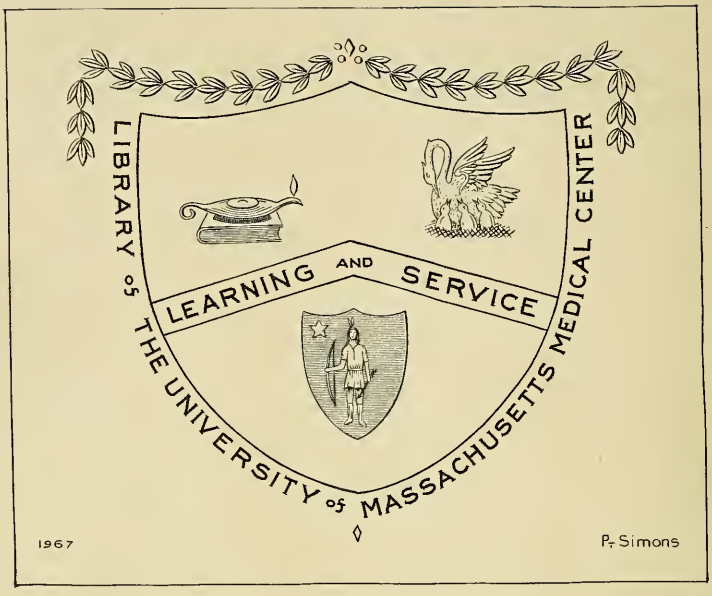
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A TEXT-BOOK

OF

PATHOLOGICAL HISTOLOGY:

AN INTRODUCTION

TO THE STUDY OF PATHOLOGICAL ANATOMY.

BY

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TRANSLATED FROM THE SECOND GERMAN EDITION,

WITH PERMISSION OF THE AUTHOR,

BY

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WITH

TWO HUNDRED AND EIGHT ILLUSTRATIONS.

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TRANSLATORS' PREFACE.

In presenting the English-reading portion of the medical profession with a translation of the valuable work of Prof. Rindfleisch, the translators scarcely deem an apology necessary. The merits of the book itself, and the fact that it fills an unoccupied gap in our most recent literature upon the subject of Pathological Histology, was judged to be an ample incentive for undertaking the labor of the translation. The work of Virchow, translated by Chance, is in many points, antiquated, and the more recent work of Billroth, translated by Hackley, occupies the ground but partially, and is professedly a work of Surgical Pathology.

Throughout, the aim has been to present the author's views with as little paraphrasis as possible; vigor or conciseness of expression was never sacrificed for smoothness of diction. A few notes or words of explanation (as few as possible), where these were judged necessary for illustrating the author's ideas, or for giving the reader a better conception of the meaning, have been added, and are inclosed by square brackets [ ].

Baltimore, Md., Nov., 1871.

DEDICATED

TO

THEODORE BILLROTH,

IN TRUE FRIENDSHIP,

BY THE AUTHOR.

Dear Friend:

I was very sorry to have been absent from home, when several weeks ago you honored it with your long-wished-for visit. How gladly would I have conferred with you of the great attainments of these memorable times, how gladly also of the small exigencies, to which the author of a text-book of pathological histology is exposed, if he will maintain his work "au courant."

It is a delicate matter, to play the rôle of an architect, with a structure, for which is given but a certain number of blocks more or less well hewn, but not the plan. One just builds haphazard; that, which yesterday still appeared firmly established and sure, must to-day be torn down in cold blood. Compare the section on pathological new formations in this second edition with the same section in the first; there has not been left one stone upon another; this we owe to our Billroth, Cohnheim, Thiersch, Waldeyer, Stricker, Köster, and many others; and how long will the present edifice last? You know that I do not complain of this. But I would complain, were some one, who perhaps after several years will turn over the leaves of this book, to forget that the views laid down in it, were the views of the author in October, 1870. It so happened to me here and there with the first edition. More than once have I had to experience the painful sensation of being regarded, by some ambitious spirit, as "older" than I really was. I grant, that I am myself partly to blame for this inconvenience, because of late years I have published but little *except* my text-book, and have found it more convenient to incorporate the

results of my own studies, so far as they merited it, in the new supplies of the text-book itself.

I beg you to bear in mind, this misconduct of your friend, also in the new edition, which is to belong to you, and leniently to judge the performance.

(Signed)

RINDFLEISCH.

BONN, November 1st, 1870.

PREFACE TO THE FIRST EDITION.

Being about to commit a new text-book to the student-youth of Germany, I am impelled to preface the same with some words enunciating the contents and the leading topics.

Pathological anatomy is one of the youngest of medical sciences. In Morgagni's writings: De sedibus et causis morborum per anatomen indagatis (Venet., 1761) are contained its beginnings. It was elaborated, as well by its founder, as by his immediate followers, in Germany by Meckel (Joh. Fr. M., Handbook of Pathological Anatomy, Halle, 1804-1805), Otto, and others, entirely according to the demonstrations of normal descriptive anatomy, and up to within the thirtieth year of our century, comprehended an assemblage of the deviations, which diseased organs could undergo in their general characteristics, their shape, size, number, situation, connection, consistency, continuity, color, and contents. Microscopic investigation, however, which placed normal histology by the side of the anatomy of Vesalius, was necessarily compelled similarly also to enrich pathological anatomy. Rokitansky and Virchow, as the founders of a pathological histology, have earned an imperishable meed in our science. It very soon appeared, however, that pathological histology must assume an entirely different and more important position to pathological anatomy, than does normal histology to normal anatomy. *Pathological histology shows, how those coarser changes of the organs, enlargements, diminutions, indurations, softenings, discolorations,*

&c., are founded upon certain changes of their structural constituents; it explains the former by the latter. Thus it ever became not only a completing constituent, but the very central point of collective pathological morphology. This is the standpoint, from which the submitted elaboration of the subject was undertaken, the reason why pathological histology has been considered in the front, the coarser pathological anatomy only in the second rank.

For the expert, I add, that this book originated more at the microscope, than at the writing-table. The numerous original studies which it contains, must therefore indemnify for what it does not offer, especially, a completely exhaustive and symmetrical treatment of each individual subject.

TABLE OF CONTENTS.

SPECIAL PART.

INTRODUCTION.

§ 1. EVERYTHING living is subjected to a continual change of its constituents. We infer this change, because we observe that certain materials are continually taken up into the organism, and others instead cast out which prove to be metamorphic products of vitalized substances.

§ 2. The movement of materials mentioned is not perceptible to the eye, even when assisted by the best optical instruments. It only becomes so whenever it experiences any disturbance, whether this be an obstacle or a special exaggeration. Who indeed is able to view the nutritive process of the striated muscular fibre in the tail of a living tadpole, or to observe the quiet coming and going of materials in an adjacent connective tissue cell? As long as these objects present a certain appearance known and defined even to the minutest point and line, we receive this "fixed appearance" as a proof that the metamorphoses connected with nutrition have in them an undisturbed progress. Only when unexpected qualities appear in the cells and other elementary parts of the body, do we think of a change of their composition which has occurred and is still occurring, and are then correctly inclined to ascribe the same to an alteration of nutrition.

§ 3. These kinds of changes already occur in the normal course of life. The period of life, that gradual growth and decay of the body is mirrored up to a certain degree in the constitution of the tissues. We must here distinguish two principal directions in which the changes of the tissues take place: formation and decomposition. The former teaches us to derive the origin and growth of the organism from a continually recurring multiplication of the cell, and an exceedingly manifold transformation of the cell form; the latter shows us that the infirmities, the frailties of the declining body are accompanied by a greater or lesser striking decomposition of the histological constituents.

§ 4. Those changes of the tissues that are produced in the course of diseases are much more important to the physician. These are entirely similar to those produced by age. Hence Virchow has not incorrectly compared those among them that are retrogressive to a kind of premature senescence. The existence of the individual cell hinges upon production and decay just as well as does the entire individual. Hence,

we will have to represent formation and decomposition as the principal natural categories of the pathologico-histological processes. But it would be unjust did we ignore, that a far greater variety of histological phenomena obtains for the province of pathology, than pertains to normal production and decay.

§ 5. Almost every disease which is accompanied by anatomical lesions shows us a variegated sequence and concomitance of progressive and retrogressive processes. These taken collectively give us the macroscopic picture which a diseased lung, liver, &c., present to us. Our task now is, in the General Part, to unweave this labyrinth, and to contemplate on all sides singly each of the retrogressive and progressive processes, in order in the Special Part, to see the anatomical pictures of disease proceeding from quantities known to us.

GENERAL PART.

1. Decomposition and Degeneration of Tissues.*

§ 6. The changes which we will consider in this first principal section, have this in common, that the tissues affected by them have entirely or partially lost their significance as living effective constituents of the body. The extent of this loss is very different in the individual processes. Several, as it appears in the extremest cases only, lead to a certain even though a very important injury to life, as the amyloid degeneration, calcification; others, as the fatty metamorphosis, extinguish the individual existence of the tissue affected, gradually but completely; we have to take in view here also necrosis itself, that is to say, the condition in which death precedes the changes. We begin with the latter.

Necrosis.

§ 7. As soon as that peculiar mutual dependence and reciprocation of parts has ceased in the human body, which emanates from their genetic unity, and which we call life, it encounters the same conditions of the outer world as do the inorganic bodies, that is to say, the only force which tends to maintain it in its form is cohesion. This, however, owing to the extraordinary abundance of water, is very limited, and hence immediately after the occurrence of death a decay of the body begins, which takes place at first slowly, then however, continually more and more rapidly, and finally leads to its complete dissolution. As long

* Nature begins her works with formation; we proceed conversely in this representation, and consider first the decomposition of that which has been completed. We do this designedly. As a knowledge of normal tissues, therefore of the material in which the destruction and solution is consummated, may be presupposed, it would in itself be a matter of indifference whether we began with the progressive or retrogressive series. Meanwhile, among the pathological new formations, we have to describe the histological course of entire diseases producing tumors, as for example, of cancer, and for this we need a knowledge of many phenomena belonging to the retrogressive series, as for example, of fatty degeneration, of cheesy metamorphosis, and others.

moreover as the outer form is in any measure retained, we call the body dead.*

§ 8. At the death of the entire organism medical skill, as is known, ceases. We might, therefore, spare ourselves the trouble of studying the changes which the death of the tissues occasions, were there not also a partial death, a death of individual parts of the organism, which we call necrosis, mortification, gangrene.

§ 9. The anatomical changes which follow the occurrence of partial death, are not the same in every case. The very various causes producing necrosis, as well as the natural situation and constitution of the dead parts, condition widely separated varieties, especially as to the amount of blood and water contained, which gave occasion to the production of a dry or moist gangrene. In the following pages we will consider these varieties also, and it will appear that these lay claim more to a microscopic and clinical than to a histological interest.

Annotation.—A large part of the collective forms of mortification may be regarded as dependent upon a total abolition of the nutritive processes. As is however known, a regular uninterrupted transmission of blood, stands foremost among the conditions of undisturbed nutrition. When, therefore, that amount of arterial blood, which in a given time flows through a certain portion of the body and thus becomes venous, sinks below the normal measure, nutrition must necessarily suffer; if the current ceases entirely, nutrition also immediately ceases. The part affected may thereby be uncommonly rich in blood; it may even be so surcharged with blood, that it may be recognized even by the naked eye, by its dark bluish-red or livid color. The microscope then shows an extraordinarily turgid repletion of the capillaries, which has led in many places to small extravasations of blood into the parenchyma; within the walls of the small and likewise congested veins are found blood-corpuscles, either singly, or in long rows, which in their situation, correspond to the boundaries of the individual layers of the walls.

If we now ask, by what means such a disturbance of the circulation could be brought about, we will most frequently find the obstacle in the afferent arteries. We will have to study more intimately, in another place (Special Part, Chap. II), those diseases of the vessels, in consequence of which, a simple occlusion (thrombosis, embolism) or a gradual diminution of the lumen of the vessel, or finally, a condition of the vascular walls is developed, in virtue of which the propulsive force of the heart is already so far consumed in the larger arterial trunks, that it has sunk to zero at the extremest portions of the body. The failure also of the force of the heart, in consequence of diseases of the heart-

* We also call inorganic nature, to which the constituents of the body now return, "dead;" the designation is, however, metaphorical here. In the common use of language, we mean by the expression "dead," that a body although still exhibiting organic structure is no longer the seat of organic functions.

muscle, or in consequence of a general debility, such as typhus especially leaves behind, is able to bring about a disturbance of the circulation in the most extreme parts of the body in so high a degree, that gangrene is thereby produced. In gangrena senilis, which is generally observed at the toes and the foot up to the knee, both forces generally act jointly, namely, changes of the heart-muscle and diseases of the vessels. Compression of the arteries, as for example by a compressing tumor, must naturally have the same unfavorable effect upon the circulation of the blood throughout the parts supplied by the arteries affected. An enduring convulsive contraction of the muscular coat probably most rarely effects such a considerable diminution of the lumen of the afferent artery, that a stagnation of the blood circulation is thereby produced. Still it is believed that we must in this way explain gangrene of the remoter parts after the abundant use of secale cornutum.

The interruption of the circulation of the blood may also have its seat in the capillaries. The occurrence is of especial interest, in reference to exudation or a new formation in the parenchyma of a part, producing a compression of the capillaries coursing therein. As an example we here mention diphtheritic inflammation, in which the death or gangrenous ulceration of the part affected supervenes upon an exudation into the substance of the mucous membrane or the outer integument. Yet to this place also belongs a great part of the pre-eminently so-called necroses of the osseous system, where accumulations of pus, which, in consequence of periostitis, collect between the bones and periosteum, compress the vessels passing from the periosteum to the bones, and thus soon rob the outer layers of their nutritive supply. Suppuration in the Haversian canals likewise leads to a compression of the vessels and the death of the particles of bone affected (Caries). It is self-evident in all these cases, that there can be no thought of a hyperæmia of the necrosed parts; on the contrary, we may here constantly expect a decided anæmia.

An interruption of the return of the venous blood is seldom a cause of gangrene. The interruption must be so complete, as it appears, that this condition is fulfilled in but few cases. At least after pregnancy we frequently observe a thrombotic occlusion of the collective larger veins of the thigh without gangrene of the leg having been produced thereby. Consequently but a single case properly comes into question here, namely, where a part is pinched in a comparatively narrow and unyielding outlet; as, for example, a coil of intestine in the neck of a hernial sack. The flaccid walls of the veins are then compressed sooner than the arteries, and thus the return of the blood may already have ceased long before its afflux is interrupted; hence a decided hyperæmia of the necrosed portion is also to be expected here.

All the causes of necrosis hitherto discussed agree in this, that the abolition of the normal exchange of the blood cuts off the exchange of

material and the life of a part. The interruption of nutrition, however, may also, independently of the circulation of the blood, affect the intermediary interchange of material of the parenchymatous islands, which are inclosed by the capillary loops. Almost all the changes of this kind, however, develop themselves gradually, and the changes of the tissues caused thereby, which characterize themselves, in opposition to those of necrosis, by a gradual extinction of life, constitute the contents of the following chapter. We may only regard, as true necroses of this kind, the death of such organs, which, like cartilage and the cornea, whose structure is totally non-vascular, have been everywhere cut off by suppuration from a connection with surrounding parts. Here the circulation in those vessels, which formerly conveyed nutritive material to these organs, by no means stagnates; the interchange of material, however, from cell to cell, upon which cartilage and cornea alone depend, certainly ceases.

Furthermore, we have still those cases of necrosis to mention where the death of a part is produced by external actions of a mechanical or chemical kind, crushing, concussion, desiccation, corrosion, or poisoning by a ferment. We are here dealing with a violent disturbance of the molecular arrangement, which is incompatible with the continuance of any vital action.

§ 10. If it is a prominent property of living tissues, in the midst of fluids, which of course must be suitable, to dissolve albuminates and their derivatives, and still retain their own form and constitution, so it is just as certain a sign of the occurrence of death, that they now no longer withstand solution themselves. We already recognize this universal token of the changes of mortification in this, that the dead part loses its elasticity, its *turgor vitalis*, and becomes withered, soft, doughy. In case now a too copious evaporation of water is prevented at the surface of the dead part, which is however already fulfilled by the presence of the epidermis, then the 81 per cent. of water, which the normal organism contains, with the addition of the water which forms in the decomposition, appears to be sufficient to effect the solution of the collective solid constituents of the body, with the exception of the bones. In the meanwhile, as was evident in the annotation, an unusual plethora of blood of the affected part is a persistent phenomenon in the majority of cases of gangrene. The blood is by far the richest tissue, in water, of the body. The mortifying part will hence contain a greater abundance of water, at the expense of the healthy part, than it normally does, and therefore in better condition to be dissolved in the water contained in it.

This plethora is also a measure for the other macroscopic appearances; namely, the coloring matter of the blood, a short time after the occurrence of death, leaves the blood-corpuscles, and colors first the serum, afterwards, however, all the tissues, which naturally have either

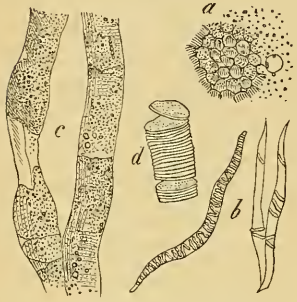
no color at all or but a very slight one. The vascular walls and the loose cellular tissue around the vessels become colored thereby through imbibition, so that the course of the veins may be recognized by bluish-red stripes and spots, which, if the gangrene is of an external part, gives the skin a blue, marbled appearance. Finally, all the parts become uniformly saturated with blood; even the fat of the adipose tissue forms no exception. The red-colored serum penetrates to the surface of the cutis in external parts. The disintegration of the rete Malpighi produced in the meanwhile favors a loosening of the impervious epidermis, so that the accumulation of serum sometimes leads to the formation of bullæ, generally, however, to the continuous detachment of the epidermis in larger patches. In the latter event there ensues, if the evaporation of water is not prevented by other means, a rapid desiccation of the superficial parts exposed to the air. Impregnated as they are with the coloring matter of the blood, in this desiccation they assume a very dark, almost black coloring (Gangræna sicca; Mummification). As far as the desiccation extends, the process of decay is for the time being arrested. Desiccation is a means of killing living parts, as may be seen in the formation of every scab; it is, however, also a means of preserving parts from further decay. All, therefore, that we have to state concerning gangrenous changes of the tissues only occurs by the presence of a sufficient quantity of water for solution; this refers first to gangrene of inner parts, then of outer, but not of parts exposed to desiccation.

§ 11. The blood undergoes decomposition more rapidly than all the tissues. The morphological changes then occurring may be stated in few words. It has already been mentioned that the coloring matter leaves the blood-corpuscles, in order to be gradually imbibed by all the tissues of the dead part. Our attention will be again occupied, further on, with the dissolution of these bodies. The colorless protoplasm dissolves under moderate intumescence and disappears from view. There is soon no longer a single intact blood-corpuscle to be found.* The case is to be pointed out as an exception where variously sized aggregations of very intensely brownish colored blood-corpuscles are yet discovered in an already far advanced stage of mortification. The edges

* Alexander Schmidt has proved experimentally that in a layer of blood of the thickness of scarcely a line, in contact with the air and protected from evaporation, the blood-corpuscles disappear in a very short time: in the blood of dogs, after fifteen to eighteen hours; in horse-blood, after three days; in beeves' blood, to be sure, only after eight to ten days. In the beginning, the blood only becomes lake-colored, and we then see, especially in dogs' blood, the corpuscles first become decolored, changed in form, and according to the number somewhat separated. At a later period, the discs having become colorless, are completely dissolved. This decoloration of the corpuscles, the passage of the coloring matter into the serum, and the solution of the colorless stroma, are the joint results of the oxidizing action of oxygen. (A. Schmidt, Kleine Physiol.-Chem., Untersuchungen. Virchow's Archiv, xxix.)

of such aggregations (Fig. 1, *a*) appear almost regularly notched; the outermost corpuscles show a disintegration into minutest colored granules, and this disintegration may indeed be regarded as the final destiny of all.

Fig. 1.



The gangrenous disintegration of tissues. *a*. Aggregation of blood-corpuscles. *b*. Smooth muscular fibres. *c*. Striated muscular fibres. *d*. Breaking up of same into Bowman's discs. 1-300.

§ 12. The changes of nucleated cells form the second group of necrotic phenomena. We may here state the proposition at the commencement, that the nucleated clump of protoplasm, as soon as life is really extinct in it, comparatively soon undergoes solution. The disintegration is introduced and in a certain degree prepared by a phenomenon, which in striated muscular fibre has for a long time been designated as the rigor mortis, and which essentially depends upon the coagulation of that viscid albuminate, in which all the formed constituents of the cell, including the nucleus and the protoplasm granules are imbedded. The protoplasm becomes immovable by coagulating, and, indeed, in a position corresponding to that of the cell in repose; the granules also, which previously showed perhaps some molecular motions, now stand still; the entire appearance becomes cloudy,* as though dusty, and finally breaks up into relatively large granules, which then become smaller and disappear from view. The nucleus, which at first stood out prominently, likewise takes part in this disintegration.

§ 13. The course of these changes is naturally modified, accordingly as the cells have already undergone this or that physiological metamorphosis. Without saying more, our description only applies to the cells of connective tissue, of the rete Malpighi and those of the deeper layers of epithelium corresponding to the rete; also to glandular cells and lymph-corpuscles. The cell membrane, which we recognize in the older epithelial cells, opposes an energetic resistance to solution. These cells therefore maintain their outer form for some time, after nucleus and protoplasm (here the cell contents) have already broken up into granules, so that anucleated epithelial cells regularly belong to what is found in dead parts. The cells of the epidermis distinguish themselves in this relation, which bid defiance to the necrotic process in the same degree as they have advanced in the process of becoming horny.†

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* Kühne missed these appearances in the cells of areolar connective tissue, but found them in the cornea cells of the frog. (W. Kühne, Untersuch. über das Protoplasma und die Contractilität. Leipzig. Engelmann, pp. 121, 130.)

† Herewith we must of course not forget that the change into horny matter itself denotes a gradual transition from life to death. In the process, by the way, we can also establish a diminution and final disappearance of the nucleus.

§ 14. The smooth muscular fibres also, although a cell-membrane cannot be conceded them, still preserve their peculiar form tolerably long, so that the nucleus has already broken up to an elongated dotted mass, when the outlines may yet be followed with all exactness. The phenomena of the rigor mortis have yet been but little investigated for the contractile substance of smooth muscular fibre. The only pertinent communications are derived from Heidenhain,* who describes certain phenomena of coagulation, which occur in smooth muscular fibre sixteen to eighteen hours after death: the cells receive at first a dusty or sandy appearance, derived from innumerable very minute, dark, dot-like granules, which are diffusely scattered throughout their contents. At a further stage these immeasurable molecules move together into regular grayish-shaded figures, which continuously unite into coarser, strongly refractive, elongated, straight or crooked particles, which are imbedded in an unconsumed clearer substance. These particles are at one time scattered without rule in the cell, then they are tolerably regularly transversely stationed, and at tolerably equal, greater or lesser distances from each other in the interior of the cell, so that the cell receives a transversely striated appearance. (Fig. 1, *b*.) I can confirm this statement from my own experience. We regularly find this disintegration in the so-called softening of the stomach, a swelling and breaking up of the gastric walls, which was formerly regarded as a disease, but at present passes for a post-mortem phenomenon. (Elsässer.) (Fig. 1, *b*.) The further decay of the muscular fibres so changed is their dissolution into a slimy substance drawing out into threads, in which, however, these dot-like bodies remain yet visible for a long time.

§ 15. The striated muscular fibre presents in its necrotization somewhat more complicated relations than the cells hitherto considered. This is then the place to enter somewhat more minutely into the phenomena of rigor mortis. In from twelve to fourteen hours after the occurrence of death all corpses, with the exception of those suffocated by charcoal vapor or sulphuretted hydrogen, those killed by lightning, or dying from putrid fevers and long-continued debilitating diseases, fall into a peculiar stiffness, which lasts, perhaps, twenty-four hours, and, observed more accurately, amounts to a pretty considerable shortening, thickening, and induration of the voluntary muscles. Even in such limbs as are suddenly robbed of their supply of blood, we observe the same behavior of the muscles; we can produce the same experimentally not only by interrupting the supply of blood, but also by heat and cold, over-exertion, mechanical injuries and chemical agents, but most rapidly by distilled water.

Numerous investigations, of which we owe the latest and most ex-

* Heidenhain, Gerinnung des Inhalts der contractilen Faserzellen nach dem Tode. (Studien des Physiol. Instituts zu Breslau, i, 199.)

haustive to W. Kühne,* have left no doubt concerning this, that this stiffening of the muscular fibre depends upon the separation of a solid albuminate from the muscular juice. This coagulum (myosine, Kühne) forms a white, but slightly transparent mass, and thence causes a striking opalescence of the stiffened muscular fibres, which is conjoined with a discoloration verging upon brown.

Rigor mortis is indeed the first step towards death, but a step which can be again recalled. We can very readily produce rigor mortis of the thigh of a frog, by tying the afferent arteries, and see the normal condition return by removing the ligature. If, however, the question is of a persistent death of the muscular fibre, its continued disintegration will also follow its stiffening. That which may be seen by the naked eye, is primarily the loss of the bright red color of the muscle, which, if an imbibition of the dissolved hæmatine does not occur, gives place to a dirty red or grayish-yellow; furthermore the cohesion of the muscles changes, so that finally, they either run into a gelatinous, smeary mass, in which no trace of the former fibre-structure is visible, or also into a fragile, dirty gray, tinder-like substance, in which indications of longitudinal striæ still occur. The microscopic appearances are much more monotonous. The transverse striæ and the nuclei disappear under a dense cloud of very minute, dark points; fat-globules and reddish pigmentary granules show themselves partly in and partly beside the contractile substance; the latter tears across at short distances; the fragments melt, so to speak, away from the edges; the sarcolemma holds out yet for a time, and when it also finally falls into decay, it only contains small formless lumps of the former contents, which are mingled with the remaining detritus. (Fig. 1, *c.*)†

We may expect a somewhat different mode of dissolution, only in cases where the gelatinous condition of the disintegrating muscular fibre mentioned above, is very decidedly marked. I observed this condition, and corresponding to it a disintegration of muscular fibres into Bowman's discs, for the first time in an almost demarcated gangrene of half the foot, and have since once again had the opportunity of confirming this observation. (Fig. 1, *d.*)

§ 16. Nothing has as yet been learnt concerning the necrosis of nerve-cells, and but little concerning that of the peripheric nerve-fibres. We know, that the thicker nerve-trunks are wont to maintain themselves for a comparatively long time, as peculiar structures within depôts of mortification, whilst their finer ramifications generally soon dissolve. The coagulation of the white substance of Schwann of the nerve may

* W. Kühne, loc. cit.

† According to Falk (Centralblatt, 1866, p. 434), the striated muscular fibres move closer together before their disappearance under the granular cloudiness, and before their final dissolution a longitudinal division of the contractile substance not infrequently occurs.

precede all other changes, similar to rigor mortis of muscular fibre. In consequence of which, that fluid, in a normal condition entirely homogeneous, which closely surrounds the axis cylinder and is externally limited by the neurolemma, collects into larger and smaller drops, which are separated by a clear fluid. The dark, frequently involuted contours of these drops give the entire fibre an irregular appearance (Fig. 8, *a*), which has not inappropriately been compared to the curling of smoke-clouds. The chemical changes occurring here, whether the drops of myeline (Virchow) are to be regarded as a separation from the nerve-medulla, or only as a regrouping,* we do not yet know, although the phenomenon has been known since Leeuwenhoek's time. The continued advances of decay are marked by a strong intumescence of the whole nerve-trunk, whereby then the individual fibres appear extraordinarily opaque, the neurolemma indistinct, and the axis cylinder entirely disappears. The complete dissolution advances more rapidly at some places than at others, so that a similar varicosity is observed here as we observed in the muscular fibre shortly before its definite disintegration.

§ 17. Adipose tissue plays a far more important part in the process of mortification. The fluid fat leaves the cells with the greatest facility, and the liberated globules, which then collect to larger drops, not only give the ichor (see § 22) a peculiar emulsion-like appearance, but also diffuse themselves extensively throughout all the mortifying tissues, so that we cannot easily obtain a preparation of the mortifying parts where fat-globules are not present in large amount in all clefts and interstices. If we bring the adipose tissue itself under the microscope, as a rule we do not observe a single fat-cell which yet contains the normal amount of this material, but we must also add, none which has entirely given up its contents. The drops are mostly reduced to one-half and less, and not infrequently also broken up into smaller globules. It is just this fat remaining in the cells which is so easily impregnated with the coloring matter of the blood, so that not only does the cell-membrane and the loose connective tissue between the fat-spaces appear red or reddish-yellow, but also the entire adipose tissue. Crystalline deposits may indeed also occur within the cells; they are, however, incomparably more frequently to be observed in the escaped fat, wherefore they constitute an unfailing constituent of the ichor of mortification. (See § 23.)

§ 18. The first change which the fibres of loose connective tissue experience, consists in that they swell up. They by no means become more transparent by this swelling out, as perhaps when treated by acetic

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* G. Walter (Virchow's Archiv, xx, 426) conjectures, that the pre-existing albuminates of the tubular sheath coagulate, and thereby a separation and flowing together of fats soluble in ether takes place into larger portions.

acid, but on the contrary they assume an opaque, strongly refractive quality. To this is almost regularly added the saturation with the coloring matter of the blood, already several times mentioned, which causes a coloring, whose intensity stands in inverse proportion to the amount of water contained, for it is scarcely necessary to say, that the degree of tumefaction depends entirely upon the quantity of water present. Evaporation and resorption of the parenchymatous fluid immediately become apparent by a corresponding desiccation of the connective tissue fibrillæ. The black, coal-like substance, however, into which the cutis is converted in gangræna sicca, is transparent and of a ruby-red color in very thin sections. When, on the contrary, the tumefaction of the fibres continually increases, they receive a granular appearance, become indistinct in their outlines, until they finally liquefy into a cloudy, slimy mass.

§ 19. The formed parts arising from the basis-substance of connective tissue are incomparably more capable of resistance than the latter. As such we do not so much regard the clear, homogeneous membranes (capillaries, tunicæ propriæ, basement membranes), concerning whose destruction in mortification there are no certain statements, as especially *elastic fibres and fibrous network*. The well-known durability of these in all possible chemical reagents preserves them also against the less energetic agents of the process of mortification. The physician, therefore, with confidence expects that gangrene of the lungs will, among others, infallibly betray itself by the appearance of elastic fibres of the lungs in the patient's expectoration. If at length the elastic fibres are also attacked by the destructive process, they lose their normal elasticity, appear less curled; not infrequently they swell up, and may at last liquefy into a gelatinous mass.

Those firmer, more dense, connective tissue fibrils, which form the tendons, and which also occur otherwise in fibrous membranes (dura mater, sheaths of tendons, of muscles and vessels, periosteum), behave similarly to elastic fibres. The first sign that the structures mentioned (we have the tendon especially in view) are undergoing moist gangrene, consists in a loosening of the individual parallel bundles of fibres, which is however to be placed more to the account of the intermediate connective tissue supporting the vessels, is that this softens and disintegrates. Later, however, the so-called secondary and tertiary fibrillæ also separate from each other, the tendon becomes a mass of delicate filaments, which compare with the normal structure as combed out hemp does to a well twisted cord. Even in this condition, as a unit it is torn asunder with difficulty; only at a late period do the fibres begin to break up into single granular striæ, like strings of pearls, and then into the smallest molecules, and thus vanish from sight.

§ 20. Cartilage is one of the firmest tissues of the body. The chemical combinations of the matrix (intercellular substance) are with diffi-

culty soluble, and it may principally proceed from this cause, that large pieces of cartilage, for example, loosened articular cartilages, set necrotic destruction at defiance for so long a time. Should the latter nevertheless occur, it exhibits itself, regarded as an entity, as a slowly progressing peripheric melting away; the cartilage thereby becomes transparent and assumes a reddish color. That this discoloration proceeds from a saturation with the dissolved coloring matter of the blood, cannot at all be established as probable in all cases; especially does the constant occurrence of the discoloration alluded to in the cartilage of the larynx and trachea, isolated by suppurative perichondritis, oppose the acceptance of this view. Under the microscope, a granular cloudiness of the intercellular substance shows itself, which at the edges dissolves into a gelatinous mass. The cartilage-cavities are mostly filled with fat-globules, which, produced by fatty degeneration of the cells, become free by the solution of the tissues.

§ 21. Osseous texture remains unchanged in necrosis. The surgeon, who in the midst of the most striking inflammatory and ulcerative changes of a bone, by the smooth surface and well-preserved form of a piece of it, recognizes just this piece as the dead part, the sequestrum, has every reason to stand firmly by the correctness of this proposition. In the meantime it may still not be superfluous to obtain a clear idea as to how far we have to understand literally this unchangeableness of osseous tissue. Occasionally, at all events, we will have to expect upon the necrosed pieces those changes which all the bones of the skeleton undergo in the decay of the entire body. All that goes by the name of cell, bloodvessel, and medullary tissue, falls away. It however appears that a large part also of the organic matrix of osseous cartilage is lost in putrefaction, and indeed so much the more, the longer the bone is exposed to its influences. Otherwise the striking phenomenon, that sequestra regularly have a much lighter specific gravity than the bones of the skeleton, could not be explained. Moreover, cases are also known, where the sequestrum not only has lost its original smoothness by the gradual corrosion of the surface, but has also decreased in volume. And it is really not at all comprehensible why, under suitable conditions, a complete disintegration of the dead osseous texture should not occur. The presence of small quantities of acid in the circumfluent fluids would be already sufficient for this; if the salts of lime are once dissolved, the remaining osseous cartilage has no greater capacity of resistance against putrefactive decomposition than has articular cartilage and other allied structures. In the meanwhile we may stop at the fact. In another place we will have to take up the consideration as to the mode of osseous disintegration, which is very much the same in dead bones as in the living. (See Softening of Bones, Rarefactive Ostitis, Caries, &c.)

§ 22. So much concerning the disintegration of individual tissues.

Let us now cast a glance upon the fluid which is hereafter to be regarded as the rendezvous of all those things which we consider as the dissolved organism, of course not in that sense in which Moleschott has designated the blood. The constitution of the ichor of mortification is modified, as a matter of course, according to the locality of the process; gangrene of the lung must necessarily yield a somewhat different ichor from the gangrene of external parts. We can only say of the sanies gangrænosa generally, that it has a disagreeable odor, and an ugly, grayish-yellow color, which latter, by the addition of nitric acid, receives a rosy tint, first observed by Virchow. The reaction is at least not always alkaline. This, like all the other differences of the gangrenous ichor, depends upon the various chemical composition, which we must therefore look to in the first commencement of our observation.

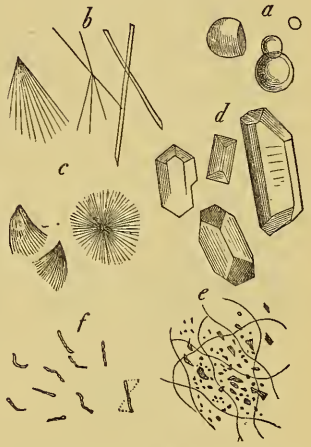
§ 23. Whilst, as we have seen, the process of decomposition presents itself in a physical bearing as a solution of the constituents of the body in water, in a chemical aspect it is to be regarded as a varied combination of the elements among each other, and with the oxygen of the atmosphere. Every plastic chemical body is embraced in a chemical tension, that is to say, its atoms have a tendency to group themselves otherwise than they are at the time grouped. Life consists and shows itself in this, that they do not accomplish the combinations striven for; death shows itself in that they do. We now have decompositions and combinations, which are different for the different chemical substances of the body, as albumen, fats, &c., but they all finally end with the formation of carbonic acid, ammonia, and water. As a considerable amount of oxygen is consumed in these processes, the whole might be regarded as a slow process of combustion; in the meantime the certainly very manifold metamorphic bodies are by no means all known. Several of them are volatile, and when largely developed occasion the so-called emphysematous or crepitant gangrene; at the same time these are they which offer the well-known offence to our sense of smell (sulphuretted hydrogen, ammonia, sulphuret of ammonia, valerianic and butyric acids); others, without being volatile, are soluble in water; others yet finally separate during their formation in a more solid form, so that here, therefore, after the complete disappearance of the histological forms, a number of microscopic objects are produced anew, of which the following are the most interesting:

a. Leucine—in gangrenous processes of the lung, liver, spleen, and pancreas—separates in the form of a white, opalescent substance, which partly forms homogeneous drops or globules, partly bodies of concentric layers, and finally partly stellate spheres of minute crystalline needles*

* Virchow says in regard to the interior aggregation of these various forms (Archiv, viii, 337): "If we permit leucine to crystallize from a solution, we constantly see at first very minute granules of a rounded form arising in the minutest drop of a viscid mass, which are distinguished from fat-globules by being less refractive, and

(Fig. 2, *a*). *b*. Tyrosine—generally to be found along with leucine—forms satiny, white needles, which either remain isolated, and may then attain an appreciable length and thickness, or may unite into beautiful sheafs or rosettes (Fig. 2, *b*). *c*. Margarine—a mixture and crystalline separation of the solid fats, stearine and palmitine—occurs with extraordinary frequency in gangrenous tissues. We meet with individual minute needles, or groups of such, which then radiate from a common centre (Fig. 2, *c*). *d*. Ammoniaco-magnesian phosphate ($PO_5\left\{\begin{matrix}2MgO\\NH_4O\end{matrix}\right\}+12$ Aq.) is only found in alkaline or neutral ichor. The crystalline forms occurring most frequently are combinations of the rhombic, vertical prisms, having a great similarity to the lid of a coffin (Fig. 2, *d*). *e*. Pigment bodies—with the exception of sulphuret of iron, collectively produced by the co-operation of the coloring matter of the blood. We meet these among the floating particles of all such discharges from gangrenous parts containing blood, and in the tissues of such parts themselves. The variety of their forms is great. A certain rust-colored pigment may occur most frequently, yellow to dark brownish-red colored granules, and heaps of granules, which yet stand tolerably close in a chemical relation to hæmatine, and are also found with hæmatoidine in non-gangrenous, so called pigmentary metamorphosis of the tissues. As being characteristic of necrosis, we regard only the so-called gangrene particles, very minute, only to be recognized by strong magnifying powers, black particles of entirely irregular outline, which remain unchanged in most of the reagents. It is not at all proven that these gangrene particles are to be regarded as something occurring exclusively in putrefactive decomposition; on the contrary, many circumstances indicate that they are identical with melanine, to be considered hereafter (Fig. 2, *e*).

Fig. 2.



Products of gangrenous disintegration. *a*, Leucine; *b*, Tyrosine; *c*, Fat-crystals; *d*, Ammoniaco-magnesian phosphate; *e*, Gangrene particles (black pigment); *f*, Vibriones. 1–300.

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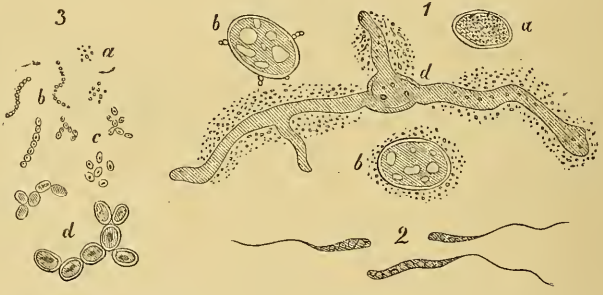
by their paler circumference. These often combine by twos or many, and form large 'drusy' figures, or figures radiating in long needles from a point. They remain more isolated in very slow crystallization, each grows by itself, and in that they often exhibit concentric layers, they stand out continually more distinct as globules of a light yellow color. Very frequently we recognize nothing therein of a fine composition of needles; at other times, on the contrary, masses form, which consist of closely arranged needles, which distinctly project beyond the edges as isolated points." The larger spheres also may grow together. They thereby mutually flatten themselves, so that we not unfrequently meet one-sided flattened spheres, which are isolated in preparing them (Fig. 2, *a*).

§ 24. The occurrence of living organisms in gangrenous parts deserves special mention. They are, in the first place, the ordinary superficial layers of mould (aspergillus, oïdium), such as we find in all mouldering bodies sufficiently moist; but, besides these, the so-called vibriones, which are met with in the ichor and in the interior of decaying organs, in immense numbers. It was not for some time known whether the minute, linear bodies, in lively, rotating, whirling, and swinging motion (Fig. 2, *f*), should be reckoned among plants or among animals. The studies of later years have in so far given us some light, as the vibrios thereby appear to be placed, without doubt, in a close relation to fungi. A series of observations by Madame Joh. Lüders* are the most worthy of note, which prove that the protoplasmatic contents jut out in minute portions from the spores of various fungi in putrefactive fluids, and that these portions, which are soon provided with a lash or tail, and undergo lively movements, are to be regarded as vibriones (Fig. 3, 1, 2). If it should be confirmed that these vibriones

Fig. 3.



1. Spores and germ-threads of Bothrytis acinorum cultivated in the washings of flesh. *a*, A recently produced spore; *b*, the same after four hours; *d*, after forty-eight hours, both covered with vibriones, 1–500. 2. Wandering vibriones coming from the mucor germ-threads into the washings of flesh, 1–800. 3. Yeast formation from vibrional germs. *a*, Germs; *b*, *c*, *d*, the same as vesicles which become ever larger, and finally form the cell-colonies of yeast. After Lüders.

in fermentable media grow into yeast-cells (Fig. 3, 3), without which fermentation could not proceed, a field of the most influential activity would be thereby assured to the lowest organisms. Pasteur,† namely, who has published beautiful studies concerning vibriones, accepts, that true decay everywhere is only produced by vibriones, and regards these as the visible ferments of decay; he, however, unaccountably just excludes gangrene from his observation, since he will not concede this to be a true process of decay.

2. Conditions of Involution.

a. *Fatty Degeneration.*

§ 25. I have designated in the heading, as conditions of involution, the changes of the tissues which will occupy us in the following para-

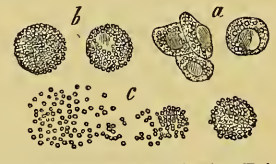
* J. Lüders, Schultze's Archiv für mikroscopische Anatomie, Bd. iii, page 318.

† L. Pasteur, Recherches sur la putréfaction. Comptes Rendus, lvi, 1189–1194.

graphs, and by this term wished so far to determine for them the general character, that a gradual transformation and final destruction of the normal form goes hand in hand in them with a parallel decrease and final extinction of the normal function of the parts.

§ 26. Foremost under this definition occurs a metamorphosis of the *cells*, which is marked by the occurrence of fat-globules in the interior of the cell, and is hence called *fatty degeneration*. For a time no unanimity was attained as to whether the globules of fluid fat soluble in ether, of a dark contour, white in reflected light, first appeared in the cell contents, or in the nucleus, or even in the nucleolus. The possibility of a fatty degeneration of the nucleus, and eventually of its nucleoli, is indeed denied by no one at present, nay, we must accept, that in every complete fatty metamorphosis of a cell the nucleus and nucleoli are also destroyed; the protoplasm, however, forms in all cases the starting-point of the destruction, in cells with membranes the cell contents. This substance, in the normal condition exceedingly finely granular, contains at first the fat-globules in very small number. Small groups of two to ten especially are ordinarily found in the immediate neighborhood of the nucleus. These globules never flow together into large drops, as we very characteristically find in such particles of fat which have penetrated from without into the cell (see below, fatty infiltration), but they remain separated from each other by thin layers of the protoplasm. The more they increase, the smaller will the outer portion of the cell not yet infiltrated become; finally this entirely disappears, and the fatty globules reach the contour of the cell. The nucleus now also becomes invisible, which, up to this time, could be recognized as a clear spot in the midst of the dark mass of fat-globules, and could be rendered distinct by tinting with carmine. (Compare adjacent Fig. 4 with this and the following §§.)

Fig. 4.



The fatty metamorphosis. Epithelium of the pericardium in dropsy of pericardium. *a*. Cells which still show the normal form and arrangement. First appearance of fat-globules. *b*. Granular globules, the one with a nucleus still visible. *c*. Granular globules disintegrating to fatty detritus.

§ 27. During the process just described, the cell, on the one hand, has very considerably increased; it frequently attains three to four times its former diameter; on the other hand it has assumed a completely spherical form, indifferently, whether it were previously round, or had a cylindrical, a flat, or a spindle form. They are now called "granular corpuscles,"* and by this term we understand a globular ag-

* The expression granular corpuscles is decidedly to be preferred to the older "inflammatory corpuscle." Gluge, who found these bodies in the commencement of pneumonic infiltration of the lung, regarded them as characteristic marks of inflammation. It was proved later, that these are the fatty degenerated epithelium of the lungs, which were displaced from their seat by the œdema preceding the inflammation, and then disintegrate.

gregation of fat-globules, which are held together by an albuminous intermediate substance.

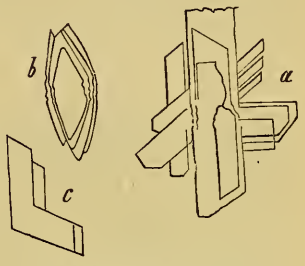
A large amount of granular corpuscles gives a fluid, which suspends them, or a tissue, in whose interstices they are deposited, a whitish-yellow, or a butter-yellow appearance. Thus colostrum, that is to say, the milk which is poured out by the mammary gland in the first days after parturition, appears not as a white, but as a yellowish, viscid fluid, which, by quietly standing, soon separates into a transparent, serous part, and a cream-like mass collecting at the surface. The latter almost entirely consists of granular corpuscles, which are here produced by a fatty degeneration of the glandular epithelium, and are called colostrum corpuscles. In a similar manner, in order to continue the physiological example, do the corpora lutea of the ovary owe their name to a fatty degeneration of the cells of the membrana granulosa, which is found in all evacuated and disintegrating Graafian follicles.

§ 28. We may conveniently term the last act of fatty degeneration as a lactification ("vermilchung"). The granular corpuscles disintegrate, in that the albuminous substance, which hitherto cemented and held them together, dissolves in the surrounding, constantly alkaline fluid. A lively to-and-fro oscillation of the fat-globules (Brown's molecular motion) gives notice of the impending disintegration; then the outermost globules leave the periphery of the cell—as we observe this and the whole course of the phenomena, especially well, in the cells of cancer-juice—and scatter themselves uniformly throughout the fluid, whilst the conglomeration becomes continually smaller, to finally disappear without any remains whatever. The emulsive fluid in which the fat-globules are now suspended, the *fatty detritus*, has its physiological type in the secretion of the mammary glands; the more uniform dispersion of the refractive bodies produces a whitish or even entirely white color, as we also see in artificially prepared emulsions.

§ 29. If milk is injected into the abdominal cavity of a rabbit, it disappears after a short time; the resorption takes place still more rapidly in the subcutaneous cellular tissue. Milk and with it all fatty detritus are absorbable substances, and are also regularly absorbed, when no particular conditions prevent absorption. With reference to the latter, the case deserves particular mention, where the products of fatty degeneration are inclosed in a cavity, whose walls are in a state of inflammatory irritation, and therefore more disposed to production than to resorption. They, then, undergo a further series of metamorphoses. The fats are partly saponified, they partly separate in solid form, which we have already learned to know in necrosis. Finally there ensues an abundant deposition of crystals of cholesterine, whereby the dirty white mass, pulpy or crumbly according to the contents of the fluid, obtains a peculiar, glistening appearance. (Atheromatous pulp, Bran-like pulp.)

Cholesterin, which we here meet for the first but not for the last time, is yet an exceedingly questionable body, in spite of manifold investigations. As it is found in the brain and spinal marrow under entirely normal circumstances in enormous quantities (40 per thousand), it may not without further proof be regarded as an excrementitious substance. That it constitutes a never failing constituent of the bile, is explained by this, that bile is just one of the few fluids which can contain it in solution. Chemistry tells us, that beside bile only solutions of soap and fatty oils take up a part of it. This difficult solubility in animal juices is one of the most prominent peculiarities of cholesterin, and is the cause why we meet it so often in the solid form.

Fig. 5.



Crystals of cholesterin, after Virchow.

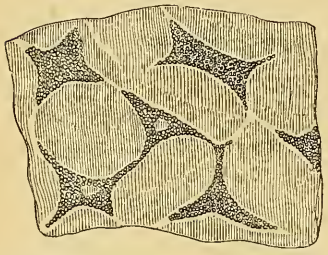
The regular crystalline form of cholesterin is a rhombic tablet, whose angles are constantly =79° 30′ and 100° 30′. These tablets commonly lie together in heaps, with their long sides parallel, without covering each other. The interesting varieties of their forms have undergone a most exhaustive analysis by Virchow; but in this regard we must refer partly to the annexed representation, and partly to the original treatise. (Virchow, Archiv, xii, 101.) It is judicious to make use of micro-chemical reagents, for the sure discrimination of cholesterin from similarly crystallizing substances. These are very characteristic of cholesterin. A drop of concentrated sulphuric acid, allowed to flow slowly to the preparation, causes the cholesterin tablets "to melt away from the edges and to assume a fatty appearance. After some time the tablet becomes movable, membranous, at times it turns over, at other times it draws together and gradually, in that the mass continually decreases in periphery, we have arising before us a dark brown-reddish colored drop." (Virchow, Würzburger Verhandlungen, 1850, bd. i, s. 314.) The simultaneous action of sulphuric acid and iodine causes, in the condition of the commencing decomposition of cholesterin, a fine blue color.

Now as to what specially concerns the occurrence of cholesterin in the atheromatous pulp, the assumption that it is first taken up by the oily and saponaceous constituents of the detritus, and again precipitated in their decomposition, without doubt corresponds most to the otherwise known properties of this body; meanwhile future investigations must decide this point.

§ 30. We have hitherto followed the fatty metamorphosis in the more isolated cells. It is now incumbent upon us to show how, in the various modifications which the form of the cell protoplasm experiences, a difference of the process is also brought about. These are naturally dif-

ferences entirely relating to form, of an external kind. We therefore may not expect in cells, which have the form of a long-rayed star, and have thereby departed very far from the primitive spherical form, that the aggregation of fatty granules should be completely spherical. The degenerated connective tissue corpuscles of the innermost coat of vessels (Fig. 6) may serve as an example how the aggregations of fatty granules may also exhibit polygonal forms. In a similar manner the smooth muscular fibres also, as aggregations of fatty granules, retain their original spindle form.

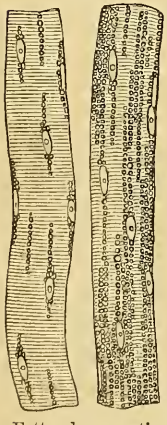
Fig. 6.



Fatty degenerated connective tissue-cells of the inner vascular membrane. 1-300.

The protoplasm of striated muscular fibre has an exceedingly complicated form, which also prevails in its fatty degeneration. The doubly refractive muscular particles (sarcous elements, Bowman), which we regard as depositions of the protoplasm, form in their longitudinal arrangement the varicose fibrils of authors, and these lie so together in the primitive bundles, that the nodules on the one hand are placed upon a level with the constricted points on the other. If we now imagine to ourselves a space, which remains vacant in this arrangement of the muscular particles, filled by the viscid protoplasm, there results, as the form of the latter, a system of varicose threads with incurved edges, which come into apposition with their thicker portions at those planes where the fibrils are thinnest. In larger groupings this happens only in the immediate neighborhood of the nuclei, which there, where they are imbedded, force the fibrils apart, and thereby form a spindle-shaped interspace, whose permeation remains to be accomplished by the protoplasm. These small conoidal projections at the nucleus, are they in which the first fat-globules appear. We then see them arranged behind one another, in very minute and elegant rows, like strings of pearls, in the longitudinal axis of the primitive bundles, and originating or exactly corresponding to the nodulated threads of the interfibrillar protoplasm. The transverse striation, which also only depends upon the regular arrangement of strongly refractive bodies, must naturally become indistinct in the same measure, as the much stronger refractive fat-granules take the upper hand, and injure the effect produced by light upon the Disdiaklasten groups.* In far-advanced cases of disease we see nothing but the fatty

Fig. 7.



Fatty degeneration of striated muscular fibres. 1-300.

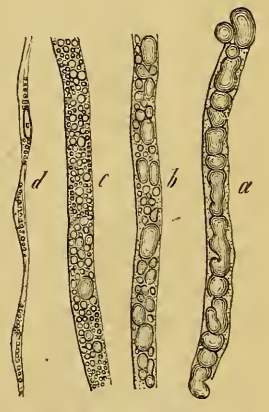
* Disdiaklasten groups (Brücke) = sarcous elements = muscular particles.

detritus, which is here contained as a fluid in the same sarcolemma tube. (Fig. 7.)

§ 31. The chemico-physical process, which lies at the basis of the fatty degeneration of the cells, is not indeed known with sufficient perspicuity. In the meantime we may set aside the opinion, as though the fat-globules attained the interior of the cells by intussusception; the fact that muscle, in which we recognize a medium degree of fatty degeneration, nevertheless does not exhibit a greater percentage of fat than does the normal, controverts this. The possibility only remains, that the fat-globules originate in the interior of the cell. But are they to be regarded as the production of a disturbed exchange of material of the cell, or as the products of decomposition of the cell-substance? The view seems mostly to recommend itself, that we are investigating phenomena the opposite of those which accompany the cell-formation. As we know from the composition of the yolk, the formative material of the cells consists of albuminates, which are abundantly mixed with fat. We further know from the chemical analysis of muscular fibres, that they contain a not inconsiderable amount of *invisible* fat, so that we have reason to accept an amalgam-like combination of fat and albuminates in the cells. Fatty degeneration is a "re-separation" ("Wiederscheidung") of this amalgam, in which the fat again appears free and in large globules in the protoplasm. That an appreciable enlargement of the cell occurs herewith, is explained by this, that the same amounts of fat and albumen, in order to exist together separately, take up a greater space than in their former interpenetration.

§ 32. The microscopic processes, which take place at the peripheric portion of a divided nerve, might be regarded as an excellent confirmation of views just stated concerning fatty degeneration, if it should be proved that the coagulation of the white substance of Schwann, described in § 16, is to be received as the commencing separation of an amalgam of albuminous and fatty bodies. For, according to the uniform description of all authors who have occupied themselves with this subject, the further changes are but a continuation, so to say, a further fulfilment of those still obscure phenomena. The large myeline drops of dark contour disintegrate, in the time of two to four weeks, into smaller and smaller drops, which can no longer be distinguished from fat-globules by their microscopic and microchemic behavior. Beside these, very small, pale protein molecules still arise; a fatty granulated detritus is produced, which is preserved for some time in the

FIG. 8.



Fatty degeneration of the doubly contoured nerve-fibres, as this presents itself in the peripheral portion of a divided cerebro-spinal nerve. *a*, after the lapse of half a week; *b*, of two weeks; *c*, of four weeks; *d*, of two months. 1-300.

neurolemma tubules, then however disappears by way of resorption. The axis-cylinder remains intact in the disintegrated medullary sheath perhaps six weeks. If within this time the connection of the peripheric, degenerated piece with the central stump is restored, the tubular sheath again fills up with the white substance, and the axis-cylinder performs its former offices; where this does not take place, it also, and that too before the resorption of the fatty detritus is entirely completed, is destroyed by granular cleavage. The empty neurolemma now falls into longitudinal folds, and only shows at intervals an elongated aggregation of fat-granules, within which we can make a nucleus distinct by coloring with carmine.

§ 33. We may conveniently adduce the fatty granulated metamorphosis or the cheesy degeneration of cells as a variety of fatty degeneration. The term cheesy degeneration, chosen by Virchow, denotes a close resemblance of the yellowish-white, compact, homogeneous, friable or smeary mass, which is the final product of this metamorphosis, with certain kinds of cheese.

It was formerly believed that only tuberculosis could give occasion for the formation of the substance mentioned; this was looked upon as a direct separation of the morbid material from the diseased blood, and it was thence called "imperfect or crude tubercle." The expression tuberculization was about equivalent with what is now called cheesy degeneration. Reinhard, who first shook the belief in the specific nature of this deposit, was also partially misled, as he declared this to be entirely inspissated pus; it was reserved for Virchow first to place the matter in the true light, in that he described the "cheesy necroses" as a tolerably prevalent mode of decomposition of tissues rich in cells.

§ 34. As we will remember, from the representation of fatty metamorphosis, a certain quantity of fluid is required for the accomplishment of the true disintegration of cells, in order to dissolve that albuminous substance which holds together the fat-globules of the granular corpuscle. If this fluid is wanting, which is especially the case when large masses of newly-formed cells are to but a slight extent or not at all penetrated by afferent bloodvessels, the process of fatty metamorphosis experiences a modification, which is analogous to that we have already learned to know in the relation of gangræna sicca to gangrena humida. The cells desiccate, they shrivel into relatively small, deformed, mostly angular shapes, in which we distinguish, besides the fat-globules already present, a large number of granules, the so-called protein molecules. The greater the loss of water the more does the whole condense into a compact, yellowish-white mass, in which, after the lapse of years, the remains of cells may yet be demonstrated. We can of course but partially succeed, by the addition of water, in restoring the pristine form to these desiccated cells; we generally observe that the molecular heaps soon disintegrate in the water

added and form a certain emulsion-like detritus. This is also their behavior, when, in the organism itself, a redundant saturation and a recurrent softening of the cheesy substance occurs. We will learn to know this process as an exceedingly destructive phenomenon in the history of tuberculosis, and thereby to make the observation that the softening occurs by preference in such caseous material which lies at an inner surface of the body, be it of the respiratory or digestive tract, and has therefore yet other sources of water beside the surrounding nutritive fluids. In such parts as have no free surface communicating with the outer world, as in the lymphatic and mesenteric glands, the bones, the brain, and spinal marrow, the cheesy deposits soften more rarely. On the contrary, not infrequently an increase of consistence occurs in the cheesy lymphatic glands, a true calcification, in that the salts of lime are deposited in their interior.

§ 35. Let us in conclusion take a view of the occurrence and extension of the fatty metamorphosis. We have already frequently had occasion, in the course of description, to touch upon this point; it now only remains to obtain a summary thereof.

First of all, we may regard fatty metamorphosis as the regular mode of decomposition for many tissues liable to a rapid change. The epithelial formation especially here stands in the foreground. If we scrape the surface of a serous membrane with a scalpel, after having somewhat moistened it, we will seldom fail in obtaining in the fluid scraped off, even in entirely normal cases, a certain number of fatty-degenerated epithelial cells. Before others, the epithelium of the mammary and sebaceous glands principally fall into the physiological fatty metamorphosis, then however also those of the lungs, and in cats and dogs those of the kidney. Whether it is correct that the effete colorless blood-corpuscles find their final destruction by fatty degeneration, must provisionally remain a question; certain it is, that we always meet with several granular corpuscles in the blood of amphibia, which however might also of course be derived from the epithelium of the vascular walls.

To the cases hitherto mentioned fatty metamorphosis as a component part of senescence immediately connects itself. The decrease in the energy of the nutritive processes which old age brings with it, makes itself particularly felt where the conveyance of nutritive material is already in and for itself complicated and—if this expression will occasion no misunderstanding—is more difficult. We here again mean those great continuities of non-vascular tissues which we encounter in cartilaginous organs and in the transparent media of the eye. Hence we find, in old men, the cells of the laryngeal and tracheal cartilage so frequently degenerated and the cartilage spaces filled with one or more fat-globules. Here belongs the arcus senilis, a fatty degeneration of corneal corpuscles, along the insertion into the sclerotic, and the "ge-

rontoxon lentis," a long time stationary, then however an advancing opacity in the region of the posterior zone of division of the nucleus and the cortical substance of the crystalline lens, up to the formation of a nuclear sclerosis.

But not only the non-vascular, but almost all the tissues of the body, nay, even the vessels themselves, may become the points of attack of fatty degeneration in old age, and in analogous conditions of debility induced by wasting diseases. The muscular structure of the heart here occupies the foreground. As, however, we do not intend an exhaustive, but only a compendious description, we will hasten to the last and most important, exclusively pathological category of fatty metamorphosis. This always occurs where a disproportion exists between the means of nutrition and the parenchyma to be nourished. Such a disproportion can occur as well by a decrease of the means of nutrition as by an increase of the parenchyma to be nourished. If a small vessel of the brain is occluded by embolism the circulation throughout the extent of its course does not indeed entirely cease, because of the numerous anastomoses with neighboring vessels, but there occurs in them such a retardation, leading even to temporary stagnation and hemorrhage, that a disturbance of nutrition and fatty metamorphosis are the consequences. (Yellow softening.)

The disturbance of the circulation occurring in the course of inflammation, has a no less injurious influence upon the nutrition of parts. The means of nutrition are here also insufficient. In the meanwhile inflammation commonly just presents a combination of this and the second cause of nutritive disturbance mentioned, namely, the increase of the part to be nourished. The œdematous saturation of the latter is already a disturbance in this sense; it is however pre-eminently the massy new formation of cells which occasions the regressive metamorphoses, as well here as in a certain number of tumors (as, for example, cancerous and tuberculous new formations).

b. *Cloudy Swelling.*

§ 36. By the term "cloudy swelling" we understand an acutely occurring swelling and a granular cloudiness of the protoplasm, which probably depends upon a separation of certain albuminates dissolved in the juices of the protoplasm. The change occurs in very varying degrees of intensity, from a slight and very minutely-granular opacity, without any increase of the volume or deformity of the cell, up to an obscuring granulation, entirely hiding the nuclear forms, which is furthermore combined with a pretty considerable enlargement and tumid rounding of the elements. Acetic acid dissolves these bodies, wherefore a mistake for the fatty metamorphosis is, at least in the early stages of the affection, impossible. At a later period the mistake may occur so much the more easily, because the cloudy swelling, in all cases

where it does not immediately recede and the cells return to their normal constitution by the solution of the granules, proceeds without interruption to fatty metamorphosis, and thus produces the destruction of the cells.

§ 37. The pathological significance of cloudy swelling was looked upon by Virchow, who first described it in 1850, as being a nutritive irritation, that is to say, an incitation of cells to take up an abnormal amount of nutritive material. Even to-day, we yet see in it the consequence of an irritation of the cell, and know, that particularly the direct action of various mineral, vegetable, and animal poisons is able to produce a cloudy swelling of the glandular epithelium. (See Parenchymatous Inflammation of the Liver and Kidneys.) The question, however, whether it is an active or a passive process, appears to be answered constantly more in the latter sense, so that I should not be disinclined to suppose a kind of corrosion, in consequence of which the dissolved albuminates of the protoplasm coagulate, and, as in rigor mortis, become visible in small granules.

c. *Mucoid Softening.*

§ 38. A further group of conditions of involution of tissues may be comprised under the term of mucoid softening. We understand thereby a gradual liquefaction of tissues, which is rendered possible, in that the solid albuminates, which form cells and intercellular substance, pass into the soluble modification. Among the chemical bodies which are formed by this transformation, *mucus* occupies a prominent position, because on account of its considerable capacity of swelling out, it relatively demands much space, and therefore becomes already striking to the naked eye.

§ 39. The chemistry of mucoid softening must only temporarily occupy our attention at this place. Taken altogether, this is based upon those proteus-like metamorphoses, which the nitrogenous histogenetic bodies experience in the interior of our organisms, and which exhibit them to us as so many variations of a certain substance lying at the foundation, but hitherto sought for in vain.

From the very soluble peptones and alkali albuminates of the contents of the stomach and intestines arises at first in the blood the serum-albumen. This with the nutritive fluid penetrates throughout all parenchymas, and becoming solid, contributes towards the structure of tissues. It appears the least changed in the protoplasm of the cell, while collagen and chondrigen of intercellular substances, in their behavior towards reagents, deviate not inconsiderably from the albuminates, and may therefore be called albuminoids. The conversion into mucin, which collagen and chondrigen experience in mucoid softening, again brings these bodies nearer to albumen, only the sulphur is wanting to the mucin. Otherwise an unequivocal analogy with albuminates is expressed

as well in their elementary composition as in their behavior towards alkalies. All naturally produced solutions of mucus react alkaline, and mucus is generally only soluble by the combination with a free alkali. For if we treat a mucus solution with acetic acid, it becomes so much the more viscid the more the alkali combines with acetic acid, until finally the mucin separates in thick flocculi. It is, particularly, this latter peculiarity which approximates mucus to the albuminates. These also only properly occur in the organism in alkaline fluids, and we know that at least a portion of them are retained in solution by free alkali. This portion, which presents itself almost as an organic salt, in which the albuminate represents the acid (acid-albumen, Panum), is on that account designated as alkali- or soda-albuminates.

A true soda-albuminate then also forms the nearest and last product of metamorphosis of the mucoid softening, and this impresses the seal of a high probability upon the close relationship, brought into notice by us, of mucin with the albuminates.

Soda albuminate distinguishes itself from ordinary albumen by its greater solubility in water, but also by the greater facility with which water may be withdrawn from it. If we place crystals of common salt in a fluid which contains soda-albuminate, this will separate according as the solution of the salt advances, as a white, finely granular substance in the upper part of the fluid (Virchow). Hence, also the appearance, that the so-called casein pellicles so easily form upon alkaline solutions of albumen during evaporation. According to the latest investigations casein is completely identical with alkali-albuminate. With the formation therefore, of this body, a circle of metamorphoses completes itself, which lead back from the casein of milk to the albumen of the blood, the formative material of cells and the intercellular substances, collagen and chondrigen, from here to mucus, and finally to casein. Physiological chemistry demonstrates more of such sequences. Excluding the glue-yielding substance, the albuminates may directly transform themselves into mucus, which the formation of mucus in the epithelial cells of the mucous membrane proves. The stage of mucus formation may also be omitted; we saw this in fatty degeneration, where the protoplasm of the cells without further change, became a cement for the fat-globules, soluble in alkaline fluid. On the other side, instead of mucin, other albuminoid bodies may occur in the chemistry of softening; hence, we have pyin; which beside mucin is formed in purulent melting down of connective tissue; to this place belongs that enigmatical albuminoid of colloid degeneration to which we will devote a special consideration.

§ 40. If we now pass to the *morphology* of mucoid softening, we will find principally two questions to answer: how does the solution of the old forms of tissues present itself? and what *new forms* are perhaps produced by the metamorphosis? Touching the first of these two

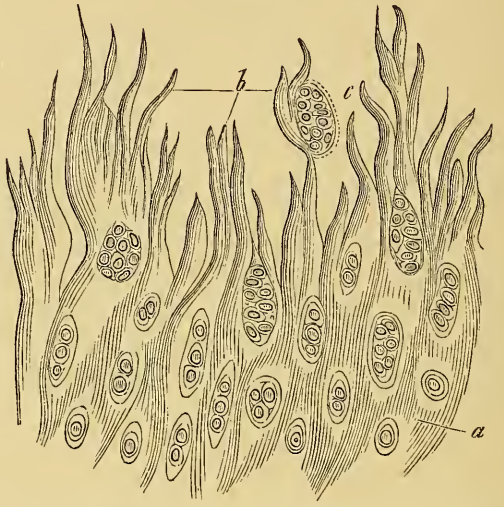
questions, the history of the preparation of mucus upon mucous membranes, like that of cartilage and bone softening, gives us a certain, although but scanty information.

That the mucus which covers the surface of our mucous membranes, is produced upon the spot and place, and indeed by the epithelial cells, is certain. If to peeled off epithelial cells we add water in sufficient quantity, there arise, under the eye of the microscopist, in the interior of the cells, large transparent mucus-globules, which press aside the remaining parenchyma of the cell together with the nucleus and cause them to appear as an appendage; finally, however, they pass out and leave behind the cell-body in a very mutilated condition. The presence of mucus in the epithelium is proven by this simple experiment. We feel tempted to place upon an equality the formation of mucus in the cell-protoplasm with the induration of the cells of the epidermis, for which the chemical similarity of mucin and keratin yet particularly invites us. Then, of course, the mucus formation would have to be conceived as at the same time a mucus transformation, and we would have to accept with Frerichs, Donders, O. Weber, that a certain amount of effused mucus represented a certain number of cast-off epithelial cells, consequently the epithelial cells were cast off in the preparation of the mucus. I cannot, without further consideration, declare my agreement with this consequence. I am far more convinced, that in general mucus is only cast out by the cells, and that a complete destruction of the cells only takes place exceptionally into mucus (for example, in mucous catarrhs).

§ 41. There is a situation, where we can study likewise upon a physiological model, what concerns the visible processes in the mucoid softening of the matrix of cartilage, I mean the cartilage of symphyses and the intervertebral cartilages. Luschka has correctly characterized the changes produced by age in the last-mentioned organs, as an incomplete formation of an articular cavity. A slowly progressing softening of the cartilaginous coverings of the opposing surfaces of neighboring vertebral bodies, becomes the means for the formation of a cavity. The anatomical picture, however, which we find in this and in every softening of cartilage, is exceedingly characteristic (Fig. 9). The homogeneous matrix shows shaded striæ placed vertically to the free surface, which hereafter present the first indication of a fibrous cleavage. The actual splitting up into fibres then ensues nearest to the surface, in that the individual fibrils separate and float in the articular fluid; their free ends rapidly taper and end with an indistinct point. This is the place where the intercellular substance is dissolved and melted down in the manner of a mucoid metamorphosis. The accompanying process in the cartilage-cells has not the character of a retrogressive, but of a progressive change, in that the advancing cellular formation by division has the consequence, that in place of a single superficial cartilage-cell,

groups of from two to twenty are found. These nests of cells, surrounded by a capsule and a residue of the intercellular substance, reach the fluid of softening, where they fall into the colloid degeneration.*

Fig. 9.



Softening of cartilage. Vertical section of an articular cartilage in malum senile articulorum. 1-300.

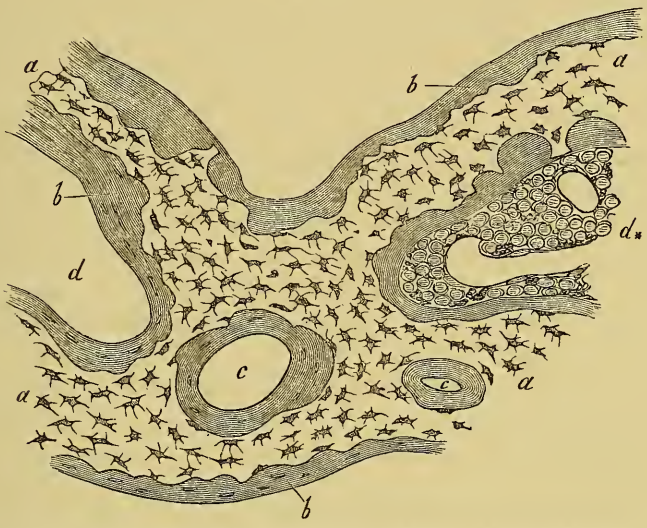
A peculiar complication is introduced in the softening of osseous tissue, in that its basement-substance is impregnated with the salts of lime, which must previously be dissolved and removed before the liquefaction of the basis-substance can take place. It is now, however, shown that in very many cases of osseous resorption, both of these forces, namely, removal of the lime and the liquefaction of the basis-substance, take place so simultaneously, that the osseous tissue at the edge of the resorptive process is defined with a very sharp, and also peculiarly serrated line,† towards the adjacent tissues, and nothing is to be seen of the peculiar manner of the solution of the basis-substance. Only in one case, namely, in the atrophy of bone, designated from of old as the softening of bone (osteomalacia), is the solution of the salts of lime separated by a long interval of time from the liquefaction of the osseous cartilage. We can therefore observe, upon every trabecula of the

* I cannot assent to the ingenious view of Kölliker, that the numerous white clumps which may be observed with the naked eye in the intervertebral jelly, are proliferated cells of the chorda dorsalis, but regard them, based upon the analogy with the pathological softening of cartilage, as nests of cartilage-cells liberated by softening of the cartilage, then, however, having undergone colloid degeneration.

† The so-called lacunæ of Howship (Fig. 10) are produced, in that the removal of the salts of lime from the osseous tissue progresses more rapidly in certain directions than in others. It appears that the direction in which the rays of the bone-corpuscles stand to the surface, from which the resolution takes place, exerts here a definite influence. (Compare diseases of bone.)

spongy substance, or the compact substance rendered spongy, of an osteomalacian bone, that a broad seam of osseous cartilage without lime exists, which encompasses on all sides the yet unaltered osseous tissue (Fig. 10). The osseous cartilage, now the immediate object of softening, shows a striation corresponding to the lamellæ; and we may

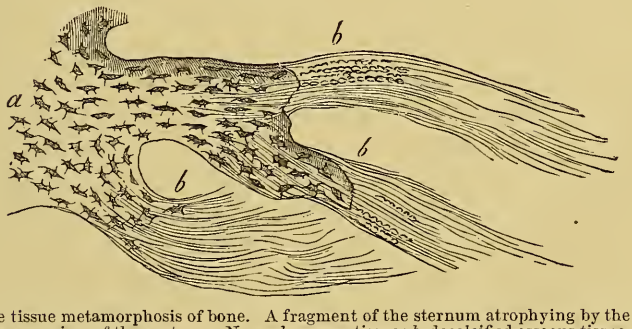
Fig. 10.



Softening of bone. Fragment of bone from the spongy substance of an osteomalacious rib. *a*, Normal osseous tissue; *b*, decalcified osseous tissue; *c*, Haversian canals; *d*, medullary spaces; *d**, a medullary space filled with red medulla. The laminæ of the capillaries are open. 1–300.

regard these striæ as the analogues of those parallel shaded striæ in the softening matrix of cartilage. That this, here also contains the indication of the formation of fibrils, is evidently shown in those cases where bony tissue becomes atrophied and disappears, from the pressure of an adjacent and enlarging tumor. If we examine the bone in the

Fig. 11.



Connective tissue metamorphosis of bone. A fragment of the sternum atrophying by the pressure of an advancing aneurism of the aorta. *a*, Normal osseous tissue; *b*, decalcified osseous tissue undergoing fibrillar disintegration. 1–300.

neighborhood of such a margin of resorption, by removing the periosteum, and then taking away small particles of the compact substance

with the forceps, and placing it under the microscope, we can unequivocally convince ourselves that the osseous tissue from which the lime has been removed is converted into fibrillar connective tissue (Fig. 11). I have convinced myself, by an exquisite preparation in the pathologico-anatomical collection at Giessen, that the same metamorphosis is the means by which actual connective tissue membranes form themselves around osteomalacian depots in the interior of bones, within which the medullary tissue degenerated to a red pulp, gradually converts itself into a thin, serous, colorless fluid (cystoid degeneration of the osseous system).

§ 42. What, in the preceding remarks, we have extracted from the anatomical morbid representations of the atrophy of cartilage and bone, contains the little that is generally known of the visible processes of the softening of the intercellular substance. In most cases, the question will be concerning a simple tumefaction with an obliteration of the old forms. Our knowledge of the new forms, which are especially occasioned by the production of mucus in the organs and tissues, is incomparably richer.

Mucus is a substance extraordinarily capable of swelling by imbibition; the smallest quantities of it are able to saturate comparatively large amounts of water. Such saturations show, in regard to consistency, all gradations, from a tough jelly to a sticky synovia, capable of being drawn out into threads. Whether we are correct in designating these as solutions, has not yet been decided; the solubility namely, of mucus in a physical sense, is particularly denied by several authors. This much is certain, that it belongs to Graham's colloid substances,* and that it stands foremost among these. Mucus has almost no capacity for diffusion, and this peculiarity is of the greatest importance, for its occurrence in the organism in general, and in softening in particular. Mucus can never—we assert this by looking to its colloid nature—as such, pass out from the bloodvessels into the tissues, or from the tissues into the blood. The homogeneous membrane of the capillaries would allow it to pass neither in the one or other direction. Inasmuch, however, as we can never discover even a trace of this substance in the blood, we are justified in the further conclusion, that mucus, upon the one side, must everywhere be regarded as a local production of the tissues, and upon the other side, that it will remain in the situations where it was formed, until it is either mechanically removed, or is converted into a body capable of being resorbed. This incapacity for resorption has no striking results, where the formation of mucus occurs at the outer sur-

* Annalen der Chemie und Pharmacie, bd. 121, s. 1. Graham calls attention to the fact, that we must distinguish with respect to the capacity of diffusion between colloid and crystalloid substances. Crystalloid substances diffuse rapidly and easily, colloid substances but little or not at all. Gum, starch, dextrin, mucus, albumen, and gluten belong here.

face of the body. The physiological secretion of mucous membranes, in which the epithelial cells function as the mucus-preparing organs, not only belongs here, but also several processes belonging to the category of softening, as for example, the mucoid metamorphoses of fibrinous pseudo-membranes and other fibrinous excretions in inflammations of the respiratory tract, &c. The incapacity for resorption of mucus, however, leads to striking and characteristic morphological effects, where it occurs within the interior of the body, be it within a closed cavity, or be it as the substitute for destroyed tissues, as in softening, now under consideration. The mucus is here qualified for an anatomical function, which is performed in a superior manner only by the colloid substance (see following section) namely, that it participates, although itself amorphous, yet as a not quite liquid interposed material, in the composition even of permanent structures and textures.

The formation of mucous tissue stands foremost in this respect. A connective tissue, whose basis-substance has undergone mucoid softening, and whose cellular elements have been somewhat separated by the tumefaction consequent upon the softening, whose form, however, has not necessarily been altered, we call, according to Virchow's example, mucous tissue. Mucous tissue has a far greater diffusion in the fœtus than in the completely built up organism. The entire subcutaneous cellular tissue is originally a subcutaneous mucous tissue. At the period of birth, excepting the jelly of Wharton of the navel-string, there is only yet found a small, but not on that account any the less very important remains of mucous tissue in the vitreous humor of the eye, which remaining with a wonderful stability of composition, continues until the end of life. The occurrence of mucous tissue in pathological spheres is much more various. We know tumors, which consist entirely of mucous tissue (myxoma), tumors, which secondarily metamorphose themselves into mucous tissue, as enchondroma, lipoma, and sarcoma; in syphilitic nodes the mucous tissue is constant; in fungous granulations and other inflammatory new formations, it is a structural element occurring here and there. We reserve the detailed account of all these occurrences for the description of inflammation and tumors.

Touching the remaining structural performances of mucus, conditioned by its incapacity for resorption, particularly its cystic and cystoid depositions are here to be considered, the former conditional upon an occlusion of an excretory glandular outlet, the latter upon circumscribed softening of connective substance. The latter group, which alone interests us here, distinguishes itself in its origin from the formation of mucous tissue, in that the cells show a less indifferent, more active or more passive behavior, whereby they become more movable, and appear as floating portions of the fluid of softening, or it may be they are entirely destroyed.

§ 43. The conditions for the production of mucoid softening are nearly

unknown to us. Were it not for the circumstance that it converts things having a distinctly marked anatomical form, into amorphous, homogeneous substances, finally, incapable of being resorbed, our warrant for representing mucoid softening among the regressive metamorphoses might appear doubtful. It always remains characteristic, that mucoid softening of the basis-substance of connective tissue upon the one side, arises without any essential change in the form and arrangement of the cells (mucous tissue) on the other side, may be combined with the most various progressive and retrogressive impairments of the cells.

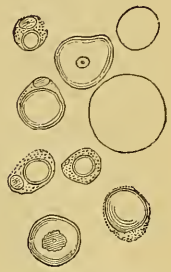
d. *Colloid Degeneration.*

§ 44. Let us pass to the last member of the series of conditions of involution. Colloid degeneration stands in a sisterly relation to mucoid softening. The macroscopic and even the microscopic appearances are so similar in certain parts, that it required a long time before we learned to distinguish a connective tissue with a mucoid softened basis-substance (mucous tissue) from such a one with colloid degenerated cells. This external similarity has nowhere caused as great a confusion as in the nomenclature of tumors, where the names, colloid, collonema, sarcoma gelatinosum, hyalinum, carcinoma colloides, &c., were promiscuously used, now for the one, and now for the other. And upon what is this similarity based? Upon the uniform occurrence, here as there, of a diaphanous, tumefied, gelatinously trembling substance, which is penetrated by fibres combined net-like. Already the perception, that in the one case this fibrous net consisted of stellated, anastomosing cells, in the other of the remains of the fibrillar basis-substance, must have produced a separation of mucoid and colloid tissues, which has also then been justified by further investigations. Above all, colloid degeneration is characterized by a chemical body, which distinguishes itself from mucus by its indifferent behavior towards the mucus reagents, especially acetic acid, and by its elementary composition, which places it among the sulphur-containing albuminates. The circumstance, that it, at least originally, is always a cellular metamorphosis, is not less important for the particular position of colloid degeneration.

We hereby, at the same time, touch upon the essential point of the anatomical process. The only form in which the colloid substance comes to the microscopist's view, is a colorless, transparent globule of fat-like refraction, the so-called colloid globule. How do these colloid globules arise? how are they produced from pre-existing cells? Two ways are possible, namely, either the protoplasm of the cell takes on uniformly, in all places, a homogeneous, strongly refractive state, the entire cell converts itself more and more into colloid globules, within which we can yet for a long time recognize the centrally situated nu-

cleus, upon the addition of proper reagents;* or else, the colloid-globule appears at a certain spot of the protoplasm alongside of the nucleus, according to some, also instead of the nucleus. At first small, in the sequel it grows so considerably that the remaining portion of the cell is pressed to one side, and appears as an appendix of the globule. It is about this time that the cells readily assume the form of a ring surrounding the globule; a seal-ring, if the nucleus yet existing causes a prominence of the periphery at one point. (Comp. Fig. 12.) Finally, the colloid-globule loosens itself from the place of its formation, and leaves behind the remains of the cell, as a crumbling, in a little while disintegrating granular mass.

Fig. 12.



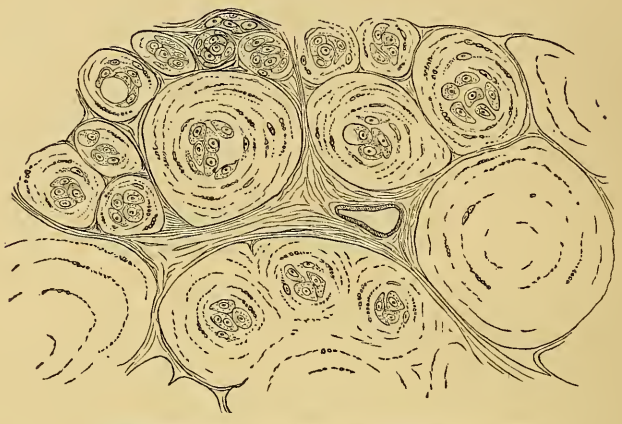
Colloid degenerating cells from a colloid cancer.

The colloid-globules, whether produced in the one or other manner, continue yet to grow for some time, that is to say, to swell up, for they become continually more indistinct thereby, until their index of refraction has equalized itself with that of the already existing colloid mass, so that in the true sense of the word they swim therein. As colloid-substance, like mucus, is a body extraordinarily capable of swelling by imbibition, it makes the colloid metamorphosis comparatively easy to be observed by the naked eye. Small groups of ten to twelve cells, which, previous to the metamorphosis, did not at all exist for the unaided eye, afterward form a small indeed, but still distinctly visible gelatinous granule, as we have already mentioned of the colloid degenerated cellular mass of the nucleus gelatinosus (§ 41). The larger the gelatinous granule becomes, so much the more does the amber-yellow color, the transparent and gelatinous tremulousness become prominent. These peculiarities, however, are only retained up to a certain size of the granule, or it were better to say, up to a certain period of development. Then the substance becomes more capable of being drawn out into threads; finally, altogether thinly fluid. The chemical final product of the colloid metamorphosis is, as with the mucoid, soda-albuminate, the morphological, either a smooth-walled cyst, or even an entire system of intercommunicating cysts, the so-called formation of alveolar cavities. In order to understand this, we must take into consideration that, especially in the pathological colloid-formation (colloid cancer), very many colloid-depots develop immediately beside each other. The basis-substance of connective tissue in which they arise may suffice for a time to isolate the individual colloid-granules from each other; if, however, these become larger, the walls of division atrophy, and, by a more or less complete confluence of the neighboring cavities, an irregular cellular division of the space takes place, which we, with a certain

* I recommend oxalic acid carmine (prepared according to Thiersch's direction).

degree of propriety, compare to the alveolar division of the lung parenchyma (Fig. 13). (See, in addition, the section on colloid cancer.)

Fig. 13.



From the section of a colloid or alveolar cancer. 1–300.

3. Conditions of Infiltration.

§ 45. The degenerations belonging to this group deserve the designation of retrogressive metamorphoses less than those hitherto treated. Thus the structures affected by them preserve, even in advanced states of the change, their external form, at least in so far that we can be in no doubt concerning their identity in changed and unchanged conditions; that is to say, that we may recognize them as cells, vessels, &c. In unison herewith the physiological action also appears never entirely to cease, although the greatest varieties exist in this respect; while the amyloid and calcareous deposits occasion an injury of the organic functions, scarcely compatible with life, the pigmentary and fatty infiltrations are comparatively easily borne. With all, however, a certain amount of damage to physiological activity, proportional to the degree of change, is undeniable, and this is the reason why we must reckon the changes among the "retrogressive."

As a special characteristic of these, we pre-eminently state that the question is everywhere concerning *intussusception and deposition of materials from the blood.* While other constituents of the nutritive fluid, the cells, &c., pass traceless, these materials are retained, like the precipitate upon a filter. An abnormal accumulation in the blood of the materials under consideration, stands foremost among the causes which condition and favor the intussusception. We have, therefore, not infrequently to deal with a simultaneous or preceding adulteration of the blood, a dyscrasia which, leaving out of consideration the clinical phenomena of the general ailment, makes itself known by occasioning the same anatomical disturbances at the most different points of the

organism. This relation to a dyscrasic condition of the blood may be followed even into the histological detail; at least I believe the peculiar fact, that not infrequently the smallest arteries, transition and capillary vessels, become the first points of attack of the infiltration, is only to be explained in this sense, namely, just here the centrifugal nutritive stream passes the walls of the circulatory apparatus; if, therefore, the plasma of the blood carries a material which is prepared to deposit itself in the cells, connective tissue, and homogeneous membranes, then this material will have the first opportunity for being deposited in the elementary structures of the walls of the vascular system of the region in question.

Besides the dyscrasia, the local dispositions, the conditions and peculiarities of tissues play a prominent part in the etiology of infiltration. In the first place, all organs in an existing dyscrasia are not uniformly fitted for taking up the peccant material; for example, in an abnormal amount of fat in the blood, the liver and the areolar connective tissue are more so than the remaining parts of the body; in the presence of superfluous salts of lime in the blood, the lungs are the preferred depository; amyloid degeneration also attacks the organs of the body one after the other in a certain sequence; first of all the kidneys, then the spleen, the liver, and so on. Finally, however, we must recognize the possibility of purely local causes of production. This occurs most strikingly in pigmentary metamorphosis, to which hyperæmia, hemorrhage, and inflammation, give by far the most frequent occasion; only a few, but certainly the most important and interesting pigmentary conditions, are to be referred to a constitutional affection, like the melanotic and melanæmic discolorations, the "bronzed skin" of Addison. We will yet frequently have the opportunity, in the course of this description, to return now to the local, now to the general character of the conditions of infiltration. These preliminary remarks were only intended to inform us as to their position in the natural history of diseases, and to establish the characters of the group.

a. *Amyloid Infiltration.*

§ 46. If we now turn to the amyloid infiltration (lardaceous, waxy degeneration, vitreous swelling—glasige verquellung), we unfortunately immediately encounter an undeniable dilemma in connection with the definitions just given, as we are not able plainly to name the material which was previously contained in the blood, and which from there infiltrated the tissues. The infiltrate of the tissues is, according to the elementary analysis of Kekule, an albuminate; but it is an albuminate which distinguishes itself from fibrin, albumen, &c., in that it becomes bluish, violet, and red, upon treatment with iodine; a brownish-red shade occurs most frequently herewith, which we can best compare to

the red of polished mahogany wood, and may call it a "mahogany red.' This peculiar color-phenomenon, which occurs only in a similar manner with bodies of the starch series, taken together with the circumstance that the substance occasionally, like vegetable starch, presents itself as bodies with concentric layers, induced its discoverer, Virchow, to give it the name "amyloid." If we now search the blood for an albuminate reacting similarly, we will search in vain, even in persons whose organs have undergone amyloid degeneration in the most extensive manner. In fact, we can only indirectly attain the conviction that amyloid degeneration is nevertheless a genuine infiltration.

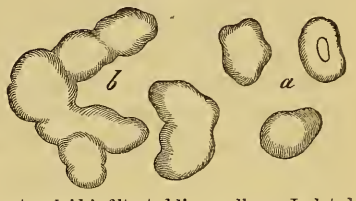
As an amyloid substance can only attain the property of reddening upon the addition of iodine, in the tissues themselves, outside of the blood-tract, it becomes of consequence, to exhibit an example, how an albuminate, which is derived from the blood, and is a well-known constituent thereof, may become amyloid substance outside of the blood-tract. This problem, in my opinion, has been solved by the observations of Friedrich and Biermer. One who has ever occupied himself with experiments on blood-extravasations, will immediately recognize the bodies with concentric layers, which both of these investigators found in hemorrhagic depots of the lungs, as deposits of fibrin about small heaps of blood-corpuscles, fragments of tissue, particles of charcoal,* &c. As some of these bodies showed the iodine reaction, the fibrin of the blood had doubtless been converted here into amyloid substance. We do not wish to say thereby that an impregnation with fibrin may now already be regarded as the essential thing in amyloid infiltration. It suffices to accept, that an *albuminate of the nutritive fluid on its way through the tissues is detained and separated in a solid form.* As it is the prominent peculiarity of the fibrinogenous substance to be constantly at the point of becoming solid, of course it will be just this albuminate of the blood that will have the first claims to our consideration; nay, if we follow the course of amyloid degeneration in detail, we will yet find much in favor of this opinion; but the matter is, at all events, not yet so mature as to be further discussed at this place.

§ 47. Let us now take a view of the histological processes. The amyloid infiltrated cell distinguishes itself from the normal by its greater circumference; this exceeds the normal measure generally one-

* It is very instructive to every one, who is interested in the pathological histology of the lung, to devote a passing glance at the microscopic forms of charcoal-dust. We see bodies there, which by their peculiarly pointed, angular forms and their color, in thin layers, translucent and brownish-red, could very easily give occasion for mistaking them for blood-crystals. We find particles of charcoal in very many lungs; for their extraordinarily pointed projections and sharp angles cause them, when inspired, to penetrate into the soft parenchyma of the lung, and to remain fixed, sooner than other foreign bodies. We may be entirely sure, however, of the carbon nature of such crystal-like bodies, if they have circular holes. (Virchow's Archiv, x, taf. iii, fig. 5.) These are the porous canals of the pitted cells of coniferous wood.

third, it may, however, be two-thirds, or even twice as large. Hand in hand therewith goes on a certain deformation of the cell into plump, clumsy forms; the characteristic contours are effaced, the angles and edges are rounded; that which is the most striking, however, is the homogeneous, colorless, translucent, slightly opaline appearances of these cells. The nucleus is no longer to be recognized. Everything points to a very intimate permeation of the protoplasm with a strongly refractive substance, which causes all inequalities produced by lesser effects of light to disappear. (Fig. 14, *a*.) If several amyloid degenerated cells are in immediate contact, they are wont to coalesce into irregular shapes, mostly elongated clumps, upon which the lines of division of the individual elements may no longer be determined. (Fig. 14, *b*.)

Fig. 14.

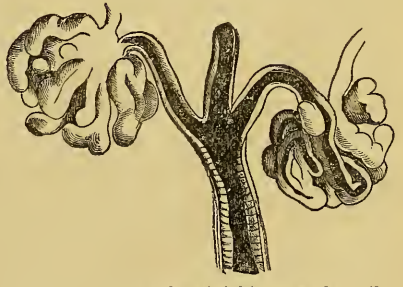


Amyloid infiltrated liver-cells. *a*. Isolated cells. *b*. A fragment of the liver-cell network, in which the dividing lines of the individual cells are no longer visible. 1–300.

§ 48. The amyloid infiltration of non-cellular textural elements is at all points analogous to that of the cells. Everywhere the same intumescence, deformity, and vitreous translucent homogeneity. We know it to be thus in structureless membranes, basis and cementing substances of all kinds. If another proof were necessary for calling amyloid degeneration with propriety an infiltration, this entirely uniform manner of appearing in parts so histologically different, would indicate it. This conviction, moreover disputed by no one, receives, however, the seal of the highest probability, if we trace the course of the degeneration in the individual organs. In this connection I refer to the appropriate sections of the special part of this work, and will only here yet make mention of the *vessels*.

The fact that small arteries, transition and capillary vessels, are the preferred and mostly the first points of attack of all infiltrations, I believe I have placed in the correct light already above (§ 45). The amyloid infiltration stands foremost in this respect. Here every diseased condition of an organ is brought about by disease of the afferent vessels. That gradual advance of the infiltration from within outwards is very distinctly reflected in these latter. At several spots the inner coat with the adjacent homogeneous limitary membrane only shows the vitreous tumefaction; further on, the muscular

Fig. 15.



Amyloid infiltrated Malpighian vascular coil of the kidney. 1–300.

fibres of the middle coat also take on the homogeneous, glistening, somewhat indistinct appearance, and in the graver forms, such as were described by Beckmann upon the thyroid artery, the infiltration even extends into the adventitious coat and the surrounding connective tissue.

The inevitable result of this degeneration is a corresponding diminution of the lumen of the vessel. The lumen is diminished by the swelling, and this swelling may proceed to complete impermeability. The accompanying representation (Fig. 15) shows the partial amyloid degeneration of a Malpighian vascular tuft of the kidney; we see how the blue injection, during life therefore the blood, could only penetrate into those capillary loops, which do not show that homogeneous glassy appearance. The addition of iodine causes the rete mirabile to exhibit an alternation of blue and red loops, by the way a very elegant sight. (Fig. 15.)

§ 49. In the degeneration of vessels, we have at the same time the principal cause of the microscopic anomalies which the amyloid degenerated organs present; namely, by reason of this a greater or less marked anæmia becomes decidedly prominent. It is true, this anæmia is not exclusively caused by the tumefaction of the vessels, but also because the degenerated parenchyma occupies a greater space than the normal, and thereby exerts an external pressure upon the vessels, as we can particularly establish in amyloid degeneration of the liver. Here, not the capillary loops, but the liver-cells lying in the capillary loops, are the principal depots for the amyloid substance, and the anæmia of the lardaceous liver is therewith complete.

The smaller the share, however, which the blood takes in coloring an organ, so much the more does its intrinsic color become prominent. This also particularly obtains in amyloid degenerated organs, and hence we observe upon them, in the same measure as the infiltration advances, so much the more does the peculiar color and nature of the amyloid substance become prominent. The parts become pale yellowish, or grayish translucent; soft as wax, the impressed finger leaves a lasting pit behind. Where the degeneration is altogether complete (certainly a rare case, and as yet only observed after the manner of depots in the thyroid gland and the spleen), the comparison to white wax, which Virchow advanced, is entirely appropriate.

§ 50. The form of amyloid degeneration hitherto described is found most frequently after long-continued suppuration in the osseous system, caries of the vertebræ, necrosis, &c.; furthermore, it is not a rare attendant upon constitutional syphilis, less frequently upon tuberculosis of the lungs and other cachexias; upon all cases where we can unconditionally presuppose a dyscrasic constitution of the blood as a basis.

We have yet but few words to add concerning the local production of amyloid substance. We have already mentioned the stratified concretions in hemorrhagic depots of the lungs. There it was the fibrin

of the blood, which, after lying a long time outside of the vascular tract, showed the iodine reaction; it meanwhile appears that other albuminates and albuminoids can also experience the same metamorphosis. The stratified concretions, which are never wanting in the glandular tubules of the prostate gland of the adult, afford us an example, how in the (mucus or colloid?) secretion of a gland, an albuminate may separate in a solid form, generally about individual cells or heaps of cells, and then—although not without exception—shows the iodine reaction, and indeed more of a bluish or violet, less of a reddish tint (Fig. 16). These bodies may attain a considerable size by the deposition in layers of the same substance; it also occurs that two or more lying together receive a common envelope, then we can recognize them even with the naked eye and test their behavior towards iodine.

Fig. 16.

Stratified amyloid concretions from the excretory ducts of the prostate.

Finally, those frequently mentioned, concentrically stratified bodies, which we regularly find in the ependyma of the ventricles of the brain, and in enormous amount in the so-called gray atrophy of the nervous structure, are of entirely local significance. Whether the question here is about amyloid infiltrated cells, or about concretions, is not yet decided; yet the striking uniformity of size and the dispersion of these bodies, not entirely without rule, in the ependyma of the ventricles, may be more in favor of the first view than of the second. The color which they present upon adding iodine is a pale blue, which, however, may be converted into violet by sulphuric acid.

b. *Calcification.*

§ 51. Calcification plays a less important part in pathology than does amyloid degeneration. We understand by this, the infiltration of tissues with phosphate, and carbonate of lime in the solid form. The most extensive, but also in its way very peculiar, physiological model, is the deposition of the salts of lime into the basis-substance of the osseous tissue. On the contrary, all the crystalline deposits of the secretions, which, for example, occur in the urinary passages as sediments and incrustations, do not belong here.

We must open the consideration of lime infiltration with a preliminary question, whose answer is of so great interest for the comprehension of the phenomena that it immediately becomes the main question. Whereby are both the phosphate and carbonate of lime retained dissolved in the blood and the parenchymatous juices, and what circumstances may we regard with probability as the condition of their deposition into the tissues?

Our answer to these questions is piecemeal. From the intimate com-

bination of all albuminates with small quantities of phosphate of lime, which remain behind as ashes in their combustion, we might derive the impression that it was chemically united to the albuminates in animal nutritive fluids, and must be soluble in water in this combination. (Gorup-Bezanez.) Leaving this hypothesis out of consideration, the fact is to be adduced that phosphate of lime, and still more exclusively carbonate of lime, are soluble in such fluids as contain *free carbonic acid.* The blood, as well as the nutritive fluids of the body, belong to these fluids. It is therefore at least probable that free carbonic acid functions as an important, it may be the most important, solvent for the salts of lime. (Gorup-Bezanez.)

It was already disagreeable that we had to answer the first part of the question proposed above with a "may be." So we fall right into a dilemma, when the aim is to bring forward a satisfactory representation as to the *causes of the deposition* of lime. We must meanwhile here also make at least a trial. The circumstantial but only correct way for this is to pass in review before us all the known cases of calcification, in order at the conclusion to propose to the muster the question: What have the localities, where we find the lime deposits, in common with one another, and to what extent does this general peculiarity qualify them as depots for lime? It is herewith inadmissible to take into consideration those cases of lime-infiltration where an extensive, simultaneous resorption of the salts of lime from the osseous system permits us to conjecture with certainty a supersaturation of the blood with lime—a lime dyscrasia—because here the idea is too obvious that the blood can only retain in solution the salts of lime up to a certain point of saturation, and then the deposition in a solid form at this or that point must ensue. We must confine ourselves exclusively to lime-infiltrations of a local character, and will begin with the physiological occurrences.

§ 52. Genuine osseous tissue is produced, in that, in a connective tissue richly provided with blood-capillaries, and in those parts of the territories of the vessels or parenchymatous islands, which upon all sides are the most remote from the vessels, there first arises a dense basis-substance which incloses the cells becoming stellate, in regular interspaces, thereupon however itself experiencing an impregnation with the salts of lime. This is the fundamental phenomenon to which both the formation of bone from membranes, as well as the formation of bone from cartilage, may be traced back. In both cases the first outlines of the medullary spaces are given in this manner; the regular repetition of this deposition, inclosure of cells, and calcification, leads upon the one side to the formation of the compact osseous substance, concentrically stratified around bloodvessels, on the other side to a diminution of the original medullary spaces to the lumen of the *Haversian* canals. In regard to the detailed study of these things, I refer to the

text-books of normal histology. The circumstance that the first deposition of the salts of lime ensues into those neutral lines, which we may conceive just as well as limitary lines, as the intermediate line of the territories of vessels, is of especial importance to us. It is self-evident that these lines come together at certain points, and must form a similar network to the capillaries themselves, which also the aspect of a young osteophytic formation, or of a long bone at the edge of ossification toward the cartilage, completely confirms.* It occurs to us in this connection that, in other connective-tissue parenchymas, the lymphatics with greater consequence show a similar relation to the bloodvessels. In 1859† I already called attention to this, that the lymphatics of the tail of the tadpole always appeared in those parts of the parenchyma that were farthest removed from the bloodvessels. Since, then, the course of the lymph-capillaries has been the subject of numerous investigations, and this fact has been constantly reaffirmed (compare, for example, Von Recklinghausen, Die Lymphgefässe und ihre Beziehung zum Bindegewebe, taf. i, fig. 1). This course is connected with the function of the lymph-capillaries as drains for superfluous nutritive fluids, since wherever the currents going out towards all sides from the capillary vessels meet together, there is provision made for a corresponding discharge by drainage-tubes. I will show further on in what manner this diversion to a distant part may become profitable to our consideration. At present I will only add the remark, that the true osseous tissue is one of the few textures which is entirely deprived of lymphatic vessels.

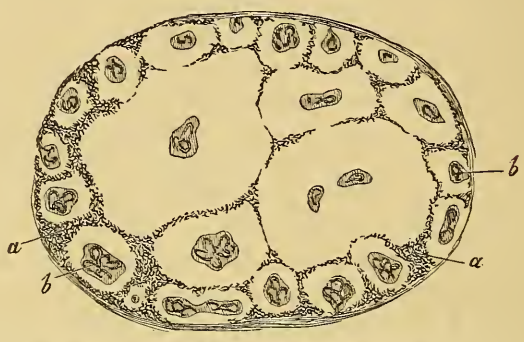
As the individual vascular territories of young bone are indicated by lime-infiltration, so the bone as a whole also limits itself towards the cartilage by a zone infiltrated with the salts of lime, one-half belonging to the cartilage, and the other to the bone, the same zone of calcification which has obscured for so long a time the formative process of bone. More accurately expressed, it is not the idea that this common boundary belongs to the bone, but to the sum of the most exterior medullary spaces, contiguous to the cartilage, and supplied by the ultimate loops of the arteria nutritia. This is plainly shown in that disturbance of the growth of bone, which we call rachitis. Here individual terminal medullary spaces extend far into the very wide proliferating layer of the cartilage. The calcified zone is interrupted at many points, and Virchow had already observed, that we find instead small depots of calcification, to a certain extent the dispersed pieces of the calcified zone, farther up in the cartilage. If we make a transverse section in this region, we may observe how the whole cartilage is subdivided, by this infiltration of lime, into elongated rounded fields of unequal size, in whose centre we can recognize one of the encroaching

* See Osseous System, Exostoses.

† De Vasorum Genesi. Inaugural Dissertation, Berlin.

medullary cavities, with its centrally located vascular loops. Therefore, here also the infiltration of lime occurs as the bounds of the vascular regions, and again in a tissue, which exhibits lymphatics, neither in the lines of demarcation mentioned, nor generally.

Fig. 17.



Calcification of cartilage. Transverse section through the proliferating zone of a rachitic cartilage of the epiphysis. 1–10.

I believe that, already upon the basis of these data of normal histology, that I may express the opinion that peculiarities of the movement of juices, especially a certain slowness, relatively a stagnation thereof, which may be supposed with probability, because of the want of lymphatics at the places alluded to, stand in a not altogether accidental causal relation to calcification. If, however, this is the case, we would have to imagine to ourselves the precipitation of the salts of lime as occurring thus, *that the solvent thereof, the free carbonic acid, leaves the stagnating nutritive fluid by its great capacity for diffusion, and is excreted in other ways, and by its escape, leaves the insoluble salts of lime behind.*

§ 53. If we now pass to pathological calcification, we will see this occurring, especially as a secondary production, in consequence of inflammation and new formation. They are either the new formations themselves, which calcify, or they are those remaining parts of diseased organs, which do not themselves participate, but are surrounded and permeated by the products of inflammation and new formation. To what extent here in each individual case we can likewise adduce with great probability a disturbance of the circulation of juices, as a causal force for the deposition of the salts of lime, will show itself in observing individual cases. Calcification is observed in the various tissues, connective tissue, vessels, cellular and glandular tissue, muscles, both smooth and striated, most frequently, however, also in the pathological states of the calcification of cartilage. After long-continued catarrhs of the respiratory mucous membrane, the cartilages of the larynx and trachea, and in chronic suppurations of the vertebræ, the intervertebral discs are wont to calcify; the costal cartilages of old persons not infrequently share the

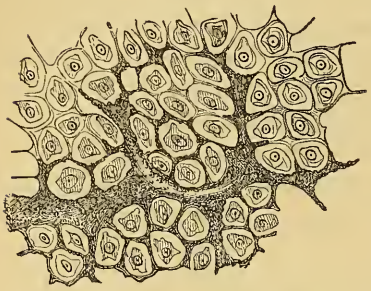
same fate; finally, calcification shows itself in those small globular portions of cartilaginous tissues, which we have learned to know upon the one side as structural elements of cartilaginous tumors, upon the other side, as excrescences of articular cartilage and synovial membranes. In all these cases the first deposit of the salts of lime occurs at the most interior, the furthest removed regions, of the cartilaginous structures, in regions where certainly the circulation of nutritive fluid takes place with the greatest difficulty, probably stagnates entirely. It therefore also appears justifiable from pathology in the meantime, to regard the deposition of the salts of lime as the result of a retardation, relatively a stagnation of the nutritive fluid.

§ 54. We will, in the next place, learn the histological detail of lime-infiltration as a marked example from the history of the development of cartilage. We are here dealing with a connective substance, with cells and a basis-substance. It has not been explained why, at one time the cells, at another the intercellular substance, are the first points of attack of the calcification; enough that they may both be so; it is also a characteristic feature of this infiltration, that the most various textural elements are accessible to the changes. The so-called calcareous granules form the first visible effect of calcification, small, round-cornered corpuscles, black by transmitted light, glittering white by reflected light, which are more or less closely sprinkled into the tissue affected, let us say at first into the basis-substance of cartilage. These bodies were actually held for the salts of lime themselves, and it was supposed that we could find in them crystalline forms; but we were deceived. The calcareous masses may constantly receive their principal peculiarities, namely, their solidity, their white, opaque constitution, from the impregnated salts of lime; nevertheless we must distinguish upon each of them—first, a particle of basis-substance of similar size, and second, the impregnated salts of lime. Without this distinction, or better, association, all further changes would not only be inexplicable, but absolutely impossible; namely, after the basis-substance has been primarily, markedly obscured by the calcareous masses, it attains in consequence a homogeneous, sheeny appearance, as we know it of the basis-substance of bone; it however evidently attains it, in that the calcareous masses come to lie ever closer and closer, finally come into contact, and immediately disappear as bodies to be distinguished individually. As the basis-substance now, after complete calcification, has exactly the same volume as before, the salts of lime cannot possibly occur in such large portions, as these granules, together with the proper basis-substance; the calcareous granules must, therefore, be regarded as basis-substance + the salts of lime.

Now, therefore, and as long as the basis-substance alone is calcified, the appearance is presented to us of a white, sheeny figure, branched netlike, which is so much the more elegant, the more space the cells occupy, and

the smaller, in consequence, the trabeculæ of the basis-substance are. (Fig. 18.) Rokitansky also describes a globular separation of calcified basis-substance, which especially occurs in fibrous cartilages and enchondromatas. I have likewise seen this globular deposition. It is not to be mistaken for the granular deposition. On the contrary, Rokitansky correctly places it by the side of calcification of fibrillar basis-substances.* The globules, or rather discs, are the transverse sections of calcified fibrillæ. When, therefore, we meet with the globular deposition of calcified basis-substance in fibro-cartilaginous structures, this presents in itself nothing remarkable; that, however, the basis-substance also of hyaline cartilage, under proper circumstances, is capable of a dissolution into fibrils, the history of softening has already taught us.

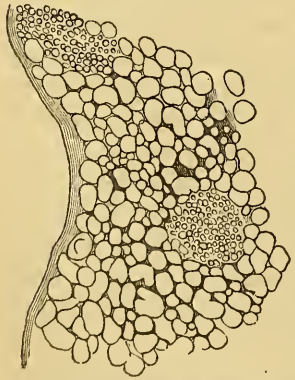
Fig. 18.



Calcification of cartilage. A free body in the elbow-joint, in cross section. 1-300.

Calcification of cartilage leads to entirely different optical results, when the *cells* are the part first attacked. A peculiar thickening (sclerosis, Virchow) of the cartilage-capsule precedes in these cases all other changes. The thickened capsule takes up the salts of lime, and indeed not always as clouds of calcareous granules, which certainly occurs most frequently by far, but also in the manner, in which Kölliker first saw it in rachitis,† that the impregnation of lime only characterizes itself by the gradual production of a whitish opalescence in reflected light, whilst the structure *never loses its transparency.* To the latter circumstance we owe the perception, that this entire series of transfor-

Fig. 19.



Cross-cut of an ossified pleuritic pseudo-membrane (after Rokitansky).

* The phenomenon of globular deposition occurs most beautifully in the calcification of tendons, and has here undergone a very exhaustive investigation by Lieberkühn (Reichert and Du Bois, Archiv, 1860, No. 6, p. 824 ff). It is thereby to be remarked, that between the discoid, transverse sections of the fibrillæ, occasionally larger or smaller interspaces remain, which often look delusively like bone-corpuscles, because of their inwardly curved, serrated outlines. If, meanwhile, we consider the extraordinary variations in size and form which these things undergo, we will, even without having recourse to a longitudinal section, obtain the conviction that we are dealing with incidental forms, determined by the contiguous circles. Compare herewith Fig. 19, which represents a transverse section of an ossified pleuritic pseudo-membrane.

† Compare herewith the history of rachitis under "Diseases of Bones."

mations still does not properly affect the cellular substance itself. It remains, up to the very end, a decidedly capsular process. The capsule continues to thicken inwardly. In consequence, the space of the original cartilage-cavity becomes constantly smaller and smaller; it simultaneously loses the spheroidal form. As, therefore, the thickening of the cartilage does not follow uniformly at all points, but funnel-shaped clefts (analogous to the porous canals of lignifying vegetable cells) are spared at regular small distances, there finally results for the portion retaining cells, a serrated, ramified shape, such as could not be imagined more like the corpuscles of bone. If the basis-substance has simultaneously or even supplementarily proceeded to the vitreous translucent stage of calcification, we may speak of a direct ossification of hyaline cartilage. This sort of spurious osseous tissue, which compares with the genuine (§ 52), just as other calcified connective substances, tendons, fasciæ, coats of vessels, &c., rarely occurs, and always only in small portions, as in cartilaginous tumors and in the spongy substance of rickety bones, where it forms small inserted pieces near the edge of ossification of the cartilage.

So much concerning the histological detail of the calcification of cartilage. The individual features recur in the most various tissues. If meanwhile we do not wish to anticipate the special demonstrations, we must here satisfy ourselves with the remark, that in calcification the question is everywhere about a true infiltration. The forms of the infiltrated tissues, at least in their coarser outlines, never become indistinct; as a rule, by the chemical solution of the salts of lime (hydrochloric acid), we are able to restore the structures as they previously were.

c. *Pigmentation.*

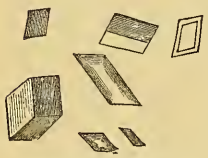
§ 55. In that we pass to pigmentation (chromatosis), we enter upon one of the most interesting regions of pathological histology. Its limits are somewhat indistinct. I therefore observe in advance, that it is not my intention to bring into consideration every change of color, which is occasionally observed in diseased parts,* as a pigmentation, but exclusively those positive colorations, which are produced by the infiltration of a coloring-matter into the tissues. Red, yellow, brown, and black pigments, with every imaginable intermediate tint, may occur in this way as infiltrates. In the latter instance, however, they all proceed from one and the same pre-existing red coloring matter; I mean the hæmatine of the blood-corpuscles.

We do not exactly know the chemical composition of hæmatine; we do not know how it is formed. Itself most probably an albuminate, in

* Have not almost all the changes of tissues hitherto considered, been simultaneously the causes of a particular coloring or decoloration of the tissues? The coefficients of refraction and therewith the optic properties of tissues, may be altered by desiccation, by shrivelling, and by induration.

the red corpuscles of the blood, it is most intimately combined with another colorless albuminate, globulin. This combination, under proper circumstances, shoots into long, red needles (hæmato-crystalline). In order now to find it intelligible, that even yellow, brown, and black pigments are derived from the coloring matter of the blood, it is indispensable to cast a glance at the physiological metamorphoses of this body. The most important of these, and in a certain measure the model for all, is the metamorphosis into biliary coloring matter. A mysterious darkness has hung for a long time over this in itself so plausible a process. It correctly appeared to be doubtful, to derive a chemical body, which is exclusively produced by the activity of the liver-cells, from a definite constituent of the blood, only because it possessed similar optical properties. These scruples are at present as good as removed, and particularly by the following experiences: at points, where previously an extravasation of blood had taken place, there is not rarely found hæmatoidin, small, fire-red crystals of the rhombic system. (Fig. 20.) No one will, indeed, doubt that this hæmatoidin is a derivative of the coloring matter of the blood; meanwhile it contains no iron, like hæmatin, and gives with active oxidizing agents, for example, concentrated sulphuric acid, the spectral colors. It is now scarcely necessary to bring forward, that just these properties, which distinguish hæmatoidin from the coloring matter of the blood, approximate it to the biliary coloring matter. It became at least very probable thereby, that the biliary coloring matter must be regarded as a derivative of the blood-coloring matter, and this probability became a certainty, when Valentiner came forward with the discovery, that we could extract hæmatoidin by means of chloroform from dried and powdered bile. In fact we obtain in this manner a crystalline coloring matter, which at first glance is not at all to be distinguished from hæmatoidin. Nevertheless the observation of Valentiner has had to undergo a slight correction. Städeler found that the crystalline coloring matter of bile (bilirubine, $C_{32}H_{18}N_2O_6$) does not only distinguish itself by the unimportant deviation in the angles of the crystal, but also by containing two atoms more of carbon than does hæmatoidin ($C_{30}H_{18}N_2O_6$, Robin). This difference is of course judged even by Städeler as being too slight to shake the position, that biliary coloring matter is formed from the coloring matter of the blood. The senescent red blood-corpuscles lose their coloring matter, which imparts itself to the serum, from thence is taken up into the liver-cells, converted into biliary coloring matter, and removed from the body with the excrement. Previous to this removal, however, it undergoes, especially by long retention in the gall-bladder, a further metamorphosis into yellow, green, brown, and black shades,

Fig. 20.



Crystals of hæmatoidin (after Virchow).

which Städeler designates as bilifuscin ($C_{32}H_{20}N_2O_8$), biliverdin ($C_{32}H_{20}N_2O_{10}$), biliprasin ($C_{32}H_{22}N_2O_{12}$), and bilihumine. We observe, that bilifuscin distinguishes itself from bilirubine by containing 2 atoms more of HO, the biliverdin from bilifuscin by 2 more atoms of O, biliprasin from biliverdin again by 2 more atoms of water, while bilihumine is a black, insoluble, very highly oxidized body.

§ 56. The scale of colors just presented is, as has already been mentioned, the paradigm for the course of all the other pigmentary changes, both physiological as well as pathological. The former, which I only here touch upon passingly, are produced in that other cells also have the property, or still attain it in advanced life, like the liver-cells, to withdraw the dissolved coloring matter of the blood from the serum, and to condense it in themselves; thus the epithelium of the choroid, the rete Malpighi, certain ganglion-cells. The black pigment of the lungs alone deserves a particular mention. I have already called attention, in a note at page 52, to the fact how small particles of vegetable coal, especially charcoal, become fixed in the lung, and then may give occasion for mistaking them for pigments. We will therefore not be averse to refer, even though but a small part of the pigment of the lungs, to inhaled carbon.* This opinion will certainly not be shaken by this, that the lung-pigment shows itself extraordinarily steadfast towards means for its reduction, which at least allows us to conclude upon a large amount of pure carbon. The observation, also, that occasionally the lung-pigment occurs inclosed in cells, can no longer be available for opposing the coal-dust theory, as we have lately seen with our own eyes, how soft cells, for example, colorless blood-corpuscles, can take up small solid particles into their protoplasm. In spite of all this, but a small part of the lung-pigment can be regarded as inhaled charcoal; another part is undoubtedly derived from the coloring matter of the blood. This shows itself upon the one side in the anatomical uniformity of this and other pigmentations; upon the other side, in that the lung-pigment, under entirely the same conditions (hyperæmia, hemorrhage), experiences a pathological increase, by which other organs become the seat of pigmentary formation. It is also entirely credible, that the blood-pigment would undergo an incomplete combustion into animal coal, at a spot where the interchange of gases is so extraordinarily lively, more rapidly than at other places.

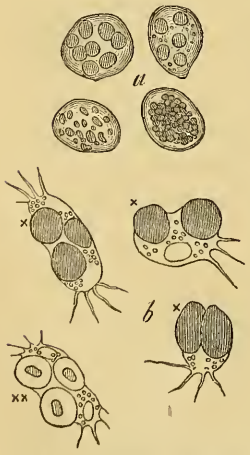
§ 57. If we now turn to the pathological chromatoses, we have already intimated in the preliminary remarks that the great majority of these occur in consequence of local disturbances of the circulation. These pigmentations are of an extraordinarily durable character, and hence not only indicate persistent hyperæmias, but also form a kind of landmark, that this or that organ, this or that spot of an organ, had previously been the seat of a hyperæmia. Moreover, that every hyper-

* Compare dust-inhalation diseases, under head of "Lungs" (anthracosis).

æmia does not leave a pigmentary formation behind, is self-evident; we can even make the assertion that only those hyperæmias do this where blood is extravasated, or is brought to a persistent stagnation in the vessels. If we reflect that, leaving entirely out of consideration bulky hemorrhages, also acute inflammations, and not less the stagnant hyperæmias which lead to smaller, but so much the more numerous, extravasations in the capillary region, we will already find this assertion in itself less venturesome. It, however, receives its proper justification by the anatomical facts.

All purely local, that is to say, all pigmentations not depending upon a dyscrasia, demonstrably take their departure from larger or smaller portions of entirely stagnant blood. Occasionally they are but a few blood-corpuscles, which have not even passed entirely through the walls of the vessels, but have perhaps remained sticking in the adventitious coat; but much more commonly they are small stripes and drops of blood, or even larger bodies of blood, which lie *beside* the vessel in the parenchyma. At this place we have not to enter upon the manifold changes which these kinds of blood-portions in the stagnant condition may in general experience (organization, suppuration, &c.), we have only therefrom to bring forward that important cause of pigmentation, that the blood-discs gradually become decolored, and place *their coloring-matter in a soluble form* at the disposal of the neighboring tissues. We have already learned to know something similar in the putrefaction of blood. From this it follows that the surrender of the coloring-matter is a phenomenon, which not only accompanies the sudden death of the blood-corpuscles, but also induces those metamorphoses which we here trace more to a similar destruction or to a continued existence in another form.

Fig. 21.



Cells containing blood-corpuscles; *a*, of the human being; *b*, of the frog. 1–300.

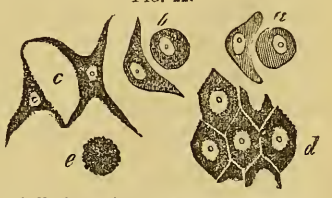
Annotation.—We take this opportunity of mentioning in few words the case where the coloring matter of the blood forms pigments without leaving the blood-corpuscles,—I mean the so-called *cells containing* blood-corpuscles. The question concerning the origin of these large, round or roundish structures, which contain a number of red blood-corpuscles in a colorless, homogeneous basis-substance (Fig. 21, *a*), was formerly regarded as more important than now. It was believed that by this example we could support the doctrine of the formation of cells by *investment* (Umhüllung). At present it has lost that histogenetic interest. It appears that these bodies do not form everywhere in the same manner. In stagnating blood of amphibia I have convinced myself that conglomerations of colored and colorless—that is, decolored blood-corpuscles—produce the optical effect of cells containing blood-corpuscles (Fig. 21, *b*). According to Preyer ("On Amœboid Blood-Corpuscles," Virchow's Archiv, xxx, 417), a similar optical effect is produced, in that the red contents of stagnating blood-

corpuscles of the frog escape in smaller and larger drops, which become incorporated in the contents of neighboring amœboid cells, like the granules of cinnabar, or such other solid particles as present themselves. This may only be applicable in limited measure to the cells containing blood-corpuscles of mammals, as the blood-corpuscles lie more central here, and are inclosed on all sides by a homogeneous border. The opinion only appears to me admissible here that a secondary separation of fibrin has formed about a group of blood-corpuscles. We would then be dealing on a diminutive, or the most diminutive scale, with a phenomenon, which, as we will see, repeats itself in all depot-like (heerdweisen) hemorrhages in even larger dimensions. The colored blood-corpuscles undergo supplementary metamorphoses in this their investment; they lose their rounded contours, become darker, and finally shrivel together into a deep brownish, or black heap of pigment.

§ 58. If the coloring-matter of the blood and the granules have escaped, and have diffused themselves into the surrounding tissues, it is shown that all the constituents of tissues are not uniformly susceptible to the pigments forced upon them. We observe an affinity entirely similar to what we know of the impregnation of dead tissues with carmine solution. The cells have a greater attraction for the coloring matter than the intercellular substance, homogeneous membranes, elastic fibres, &c. Hence the cells, already in this state, appear most intensely saturated with a yellow or brown tint. Coloring by hæmatin, however, distinguishes itself from that by carmine in this, that the nucleus does not again furnish a particular centre of attraction within the cell for the coloring matter. On the contrary, just the nuclei remain untouched, so that we may especially observe them at a later period as colorless discs within the colored protoplasms.

Upon the stage of diffuse imbibition follows that of granular or crystalline precipitation of pigments. This phenomenon we have also already met with in mortification. Therefore, and because it not only occurs in the constituents of tissues, but also in the free fluid *between* the constituents of tissues, we are justified in regarding this as a purely chemical process, which has nothing to do with the vital properties of the parts. It is correct that the crystalline deposits (hæmatoidin), in which least of all we can think of a co-operation of the cells, are found more frequently in the free fluid than in the cells; meanwhile colored crystals have also been discovered in the cells, and conversely, the granular pigment occurs just as well outside of as within the cells, which, by the way, is so commonly found that the hæmatoidin crystals may be regarded as a great rarity. This granular pigment consists, as the name already expresses, of the smallest, yellow, brown or black (melanine)-granules, which lie together in heaps, and under proper conditions fuse into larger, more homogeneous lumps. If they fill out the protoplasm of

FIG. 22.



Cells in various stages of pigment-infiltration. *a*, *b*, *c*, *e*, from a pigment-cancer. *d*, pigmented vascular epithelium from same. 1-300.

a cell, the colorless nucleus is partly pressed to one side, partly surrounded on all sides, it appears as though the pigmented cell had a round gap or a hole. In flat cells, where the nucleus extends from one wall to the other, this form is retained, as the choroidal epithelium furnishes us with an example; in roundish cells the nucleus also finally becomes invisible, and we have a colored corpuscle, upon which only the external form of the cell is yet to be recognized.

§ 59. That the function of cells essentially suffers under this infiltration is not probable, because we observe a partial infiltration of pigment upon many, even the most important elements of the body. I am reminded of certain groups of motor ganglion-cells in the peduncles of the brain, whose regularly exhibited pigmentation has given occasion to the designation of this region as substantia nigra or ferruginea. In general, however, this question cannot well be discussed just in local pigmentations, because it is impracticable to separate the hindrances to function, which are caused by the infiltration of pigment, from those which have been left behind by the preceding local ailment. For this, certain dyscrasic infiltrations of pigment offer us much more favorable opportunities. We observe melanemia, which may be regarded as a dyscrasia, in so far as a locally produced, especially in the spleen, black pigment, from hence reaching the blood, and forming for a time an abnormal constituent thereof. If the deposition of this pigment causes grave disturbances in the capillaries of the brain, these are disturbances which would also be occasioned by other obstructions of these vessels, and cannot be laid to the account of the pigment as such. That discoloration also of the normal skin, which Addison derives from an affection of the supra-renal capsules, is not to be adduced here, because of the great obscurity which accompanies the entire process. On the contrary, the history of pigmentary sarcoma (S. P. Neub) shows us, that there are morbid dispositions of the blood, in which massy cellular formations occur at the most various points of the body, and the newly-formed cells fill themselves entirely or partially with a granular black or brown pigment. The mechanism of this coloring is the same, as in the cells of the rete Malpighi, the choroidal epithelium, &c. And they are just the choroid and the outer integument from which, as a rule, the development of the first melanotic tumors proceeds. The cells withdraw the diffuse coloring matter from the nutritive fluid, according to O. Weber of course also from capillary hemorrhages, which may accompany the change. Be that now as it will, the course of the pigmentation, here as everywhere, proceeds from the state of diffuse imbibition. The coloring matter condenses and is precipitated. The colorless sarcoma-cells have become pigmented sarcoma-cells. No one will however deny that these pigmented sarcoma-cells, thereafter as previously, retain their highly pernicious vital properties and assert them to the injury of the organism. In

my judgment it is inadmissible to speak of a pigmentary metamorphosis in the same sense as of a fatty metamorphosis. For even if we make the observation, that in the scraped off juice of melanotic tumors innumerable minute particles of coloring matter, and therewith such cells occur, in which the granules of coloring matter are affected with dancing movements, and separate under our eyes from the cell, yet we can only see an occurrence in this, such as finally all sarcoma-cells experience; and the numerous fat-granules, which are observed between the granules of coloring matter, but of course difficult to be distinguished from them, make it probable that we are dealing with a fatty metamorphosis.

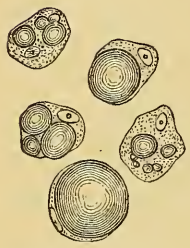
§ 60. Besides hæmatin, the coloring matter of bile must also be mentioned as a source of abnormal pigmentation. If meanwhile we are entitled to the opinion, that the biliary coloring matter is produced from the coloring matter of the blood, we must also regard biliary pigmentation only as a subdivision of sanguineous pigmentation. We meet these exclusively in the bile-preparing and bile-conveying organs. It may be, then, that we may esteem jaundice (icterus) as an infiltration of pigment. In icterus, together with the whole bile, the biliary coloring matter has also been absorbed from the biliary passages into the blood, and the consequence of this is, that, so long as this condition continues, the collective tissues of the body, as far as the nutritive fluid reaches, assume a yellow tint. Never, however, or yet, only very exceptionally, does it come to a deposition of solid biliary pigments; the pigmentary imbibition does not become a pigmentary infiltration. The latter occurs, as has been already stated, only in the liver and in the biliary passages. Virchow found in the epithelium of the gall-bladder crystalline depositions of bilifulvin, and a granular biliary pigment of yellow, brown, but particularly of black shades, is found in the liver-cells, not only when the efflux of bile, but also when the efflux of blood from the veins of the liver is hindered or injured. An atrophy of the pigmented cells may also simultaneously be produced here; yet it is also not allowable here to regard the pigmentary infiltration as the cause of the atrophy, as will be shown from the history of the pigmented nutmeg liver, cirrhosis, &c.

d. *Fatty Infiltration.*

§ 61. The last member of our group, and of passive changes of tissues in general, is fatty infiltration; not to be mistaken for that fatty metamorphosis, which we learned to know already among the conditions of involution of tissues. Whilst there the fat-globules appeared as the forerunners of approaching destruction, they are here nothing else, but in the worst cases a superfluous constituent of the cell; whilst there they appeared as a product of decomposition of the cell-body, they are here a substance conveyed from without and retained in the protoplasm, therefore most properly infiltrated. Corresponding to this, the ana-

tomical picture of fatty infiltration is also an entirely different one from that of fatty metamorphosis. Both only agree in the point, that generally the minutest fat-globules appear in the interior of the cell-protoplasms. While, however, in fatty metamorphosis these fat-globules continually become more numerous, without ever flowing together to larger drops, we have here the spectacle of a true formation of fat-cells. (Figs. 23 and 24.) We rarely see more than two, at most three isolated globules in a cell, and even these hasten, if the expression is allow-

Fig. 23.



Fatty infiltrated liver-cells. 1–300.

Fig. 24.

Fatty infiltration of connective tissue. 1–300.

able, to flow together into a single large drop. The protoplasm with the nucleus is pressed aside in the same way as we saw it in colloid degeneration. The larger the fat-drops become—and in the fat-cells of a lipoma especially they attain a very respectable size—the more difficult does it become to convince ourselves of the presence of certain remains of the protoplasm and the nucleus. Nevertheless, it is not permissible to doubt of their presence in general, as the nuclei regularly reappear upon the occurrence of resorption of the fat. (Fig. 25.) The function of fatty infiltrated cells can be just as little regarded as completely destroyed. We know that a liver whose cells have collectively undergone the metamorphoses in question, nevertheless yields bile, even though it cannot be called either abundant, nor concentrated, nor properly brown. The function is injured, but not at once abolished, even in cases of the greatest extent. It is scarcely necessary to repeat, that after the removal of the infiltrate, which, as already mentioned, entirely and universally lies within the region of possibility, with the old form the old function of the cells also returns.

Fig. 25.

Atrophic adipose tissue.

§ 62. It cannot be stated with certainty what the peculiarities are which qualify the cell-protoplasm in general and the protoplasm of certain cells in particular as depots for fat. That the presence of glycocholate and taurocholate of soda make the animal tissues particularly accessible to fatty infiltration, is partly proven by experiments, partly taught by experience, inasmuch as the entire bed of the bile current, from the intercellular ducts of the parenchyma of the liver to the large intestine, is accompanied by the phenomenon of fatty infiltration. Nevertheless, the moistening with bile can only be regarded as one factor of the production of the infiltration. A second is, that fat in a minutely divided state from the neighboring parts must be at the disposal of the affected tissue. Whence this fat comes is indeed for the economy of the entire organism a vital question, for the process itself it is a matter of indifference. Hence in the intestine we see the food-pulp [the chyme] yielding the fat, the liver-cells taking it up from the serum of the blood, and the epithelium of the biliary ducts from the bile itself, as Virchow has shown.

After all this we certainly cannot doubt that saturation with bile furnishes an uncommonly important force in fatty infiltration. Beside the liver-cells and the epithelium of the biliary passages and the intestine, other cells of the organism also are disposed to fatty infiltration, principally the cells of areolar connective tissue, which, by this metamorphosis, are converted into adipose tissue. Subcutaneous or subserous connective tissue stands foremost in this respect, then follows the interstitial connective tissue of muscles, especially of those which are exercised but little, or are even placed in a state of pathological rest (immobility of joints, paralyses), finally the subfascial, subsynovial and submucous connective tissues.

§ 63. All these tendencies especially obtain when the blood carries more than the ordinary quantity of minutely subdivided fat, when a *fat dyscrasia* exists. We recognize such a one in that the serum is cloudy, opalescent, whitish. Microscopically, we recognize either larger fat-particles, or the emulsion is so minute, that, even with high powers, we can recognize nothing. By agitating with ether, however, we can clear every serum of this sort. If we allow it to stand, the fat will separate and rise to the surface as cream.

We find the serum lacteum perhaps three hours after a meal, and hence it is not wonderful if persons that eat much and abundantly obtain a fatty infiltration of the connective tissue (corpulence; obesitas, polysarcia). Thereafter, according to experience, fat accumulates in the blood of such persons, as drink much brandy, in diseases of the lungs, where the fat ingested and conveyed to the blood is not entirely consumed. In both of these cases the liver is the principal depot for the surplus fat. *Fatty metastases* also occur, diseases in which fat is resorbed at one place in order to be deposited at another. Tuberculosis

of the lungs is not rarely accompanied by such a fatty metastasis of the panniculus adiposus to the liver; as here, however, we could also suppose a deficient oxidation, such cases are of greater importance where this fatty metastasis directly constitutes the essence of the disease or accompanies the diseasing of another organ, as the lung, as I have observed it in a case of a woman of twenty-seven years, where, in the course of fourteen days, the fat was conveyed from one place to another.

II. PATHOLOGICAL NEW FORMATION.

1. General Considerations.

§ 64. The pathological new formation forms the natural contrast to the changes of the tissues hitherto considered. We thus designate every production of the constituents of tissues exceeding the normal measure. The various forms of the pathological new formation are of an exceedingly different value, as well for the organ in which they are seated as for the organism as a whole. If we could establish in the retrogressive metamorphoses everywhere, a certain loss in the physiological capability of functioning, yet we are not in a similar situation in regard to new formations; least of all can we speak of a general exaltation of the capacity for functioning, as we might perhaps have imagined from the contrast; at most, we may speak of an alteration of the functional capacity, and thereby not much is said. In order, however, to obtain from the very beginning the right basis for understanding and comprehending the pathological new formation, it is just as profitable as correspondent to the principles of modern pathology, if we first make the trial, of regarding it as an *excess of the physiological new formation;* that is to say, of the normal development and the normal growth of organs. A short historical review teaches that this principle has indeed always been kept in view, but until now has not been carried out with vigor and consistency.

§ 65. I will not go further back than to John Hunter. In his renowned work, Experiments upon the Blood, Inflammation, and Gunshot Wounds (translated into German by Hebenstreit, 1797), this author develops the opinion that an exudation of *plastic lymph* is the first point of departure of every new formation. Plasticity as an indwelling force of the exudation, of its own accord determines it for the production of all kinds of tissues. The first thing, which in all cases comes to be developed, is a peculiar system of bloodvessels; this is thereafter answerable for the future processes, yields new quantities of plastic lymph, &c. In such representations, which moreover are supported by the most careful observations, the conviction is not indis-

tinctly expressed that the new formation is something foreign to the organism, obtruded—or, to use a word ready coined, a parasite. Hunter attained this principally by comparing pathological new formations with the development of the chick in the hatching egg. He did not know of the cell, and regarded the punctum saliens as the beginning of the history of development.

The discovery of the cell and the perception soon following, that even in the embryo, before the formation of a heart, cells are already present, must necessarily modify the Hunterian theory. The formation of vessels appeared as something secondary, and as we even attained the certainty, that, leaving out of consideration that first foundation of a vascular system, every formation of a vessel is only an extension of the vascular tract already existing, with the "peculiar system of vessels," of new formations, a good portion also of their individual nature was overthrown. The question generally was no longer asked: How do new formations arise, but how do cells arise? But even in this manner of putting the question the same alternative recurred which had just been discussed in regard to the vessels; namely, in the next place such theories were created as permitted the cell to arise *spontaneously*. Plastic lymph, or rather the plasticity of lymph, remained thereafter as before the producer of tissues. It was now designated as cytoblastema, or briefly as blastema.

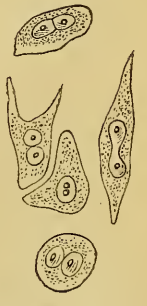
It would carry me too far were I completely to discuss the one or the other of these theories. Therefore let the declaration suffice that at first the theory was very absolutely proclaimed. An exudation of the plasma sanguinis yielded everywhere the blastema. Then it was supposed that in the pure fluid minute granules were primarily formed, these collected together to nucleoli; further on into nucleus, and finally a cell. At a subsequent period one was more careful, and connected the possibility of cell production with the condition that at least the elementary granules must exist preformed in the blastema. We can in general not mistake that one period of the transition and hybrid theories led over to the thesis proposed by Virchow: Omnis cellula e cellula. Wherever cells occur in the organism they are the offspring of other cells, which no longer exist; they are the heirs of their existence, though not always of their peculiarities and vital properties. Hereby the question concerning the production of cells was in a manner answered, which the answer of to-day yet shows to be a sure acquisition of science. The cells, also, which we find in pathological neoplasms, are produced by the division of pre-existing cells. The question only is, what cells? Virchow, whose authority on this subject became the standard throughout a full decennium, developed the view that the cells multiplied by division at the spot and place of the tumor; that, therefore, the newly formed tissues substituted a certain amount of the normal constituents of the body. In opposition to this we owe to Colnheim

the more certain proof that an emigration of colorless blood-cells from the vessels, therefore a plastic exudation in the most proper sense of the word, may furnish the material for the pathological new formation. These cells are also naturally the products of division; the parent cells, however, are distant from the place of the new formation, in the blood, in the spleen, in the lymphatic glands. Of course by this the possibility of a localized new formation is not excluded. The latest investigations of Stricker upon inflammation have rather proved that beside the emigration there undoubtedly occurs a division of the wandering cells, and within certain limits also of the cells preformed at the locality.

§ 66. From preference for these studies of the fundamental processes we had meanwhile neglected a more careful comparison of the pathological with normal new formation. For our part we will further on endeavor, according to our ability, to remedy this deficiency; at present, however, we must likewise yet permit several general discussions to follow. In the first place we will not continue in the assurance that cells proceed from cells, but we will take a more accurate view of the histological detail of this process. The cells of the fully formed organism have experienced so manifold alterations, connected with their physiological function, of the original cell form, the nucleated lump of protoplasm, that we have to expect in almost every tissue another elementary generation of the productive series. Still, we cannot mistake that several generally recurring features are present, by which an outline picture of cellular new formation can be right well delineated.

That the number of the nuclei is multiplied is a phenomenon that is not wanting in any cellular formation. That this increase is caused in all cases by a *division* of the original simple cell-nucleus is in the highest degree probable. Too often has this division of the nucleus been seen, innumerable times been accurately described, how therein the nucleus elongates, becomes constricted in the centre, appears hour-glass formed or indented, until finally the connection of the two nuclei is broken, and now two nuclei instead of one are present (Fig. 26). The nucleolus also appears occasionally to participate in the process. Indented, dumb-bell shaped and double nucleoli have frequently been observed in the large vesicular nuclei of cancer-cells, where we can distinctly follow the production of the nucleolus. In spite of all this we cannot question that the division of the nucleus is observed comparatively seldom. The cause lies in the extraordinary rapidity with which the division takes place. According to all authors who have had the good fortune to observe the process of nuclear division in recently living cells, it is the work of a few seconds. To this must be added that many times they begin and again recede; in this case the indentation which had taken place again equalizes until

FIG. 26.



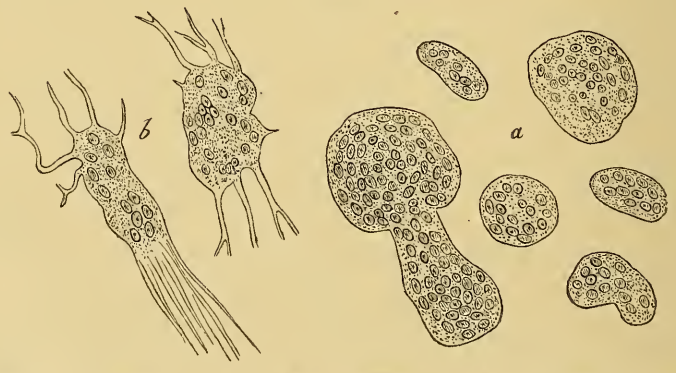
Cells with nuclear division. From a carcinoma.

it is at once suddenly carried out like a work for which repeated efforts of strength are necessary. The same is repeated later in the division of the cell, and we must keep here as there to the declaration of a renowned natural philosopher, that a positive observation is of more value than ever so many negative ones.

§ 67. Another phenomenon, which generally goes hand in hand with nuclear division, is the increase of the protoplasm of the cell. Leaving out of consideration that it is already not well conceivable how, without a corresponding increase of the volume of the individual cell, nearly doubly as great a quantity of substance can proceed from it, so has also this increase of the volume been so often the subject of microscopic observation that there can exist no doubt about it.

Hence nuclear division and increment of the protoplasm together form the first stage of cell production. It happens that a further stage is altogether not attained, that the purpose is fulfilled in a repeated multiplication of the nuclei and increase of the protoplasm of a cell. This leads to that peculiar formation which has been described by Robin under the name of myeloplaques, or cellules à noyeau multiples. These are comparatively large, simply contoured flakes of a very minutely granular, feebly refractive substance, in which numerous (from 20 to 30), round nuclei, furnished with nucleoli, are imbedded. The external form of these formations varies exceedingly. It is evidently confined to no definite formative law, but depends upon the form of the space which they fill out. Only where giant cells (Virchow) are imbedded in very soft, yielding tissues, is a form approaching the globular, or at least roundish, the rule (Fig. 27, *a*); in tissues of fibrous structure the

Fig. 27.



Giant cells. *a*, roundish (Virchow). *b*, with processes. From a muscular tumor (Billroth).

giant cells are furnished with processes at their periphery, which are to be regarded as the continuations of the plasmatic exudation, enlarging the cells into the interspaces of the fibrillæ. An observation derived from Billroth is the most instructive for this relation, where the

giant cells proceeded in the manner described from the cellular elements of muscular fibres. At the boundaries of the tumor, at least partially caused hereby, Billroth could distinctly make out a swelling of the muscular fibres together with a simultaneous separation of the fibrils. The isolated giant cells showed the forms represented (Fig. 27, *b*). I made similar observations in a new formation of connective tissue in the white substance of the brain. It is to be constantly remembered that every giant cell in fact, was produced from a cellular element originally present; an example of the unlimited means of multiplication which are placed at the command of the organism in a single cell.

§ 68. The second phase of cellular formation is the *division of the cell body itself.* Each of the newly formed nuclei acts as the particular centre of attraction for the protoplasm nearest to it; and when this attraction has the result that a certain quantity of the protoplasm also limits itself all around the nucleus, we say the cell is dividing.

The microscopic picture, which the limitation of the protoplasm mentioned presents, is not always the same. The principal difference is caused by the greater or lesser solidity which the peripheric limitary layer of the cell to be produced has attained. This limitary layer is in most cells exceedingly delicate, a "physical membrane," such as the limits of two fluids everywhere form, which will not intermingle. The larger and older the cells become, so much the more distinctly does a colorless, homogeneous, strongly refractive, doubly contoured envelope become prominent upon them, a cell-membrane in the older sense of the word.*

The physiological cellular formation, accompanying or causing the growth of the organism, appears to be exclusively fulfilled only in such cells, which either possess none at all, or but an exceedingly delicate physical envelope. Under these circumstances the process of cell-division appears, like the nuclear division, as a constriction proceeding to division of the cell-body. (Fig. 27.) The longitudinal cleavage of striated muscular fibre is only a variation of this division.

To this cellular division by constriction, pathological histology yet joins two other types of cell-division, or rather two modifications of their anatomical pictures, the cell-formation in *nucleated protoplasm*, and the *endogenous* cell-formation.

The anatomical presumption for the first of the two is upon the one

* M. Traube has sought for a chemical explanation of this process in this, that an albuminate of the protoplasm is precipitated by another of Graham's colloids (?) which acts upon the cell from without. The experiences made by Kühne upon infusoria (amœbæ) only partially agree with this view. That the membrane becomes visible in consequence of exterior irritation at the surface of the body of the amœba, is of course beyond doubt; according to Kühne, however, the irritations which make obvious the membrane are not so much of a chemical as of a physical nature (electricity, variations of temperature), and Kühne is hence satisfied to define formation of a membrane as simply a peripheric coagulation of the protoplasm.

side, the absolute want of a limitary membrane in the cell being produced, upon the other side a more massy accumulation of such thoroughly naked cell-individuals. Under these conditions, namely, the protoplasm of the one cell *appears* to us to be continued uninterruptedly into that of the other, the limits of the cell are invisible, and this self-evidently obtains just as well of the *newly produced* boundaries. If these cells therefore divide, we would only be able to perceive the division in this, that two nuclei, which were produced by the division of a single one, and therefore originally lie close together, that these were a little separated. What in point of fact we do observe, are only the various stages of nuclear division.

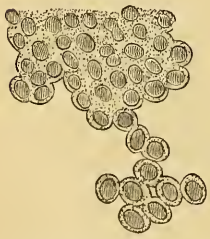
They are just the most luxuriant cell-proliferations, granulations, soft cancers, and sarcomas, in which we find this nucleated protoplasm. This distinguishes itself from the many nucleated giant cells upon the one side by the greater massiveness of the accumulation, upon the other by its behavior towards reagents; namely, while the giant cells behave, under all circumstances, as an inseparable entity, a small addition of acetic acid, chromic acid, &c., suffices to break up the nucleated protoplasm into its elements. We then very commonly observe upon the small fragments surrounded by the acetic acid water, how everywhere at the periphery the cells with dark contours disconnect themselves, how the dark contouring reaches just as far as the isolation, and then bounds the yet connected cell-mass with a line composed of segments of a circle. (Fig. 29.)

Fig. 28.

Cell-division. *a*, from a luxuriantly proliferating granulation; *b*, division of striated muscular fibres.

Touching *endogenous* cell-formation, this is also to be regarded only as a modified cell-division. Namely, if a cell with a completely indurated layer, for example, an older epithelial or cancer-cell, is stimulated to production, the process is confined to the interior, non-indurated portion of it. We have here a nuclear division and a limitation of the protoplasm about the newly produced nuclei. Then, however, the resistant cell-membrane prevents the separation of parts of the cell which have become independent, and we obtain more or less characteristically the *picture of a parent-cell which incloses a brood of daughter-cells.* (Fig. 30, *a.*) It is self-evident that the daughter-cells are smaller than the parent-cell; they are always round, and as a rule bear the impress of pus-corpuscles. It is not necessary therewith that the collective nuclei produced by division also become the central points of those cells; as a rule, one or more of them remain over, so that the impression might be produced, that the whole

Fig. 29.



Nucleated protoplasm. Fragment from a granulation.

endogenous cell-formation was accomplished apart from the nucleus by a globular separation of the protoplasm with generatio æquivoca of the

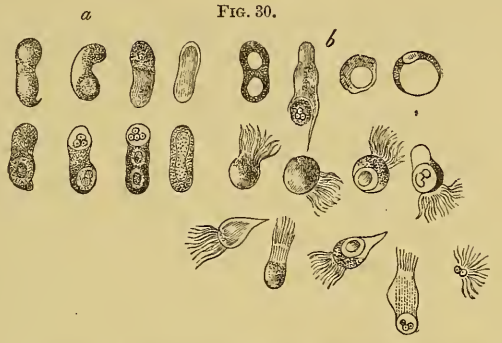


Fig. 30.

Endogenous cell-formation. *a*. Development of pus-corpuscles in epithelium. *b*. Cells with brood-spaces.

nucleus. Truly, for the time, this question must not yet be regarded as solved.

We are not yet informed, upon the whole, concerning the nature and manner, how the endogenous cells become free. Two ways are possible, namely, either the non-participating remainder of the parent-cell dissolves in the surrounding fluid, and then the endogenous cells are by that very circumstance free, or, the endogenous cell slips out. In the latter case a little fluid collects, in the first place, around the daughter-cell; the daughter-cell loosens itself in its position, and by the aid of amœboid movements slips out. If this is accomplished, the cavity of the parent element no longer widens. We have the impression, to use Virchow's language, as though a hole were made in the cell by a punch. (Fig. 30, *b*.) We may conveniently leave the old designation of these things as brood-cavities or brood-cavity-cells untouched, although Virchow in their discovery and naming proceeded from the view, that at first the empty cavities were produced in cells, and then cells in the cavities, by generatio æquivoca.*

§ 69. It lies in the nature of the subject, that not only does the histological detail of new formations admit of a schematic representation, but that we can also premise several general remarks concerning their macroscopic appearance, the *forms* under which they present themselves to the unaided eye. In this connection much depends upon the station of the new formation, especially whether the new formations

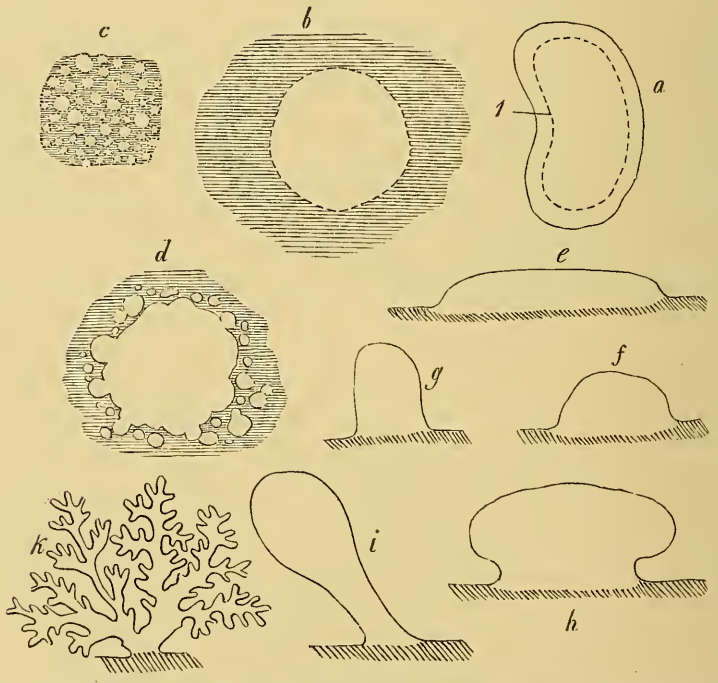
* Volkmann and Steudener have brought us to consider, whether the embracing of a cell by the soft body of a neighboring one might not delude us with a picture of an endogenous cell-formation. This must be admitted up to a certain degree, especially for the epithelial cancer-cells; still I do not believe that the entire doctrine of endogenous cell-formation would be brought in question by such an avoidable error of observation.

have their seat more in the parenchyma or more at the surface of the organs. I am perfectly conscious, that a distinction of this sort cannot be carried out with great rigor; in the meantime the question here is generally not about sharply defined, but about the most possibly useful definitions of certain technical terms invented for the necessities of the physician; the question is not about a classification of the new formations, but of a survey of their *macroscopic forms:*

A. When the new formations have their seat in the parenchyma of organs, they present themselves—

1. As a *uniform enlargement* of the organ in all its dimensions (*intumescentia*); hypertrophy, in the oldest and most unscientific sense of the word. The question then is either concerning a *uniform* increase of the *collective* tissues of an organ, or concerning an increase of volume of a structural element *uniformly distributed* throughout the

FIG. 31.



Macroscopic forms of pathological new formation. Diagrammatic. The shaded portion denotes the normal parenchyma. *a.* The uniform tumefaction of an entire organ. *a* 1. The normal bounds. *b.* The node (nodus). *c.* The infiltration. *d.* Growth of a node by infiltration. *e.* The flat swelling (bed-like). *f.* The tuberosity (tuber). *g.* The wart (papilla). *h.* The fungus. *i.* The pedieulated tumor (polyp). *k.* The dendritic vegetation (papilloma).

entire organ. Were it not more advisable to avoid the term hypertrophy in general, we should have to designate the first form as *genuine*, the second as *spurious* hypertrophy. As an example of the former, we may here mention the hypertrophy of muscles produced by work, in

which not only the muscular fibres, but also the perimysium and the vessels participate, so that the microscopic examination of the hypertrophied muscle shows nothing different from the normal. We have the same relations in certain hypertrophies of the spleen and lymphatic glands. On the contrary, as spurious hypertrophies are to be reckoned all those uniform tumefactions, which are produced by an increase of the interstitial connective tissue in glands, muscles, &c. It is an evidence how unsettled, however, the whole conception of hypertrophy is, that occasionally even fatty infiltration is admitted as a hypertrophy.

2. As *nodes* (nodus). By nodes we understand circumscribed, round or roundish tumefactions. There are nodes of the most various size, from the scarcely visible granule up to the size of a man's head. The size is directly and alone proportional to the quantity of the newly formed tissue. If we divide an organ, in which a node is imbedded, this will project more or less prominently above the level of the section. We may therefore assume, that the node acts tearing, stretching, and pressing asunder of the surrounding, but non-participating parenchyma. Herewith is also connected, that it more readily enlarges in the direction of the least resistance, and that it occasions a globular projection when situated at and in the neighborhood of the surface. More or less of all these properties are likewise determined on the one hand by the quantity of the newly formed tissue, upon the other however and in the reverse proportion, by the quantity of that tissue, which is substituted by the new formation. The node compresses and projects the more, the smaller the portion of the substance of the diseased organ which has been replaced. There are nodes, which, when they have attained a certain exceedingly inconsiderable size, cease to grow by propagating the process to the contiguous parenchyma (by apposition), and henceforth enlarge by new formation in their interior (central growth). In such cases the node almost becomes a foreign body. The mechanical injury to the surrounding parts, mentioned above, becomes so intense, that it leads to a chronic inflammation and a new formation of connective tissue. The latter presents itself, the larger the node becomes, so much the more as a capsule, which stands in firm connection with the node only at single points, namely, where the vessels run to and from it, for the remainder, however, opposes to it a moist, smooth surface, often covered with pavement epithelium. The question, whereby this loosening of the connection, without doubt originally existing, has been produced, can only be answered indirectly.

There prevails, as I believe, no difference of opinion about this, that the cavities within connective tissue, for example, bursæ, are produced by the organs in toto, sliding upon each other, and the necessary scope for this is furnished by a partial softening of the connective substance. The wide-meshed areolar connective tissue is the most subordinate;

the articular cavity is the most complete arrangement of this kind. The movement of one internal organ however upon another is entirely analogous to our case, in that an enlargement of the surface of the node is not to be thought of without a shifting of the points of contact with the neighboring parts. If we double one hand into a fist, lay it in the other hand open and then gradually inclose the fist with the fingers, we will get an approximative representation of this process. The ideas of the last but one epoch of our science diverge from ours in this, just as the former explanation of brood-cavities does from that of to-day. The capsule was supposed to pre-exist as a cystic or cellular cavity, and then that the neoplasm was exuded into this.*

3. As *infiltrations*. We here meet with the same word for the second time, but of course in an entirely different figurative sense. When we speak of a tuberculous infiltration of the lung, of a cancerous infiltration of the liver, we mean thereby a uniform tumefaction and condensation of larger sections of these organs, which is caused by a deposition of new formation in very numerous, but small depots. Therefore infiltration stands in the middle between uniform tumefaction on the one side, and nodes upon the other. It is scarcely necessary to remark, that all possible transitions exist towards both sides. Are, for example, tuberculous depots somewhat larger and more individualized, we allow the infiltration to be a granulation, and where the question is about single, circumscribed tuberculous depots, as at times in the brain, we speak of a tuberculous node. Just so the infiltration is regularly to be found at the limits of such nodes, as increase more by peripheric than by central growth. With the magnifying power of a lens, we here already remark, beside a creeping advance in the neighborhood, by which the continuity with the principal node is never interrupted, a bolder advance, which is occasioned, in that at a small distance from the periphery of the principal node, new nodules form on their own account, which enlarge toward all sides, and finally again unite with the principal node. The zone of these nodules may appropriately be designated as the zone of infiltration, and hence arises the phrase customary in the records of dissections, that the surrounding parts of a node were already infiltrated.

The transition from infiltration into uniform swelling is only determined by a greater extension of the infiltrated parts. If the whole organ is infiltrated, it is in fact not conceivable why we should not speak of a universal tumefaction of it.

B. When the new formations are seated at the surface of organs, they present themselves—

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* Upon this foundation was based the old division of tumors into cystic and non-cystic. The encysted were at the same time the innocuous, the non-encysted the malignant ones. We will see in the sequel, in how far here medical instinct has happened upon the right.

4. As a *scaling* (desquamatio). We understand by these exclusively, the abundant shedding of epithelial cells. If this is at the same time combined with a considerable secretion of fluid, we make use of the expression catarrh, in that we generalize a designation, which especially suits the catarrh of the nasal mucous membrane, in so far that here the morbid secretion flows from the nares and sinuses, καταῤῥεῖ.

5. As a *flat, bed-like* [garden-bed] *tumefaction.* This corresponds to the uniform enlargement from all sides of parenchymatous organs, and like this is occasionally designated as hypertrophy. The distinction also between genuine and false hypertrophy again recurs. That which distinguishes them from uniform enlargements, is the circumstance, that it may indeed extend over very great tracts of a membranous organ, but yet not over the whole of it; that it somewhere touches upon the sound portion, and thereby experiences a limitation as to space, which has also procured it the name of "island-like tumefaction." This occurs in many chronic inflammations of the external integument, arterial coats, in typhus and in many cancers.

6. As the *tuberosity* (tuber). The more the height of a circumscribed tumefaction increases, the surrounding level remaining the same, the more is it a tuberosity. The height and profile of the tuberosity may vary within certain limits; a very much elongated one is called a wart (papilla). The base, however, always remains the broadest part. If the base of a tuberosity decreases, its edges must necessarily hang over, the new formation appears—

7. As a *fungus*, or

8. As a *pediculated tumor* (polypus). The difference between the fungus and polyp depends essentially upon the various manner and mode as to how the diminution of the base of the tuberosity is produced. If it is only relative, that is to say conditioned by the predominant proliferation in the prominent parts of the tuberosity, we make use of the designation, fungus. The fungus has a broad pedicle and a flat top. If, however, an absolute diminution of the base is associated with this relative one, in that the top ever becoming more massy draws and drags upon its base, be this by its own weight, or be it by other forces which tend to move it about, the latter is reduced to a comparatively thin pedicle, a polyp is formed.

9. As *dendritic vegetation.* This is incontestably the highest development of form which a circumscribed elevation of the surface can experience. As the name implies, it is a tree-like ramification of the ground-plan of the same. We have a trunk, we have branches, which go off at various angles, and we have occasionally upon the smallest twigs, leaves or berries. As is known, we find the same design in glands with branching excretory ducts, the so-called racemose glands. The uniformity in the first design and development of these glands with the dendritic vegetations proceeding from the outer skin and the

mucous membranes is remarkable. In considering the latter we will observe this more intimately. Let the declaration here suffice, that, as with the racemose glands, so also with dendritic vegetations, the essential part of the whole structure is to be sought in the structural-constituents of the foot-stalk. As such we must recognize the elongated tuberosity, the papilla. And in fact no other view agrees so well with the known processes of development of dendritic vegetations. A simple papilla is in every case the point of departure. This sends out somewhere at the surface a sideling shoot, a new papilla, which forms with the original one a fork, or a trunk with two branches. This phenomenon is repeated and thus becomes the simple occasion for the most complicated arboraceous ramification of a neoplasm.

If I close this review with the remark, that all the kinds of forms mentioned are of a very transitory nature, and melt into each other everywhere at their limits, I do this especially because I do not wish to let any opportunity pass, to raze from the very foundation, the prehistological error, as though by the description of the macroscopic forms of a new formation anything had been said of its essential nature. This error was pardonable as long as more searching microscopic investigations had to battle with greater difficulties than at present; it was also pardonable, because of course certain new formations prefer the one form to another, several indeed appear only as a fungus, as a polypus, as a papilla, &c.; this, however, does not exclude the fact, that others may just as well arise in these forms. And what obtains from the external form, also obtains of the other macroscopic properties, of the size, consistence, and color of the new formations, which were formerly with the same incorrectness valued as principles of division.*

§ 70. By way of appendix, we must here yet mention a peculiar anatomical structural element, which may be associated in the most complicated manner with the most various new formations, namely, the cyst. Every sharply defined cavity filled with fluid, of a round or roundish form, we call a cyst. If in this definition the cystic walls are not mentioned, it is because, while a particular cystic wall, a sac or shell, exists in very many cases, it however does not exist in all. The contents also of the various cysts is different in the highest degree. This may be thin and clear as water; it may, however, also be more fatty, pulpy, nay, it may be so thick, that we can scarcely any longer regard it as a fluid. All this essentially depends upon the manner of production of the cysts. Accordingly we distinguish:

a. Cysts of retention. The name implies, that these cysts are produced by the retention of secretion, and we may add, that they are exclusively only such secretions as normally reach the free surface of

* Especially in the literature of tumors. Concerning this compare Virchow: Die Lehre von den krankhaften Geschwülsten. Berlin, bei Hirschwald, 1864.

the body, the skin and mucous surfaces, in order there to flow off or to be otherwise consumed. The indispensable preliminary condition of a cyst of retention is an involution of the surface, a cavity with an open mouth and ending in a cul de sac, which by any extraordinary conditions becomes occluded and thereby a cyst; that the secretion uninterruptedly flowing therein is retained and accumulates the more, the longer this continues. It is evident, that the physiological involutions of the skin and mucous membranes come foremost into consideration, I mean the excretory ducts and culs de sac of the tubular and racemose glands; that they meanwhile are not the only ones to be considered, I will show further on.

If we ask, whereby the occlusion of a glandular excretory duct may chiefly be brought about, we encounter various possibilities. The simplest but rarest kind of closure is obstruction (obturation). Solid bodies, which because of their size and weight are not able to pass the lumen of the excretory duct, almost always are produced as precipitates, concretions from the fluid secretion itself, as biliary, urinary, and salivary calculi. Rarely do obstructive masses penetrate from without into the lumen of the glandular ducts, for example, echinococcus vesicles. Furthermore, an occlusion of the excretory duct may be produced by its sticking together (obliteration). External pressure and a raw, ulcerative condition of the surface, especially if followed by a cicatricial formation, disposes to this kind of closure, which in their incomplete grades are designated as contractions (stenosis, strictura). Finally, external pressure in and for itself, is able to narrow, to fold in and to constrict the excretory duct. The possibility of this mode of production, which at a later period may be complicated with obliteration, is just of the greatest importance for the history of new formations. Not only that new formations, which are situated about the ureter, the ductus choledochus and pancreaticus, are capable by compression and constriction of making these large excretory ducts impassable, and thereby producing colossal distensions of the sections of these mucous canals situated higher up, but this process repeats itself upon a diminutive scale when the new formation affects the glandular substance itself. Individual urinary tubules, lactiferous ducts, tubuli seminiferi, &c., are cut off by interstitial new formations; the secretion accumulates; the longer this continues, so much the more does the original form of the occluded cavity, perhaps a cylindrical tubule, pass into a round or roundish form; a cyst is produced, whose wall therefore is the original wall of the glandular canal, and whose contents, at least in the initiatory stage, is the secretion of the gland itself.

A rare, but therefore none the less interesting kind of retention-cyst does not originate from glandular canaliculi, but from those cleft-like, intercommunicating spaces, which are left between the trunk, the

branches and the end-papillæ of a dendritic vegetation. At the first glance it appears as though these interspaces were not fitted in the least for cystic beginnings. They not only freely intercommunicate, but also stand in such open connection everywhere with the exterior world that there can be no question about an outlet, or still less of an occlusion of this outlet. Thus it is and remains, when a dendritic vegetation is situated upon a free, level surface. It is otherwise, however, when it projects from the surface of a cavity. Let us suppose, for example, a papilloma, which extends from the os uteri externum into the vagina. A time will come here, when the tumor so far fills out the lumen of a canal, that its walls begin to exert a lateral pressure upon the tumor, which becomes the greater the more voluminous the tumor becomes. The papillæ incline towards each other, touch one another with their convex surfaces; at length they grow together at the points of contact, and at once the open interpapillary space is divided into a number of small, tubular recesses, which are only to be distinguished from tubular glands, in that, upon a transverse section, they are not round, but are bounded by three or four incurved circular lines, the convex surfaces of the contiguous and coalescing papillæ. These tubes are just as well fitted for the formation of cysts, as are the glandular tubuli, for a further continued action of the same external pressure is only required to occasionally shut off the one or other interpapillary space at its outer opening or elsewhere in its continuity, and thereby cause the production of a cyst of retention.

By the way, just here we have a good opportunity of observing how, in consequence of the accumulation of fluid, every other form of the space of retention tends to be converted into the spheroidal form (Fig. 32). Previous to the beginning of retention the interpapillary spaces

Fig. 32.

Papilloma cysticum of the portio vaginalis. Transition of the interpapillary clefts into cysts of retention.

upon a transverse section show themselves as three and four cornered figures with incurved sides and very pointed angles; figures, such as

must always be produced by the apposition of cylindrical bodies. If the collection of fluid proceeds, these sharp angles upon the one side open more and more; they are changed into a parabola, and finally into a circle; upon the other side the incurved lines experience a gradual depression, the incurvation is finally entirely lost, and in that both of these movements meet, the transverse section becomes a circle, the space of retention a globe.

It would take me too far were I to develop in detail at this place the physical law which governs this process. I will content myself with the hint that, of all stereometric bodies, the globe with the same surface incloses the greatest volume. As long, therefore, as the contents of a hollow body grows, the extent of surface remaining the same, it must tend to the globular form. And it is thus with the cavity of retention. Besides, that of which we have an example before us prevails at very many points in the economy of the organism: I will only remind of the form of the eye, the gall and urinary bladders, the heart, &c.

b. Exudation-Cysts. The exudation-cyst is also a secretory cyst; in a genetic relation, however, it is just the opposite of the retention-cyst. The closed cavity here is not first produced by the occlusion of a recess; it is preformed. Bursæ mucosæ, sheaths of tendons, serous sacs, cerebral and spinal cavities, form the foundations of the exudation-cysts. The accumulation of the fluid also is not produced by the continuance of the normal secretion, but by an exudation, surpassing the normal measure of the serum of the blood with salts, albumen, fibrinogenous substance, and extractives in the most varying proportions. The exudation-cysts have little to do with pathological new formation; we will learn to know them under the most various designations, mostly reminding us of the watery contents, as hydrops, hygroma, hydatid, &c., in the diseased conditions of organs.

c. Extravasation-Cysts. A parenchymatous bleeding can very well be the point of departure for the formation of a cyst. Of course we would scarcely make use of the term cyst in an extravasation of blood, where the extravasation forms a shapeless, coagulated lump, and which the adjacent parenchyma in no way smoothly and sharply defines, but is irregularly torn and crushed. The hemorrhagic depot can, however, present itself primarily as a cyst; namely, when the blood is poured out between two surfaces in themselves smooth; for example, bone and periosteum, cartilage and perichondrium, and thereafter remains fluid; as a cyst may also be formed when upon the one hand the limitary parenchyma furnishes a connective-tissue membrane, upon the other hand the blood itself is resorbed through a series of metamorphoses up to a small remainder, and is replaced by a clear fluid.

d. Softening-Cysts. Under the conditions of involution of tissues, we have learned to know more than one process which leads to soften-

ing, to the formation of a pathological fluid. I especially mention fatty degeneration and mucoid softening, of which the former in the proper conditions yields a pathological milk, the latter a mucus-and-albumen-containing fluid clear as water. If the efflux or the resorption of this fluid of softening is prevented, the local accumulation of this without further conditions can present itself as a softening-cyst; it, however, will particularly do this when a sharp, smooth limitation of it takes place. That a limitation of this kind of a softening-cyst is not occasioned by an anatomically separable membrane, lies in the nature of the case. The appearance of such a membrane, however, can very well be produced in that the textural elements lying at the limits of the focus of softening are collectively in the same stage of metamorphosis, and consequently form a layer which distinguishes itself as well from the intact parenchyma as from the fluid of softening.

As long as a softening-cyst enlarges itself by the further diffusion of the process of softening into the surrounding parts; in a word, as long as it is nothing but the focus of softening, it wants a true membrane. The softening-cyst may, however, subsequently receive a membrane. In this case the softening ceases, the adjacent tissues close in organically towards the depot of softening. Like all the interior cavities of the parenchymas of the body, these pathological new formations are also lined by a continuous stratum of connective tissue, which, under proper conditions, is clothed with an epithelium, and then is entirely to be regarded as the analogue perhaps of a bursa. Henceforth all the changes which the cystic contents experiences depends upon an exchange with the bloodvessels of the membrane; if its quantity increases, an exudation from the blood is the cause of this growth. The softening-cyst has become a secretory cyst.

In conclusion, I repeat, what has already been occasionally expressed in the representation, that for the history of new formations the retention-cysts come foremost into consideration, then the softening and blood cysts; the exudation-cysts, however, as good as not at all. In naming new formations we are wont to indicate the complication with cysts by prefixing the two syllables cysto-, therefore cysto-sarcoma, cysto-carcinoma, &c.

2. Normal Growth as a Type of the Pathological.

§ 71. After these general preliminary remarks, if we pass to the division of the processes of new formation, the histological constitution alone offers us no sufficing points of support. We must take refuge in a more universal principle, and we find such a one, as was already indicated above, in that we conclude upon the attempt of carefully comparing the phenomena of pathological new formation with those of the physiological. If in the latter we distinguish the first foundation from

the subsequent growth, it is the subsequent growth par excellence which yields us the sought-for points of comparison.

The first foundation of organs is brought about by the differentiation of originally equivalent elementary parts, small, round cells, provided with large nuclei, which in uninterrupted accumulation form the germinal disc and the germinal area. The segmentation of the germinal disc into three layers, which at first ensues, has of late been frequently discussed. So much appears certain, that generally the organs of motion and sensation are produced from the upper layer, the organs of respiration and digestion from the lower layer, while the middle layer is intended for the bloodvessels and connective tissue. According to the view of His, however, who in a measure follows a work of Waldeyer, a decided contrast already becomes prominent in this primary division, between the two exterior properly organo-poietic germinal layers, which together are designated as neuroblast, and the middle germinal layer, the hæmoblast, which is not produced, as has hitherto been accepted, by splitting off from the lower germinal layer, but by an independent growth inwards from the edge of the germinal disc. It would, in fact, be very interesting if the independence of the vascular system and the parenchymas, of the nourishing and parts to be nourished, reached back even to these early stages of development. That it is present in the formation of the first vascular system, the area vasculosa, and plays an important part in the whole future development of the individual, is not to be doubted. Now, henceforth, as soon as a new organ has at any spot to separate itself from the continuity of the germ-cells, as soon as at a certain accumulation of the specific elements we remark that a muscle, a nerve, a gland, &c., is being formed, the vascular system has already sent into it a loop-formed process, and in a certain sense lays claim upon the new acquisition in the name of the whole. Herewith each new vascular loop grows out of one already existing, so that the unity and independence of the entire system constantly remains guaranteed. This law also remains unchanged for the subsequent growth, and again comes into action in the adult organism, whenever a pathological new formation offers the opportunity for it.

If we now pass expressly to this later growth of the organs, we must, unfortunately, admit at the very threshold, that our acquirements in this relation are still very limited. Upon the growth of bone only are we fully informed. The growth of epithelium is a grave question. Concerning the growth of muscles and tendons distracting accounts are in question. The point, however, around which everything here revolves, is to determine the share which upon the one side the specifically functioning elements of the organs have, in the processes of growth, upon the other, that of the vascular and connective tissue

system, which latter together we wish to designate as the inner or intermediary nutritive apparatus.

We may best begin a short representation of these processes with the growth of the *intermediary nutritive apparatus* itself. After the manner of Billroth, we distinguish a threefold manner of new formation, in what appertains to its most important constituents, the vessels. The primary form, which is only observed in the area vasculosa, shows us an immediate differentiation of the germinal cells into red blood-corpuscles and the elements of the walls. One observes how in certain directions the germ-cells unite into closer strands, then those located at the axis become colored red, and become movable in an accumulating clear fluid, whilst those situated at the periphery, which do not become natant, by that very circumstance represent the vascular wall. Of course the limit of this vascular wall towards the parenchyma is by no means sharply defined; one has more the impression of a continuity perforated by canals; upon the other side also individual cells yet loosen their connection with the parenchymatous islands, in order furthermore to move in the blood-current, and themselves to become blood-corpuscles, but these are phenomena, which only apparently stand in contradiction with the known regulations of the completed apparatus. The next step forward already explains this to us. It is the formation of the endothelium of the vessels, which, according to the very correct apprehension of Ebert (Stricker, Lehrbuch der Gewebelehre, Lief II), forms the proper foundation, the alone characteristic and universally present constituent of the vascular walls. With the formation of the endothelial tube, which is known to all my readers as a very delicate membrane, formed of elongated polygonal nucleated cells, upon the one side every separation of cells at the inner surface of the vascular walls ceases, upon the other side a determined boundary is given, beyond which, in the more comprehensive sense of the word, we may allow the parenchyma to begin, whether now this consists, as here, of germinal tissue, or of connective substance, or of connective tissue, with muscular fibres, &c.

But with the formation of the endothelial tube, the primary vascular formation also ceases. If a new vascular loop thereafter arises, this can only be accomplished with the aid of a bulging out of the endothelial tube. A bulging out of the endothelial tube is, therefore, characteristic for those forms of the new formation of vessels which Billroth has designated as secondary and tertiary. It occurs most distinctly in the *tertiary*. It is easy to establish here that at certain points the capillaries already carrying blood bulge out like culs de sac, and gradually growing, return back in a curved line to the mother vessel, or two of these growing towards each other lead to the same result, a new capillary loop. If we observe more accurately, we are convinced that these blind ends run out into certain minute threads, whose more inti-

mate relations are not disentangled without difficulty. (Fig. 33.) The most useful object for this is undoubtedly the transparent border of the tadpole's tail, but here also numerous stellated connective tissue corpuscles lie round about. If these now are connected with the vascular

Fig. 33.

Tertiary vascular formation. Border of tadpole's tail. *a*. Capillaries. *b*. Lymph-vessels. *c*. Sprouts of vessels. *d*. The same connected with a connective tissue cell. *e*. Free edge with epidermis.

processes, they may simultaneously be regarded as their processes and the capillary formation as a direct metamorphosis of cellular elements; on the contrary, if such a connection cannot be proven, the filiform processes are a special preceding foundation for the future vessel. After long, zealous endeavors, it appears finally to be proven that both take place. The vascular shoots neither seek nor avoid the cellular elements. If the direction of the forming vessel dependent upon the more general circumstances falls within the sphere of a neighboring cell-body, this participates in the formation of the vascular wall; if it falls into the boundaries of neighboring cell territories, we see the vascular shoots take their independent course. According to Stricker, we must imagine to ourselves the capillary vessels as covered upon their entire outer surface, not only at the nuclear points, with a thin mantle of protoplasm, and we would then of course have a material lying ready for the formation of our vascular shoots. That they consist of protoplasm, is proven upon the one hand by the optical similarity with the protoplasmatic processes of connective tissue cells; upon the other, by the circumstance that they may be replaced by these in vascular formation. In the opening up of the new vessel this protoplasm extends in a thin layer upon the surface of the cavity, and then condenses into a membrane, which distinguishes itself in nothing from the membrane of the mother vessel, as it then also stands in direct continuity with it. If

connective tissue cells have been used in the vascular formation, these appear after the metamorphosis as inserted constituents of the endothelial tube.

The *secondary* formation of vessels, which is observed almost only upon pathological objects, can be observed in so far as a modification of the tertiary, as the question there is also about a gradual widening of the endothelial tube. The apposition of new elements of the walls only comes into the foreground, namely, the vascular foundations are formed by a strand of spindle-shaped cells arranged parallel, which, in the subsequent opening of a central lumen, are directly converted into endothelial tube cells. The numerous varieties of this secondary vascular formation we will learn to know more intimately in inflammation and in several of the species of tumors.

§ 72. The second constituent of the intermediary nutritive apparatus is *connective tissue.* From an embryological point of view, that residue of the germinal tissue is to be designated as connective tissue, which remains over upon the one side between the bloodvessels and upon the other between the functioning tissues. Always accordingly as the parenchymatous islands of the middle germinal layer are more or less completely consumed, or dislodged in the formation of organs, do we find smaller or larger quantities of connective tissue in the composition of the organs. There are organs in which the connective tissue portion is with difficulty demonstrable, as for example, the kidneys and testicles; the acinus of the liver appears to be formed only of capillaries and liver-cells. Meanwhile small quantities of unformed connective tissue may be demonstrated with all certainty, as well in the testicles as in the parenchyma of the kidneys, and when even these are wanting, as in the acinus of the liver, the walls of the capillaries themselves take the place of connective tissue; for the cells of the endothelial tube and the cells of connective tissue are of similar dignity, as the tertiary vascular formation has already taught us, in which the latter were directly converted into the former. Beside this a plate-shaped form has been discovered by Ranvier upon the cells of the loose subcutaneous connective tissue, whereby it becomes evident that connective tissue cells are generally disposed, in the larger interfibrillar clefts, to assume the form of delicate lamellæ. As complete evidence, however, the uniformity of connective tissue cells and the endothelium proceeds from the uniformity of formative actions, of which both are up to a certain degree capable, as we will see hereafter. Of course the question here is only about the stable cells of connective tissue, the connective tissue corpuscles of Virchow; what has been said has no application to the mobile cells discovered by Von Recklinghausen.

As far, therefore, as the bloodvessels reach, so far, and still further, does connective tissue also reach. It surrounds the bloodvessels mantle-like, extends their walls into the interspaces of the organic structures,

and as the bloodvessels are all connected among themselves, the vascular system, together with the connective tissue, presents a richly articulated framework, into which the other form-constituents of the body are set. In short, the diffusion of connective tissue throughout the body is so great that it is utterly impossible to make a cut at any point whatever and not to injure the connective tissue, and not to have connective tissue contiguous at innumerable points of the cut surface.

§ 73. If we now take a view of the *circumstances of the growth of connective tissue*, the opinion in reference to this obtains tolerably undisturbed, that for each new quantity of connective tissue which arises, a certain quantity of embryonal connective tissue is requisite. The latter consists of nucleated, membraneless lumps of protoplasm, and forms, where it occurs in larger accumulations, a very soft, elastic, pale-grayish substance. It arises with greater facility wherever the necessity arises for a widening of the intermediary nutritive apparatus. There also can be no doubt, that the intermediary nutritive apparatus of the embryonal connective tissue produces itself from its own resources. This is a fundamental property and function of it, which also unquestionably plays the greatest part in the pathological growth. Only the "how" of the production is as yet the all-important question. As yet, I say, for the thing, of which we are here questioning, is so important for our general view of pathological processes, that we can plainly designate it as the central point of all past and still existing pathological systems; namely, the embryonal connective tissue, with whose origin we are now engaged, is identical with the frequently mentioned germinal tissue of pathological new formation, the plastic exudation of humero-pathological authors, the proliferation of connective tissue corpuscles of Virchow, the accumulation of emigrant colorless blood-cells which Cohnheim has taught us. In treating of inflammation we will take occasion to learn the relative facts of pathological histology; for the present, let the hint suffice, that the possibility of an emigration of colorless blood-cells and the formation of plastic exudation by accumulation and collection of these, has certainly been established; that, however, upon the other side, the possibility of a division of the existing stable connective tissue cells is not to be excluded, nay, in certain cases is to be accepted as indispensable.

§ 74. The transformations which thereupon the young connective tissue experiences, the deposition of various species of intercellular substance, and the establishment thereby of various connective substances, I may suppose as known from normal histology. (See A. Rollet in Stricker's Handbook of Histology.) We will do well here to make a rigorous distinction between these connective substances, which for themselves alone form parts of organs, between the functioning or formed connective substances, as the tissues of cartilage, bones, tendons, &c., and the functionless and unformed connective tissue

filling out clefts, which was formerly called cellular tissue. The latter only is meant by us, when we simply speak of "connective tissue;" only to this does our representation above of the diffusion of connective tissue in the body relate, of the relation of its cells with endothelium, and of its significance as an intimate constituent of the intermediary nutritive apparatus. Be it well understood, the relationship of this connective tissue with the formed connective substances shall by no means be denied; on the contrary it will be shown, that just this is of the greatest consequence for the pathological process; the organs consisting of connective substance shall only at the proper time be separated here, where the question is about the growth of organs, from that apparatus, which it just as well nourishes and makes to grow, as the muscles, nerves, glands, &c. They are also only the cells of this "connective tissue" par excellence, whose origin from embryonal cells will occupy us yet for a moment. The form which these cells assume, is essentially dependent upon the local conditions for their development. They by far the most frequently become spindle-formed, corresponding to the elongated clefts which remain for them between the connective tissue fibres; where the basis-substance allows a free development towards all sides, as in mucous membrane, they are wont to assume the stellate form, and let their processes enter into an anastomosis with each other; where finally flat clefts between larger bundles of fibres or lamellæ are assigned them, they flatten themselves out, even if now they become epithelial-like plates, or that they also in this flattening out send forth anastomosing processes, as in the cornea and the intima of arteries. Very commonly then a portion of a protoplasm indurates to a homogeneous, colorless, strongly refractive substance; we obtain stars, plates, and fibres, which are carefully to be distinguished from the plates and fibres of intercellular substance, and are very well distinguished chemically, in that they do not swell out and become invisible in acetic acid. It happens (lig. pectinatum), that the entire cell together with the nucleus undergoes the metamorphosis spoken of. Generally the nucleus with a remainder of granular protoplasm remains behind, and then as a rule takes up the centre of the indurated cell-body. Thus arises the *stable* cell of connective tissue; in this condition it continues, if pathological irritations do not arouse it to new activities, during the whole life of the individual.

§ 75. We come to the *lymphatic vessels* and *glands*. This is the third, and—we may say it with emphasis—the last chief constituent of the intermediary nutritive apparatus; the last, not according to importance, but according to time. Only when the development of the embryo ensues at a less rapid rate, when all the other organs have been founded and built up to a certain point, do we remark lymphatic vessels, still later, lymphatic glands. This doubtless is connected with the physiological significance of lymphatic vessels, as drains for the

surplus nutritive material. As long, upon the one side, as no nutritive material is superfluous, in that all is applied to the new formation, and as long, upon the other side, as the external coverings of the embryo are not too thick to hinder a free efflux towards without, so long we need no lymphatic vessels. We can also say the reverse, that luxurious new formations, catarrhs, and surface-secretions of all kinds must be produced, where the lymph conveyance is hindered, and we will find this position in pathology very frequently confirmed. The beautiful studies of V. Recklinghausen on the lymph-vessels and their beginnings have taught us, that the lymph-vessels are lined with entirely the same pavement-like nucleated endothelial plates as the bloodvessels. The same obtains of those yet more minute juice-canals, which according to the same investigator present the beginnings of the lymphatic tract in the connective tissue, and are connected by minute openings with the larger, apparently blind-ending lymphatics. The juice-canaliculi have in general the form of flat, stellated lacunæ, and are indeed for the most part identical with those cleft, and star-like cavities, in which the flattened cells of connective tissue (Ranvier) are arranged. By the elongation of the tracts of the lymph-vessels into the connective tissue, the minute communications with the juice canaliculi spoken of (Kölliker) simply widen themselves, so that from this side also the homology of connective tissue cells with endothelium appears to be proven.

§ 76. The relations of the lymphatic glands are far more difficult to estimate than those of the lymph-vessels; namely, unfortunately a complete authentic history of the development of the lymphatic glands is at this time still wanting to us. The older views of Breschet and Engel, according to which they are developed from plexuses of lymph-vessels, have been lately and indeed in a far more interesting form reproduced;* still I must declare myself against this opinion. In the preparation of J. Orth† I see with this author, as the first foundation of a lymphatic gland, a very richly vascular heap of embryonal formative tissue, which presses away from each other the fibres of the surrounding connective tissue, and thereby arranges them into a capsule for itself. A clear subcapsular space only subsequently arises at its periphery, and cleft-like openings show themselves in its interior, which in that they communicate with this peripheric space, divide the true glandular substance in the manner known into strands and alveoli. From a purely physiological standpoint the lymphatic gland appears as a local dilatation of the lymphatic tract, which is filled with a peculiar new tissue, the lymphatic glandular tissue. The lymphatic glan-

* Sertoli found, that at first lymph-canals lined with epithelium were produced, around which the connective tissue proliferates, and that heaps of cells developed in this proliferated tissue into follicular glandular substance.

† J. Orth, Lymphdrüsenentw. Inaug. D. Bonn, 1870.

dular tissue, consisting of the known reticulum and the lymphatic corpuscles deposited in it, is regarded as the principal point of production of the colorless blood-corpuscles, and, as upon the one side according to the general opinion, the red corpuscles of the blood proceed from the colorless, upon the other, that the wandering cells of connective tissue are emigrant colorless blood-corpuscles, it is regarded as the *point of production of all mobile cells* of the entire intermediary nutritive apparatus. Unfortunately this view also, like so many in histogenesis, still rests upon an insecure foundation. We must concede, that processes of division have been almost not at all observed in the lymph-corpuscles of the glands; the old, but easily established experience, that the lymph before its passage through the glands contains less cells than after it, forms the principal support for this view. What, however, if this increase of lymph-corpuscles arises from the blood-vessels? There is no manifest ground whatever, why colorless cells should not leave the vessels in the lymphatic glands just as well as in all other organs; nay, that just during the digestive hyperæmia of the digestive organs, in which the lymphatic glands take part in so prominent a manner, especially many lymph-corpuscles are furnished, speaks more for than against this explanation. Nevertheless, for my own part I decline to shake, upon observations of this kind, the representation received and in itself so plausible, that new cells are produced in the lymphatic glands by division of lymph-corpuscles. I still see in the lymphatic glands, organs, which the intermediary nutritive apparatus, so to say, itself prepares for the regeneration of its mobile cells, while it occasions at various points a circumscribed capillary ectasy with the subsequent emigration of colorless blood-corpuscles. The number of migrating cells increases supplementarily by division, and this increase leads to an enlargement of the glandular parenchyma, as long as no lymph-vessels provide for the conveyance of the surplus cells. A certain equilibrium in the production and conveyance exhibits itself at a later period, which can only be disturbed by pathological irritations.*

§ 77. The spleen ranges itself in a histogenetic relation with the lymphatic glands. The principle of the "formation of lymphatic spaces,"

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* I cannot forbear calling attention, that in the formation of lymphatic glands, as it appears to us according to this representation, we possess a valuable parallel with the numerous pathological productions of the intermediary nutritive apparatus (see following chapter). Emigration, and subsequent division of the cells, is here also the structural principle. *Contact with the tissue and relative rest* of the emigrant cells induces them, as it appears, first to essay their amœboid mobility, then to division. Division, however, of the emigrant cells, according to my conviction, is the most effectual cause of inflammatory new formations as well as of the histioid tumors; this it is which permits of their massiveness, so frequently enormous, and indeed especially then and there, where the development of lymphatic vessels remains in the background, and these cannot provide for the seasonable conveyance away of surplus cells.

as we are wont to call the local emigration of colorless blood-corpuscles, and their accumulation in the immediate neighborhood of the vessels, this principle, which we, based upon our own investigations, have represented as the most probable formative principle of the lymphatic glands, is carried yet a step further in the spleen. In the spleen, also, the vessels surround themselves immediately with lymph-spaces, which are here called Malpighian corpuscles; they then, however, undergo a complete perforation and entire separation into fibrils, of their walls. In this manner is produced a delicate spongy tissue, through which the blood trickles, to collect at the opposite side into venous effluent tubes, which penetrate this spongy tissue in all directions. The same doubts and opinions prevail concerning the function of the organ as concerning the function of the lymphatic glands, only that the splenic pulp is regarded just as well the birthplace of young colorless cells as the grave of the older red blood-corpuscles.

§ 78. So much concerning the histogenetic relations of the blood, the vascular and connective tissue systems. We note the difference between the stable and mobile cells of these. To the former belong the formerly so-called connective tissue corpuscles, the endothelium of the blood and lymph-vessels, the anastomosing and stellate cells in the lymphsinus and in the splenic pulp, finally the epithelium of the serous cavities, which according to Recklinghausen are connected with the system of lymph-vessels. The mobile cells of the apparatus are represented by the blood-corpuscles, of which particularly the colorless with the remaining nutritive fluid pass through the walls of the smaller vessels, in order, as wandering cells of the connective tissue, partly to place themselves at the disposition of the growing organs as ready building material, partly to return through the lymph-vessels back into the blood. The stable cells are produced from the mobile cells. The production of the mobile cells is as yet undiscovered. The parenchymatous cells of the lymphatic glands and the spleen have the greatest claim to be regarded as the normal matrix of the mobile cells. Still in glancing at the production of the lymphatic glands themselves we will probably have to adopt the principle, that all the colorless cells, as soon as they come outside of the circulation, begin to wander and to divide.

§ 79. If we now pass to the growth of the remaining organs, we will, in the first place, make mention of the *cartilaginous and osseous systems*. It is known that upon sections of youthful cartilage, almost without exception, the cells are divided off in the basis-substance in groups, or at least in pairs. We recognize the juxtaposition of two cells by this, that they always have a convex and a flat side, of which the flat sides are in apposition. One involuntarily believes to have before him the two halves of a globular body. That however we are in fact dealing with cellular division, we recognize in such pairs of cells,

which are yet united by a common capsule. If to this evident proliferation of cells we yet add the interdeposition of new basis-substance, which properly separates the cell-halves, now become independent cells, we have the known model, according to which the growth of cartilage is said to ensue. I do not wish to involve in doubt the importance of the observed fact, but must decidedly guard against the opinion, as though by this interior increase of cells and tissue, the greater part also of the growth of cartilage were accomplished. Cartilage has a peripheric growth as a chief feature. The perichondrium yields embryonal cells, which, in the next place, surround themselves with a mantle of hyaline basis-substance, which forms an entity with the basis-substance of the existing cartilage. The more frequently this process is repeated, the more abundant in cells does the cartilage become. Those cells, which originally lay at the periphery, gradually move towards the centre; and now only is it the time to speak of that second impulse to growth, namely, the gradual enlargement and subsequent division which the cells experience when they advance towards the middle of the piece of cartilage. In this process each element is divided once up to three times. The division constantly ensues in a plane vertical to the longitudinal axis of the cell, and only at the thickest point of the element, so that the most exceedingly characteristic forms result for the daughter and granddaughter cells. Half-spheres, quarter-spheres, cones, &c., are maintained during the entire life, because of the firmness of the basis-substance; and as because of the same ground the products of division are but little separated from each other, we may still perceive in the cartilage of an old man of ninety exactly the same types, which in youthful cartilage induced us to attribute so great an importance to the interior growth of cartilage; we can still see whether an original cartilage-cell have divided once, twice, or thrice, ere it became quiescent.

Quite independent of the phenomena of the growth of cartilage, there is a peculiar metamorphosis of hyaline cartilage, which we, leaving out of consideration pathological things, meet everywhere, where the cartilage touches a still growing bone. Whether the cartilage actively participates in the formation of bone, whether cartilage-cells, or even only the offspring of cartilage-cells, become cells of medullary spaces, that is to say, the corpuscles of bone, has not yet been positively decided. The metamorphosis in question, however, must be regarded as a passive participation, in so far as thereby at points of the unyielding hyaline cartilage a soft material is deposited, which offers no resistance to the extension of the osseous trabecular system, and to the ingrowth of the medullary papillæ. The cartilage-cells anew fall into a process of proliferation, which because of the simultaneous liquefaction and partial resorption of the intercellular substance, assumes very considerable dimensions. From one cell are

produced eight to sixteen very large daughter-cells, which are only separated by thin trabeculæ of basis-substance, and form elongated round columns, which are placed vertical to the surface of the growing cartilage. Into this large-celled, soft tissue the vascularized medullary papillæ penetrate unhindered, as though they grew up in the open air; they break through all partitions, and only where the form and situation of the medullary space admits, there is perhaps a stronger trabecula of the old basis-substance used as a frame, to which the young osseous tissue attaches itself by layers. In other respects bone has for its production here, as in the periosteal growth, no other postulates than a vascular, embryonal connective tissue, which is produced at all its boundaries from the intermediary nutritive apparatus, whether this presents itself as medullary tissue or as periosteum. I will here refrain from going into the growth of bone in detail, as ample opportunity will present itself to me for this in the chapter on disease of bone.

§ 80. The following is known of the *growth of muscular organs:* the first muscular fibres, smooth as well as striated, arise everywhere from embryonal formative cells. These develop themselves—where smooth muscular fibres are to be produced—to the known spindle or more ribbon-like forms, while the nuclei assume an elongated, cylindrical form (rod-shaped). Where the question is about striated muscular fibre, the cell, according to Kölliker, elongates with a continuous division of the nucleus, until it has attained its appropriate length. (According to other authors, several cells arrange themselves into a fibre.) Then the striated substance differentiates itself from the protoplasm and grows into a cylinder, continually becoming broader, while the nuclei are pushed aside, and, together with the unconsumed remainder of the protoplasm, represent the muscular corpuscles.

The later growth of entire striated muscles is said by Kölliker to ensue entirely by an increase of the thickness and length of the already existing fibres. According to Weissmann and Kühne, a peculiar longitudinal cleavage of the primitive tubes concurs with this, which was studied by Weissmann upon the muscles of frogs, by Kühne upon the muscles of rats and mice. A considerable increase of nuclei and the finely granular protoplasm at the place of entrance of the nerves was described by Kühne. Weissmann saw the nuclei arranged in a long row which divided the contractile substance of the muscular fibre into two parallel stripes. Kühne saw two muscular fibres in one sarcolemma tube. This is all the data, which indeed a probable, but by no means distinct anatomical representation of the process of the cleavage of muscular fibre, can give us. There is nothing said anywhere of a subsequent supply of embryonal formative cells for the addition of new primitive tubes. It is otherwise in pathological cases. The regeneration of divided muscles by muscular tissue is indeed yet very doubtful;

the regeneration of muscular fibre, however, in typhous myositis, is undoubted, as we will see in due time. In this, however, the circumstances are so complicated that we could not say without scruple the regeneration ensues only out of embryonal formative cells.

We can express the proposition much more confidently in relation to the organs formed of smooth muscular fibres, that in their growth, beside the thickness and length of the cells, their number also increases. Bifurcated divisions have been repeatedly observed in single smooth muscular fibres of the gravid uterus.* As, however, a multiplication of nuclei, perhaps a double nucleus, has never been observed in these cases, it is very doubtful whether we can upon this admit the opinion of a fissiparous multiplication of smooth muscular fibres. It is especially doubtful in face of the concise representation of Kölliker, who could follow in these objects the production of muscular fibres most beautifully and into all their transitions.† The embryonal formative cells, which are necessary for this, are furnished by the intermediary nutritive apparatus, and may leave the vessels as colorless blood-corpuscles.

§ 81. In reference to the *nervous system* we have hitherto universally been of the opinion that the growth of the nerve fibres proceeds everywhere by the addition of embryonal formative cells. The regeneration of divided nerves by means of interdeposited germinal tissue appeared undoubted, and has also as yet, not been replaced by any other teaching. In opposition to it a current has lately made itself perceptible, which might indicate the advance of the ends of the nerves into the growing parts of the body, and the elongation thereby conditioned, as a growth of the tip end without the apposition of new elementary parts. Besser has defended with skill the opinion for the brain that all ganglion cells of later development exist as the preformed so-called neurogliar nuclei, and are already present in the first foundation of the organ.

§ 82. After this the important question yet remains to us, how do the *epithelial structures* grow and repair themselves? Unfortunately there can nothing yet be said as to an exact answer to this. Meanwhile we are justified in the following considerations.

A decided distinction is at first to be made between the epithelia which grow *outwardly* and those which grow *inwards*. The former clothe the entire free surface of the organism, integument, and mucous membranes in uninterrupted connection; the latter fill up cavities hollowed out in the parenchyma of the body, and are known as glandular cells or glandular epithelium. Both systems are produced from one and the same embryonal foundation, retain also during the entire life

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* Moleschott and Piso in Moleschott's Untersuchungen, vi, 1–6.

† Compare Kölliker, Histology, 4th ed., page 567.

their connection as to space in such manner that we may regard the glandular epithelium as a direct continuation and involution of the superficial epithelium; nevertheless, particularly of those upon which the appreciation of pathological changes of tissue depends, it is emphatically to be pointed out that from the very beginning the opposition mentioned above in the direction of growth is present, and that just therein the essential difference of both is founded: namely, the gland arises in this manner: cellular shoots form at the vascular and connective tissue system of the opposing side of the epithelial germinal layer, which penetrate branchingly inwards, in order finally to become hollow from the free surface up to a certain depth. This growth is decidedly central, and takes place by division of the existing epithelial cells, which is repeated again and again in the alveoli and the shoots. The intermediary nutritive apparatus remains entirely passive during this; nay, it is somewhat surprising how it uniformly melts away before the penetrating points of the shoots, and presents itself as a simple stop-gap, which is all that remains for it; it furnishes the interstitial connective tissue, the blood and lymph vessels, which, as is known in their arrangement, are entirely directed by the determined forms of the glandular tubuli, acini, &c.

§ 83. The relations prove themselves entirely different in the *outer skin* and the *mucous membranes*. Here, not the epithelium, but the vascular and connective tissue system, is the measure for the growth. They are its forms (papillæ, membranes, &c.), which determine the form of the surface, upon which the epithelium only forms a protective covering. This is to be kept in view, if we in the following considerations should find the matrix of the superficial epithelium not in itself, but in the underlying connective tissue.

The cells of every thicker epithelial stratum show among themselves certain characteristic varieties, which are universally regarded as differences of age, as phases of development. The youngest elements, which distinguish themselves by their smallness, softness, and want of membrane, lie the deepest, close to the border of the connective tissue: the nearer the surface, so much the larger do the cells become, so much the more distinct becomes a membrane upon them, and a greater or less characteristic form. This latter partially is connected with functional peculiarity (cylindrical epithelium), partially is the result of a conflict, which is occasioned on the one side by the endeavor of the cell to uniformly enlarge in all directions, upon the other by the limitary bounds, which only permit this enlargement in certain directions. A vertical section through the epithelium of the urinary bladder is the most instructive in this relation. (Fig. 34.) We can distinctly distinguish three layers here, which are formed by three characteristically different kinds of cells. Nearest the connective tissue is a simple layer of small, round elements; above this somewhat larger, pear-shaped cells, which,

with their rounded heads, are directed outwards, while the diminishing ends from above fit into the interspaces of the deepest lying round cells. That these cells, originally belonging to the deepest layer, have been raised into the second layer by the pressure from below of younger cells, therewith, however, have yet for a time remained fixed by their lower end to the place of their production, is an opinion which, in my judgment, the pear-shape thoroughly naturally explains. The cells of the third layer have at first view something exceedingly strange. They are flat, but provided at their under surface with angular projections and flat depressions, which correspond to the cell-heads of the second layer, in the same manner as the digital fossæ of the inner table of the skull to the convolutions and sulci of the surface of the brain. We can only thus understand this third cell-form, that a cell of the second layer loosening itself from its attachment to the connective tissue, and now swelling out into the cavity of the urinary bladder, is pressed flat by the centrifugally acting pressure of the periodically collecting urine, and is pressed into the grooves and inequalities of the second layer.

Fig. 34.

The epithelium of urinary bladder in section.

All epithelia do not admit of so satisfactory a representation as to the origin of their individual forms. What, however, we believe to observe everywhere, and about which there prevails no difference of opinion among authors, is the fact that the epithelial cells arise close to the connective tissue, and thereafter are pressed outwards by a vis a tergo. Hereby of course only the place, on the contrary by no means the manner of their production, is established. For this there remains to us—be it premised, that we meanwhile make no use of equivocal generation*—two possibilities, namely, either the new epithelial cells are produced by a division of the old, or they arise by pressure from behind from the connective tissue.

From the very beginning we cannot conceive why both possibilities should not exist and occur side by side. It must, however, be stated that the observations of the processes of division of epithelial cells, are as yet very scarce. The mutual flattening of epithelial cells makes it appear that one not infrequently *believes* to have before him the result of a cellular division by the formation of partition walls, since the even surface of contact of a pair of cells simulates the plane of division; therefore the utmost caution and conscientiousness is necessary here. Upon the other side, many things combine to incline us to the opinion

* J. Arnold (Virchow's Archiv, Bd. 46) has, it is true, published a study on the regeneration of epithelium, which amounts to a kind of equivocal generation, and is therewith so carefully and concisely wrought, that it deserves the highest consideration.

that the young epithelial cells grow out of the connective tissue. Burkhardt designated for the first time the uppermost layer of connective tissue as the matrix of the epithelial cells. As this investigator in the year 1859 represented to us how, according to his opinion, the young cells emerge from the connective tissue, erected themselves, and then appeared as the youngest epithelial cells, many could not resist a doubt. Since then Von Recklinghausen has directly observed the *emigration* of connective tissue cells in the cornea, and has thereby brought incomparably nearer home to us the idea that the renewal of epithelial cells is brought about by an emigration of the youngest elements of the connective tissue. The facts of pathological histology not only do not at all contradict this, but present many things which can explain the process of emigration. I only mention here the interesting observations of Biesiadetzki and Pagenstecher, who, after slight and superficial inflammation of the skin (eczema and formation of vesicles), found in all youthful strata of epidermis wandering cells, which completely corresponded to other wandering cells yet existing in the papillary bodies. (Fig. 35.) Only one circumstance is always anew brought to bear against our view; it is the fact, certainly easily to be established, that new epithelia, for example, after partial loss of the epithelial covering, by preference, nay, probably without exception, arise only in apposition and in immediate contiguity with the existing epithelium. It accordingly appears, as a production by division of the old elements cannot be proven, that the opinion is inevitable, that an embryonal formative cell can only then become an epithelial cell, when it comes in contact with such. We must believe in *a kind of epithelial infection.* This must of course just as well obtain, when embryonal formative cells, colorless blood corpuscles, &c., approach an existing epithelial stratum, as when conversely epithelial elements approach embryonal formative cells. Processes of this kind, however, are observed in fact in the transfer of cancer to lymphatic glands.

FIG. 35.

Horizontal section through a cutaneous papilla surrounded by epidermis. Migrating cells, as well in the connective tissue as between the epithelial cells. After Pagenstecher.

§ 84. With this, then, we will conclude our review of the physiological new formations. We have seen that, leaving out of consideration the first foundation of the parts of the body, which shows us that such tissue can be produced from embryonal formative tissue, the proper

growth of organs depends only in a limited extent upon a division of their specific constituents of tissue. We found one such in the glandular cells, in the striated muscular fibres, in narrower limits in cartilage, conjecturally in nerve fibres. In the epithelial-bearing membranes, the necessity of an epithelial infection, therefore at least an influence of the old cells upon the new ones being produced, appeared to take place. For all other cases the intermediary nutritive apparatus stepped in with its capacity of producing everywhere embryonal formative cells, as the carrier of physiological new formations. It probably undertakes this function as a further consequence of those duties, which are imposed upon it as the nourisher of the parts, in that it allows, beside the commonly fluid nutriment, a certain amount of colorless blood-corpuscles to pass out into the growing organs, and these without further change may be applied as building material.

§ 85. If we now enter the province of pathological new formation, we first touch upon a series of abnormal conditions, which permit themselves to be characterized as simple excesses of the normal growth of organs. They are those partly uniform enlargements, partly one-sided projections or outgrowths, which, however, entirely agree in textural and structural relations with the parental soil, therefore only condition *quantitative deformity* of the affected organs. In the nomenclature we are wont to express this circumstance by the prepositions ὑπέρ and ἐκ, to which the use of language either attaches the proliferating organ itself (hyperostosis, ecchondrosis), or also the word trophia, and therewith the meaning, that the new formation was produced by a particularly favorable nutrition (hypertrophia). We, however, prefer to renounce this genetic prejudice and content ourselves by expressing the simple fact by the words, "hyperplasia, hyperplastic." We will treat of the hyperplastic condition of the various organs in the corresponding chapters of the special part. The position which they occupy in the province of pathological new formation in general is sufficiently designated by what has been stated.

§ 86. All new formations not hyperplastic contain in themselves a *qualitative* departure from the normal processes of development and growth. It therefore appears difficult at the first view, to place them upon a physiological basis. There are, however, not so much actually existing as much more artificially produced difficulties, which stand in our way; above all, the transmitted custom of regarding the deviating evil as a ἕτερον, something foreign, introduced into the organism, of ascribing to it a parasitic existence, even a kind of personality. This view, from which the term "heteroplasia" has arisen, has a certain justification; 1st, in the presence of those new formations, which are caused by a definite poison introduced into the body, and conformably present themselves in the most various organs in the same manner, thus in syphilis, tuberculosis, typhus abdominalis; 2d, in the

sense that every organ has its own peculiar new formations, which always recur in the same forms with slight modifications, so that we, if they have progressed up to a certain point, may thereupon base a sure diagnosis and prognosis. It is, however, unjustifiable and injurious to the progress of true science if one neglects, in the study and description of what the new formations of the various organs have in common, the right of the individual organs, which requires that one regards the pathological new formation as a disturbance of *its* development, its nutrition, or its decomposition. Be it well understood, I am very far from disputing the usefulness, nay, the necessity, of general observations of pathological new formations; these observations, however, ought to proceed more upon establishing the principle of development than upon finding out certain anatomical models, according to which a new formation, for example, cancer, is built, as well in this as in that organ. Moreover, if I understand our time, it is tired of the purely external, anatomical classifications, and decides with me, that this has become scandalous in the inexhaustible multiplicity of concrete forms. We will of course therefore speak in what follows of cancers and sarcomas; we will take pains to delineate the laws of their production and their growth in bold outlines, also not to exclude observations upon their effects upon the entire organism, therewith however constantly reflecting upon the description of the individual forms in the special part, and remaining conscious that the knowledge of these is at least just as important to the physician as is the general comprehension.

§ 87. After this digression, let us take up the thread of our representation again, in that we seek the ground of that qualitative deviation from the rule of the normal growth, therefore the ground of heteroplasia, in an improper activity of one or the other factors, participating in the growth of organs. The *intermediary nutritive apparatus* occupies the first place in this regard. Very many pathological new formations are its exclusive effects, for example, interstitial inflammation, granulation-tumor, sarcoma. *Epithelium*, as the competitor of the vascular and connective tissue systems, enters the second row, and we have numerous opportunities of proving the correctness of our views on epithelial growth in its caricatures in the various forms of carcinoma. We cannot mistake that in this distribution of affairs the physiological circumstances, as I have recapitulated them, § 84, are again reflected, and we will expose ourselves to no censure if we base thereupon at least the principal division of the material.

3. Pathological new formations which are exclusively the productions of the intermediary nutritive apparatus.

1. *Interstitial Inflammation.**

§ 88. If the organism is injured or meets with any other sufficiently powerful irritation at any point, this has as a consequence for the point nearest to that affected a series of changes, which we designate as the process of inflammation. The name refers principally to the prominent part which the vascular system plays in inflammation. The capillaries are more strongly filled than usual, the part becomes red and hot. At the same time a swelling of it occurs, which is also to be partly referred to the account of the hyperæmia, partly to the extravasation of constituents of the blood taking place into the tissues. That which leaves the vessels and then infiltrates the tissues, that "inflammatory exudation," is a more lasting product of inflammation, and because of its great importance for the course and issue of inflammation will more immediately interest us in the following.

§ 89. The inflammatory exudation consists, beside the fluid parts, of embryonal formative cells, which distinguish themselves by a lively amœboid movement. Only a few years ago it was universally accepted, that these cells were exclusively produced by a division of the connective tissue corpuscles of the inflammatory focus. The persistent representation, in which we believed to distinctly perceive the process of cell-proliferation, showed us in the immediate environs of the inflammatory exudation, *instead of stellated connective tissue corpuscles*, first one, then two, then ever more numerous round cells arranged into rows, which, the nearer to the focus of inflammation, became so much the longer, and finally flowed together. At present we know that these cells are for the greater part emigrated colorless blood-corpuscles. This is proven by an experiment of Cohnheim, in which the mesentery of a living frog is stretched over a ring of cork and then directly observed. One sees how the veins dilate and the colorless blood-corpuscles first remain clinging to the inner surface of the wall of the vessel, then however, permit a process to pass through it, which swells up outside, and in this way builds a bridge, upon which the whole substance of the cell gradually creeps over. Having passed through, the cells, by aid of their amœboid movements, wander further. If a particular point of the tissue is irritated, this generally decides the direction of their course. They there accumulate more and more, and form by this accu-

* In opposition to catarrhal and parenchymatous inflammation, of which the first, so far as it comes into consideration by us, is an inflammatory process of mucous membranes (see second part). The second is identical with the cloudy swelling (see above).

mulation a certain quantity of just that embryonal formative tissue, which becomes the point of departure for all future changes. (Fig. 36.)

Fig. 36.

Cohnheim's experiment. *a*. Vein. *b b*. Contiguous connective tissue, permeated by migrating colorless blood-corpuscles. *c*. Column of red blood-corpuscles. 1–500.

With the view now advanced on the production of plastic exudation or infiltration, agrees an older perception, first appreciated by Billroth, according to which, in the inflamed parts the vessels are covered with young, round cells, even far into the tissues, but little changed. Upon the other hand that pregnant representation of the "proliferation of connective tissue" explains itself in a completely satisfactory manner by the opinion, that in it we have before us the colorless blood-corpuscles in their "migration," in which they naturally give the preference to the points of the least resistance, therefore to the interfibrillar juice-tracts, in which the stable connective tissue corpuscles are also found.

§ 90. Nevertheless it has not yet been said, that the emigration of colorless blood-corpuscles is to be regarded as the only source of inflammatory new formation. On the contrary, the question, whence does the blood take the frequently so enormous amounts of colorless cells? occasions a series of considerations which makes it our duty to use the utmost caution, when the question is about declaring the modes of generation of these cells. In this sense we greet with pleasure the beautiful investigations of Stricker, which first of all prove for inflammation of the cornea, that already in a few hours after irritation by nitrate of silver, at a time when conformably to experience the emigrant colorless blood-corpuscles have not yet advanced into the inflammatory area, the stable cornea-corpuscles exhibit a series of changes, which can only be interpreted in the sense of progressive metamorphosis. Namely, they draw in their processes; then the number of their nuclei and the protoplasm increases. About the fifteenth to the

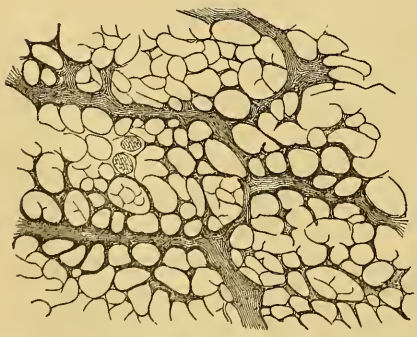
twenty-ninth hour they present strikingly large, movable, and polynucleated masses, which remind of the so-called giant-cells (see preliminary remarks). That amœboid cells are formed of these by the division of the common protoplasm is an apposite view.

The fissiparous multiplication of the wandering cells in inflammatory depots has also been certainly observed by the same author. While he directed his attention to the cells apparently lying quiet at the outer surface of the vessels, he remarked upon their surface certain shaded lines, which for a time came and went, also moved forward and backward, until finally a deeper shadow remained for a longer time in the centre of the element. The corpuscle became constricted at this point, but this constriction was yet once more equalized, until at length it led to a complete division, whereupon the two halves separated, the one to this point, the other to that. The more dense the cellular accumulation becomes, so much the more frequently may this kind of cellular division repeat itself; so much the more difficult, however, is it also to follow it up with the microscope, and this may be the reason why hitherto this has been so frequently supposed, but not proven.

As one observes, our knowledge of the origin of embryonal formative cells in inflammation is yet in full development. If we, however, reflect, that what has been stated contains at the same time the foundation for all other histological productions of the intermediary nutritive apparatus, we will comprehend the great importance which every step forwards at this place has for our whole system.

§ 91. Let us for one moment longer continue the consideration of inflammatory infiltration as a completed fact, and the effect is especially worthy of mention, which the inclosed cells exert upon the connective tissue, which in the first place lodges them. Billroth has made several statements upon this point, which appear to me very worthy of notice; namely, not only are the fibres pressed apart, but they also experience a certain melting-down and softening, so that, for example, instead of that compact fibrous texture, of which the cutis even in its most delicate parts (the prepuce) consists, there results a delicate network, which makes the impression far more of of a newly-formed intercellular substance (Fig. 37), and has certainly very often been mistaken for such.

Fig. 37.



Tissue of cutis rarefied by inflammatory infiltration. After Billroth. 1-300.

If we now pass to the further histological metamorphosis of plastic exudation, upon which, as has been already remarked, the issue of the inflammation is dependent, we distinguish in

this relation, three principal directions, namely, first to resolution; second, to organization; third, to suppuration.

a. *Resolution.*

§ 92. It is manifest, that if by our medical skill we could succeed in removing again the cells which have wandered into an inflamed organ, this organ would return to the same condition in which it was before the inflammation, provided we deduct the modification of the connective tissue fibres mentioned in the previous paragraph, which meanwhile would likewise soon disappear. The question of the possibility of a resolution of inflammation and the means of inducing the same, has therefore a highly practical interest. It might at first occur to us, to send away the cells in the same way by which they came, that is to say, to let them wander further. In this sense moist heat is applied with advantage. Exaltation of temperature also accelerates, as is known, the movements of amœboid cells. Where, therefore, the inflammatory infiltration is not great, and the inflammatory irritant does not continue to act, one may hope, by locally increasing the temperature to diffuse the already present wandering cells over a greater space, and gradually to convey them into the lymphatics. A second mode of resolution of existing inflammatory infiltration becomes possible by the fatty degeneration of the cellular elements. We saw above, how fatty degeneration converts all kinds of cells into a milk-like detritus, of whose immediate resorption naturally no hindrances stand in the way. The presence of abundant amounts of fluid in the inflammatory focus appears to be a decided condition for the commencement of fatty degeneration. Busch has made the interesting experience, that under the influence of erysipelas, massy sarcomatous proliferations disintegrated, and I have most certainly convinced myself in one of his cases, that the sarcoma-cells thereby fall into fatty degeneration. Heat would also be an appropriate remedy for keeping down a lasting hyperæmia of this kind. In spite of this double indication, the moment of time must be exactly considered, in which one may pass from the cold to the warm treatment of an inflammation. The object of the cold treatment, is by an artificially induced contraction of the vessels principally to restrain exudation, with reference to prohibiting the further emigration of colorless blood-corpuscles. We would only pass to the use of warmth, either when this indication has been fulfilled, or when it can no longer be fulfilled; for it is evident that heat is a two-edged sword. Who will be surety that instead of a dispersion of the exudation, which indeed, we would first of all desire, a stronger concentration of mobile cells shall not occur at the heated point, that is to say, suppuration and formation of abscess? A certain amount of heat evidently acts dispersing; a higher degree irritating to the process of inflammation; the former causes the already exuded colorless blood-

corpuscles to wander further; the latter causes the process of emigration to renew itself, and it increases in intensity.

Annotation.—The therapeutic complexion which I give this chapter may be an example to the student, how directly the results of pathological histology may also be applied to the practical treatment of the physician.

b. *Organization.*

§ 93. Let us suppose, now, that the inflammatory infiltration has not taken the way of resolution, then the possibility remains for it to be received as a permanent constituent of the organic unity of the body. Its reception is effected by a seasonable development of bloodvessels, and transformation of the embryonal into fibrous connective tissue. The interstitial inflammations of the interior organs furnish us the most magnificent examples of this direct organization, as we will learn to know especially in the liver and kidneys. Meanwhile none of these examples, because of peculiarities conditioned by the locality, can be regarded as models for the histological detail of the process of organization. The healing of wounds, and indeed primarily only those by first intention, can only lay claim to this honor.

In order to make the diffusion of connective tissue in the body comprehensible, I above made use of the phrase, that one could cut into no point of the body, without meeting with connective tissue, without having connective tissue contiguous to the cut surface. That this is actually so, we may conclude, among other things, from the completely typical event of those phenomena, which the reunion of divided parts brings about after actually accomplished severance of continuity. These phenomena altogether fall into the province of inflammation, and are performed by the vascular connective tissue system in a similar manner, whether the injured organ be the outer integument, or a muscle, or perhaps the liver. There certainly is a kind of reunion, which is brought about so extraordinarily rapid by the simple juxtaposition of the surfaces of the wound, that every expenditure of exudation is thereby saved. This immediate union (Macartney) is also confirmed by Thiersch (Pitha and Billroth's Handbook of Surgery). We would, therefore, have to place this in advance of first intention. In first intention there regularly occurs a cementing substance at the edges of the wound. This already appears in a few hours after the change, and shows itself, in the first place and by more exact investigation (Thiersch), as the connective tissue of the wound-surface, itself strongly infiltrated with blood-corpuscles and serum, and swelled out in the latter. In the second place, then, the emigration of colorless blood-corpuscles from the strongly dilated vessels of the neighborhood makes its appearance. The whole of the cementing substance, as well as the contiguous connective tissue, is penetrated by them, so that finally a continuous layer of embryonal

formative tissue unites the divided parts. Everything now depends upon the restoration, also, of the violently interrupted circulation. This generally takes place by secondary vascular formation (§ 71) from the still pervious capillaries. Thiersch has lately brought forward data for the individual occurrences, which, if confirmed in the significance given them by this author, must essentially enlarge our views on vascular new formation in general. Thiersch found the cut ends of the vessels closed several hours after the injury by proliferation of cells, and somewhat dilated, but rarely filled with a blood-clot. If about this time he injected a warm mass of glue, he found, after hardening the preparation in alcohol, 1st, loosened and isolated, also proliferating endothelial cells cemented to the surface of the club-shaped thrombus of glue; 2d, a peculiar configuration of this same surface, namely, numerous prickly, like broken-off processes, which perforated the vascular walls, and upon closer investigation proved to be the roots of a system of very delicate intercellular canals filled with glue. Thiersch sees in this system of canals a preliminary nutritive arrangement, a vascularization before vascularization, and by the aid of this he explains the certainly enigmatical fact, that even completely severed parts of the organism may again unite, if only they are soon enough placed in apposition again. For our purpose, upon the one hand, the proof is of interest, that the constituents of the walls of those vessels, out of which in a little while new shoots are to proceed, become spongy, and the manner in which it is done, upon the other hand the circumstance, that from this side also the histological significance of the bloodvessels is established as "intercellular," and not as intracellular canals.

The transformation of the embryonal formative tissue not applied to the formation of vessels into fibrous connective tissue constitutes the last act of first intention. As in the physiological formation of connective tissue, the cells here also become *spindle-shaped.* The great amount, however, of existing cells and their dense apposition necessitates the production here of an entirely new kind of tissue by the spindle-shaped metamorphosis of the cells, the *spindle-cell tissue.* We understand thereby a texture entirely consisting of parallel running spindle-shaped cells, which is connected by the cells with their pointed ends pushing among each other. Spindle-cell tissue, as a rule, forms rounded or slightly flattened bundles, which intervene after the manner of connective tissue bundles. There is also no doubt that the future connective tissue bundles arise out of the spindle-cell features. The question only is, whether the protoplasmatic bodies of the spindle-cells are directly transformed into glue-yielding fibres; or whether we must regard, with Rollet, the act of fibre-formation as a kind of coining of the intercellular substance. According to my experience in the case in question, that is to say, in the formation of *cicatricial tissue* out of spindle-cell tissue, the greatest part of the cell-bodies themselves, as a

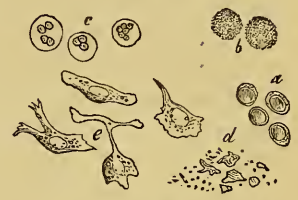
matter of fact, is converted into a mass of fibres. After a certain period of time, it is impossible to unravel even into spindle-cells the spindle-cell tissue, which one yet distinctly recognizes as such upon sections; the tissue rather breaks up into rigid, irregularly outlined, fibrous fragments, which, as the nuclei show, consist of entire groups of melted-down cells. This phenomenon can only be explained in the sense above given. The fibrous lines of cicatricial tissue do not only proceed in general from the fasciculi of the spindle-cell tissue, but neither is anything new added in this transformation. In opposition to the normal development of loose connective tissue, the entire process makes the impression of an over-hasty consumption of capital, where the judicious use of the interest would have given a far better result. I say emphatically a better result, for cicatricial tissue is anything else than a connective tissue of ideal quality. On the contrary, its fibres are rigid, inelastic and shapeless; its cells, and with them the vital capacity, are reduced down to the wholly stunted, club-shaped nuclei. In addition, cicatricial tissue has the decided tendency to shorten itself in all directions. We call this upon the whole very injurious phenomenon induration, sclerosis, retraction, and count upon its occurrence with such certainty, that we have based upon it the method of cure, of turning outwards an inwardly turned eyelid, by a cicatrix formed upon the cheek. It is scarcely necessary to say, that in this decrease of volume from all sides there can be no question about a vital contraction, but rather about a physical phenomenon; in any event the giving up of water plays therein an important part, for the white, glistening, cicatricial tissue is always dry, dense, and more difficult to cut than every other species of connective tissue.

c. *Suppuration.*

§ 94. Pus is a fluid tissue. A colorless serum contains numerous cells, the so-called pus-corpuscles suspended, and receives therefrom a grayish-white or yellowish-gray color. In the serum of pus are dissolved albumen, mucus, pyin, and salts. The cells are small and globular, are partly impregnated with minute granules, partly as though they were dusted on, so that as a rule we cannot recognize the nuclei in the interior. If we make use of acetic acid, the granules vanish and the nuclear structures come out clearly and sharply. We commonly find more than one nucleus, often three, even four. In the latter case the nuclei are small, not always regularly round, and have a peculiar sheen, indicating homogeneity. (Fig. 38.) We have sought just in these polynucleated cells for something specific of pus, and in that sense have given them the name of pus-corpuscles. Meanwhile we were deceived in this, for we again find these cell-forms also in the blood; a portion of the colorless blood-corpuscles has divided nuclei, and Virchow already

expressed the opinion that of these cells there was nothing further to be expected for the formation of blood. At a later period it was shown that in the surcharge of the blood with carbonic acid all the single nucleated colorless blood-corpuscles were converted into polynucleated, and then entirely perished. The multiplicity of nuclei here has not the import of a nuclear division in the sense, as when it precedes the division of the cell. I would sooner perceive in it a decay prior to dissolution. Besides it is not at all correct that pus only contains the one form of cells. Creamy pus (pus *bonum et laudabile*), which is secreted from well-granulating wound-surfaces, contains even predominantly uninuclear cells, which I would not know how to distinguish from the wandering cells of connective tissue. On the contrary, for example, sanious pus, which is yielded by carious bones, as a rule shows more cell-derivatives, fat-globules, albuminous molecules, &c., than pus-corpuscles. In fact, as with the colorless blood-corpuscles, there exists a transition of the uninuclear into the polynuclear elements, and these, being capable of no further development, perish through fatty and fatty-granular metamorphosis. Always therefore, accordingly as the pus is fresh or old, accordingly as it was produced rapidly or slowly, was rapidly or slowly decomposed, will we meet with uni- or polynuclear cells, or even with cellular detritus.

FIG. 38.



Pus-cells. *a*. From a well-granulating wound. *b*. From an abscess of cellular tissue. *c*. The same treated with dilute acetic acid. *d*. From a bone-fistula (necrosis). *e*. Migrating pus-corpuscles.

§ 95. When it has been said that pus may be developed in various ways, when we contrast the formation of pus here to be considered in connective tissue, with the formation of pus upon mucous and serous membranes, its formation from coagulated blood, this contrast can at present only be accepted *cum grano salis*. The chief mass of the pus is everywhere formed by the emigration of colorless blood-corpuscles out of the vessels; only that, first, the way which the wandering cells take, is directed in the one case towards a free surface, in the other towards a point situated in the parenchyma of connective tissue; and that, second, in the production of pus upon mucous and serous membranes, the participation of the epithelium in the production of pus cannot be excluded. For the production of pus in connective tissue, that is to say, the suppuration of an inflammatory exudation, which alone occupies us here, naturally the same restrictions and reservations return, which we have already had to make for the production of the plastic exudation itself. It has not been proven that all pus-corpuscles originate directly from the vessels, but upon the one hand a formative irritation of the stable connective tissue corpuscles has been proven, the breaking up of which into wandering cells is made probable; upon the other hand, divisions of the cells of the exudation have been observed. In

other respects we may regard suppuration in fact as the most direct continuation of the first inflammatory phenomena. The nature of this depends upon the unlimited continuance, upon the superabundance of the formation, whereby in a comparatively short time really colossal amounts of young cells are furnished. The impulse to suppuration of the inflammatory infiltrate, or, as the expression generally is, to a transition of inflammation into suppuration, is, in many cases, only to be sought in the too great intrusion of juices into the inflamed part, hence our antiphlogistic therapeutics always pre-eminently endeavors to prevent this intrusion of juices, at least to diminishing it. In other cases we find the cause in the quality of the inflammatory irritant; thus chemical agents, especially, however, septic ferments, bring to pass suppurative inflammations. Conversely we may expect that in such individuals, whose mass of juices is septically infected (septicæmia), every inflammation will easily take on the purulent character. Finally, there are also entirely individual predispositions to suppuration, that is to say, individuals, in whom also the slightest inflammatory irritant leads to suppuration. Still, this only by the way. We return to the anatomical course of suppuration.

§ 96. The next phase is the formation of purulent abscess. The cells primarily more uniformly dispersed in the inflamed parenchyma, leave the place of their development, and from all sides move together to a certain central spot, in which afterwards the suppurative focus (abscess, apostema) appears. By this locomotion upon the one hand, the spontaneous mobility of the cells is brought into play; upon the other, however, a greater or less transudation from the vessels, which accelerates the movement and determines their directions, as well as the point of accumulation. If this flowing together has endured for a length of time, there arises at the point of the conflux a knobby induration. Within this the vessels are compressed, the parenchyma becomes pale. With the supply of blood, however, nutrition also ceases; softening and fatty degeneration forthwith set in; in the abundant transudation the connective tissue fibres melt down and the cells loosen themselves. The palpating finger now feels fluctuation, the suppurative focus has been formed, or, to speak technically, the abscess is ripe.

After having thus seen the abscess produced, it would scarcely be necessary for us still to define the same as a cavity in the body filled with pus, if collections of pus could not occur also in another manner than the one represented, which indeed are not called abscesses, but in a histological point of view possess thoroughly the value of an abscess, I mean, namely, the purulent exudations into closed cavities, serous sacs, articular cavities, bursæ and sheaths of tendons. The size and form of the abscesses naturally vary considerably, according to this extension of their province; still, this is justified by the uniformity of their future course.

§ 97. The emptying of pus from an abscess ensues by far most frequently outwards, the bursting of the abscess. The same forces, by which the pus was collected at one point, labor to push forwards the accumulation of pus in the direction of the least resistance. The elastic tension of the part, surrounding the pus and pressed by it from its normal position, acts in the same manner, and as the pus, thanks to the great diffusion of connective tissue in every direction, touches a tissue which is able likewise to be converted into pus, there results therefrom the prevailing frequency of this outlet. The pus, therefore, presses in the direction of the least resistance. In the latter instance, this will always be the direction outwardly, the final result rupture of the cutis or mucosa. If the pus has been emptied, the cavity of the abscess has become a free, pus-producing surface; it now falls into the category of ulcers, which we will forthwith consider further.

§ 98. Meanwhile the pus is not always evacuated externally. It may also in every stage of its collection be made capable of resorption by fatty degeneration of its cells, and be resorbed. Nay, according to several newly imparted experiences, this capacity for resorption even extends to very old abscesses, already become cheesy, which for some time had preserved an unchanged extent. The cheesy material herewith, in the form of the minutest particles, reaches the blood and lymphatic systems, and can, as we will see further on, occasion the production of miliary tubercle. (See below.)

d. *Organization after Suppuration.*

§ 99. From the entire relations of pus hitherto considered, I believe it has been sufficiently shown, that it is something foreign to the organism, alienated, against which of course it is not shut out by the protective covering of an epithelium as against the rest of the outer world. The aim, therefore, is, from the moment when the abscess has constituted itself such, to restore the disturbed unity and the integrity of the organism. For this, however, the more simple means of organization considered above, namely, vascular and connective tissue formation, alone do not suffice. A new integument with an epidermis must form, and thus then is brought about that highly interesting development of form which we are wont to designate as healing by *second* intention. Of course it occurs then only in the healing of wounds where the healing of the solution of continuity did not succeed by the exact apposition of the divided parts, when suppuration renders it necessary for us to remove sutures and adhesive plaster, or when a considerable loss of substance in general makes the union of the wounded edges impossible, and the parenchyma is now open to view, unclosed, uncovered, and exposed to the action of the atmosphere, &c. But here, also, the idea is wider than the description. Entirely the same phe-

nomena occur as in the cases mentioned, where the aim is to close the organism against an abscess, or, what is analogous to an abscess (§ 96), when necrosis, burns or corrosion have made a part of the body a great source of suffering, which can only be removed by suppuration; the healing of ulcers belongs here; in a word, second intention is organization after suppuration.

§ 100. We are dealing with a free surface producing pus. At innumerable points of this, young cells spring forth, and with the cells a fluid very rich in dissolved albuminates, which pre-eminently is a transudation from the blood. At some time now, there happens close to the limits of the surface to be produced, the reverse of that which happened in the liquefaction of the plastic exudation into pus. The cells more firmly gather together. A layer of embryonal connective tissue immediately forms, which pushes on between the parenchyma of the organism on the one side and the pus upon the other. All the pus-corpuscles, which are henceforth thrown off, must pass this layer of embryonal formative tissue, which soon thickens, and is elevated in the form of small, globular tuberosities, the so-called *granulations*. The material for all further development is given in these granulations; out of them are produced the skin and epidermis; above all, however, the new vessels.

§ 101. *Vascular formation* is undoubtedly here also the most vigorous means of organization. The reason why just a greater bulkiness of the cells, also brings with it a greater frailty of the individual elements, lies in the circumstance that a great extent of a cellular collection, for example, the pus-corpuscles united to form an abscess, is difficultly, or not at all nourished. If the accumulation has attained a certain thickness, those elements which are most peripherally situated, it is true, may yet be able to take up what they require from the neighboring nutritive fluid, and to deliver their excretory matter; the further, however, we go interiorly, so much the more does this possibility decrease. Upon the one hand the excretory matters accumulate; upon the other, the nutritive material has no access. The only measure which is calculated to remedy this untoward condition is the formation of vessels; that is to say, the laying out of canals, by which on the one hand the productions of the blood-making organs are carried into the centre of the territory requiring nutriment; upon the other, the excretory matters are conveyed away from the interior of the same territory. In this manner a longer continuance and connection with the organism is assured even to larger depots of embryonal formative tissues.

§ 102. As to what specially pertains to the vascular formation in second intention, the superficial diffusion of the germinal tissue in itself, already presents more favorable chances for nutrition. Notwithstanding, at a very early period in the course of things an abundant vascular formation co-operates in facilitating this. The histological

detail is that of the secondary vascular formation: in certain central directions of the parenchyma to be vascularized, a denser accumulation of cells becomes perceptible; a strand or row of cells appears, which indicates the form and direction of the future vessel. The question, how is a tube produced from this cellular cylinder; what are the circumstances of the opening of the new vessel? we can only answer by a reference to the discoveries of Thiersch in the first intention, already noticed. As the pervious mother-vessels also, into which the foundation-structures with both of their roots are inserted, are thickly inclosed by cells, just this mysterious part of the whole process is veiled from our eyes. We know, that at a certain time the blood-current becomes visible in the axis of the foundation-structure; that by it the cells of the latter are pressed apart and henceforth appear as walls of the new vessel. I take it, the whole vascular wall is dissolved by the inflammatory irritation in individual cells and is thereby placed in a condition, which places no particular difficulties in the way of a bursting through of the blood tract. Such a representation is entirely indispensable for the further process of vascularization, in which the young vessels, still entirely consisting of cells themselves, in turn produce vascular loops; namely, as the deposition of the germinal tissue progresses externally, so the formation of capillaries also follows after internally. The capillary loops with long parallel roots spring vertically upwards in the granulations; they extend up close beneath the suppurating surface; the loop ends are somewhat widened. (Fig. 39.)

§ 103. We have reached the point of the most luxuriant production. Uninterrupted progress in this direction again leads us into a byway, namely, to the formation of the so-called "proud-flesh" (*caro luxurians*), of which, hereafter. As a rule, a new metamorphosis now occurs, which is fitted to check a too luxuriant production at the surface, and to prepare the formation of integument. The embryonal connective tissue is converted into cicatricial tissue. The transformation begins in the deepest layers of the granulations, and exhibits the same phases and transitions which we have learned to know in the first intention. Spindle-cell tissue first arises.

The plane of the layers of spindle-cells determines the direction in which the first fibrils become visible. Then follows the formation of the cicatricial tissue and the retractive shortening of the same in the manner described, § 93. Still the same phenomenon here has a more complicated effect than in first intention; namely, as was remarked, in so far as it first occurs in the deepest layers of the pyogenetic membrane, the basis upon which the granulations are seated then decreases. The surface of the wound contracts; what, however, is affected in the first place, are the vessels, which, as mentioned, spring vertically through the cicatricial soil to the surface. The vessels are constringed, diminish in calibre, nay, are in part completely obliterated. In an

equal measure the granulations lose in juiciness and volume; the production of pus is gradually diminished. In this manner, by a truly surprising co-operation of the various forces of development, there is preparation made for the last step which yet remains to be accomplished, the throwing out of an epithelial covering; the providing an integument for the surface of the granulations.

§ 104. It is correct, that as a rule the formation of integument proceeds from the edges of the granulation surface towards the centre. Meanwhile there are also exceptions to this rule. It has been repeatedly observed, that small spots covered in with integument also occur at some distance from the edges, which gradually enlarge and finally coalesce with the marginal formation. If, however, this were not a fact to be established already by the naked eye, still an accurate study of a vertical section through the edge of a healing surface of granulation (Fig. 39) would leave thereupon no doubt, that the formation of

FIG. 39.

Section through the border of a healing surface of granulation. *a.* Secretion of pus. *b.* Tissue of granulation (germinal tissue) with capillary loops, whose walls consist of a longitudinal layer of cells, decreasing in thickness from within outwards. *c.* Beginning of the cicatricial formation in the deep layers (spindle-cell tissue). *d.* Cicatricial tissue. *e.* Complete epithelial covering. The central layer of cells consists of serrated cells. *f.* Young epithelial cells. *g.* Zone of differentiation. 1-300.

integument is not produced by an independent growth of epithelium over the surface of granulation, but in that, the outermost layer of the tissue of granulation constitutes itself as epithelium. At *e* (Fig. 39)

the separation of epithelium and connective tissue is thoroughly brought out, at *f* the limits have become obscure, but at *g* we can yet recognize the future epithelium in the closer arrangement of the outer cells, even though the elements are thoroughly similar in size, nuclear structure, &c. Further along follows the suppurative surface; it looks as though the first foundation of epithelium consisted of pus-corpuscles not thrown off. If we seek for an analogue of this epithelial formation, we can only compare it to that first and foremost separation of the embryonal germinal tissue into epithelial and non-epithelial layers, and regard it as a genuine embryonal differentiation. That a certain cooperation of the neighboring normal epithelium, importing epithelial infection (§ 83) is not to be excluded in the formation of integument, is manifest. The pre-eminently frequent (according to Heine and Billroth exclusive) occurrence of marginal formation of integument may be grounded precisely upon this circumstance.

The newly formed epithelium always remains thin and dry. No one has as yet observed that regular glands or even hairs are developed from it; on the contrary, I can certify, that there are cicatricial epitheliums, in which the cellular villi characteristic of these tumors, proceed from the thin cicatricial epidermis.

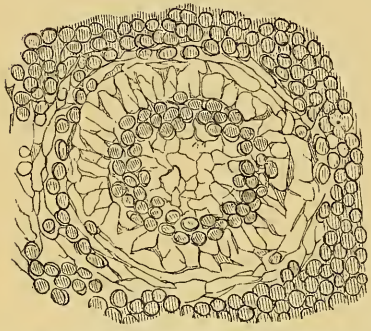
§ 105. These are the outlines of the inflammatory new formation, so far as the latter proceeds alone in the intermediary nutritive apparatus and is supplied by its means. Many interesting and important modifications are conditioned by the peculiar anatomical constitution of individual organs, and must therefore be spared for the Special Part. At this place, let us once more consider that peculiar deviation, which the second intention experiences by the formation of the so-called proud flesh.

Caro luxurians might be designated as a hyperplasia of the granulations. Instead of small tuberosities, which in breadth and height should not exceed the measure of a line, fungous masses luxuriate here, which are characterized by three or four times this volume, by incomplete dendritic organization, diminished vascularity, and a certain want of capacity of withstanding external influences. These fungous granulations distinguish themselves in a histological relation by a specially higher differentiation of the embryonal formative tissue. First of all, the more distinct formation of a stroma is universal, which is similar to the stroma of the lymph-follicles. In the formation of this upon the one side, the cementing substance of connective tissue participates, which fills out the netlike anastomosing spaces between the globular cells and now stiffens into minute, rounded filaments; upon the other side, a certain number of the cells themselves participate. These become stellate, and give at tolerably regular distances from each other the points of intersection of the supposed stroma. In order to represent the latter,

it is necessary to harden the tissue of granulation in alcohol, and most carefully to tease out a fine section.

If by this arrangement already a structure of a higher order, comparable perhaps to the connective tissue stroma of intestinal mucous membrane, is presented, this is still more the case by the production of certain globular structures, which I must declare as lymphatic follicles of new formation. (Fig. 40.) These are centrally situated within the parenchyma, equidistantly removed from all sides of the greater vessels.

Fig. 40.



Lymph-follicle, from a fungous granulation (caries fungosa). See explanation in text. 1-300.

In teased-out, very thin sections, one is readily convinced, that a very elegant reticulum, with small lymph-corpuscles imbedded, forms the principal mass of the round nodules. Towards the periphery the lymph-corpuscles hang firmer in the reticulum than at the centre, so that a border zone, very difficult to clear up, mostly exists here. Beyond this there follows a lucid border, which is penetrated by larger stellated cells, so that in fact only the proof of a communication of the structures with the lymphatic system is wanting, in order to hail them as genuine lymph-follicles. Meanwhile, I would remind, that this proof is still wanting also for the follicles of the tonsils.

§ 106. Nerve-fibres form no integral constituent of granulations; still the so-called irritable granulations are known to surgeons, and I have succeeded in discovering a great abundance of nerve-fibres in a remarkable case of this sort, which was sent to me for investigation by Prof. Billroth.

2. *Non-inflammatory Hyperplasia of Connective Tissue.*

§ 107. We above (§ 85) referred the hyperplastic conditions of organs to the individual chapters of the Special Part, since from a histological standpoint there can in general nothing more be said of them, than that they are just quantitative excesses of physiological growth. Interstitial connective tissue makes an exception to this rule, because it is only a constituent of the several organs, not an organ itself, and because, therefore, its hyperplastic increase must of necessity produce a qualitative disfigurement. Taken accurately, a great portion of the processes, which we have learned to know in the province of interstitial inflammation, may at the same time be regarded as a hyperplasia of the interstitial connective tissue. This especially obtains of inflammatory infiltration, and the transformation of the infiltrate into connective

tissue. In fact the non-inflammatory distinguishes itself from this inflammatory hyperplasia only by the slow progress of the phenomena, if meanwhile we leave the etiology out of consideration. A hyperæmic dilatation of the vessels forms in all cases the point of departure for the changes. The emigration of colorless blood-corpuscles joins itself to this, which has an increase of volume, a condensation of the connective tissue as a consequence. The decided participation of the vascular sheaths in this infiltration is particularly characteristic; these often attain three to five times their normal thickness. The transformation of the infiltrate into fibrillar connective tissue very gradually follows after, and appears in many cases (kidneys, pia mater) not at all to occur. Meanwhile the great analogy of the process to inflammation becomes of itself very obvious, so that physicians and authors are not to be found fault with for having described, and still describing it, as "chronic inflammatory." Where a determined irritant, for example, a continued or frequently repeated, although a trifling mechanical injury has occasioned the disturbance, I am likewise prepared to apply the term chronic inflammation; where, however, this is not the case, where, for example, passive hyperæmia gives the impulse for the appearances mentioned, it would be downright incorrect, if we yet spoke of an inflammation, and not rather of a simple hypertrophy or hyperplasia.

3. *Specific Inflammations.*

(*Granuloma and Lymphoma.*)

§ 108. As in this chapter we will meet for the first time the much-used term "tumor," we cannot forbear giving a short account of the purport and importance of the same. We, as physicians, are so much the more inclined to give a new formation the name of tumor, the less it exhibits the known peculiarities of the inflammatory process, and, indeed,

1. The less an inflammatory irritant can be proven as the causative agent, the more has the new formation the character of a "spontaneous production" ("Freiwillig-Enstandenen"). That there is no question here, as everywhere in nature, of an actual spontaneity, is self-evident. But we are yet so far removed from a clear insight into the etiological relations of tumors, that it is more a thing of individual conviction, whether one will follow him who regards the tumor as the localization of a pre-existing dyscrasia, a tumor-producing disease, or him who holds the local affection in all cases as the point of origin and departure of the disease producing the tumor. Billroth, in his Handbook of General Surgical Pathology, defends the former; Virchow, in his work on Tumors, the latter standpoint. Virchow, with wonderful circumspection, attempts to prove in every case, at least a local predisposition; and even though he does not succeed in entirely driving from the field the humoro-pathological reasoning, we must still concede that there are

tumors which owe their origin to a local irritation. I recall, for example, the epithelioma of the lower lip, occasioned by the continual irritation of a tobacco-pipe hanging from the teeth; of so many sarcomas, which were produced by an irritating pressure; enchondromas of bones, which proceeded from points of fracture, &c.

2. The less decidedly, with the formation of the tumor, the other cardinal symptoms also of inflammation, as pain, redness, exaltation of temperature become prominent. The physician regards it as worthy of especial emphasis, and readily believes in a complication with inflammation, when a tumor causes pain, or when an active hyperæmia with an increase of temperature accompanies its development.

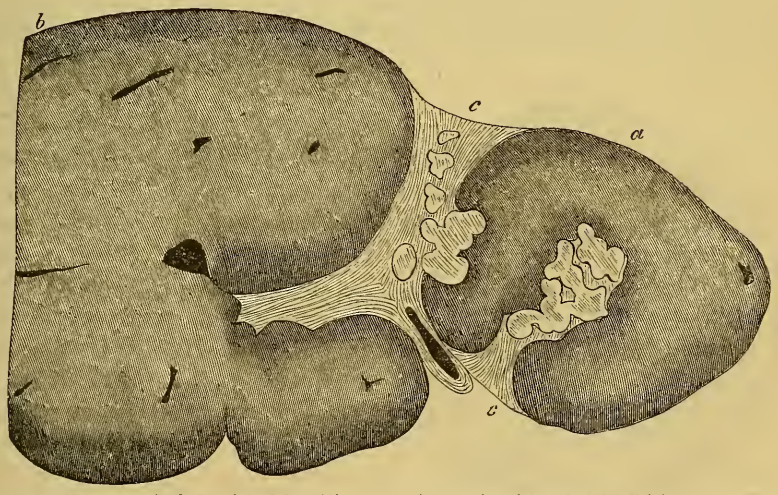
3. The less a new formation in itself contains the conditions of a perfect cure. Spontaneous cure is quite an eminent peculiarity of the inflammatory process. It, however, belongs to our delineation of a tumor, that, if left to itself, it continues growing, and if this does not occur, that it at least has a more persistent character. We may also formulate this position together with 1, as to say: inflammations do not arise spontaneously, but they heal spontaneously; tumors arise spontaneously, but they do not heal spontaneously. I am entirely conscious herewith to have expressed anything but an axiom. The case has frequently enough been observed, that pediculated tumors have of their own accord fallen off; that even the voluntary casting off of entire cancerous nodes has been observed.

If we ask after the natural grounds for this, I had almost said, instinctive distinction of the physician, we may at all events find such a one also in the circumstances of the histological development. The inflammatory new formation is essentially produced by the conflux of the mobile cells of the vascular connective tissue system at the spot of the irritation, hence the rapid appearance and almost traceless disappearance of the same; tumors in their development follow more the rules of physiological growth, hence the persistency, the organ-like character of their existence. If we reflect that an increased afflux of blood plays a principal part in inflammatory processes, we might term inflammations disturbances of nutrition, tumors disturbances of growth. Still, the question here is not universally of contradictory contrasts, only of contraries which are connected by several series of intermediate degrees. Thus one of these series proceeds from inflammation through the intermediate degrees of inflammatory hyperplasia and simple hyperplasia to those complicated hyperplasiæ which we call cancers; another proceeds from inflammation through the intermediate degree of specific inflammation to those more perfect imitations of tissue which we designate as sarcoma, enchondroma, myxoma, &c., and together term them histioid. The first of these transitions will especially meet us in the diseases of the skin, mucous membranes and glands; the second shall claim our attention at present.

§ 109. *The specific inflammatory processes* distinguish themselves from common inflammation, in that they yield, *instead of* the plastic exudation or *beside* it, certain products, which are characterized by special anatomical peculiarities. The latter are *typical* for each one of the processes, and are in general traced back to the particular quality of the inflammatory irritant. As such, in every case a *specific virus* is active, which either passes over to the organism by hereditary transmission, or is taken up by contagion, or finally is primarily formed in the organism.

§ 110. *Syphilis.* Constitutional syphilis maintains in the body a tendency to all that is called active hyperæmia, inflammation and inflammatory new formation. In the first stages of the disease they are more the superficial organs, the skin and mucous membranes, which are attacked; in the later stages, the deeper-lying organs are also laid hold of; in the anomalies of the osseous and nervous systems, of the liver and the testicles, we will particularly meet with syphilitic inflammations. Certain peculiarities of localization, of diffusion, and of the course indeed, distinguish all these inflammations; pre-eminently, however, does *a product* claim our attention, which is commonly yielded *beside* the more simple forms, seldom by itself alone; the so-called gumma syphiliticum (syphiloma, of Wagner). We may call the gumma a specific production of syphilis; the anatomical specificity, however, by no means lies

Fig 41.



Syphilis of Liver. *a.* Left, *b.* Right lobe of liver. *c c.* Connective tissue sheath, which penetrates the organ in the direction from the porta to the lig. suspensorium, and contains gummata. 2-1.

in a striking deviation of the tissue of the gumma from the known types of the inflammatory neoplasia; it rather lies in this, that within a larger depot of newly formed germinal tissue, a circumscribed, more or less globular node becomes defined, which separates itself from the remain-

ing surrounding germinal tissue by its further metamorphoses. Whilst the latter becomes fibrous connective tissue and a cicatrix, which distinguishes itself by an extraordinarily vigorous capacity of retraction (§ 93), here a mucoid metamorphosis of the basis-substance prevails, with the retention of the rounded cell-forms, at times with the formation of an anastomosing cellular net. The emphasis, however, does not rest upon the formation of mucoid tissue, for this evidently only presents one phase of the slow retrogression. The cells undergo fatty degeneration; in their stead arise round or stellate aggregations of fat-granules, which appear to be able to maintain themselves as such for a long time. Thus there result elastic, soft, yellowish-white, roundish nodes, which are imbedded in a depot of newly formed connective tissue, the specific syphilitic tumor, the node or gumma syphiliticum. Recent gummata may be brought to complete resorption by proper medication. Subsequently the node becomes caseous, while the surrounding connective tissue becomes a compact, cicatricial induration, which by its composition may effect deformities of the highest degree in the diseased organs. (Fig. 41.)

Whether it is justifiable already to designate the induration of the primary chancrous ulcer as gummous, I will not decide. The actual microscopic appearance (Fig. 42) is that of a small cellular infiltration of the connective tissue, which is noted not so much by the amount of the infiltrated cells, as that these cells *very uniformly* fill all the interstices, which exist upon the one side among the vessels, upon the other between the connective tissue fibres. By this means the swelling attains an elasticity, which appears to the palpating finger as hardness, while upon the other hand the vessels remain pervious, and the nutrition of the part is not interrupted. This immovable fixedness of the cellular infiltration at a determined point of the development, has undoubtedly something of a peculiarity, and reminds of the gumma tissue; however, whether similar indurations do not also occur without syphilis, can only then be said with certainty, when the histology of inflammatory indurations in general have been better investigated than at present.

FIG. 42.

Syphilitic induration. *a*. Vascular lumina. *b b*, and all clear places, are bundles of connective tissue, which are pressed asunder by a uniform, small-celled infiltrate. 1–300.

Annotation.—Biesiadecki seeks the ground of induration in a certain rigidity and dryness of the connective tissue fibres; former authors sought it in the

quality of the exudation (Ricord, plastic lymph ;) Michaelis, exudation flakes, &c.).

§ 111. The syphilitic new formation may at the same time serve as a model for the *leprous* disturbances and those caused by the *infection of glanders*. In these also besides the simple inflammatory processes there is produced a specific tumor, which persists for some time at the lowest grade of textural development, without change, in order at a later period either to suppurate and burst, or to wither by fatty degeneration (details under Diseases of Skin, in Special Part).

§ 112. *Typhus.* What distinguishes the typhus process in comparison to a simple acute inflammation, is the higher development, "approaching the epithelial," which the individual cells of the infiltrate experience. The acme of the typhous changes, as we will learn to know them more intimately in the "anomalies of mucous membranes" (Special Part), is termed *medullary infiltration.* If we investigate this infiltrate, we find cells, which are noted, in opposition to simple lymph-corpuscles, for the great amount of the protoplasm. The protoplasm of the lymph-corpuscles scarcely equals the space occupied by the contained nucleus, while here the protoplasm at least occupies as much, on an average, however, somewhat more space than the nucleus. The *typhus cell* represents the lowest grade, in a certain manner the first foundation of an epithelial development; it appears, however, that this intumescence of the protoplasm is wanting above all in the continuance and solidity of epithelial development, as the typhus cells only maintain themselves for a short time at this acme, in order then most speedily to fall into the retrogressive processes.

Annotation.—The lukæmic tumor stands very close to the typhus in a purely histological relation ; still it must not, without further consideration, be reckoned among pathological new formations (see chap. i, of Special Part).

§ 113. *Tubercle.* Tubercle represents a third type of specific inflammation. In speaking of fatty metamorphosis, I have already pointed out that the pathological anatomy of to-day does not understand by tubercle and tuberculization what was generally understood by these but little more than a decennium ago, namely, every yellowish-white, friable or smeary, in one word, cheesy mass, which is deposited at any point. We call tubercle *par excellence*, singly and alone, a certain originally gray, translucent, very compact nodule, which is seldom larger than a millet seed (miliary), but, however, is found in many, nay, in innumerable numbers together. The confusion of names and ideas which this distinction, already founded by Reinhard, but strictly carried out by Virchow, has occasioned, is not decreased by the circumstance that in fact cheesy inflammation, and miliary tuberculosis, very commonly occur side by side. The latest times have also brought very interesting disclosures upon this point; namely, according to a series

of investigations, which were started by Villemain, continued by Klebs and others, and brought to a certain conclusion by Cohnheim, the introduction of the "cheesy detritus" into the juices of the individual, results in the occurrence of "miliary tuberculosis." It is therewith a matter of indifference whether the cheesy material is transferred by inoculation, or whether it arises in the organism itself. Accordingly, the smallest particles of the cheesy detritus would have to be regarded as a poison, which, by direct irritation, occasions the tuberculous new formation of certain (we will soon see which) constituents of the tissues. This much is certain, that the formation of tubercle is the expression of a commenced dyscrasia, a corruption of the juices, which in many cases diffuses itself from a point throughout the organism; in others probably (?) is already congenital.

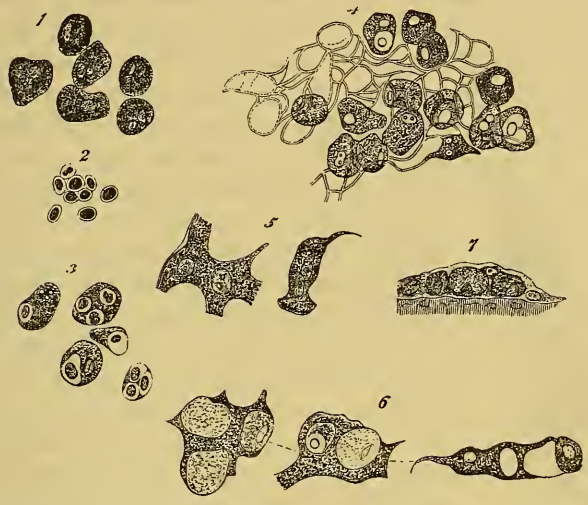
There is scarcely an organ of the body in which we do not occasionally meet with tubercles; the lungs, however, and the intestine are the localities by far most frequently visited. The extensive disturbances of an ulcerative kind, which the origin and especially the disintegration of tubercle produces, are treated of amply in the Special Part; here we can only speak of that which is the same everywhere; namely, the histology of the gray, miliary nodules, and that which we know of the histogeny of the same.

§ 114. If we lightly pull to pieces a miliary tubercle with needles, we will soon succeed in isolating its following minute constituents: Fig. 43, 1, larger cells of round, more frequently of rounded angular form, and their principal mass formed of a finely granulated, strongly refractive, probably very dense substance. The sharp contour, that is to say, the smooth surface by which the cell is inclosed externally, permits us to assume a cell-membrane, although such a one is not to be proven by means suitable for this purpose, as elevation by the addition of water, crushing, the perception of a double contour. In the majority there is present a relatively not large, single, right strongly shining round nucleus, which is mostly excentrically situated, but rarely so that it occasions a lateral protrusion at the cell-surface. In some there are found two, three and more of such nuclei, which doubtless were produced by a division of the originally single nucleus, inasmuch as the middle stages also of nuclear division, namely, elongated, slightly and more deeply constricted nuclei, are found. This nuclear division is to be regarded as a preparation for an endogenous development of small cells, exceedingly dissimilar to those just described, which, it is true, is not always carried out, so that even in the oldest tubercles we yet meet with polynucleated giant cells (Langhans).

Fig. 43, 2, presents the second form of cellular elements, as they may be isolated in greater numbers by tearing up a miliary tubercle. They have nothing in common with those previously mentioned, except the shining, darkly contoured nucleus. In all other parts they are distin-

guishable from them, and indeed at once by their far smaller size, which makes it possible for them in their endogenous origin for three or more to find room in the former; otherwise, however, by their protoplasm being translucent, homogeneous, and of a weak, refractive power, while just

Fig. 43.



Elements of miliary tubercle presented by teasing out. 1. The large tubercle-cells. 2. The small tubercle-cells. 3. Endogenous cell-formation. 4. Fine-meshed network from the interior of a miliary tubercle; the cells partly removed by brushing out. 5. Torn-off shreds of adventitia of a small cerebral vessel from the surroundings of a miliary tubercle. Division of nuclei at the inner surface of the adventitia. Finely granular protoplasm accumulated in a continuous layer of considerable thickness. 6. Formation of tubercle-cells. 7. The border of a small vessel, in whose adventitia is a development of tubercle-cells.

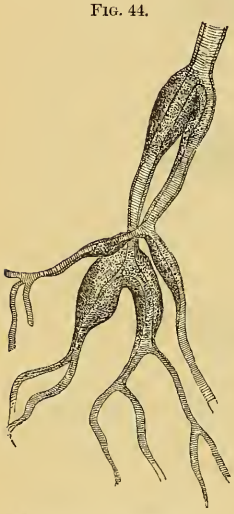
in reference to this we had to state a very characteristic behavior of the larger cells. The latter difference makes it possible for us to recognize the younger cells in the interior of their mother. The appearance of clear areas around the nuclear structures of the latter immediately marks the occurrence of endogenous development, which we regard as completed when the clear area has cut itself off by a sharp line from the surrounding, finely granulated, and strongly refractive substance of the mother cell. To this place belong the structures which have been very frequently observed, and are delineated in Fig. 43, 3.

These cells form the principal mass of miliary tubercle. After we have removed these by brushing and washing them out, that which remains is the finely-fibrous network, represented (Fig. 43, 4), to which we will return further below.

§ 115. Let us now pass on to satisfy the second of the principal questions; how are the miliary tubercles produced, how developed? We will expect from the beginning that in general the vascular and connective tissue systems must also be regarded as the origin of these new formations. There is, however, no connective tissue of the organism, as numerous observations have proven, so readily disposed to the forma-

tion of tubercle, as that which forms the adventitious coat of the smaller arteries and the transition vessels. If, for example, we observe a tuberculous pia mater, we will readily establish the phenomenon that the gray nodules from preference follow the more minute ramifications of the arteries. *They are placed as lateral projections, singly or united to small groups, upon the larger branches, while upon the more minute branches, and the almost capillary vessels, they present themselves as spindle-shaped varicosities, which occupy the whole circumference of the vessel.* (Fig. 44.) The largest among them show a whitish opacity, which begins in the centre and extends towards the periphery. This opacity is the expression of a fatty-granular metamorphosis, a cheesy modification, which of course represents the regular decomposition of the gray nodules. We take it, that it first attacks the oldest, the first produced, centrally lying cells, so that the sequence of changes, in point of time, which the miliary tubercle suffers, represents itself in space by the formation of concentric zones, of which the outer are formed by the tubercle-cells themselves, and the inner by the cheesy product of their transformation. If this view is correct, we would conversely have to seek for the development of the elements of the tubercle at the periphery of the little nodules.

Fig. 44.



Miliary tubercles adherent to a cerebral vessel.

The adventitious coat of the smaller cerebral vessels contains in regular arrangement very pale, flat, round nuclei, supplied with nucleoli. We can perceive these just as well upon loosened shreds of the membrane as upon the intact vessels. In the latter case they present themselves as staff-shaped structures imbedded between the outer contour of the vessel and its muscular coat. These nuclei are not naked, but lie in a small amount of finely granulated substance, which from preference is collected in the longitudinal direction of the vessel. A second contour, which surrounds the nuclei in a narrower or wider circumference, according to His, is made more distinct by treating with nitrate of silver, which assures the membrane the significance of a lymphatic *endothelial tube*, although a positive knowledge concerning its relations to the lymphatic system has not as yet been obtained. From this membrane, and indeed in its peculiarity as a lymphatic endothelium, the new formation proceeds. A considerable increase of the protoplasm surrounding the nuclei is the first act of our process. Simultaneously therewith is a multiplication of the nuclei by division. (Fig. 43, 5.) The nuclei move apart, and while in some the process of division may be repeated, in others a peculiar change occurs. Instead of the flattened, discoid

form, they assume one more globular, and in consequence become smaller; previously very pale and finely granular, they now become strongly refractive and homogeneous, in short, they assume the external appearance which we have stated as characteristic of the nuclei of the tubercle-cells. Simultaneously changes occur in the immediate surroundings of the nuclei. The protoplasm at that place becomes more strongly refractive, therefore probably denser, so that the nucleus appears surrounded by a feebly shining globule; at the border of this globule a line is exhibited, primarily ill-defined, but afterwards sharply prominent, and by this the whole structure is inclosed externally, the tubercle-cell complete in its essential parts. Fig. 43, 6, represents torn-off fragments of the adventitia from the limits of the growth of a small tubercle; in the thickened layer of the protoplasm we observe upon the one side elements ready formed or developing, upon the other spaces, which correspond to them in form and size; the cells have fallen out in the preparation. Fig. 43, 7, shows the border of a small vessel, in whose adventitia several tubercle-cells, and beside these nuclei, are imbedded.

In the commencement the formation of these cells is so sparse, that broad bridges of protoplasm remain standing between them, as we can also see in Fig. 43, 6. In the same measure that they become more abundant, are these bridges consumed; the newly formed elements touch and flatten each other somewhat. Then there remains but a small residue of protoplasm. This fills up that system of communicating spaces, which must always remain between contiguous globular structures,—a delicate network, in whose meshes the tubercle-cells are deposited. Fig. 43, 4, shows such a network, from which the cells have been partly removed by brushing. It consists of fine round filaments, which here and there spread out into small, three-cornered membranes. Where this is the case, two neighboring cells did not come into immediate contact, so that a thin, more extensive layer of protoplasm has remained between them. Nuclei are also yet found at individual points of union of the network. The whole resembles, as we observe, in a certain degree the more minute trabecular net which is found in the interior of lymphatic glands, so that already upon this ground, I could not formerly withstand the temptation of drawing a parallel between the tuberculous tissue upon the one side, and the tissue of the lymphatic glands upon the other, and in unison with another expert (Virchow) of straightway designating tubercle as a lymphoid or lymphomatous new formation. What, however, especially determined me to this comparison, was the similarity of tubercle with the formation of lymphatic sheaths around vessels, which I regard as the formative principle of lymphatic glandular substance. Meanwhile, however, it has been shown that the origin of miliary tubercle is by no means confined to the neighborhood of a bloodvessel, but only to the presence of an en-

dothelium. The endothelia of the lymph-vessels, the serous membranes, the bloodvessels (Schüppel), are the cells of the body by whose specific irritation is formed the most essential part of the miliary nodule, and from this only is derived the preference of miliary tubercle for this locality, that in fact the lymph-vessels also by preference take their course in the immediate surroundings, in the adventitious coat of the bloodvessels. (Compare with this the occurrence of tubercle upon serous membranes and in the lung, in the Special Part.)

4. *Histioid Tumors.*

§ 116. In the capability of the intermediary nutritive apparatus, of producing embryonal connective tissue at almost every point of the body, those higher histogenetic actions are also founded, which we in the more contracted meaning of the word, term excrescences, more correctly, however, histioid tumors. The interior continuity of their elementary parts is characteristic of histioid tumors. The majority of them consist generally only of one tissue; where, however, more tissues participate in the composition, they are never found in a differential apposition determined by sharp limits, as epithelium and connective tissue, but they organically pass into each other. This intimate continuity is declared also from the original interior uniformity of the foundation of the tumor, which in all cases is given by a certain amount of embryonal formative tissue. From this only by subsequent differentiation do the higher types of tissues proceed, and indeed, with a peculiar predilection the connective substances, the connective tissue itself with its varieties (fibroma and sarcoma) occurring in the inflammatory process, the cartilaginous tissue (chondroma), the osseous tissue (osteoma), the adipose tissue (lipoma), the mucoid tissue (myxoma), the higher anomalous tissues, the muscular tissue (myoma), and the nervous tissue (genuine neuroma) are more rarely produced. The manner of the production again is exactly the same as in fœtal development, that is to say, a certain amount of embryonal formative cells are converted into cartilage, bone, fat, and muscle-cells, while the remainder is converted into connective tissue, and beyond this the whole is divided by a sufficient vascularization into nutritive territories of the entire organism. Herewith upon the one hand the connection of the tissues among themselves is preserved, upon the other these with the organism; the new formation appears as an organ, although defectively built and unnecessary. Without the integrity of the body being attacked, colossal new formations often arise, which need only to be removed by the knife, in order to re-establish the previous status.

§ 117. What I last said, of course does not obtain without restriction. Unfortunately, there are also among the histioid tumors, a number to which we must ascribe a pernicious character, *malignitas*.

We call those tumors malignant, which are not only dangerous to the sufferer, but which threaten the life of the patient in a very decided way, in that they occasion a constitutional disease, which is incompatible with the salutary continuance of the entire nutrition. This general affection (cachexia) shows itself in a prostration of energies, diminution of the amount of blood, wateriness of the blood, emaciation, sallow complexion, profuse sweats, diarrhœas, hemorrhages, &c., to which the patient finally succumbs.

We have not been able up to the present time, to prove chemically or microscopically, the basis of this general affection. The question, how and by what means the malignant tumor induces the cachexy, likewise yet awaits to be answered. Those who regard the tumor as primarily a local affection, have a very intelligible interest in identifying the described marasmus, which is always secondary, with the constitutional disease producing the tumor of the humoral pathologists, and to make both taken together dependent upon an infectious activity of the malignant tumor. This representation interests us very peculiarly for this reason, because one at least is raised above all doubt that from the first tumor there goes out an incitation for the formation of new foci of the same kind of tumors, and gradually diffuses itself throughout the entire organism. In this diffusion of the formative irritant, the so-called infection, we distinguish three periods of time.

§ 118. In the first period this only extends to the immediate surrounding of the primary focus of the tumor. It constantly causes the formation of new foci at the periphery, which afterwards coalesce with the principal focus. Peripheric infiltration therefore (§ 69, 3) is the standing method of growth of malignant tumors. We must herewith accept, that the impulse to the new formation precedes for a space of time the new formation itself. This teaches us the so-called *capacity of recurrence* of malignant tumors. Let us suppose, namely, that, in order to check the disease, we have removed the whole tumor together with its zone of infiltration. The cut surface appeared to us after the operation to lie entirely in the sound tissues; nowhere could we perceive even but a trace of an already effected pathological proliferation; notwithstanding which, in most cases we would gain the sad experience, that just at the place from which we removed the first tumor, in the midst of just the tissues which at the time of the operation appeared to us yet entirely normal, after some time, there arises a new tumor of the same kind, the recurrence. We are therefore necessitated, if we do hold to the noncraseological standpoint, to the view, that for a time we cannot observe upon the tissues, whether or not they have already been affected by the formative irritant.

§ 119. The second stage of the diffusion of the pathological irritant of development is marked by the affection of those lymphatic glands, which take up the lymph of the region first diseased. That hereby

the question is about the transportation of an irritating substance in the lymphatic tract, can underlie no doubt. The question only is, What is transported? We might suppose cells. It is known that even still coarser particles, for example, insoluble coloring matter, which in tattooing is rubbed into the wounded skin, are taken up by the lymph-vessels, carried to the nearest lymphatic glands, and there deposited. May we, however, use this analogy with a clear conscience? After recent wounds the lymph-vessels gape and are then well fitted for taking up solid bodies; can we also suppose the same of the lymph-vessels in the surroundings of a tumor? The granules of coloring matter are either heavy or sharp or hard granules, which by virtue of one of these properties and assisted by rubbing the tattooed spot of skin can penetrate in any desired direction into the soft parenchyma of the body and up to the lymphatic tract; we cannot say the same of the cells. We must therefore reject *this* analogy, but of course not the possibility therewith, that the infection of lymphatic glands may depend upon the transportation of cells. On the contrary, thanks to the discovery that young cells in virtue of their amœboid movements can pass through the connective tissue in all directions, we no longer need this analogy, and with a probability bordering upon certainty we may refer the infection of the lymphatic glands and the whole body, to the elements of the tumor themselves, or such younger cells as have come into contact with them and were infected.

The affection of the lymphatic glands is regarded as a sign of the infectious capacity of a tumor, and in so far as an unfavorable phenomenon. Beside this the favorable circumstance brought forwards from various sides, that by the closure by swelling of the lymph-tracts in the lymphatic glands the injurious ferment is prevented from imparting itself to the remaining organism, disappears. At another place we will learn to know the detail of these closures by swelling and concede the great probability that the infection is *retarded* by this. Meanwhile there the question can only be of a temporary delay, not of a prevention.

§ 120. The third and last period of the propagation of the tumor teaches us, that notwithstanding the sacrifice of several lymphatic glands the whole organism has incurred the morbid disposition. We call the secondary occurrence of foci of tumors in other regions of the body *metastatic formations*. Whether we are justified in this nomenclature by this, that actual parts of the body are subsequently displaced from the original focus of the tumor and the affected lymphatic glands, is subject to the doubts already discussed above; in the blood, through which the transportation must yet incontestably take place, we have, as yet, in spite of zealous investigations, met with no elements of the tumor. Consequently it may be more advisable, for the time being,

in this case, also to continue in the opinion of a fermentative body in the blood.

The unbeliever in dyscrasia sees in the described irradiation of the developmental irritant, from the point of its first production, a palpable representation of the relations in which every malignant new formation stands to the organism. The advocate of the primary constitutional affection has, in opposition to him, a far more difficult position. Still he may insist that (1), the cachexy is not without further ceremony to be identified with the infection, and (2), that the developmental irritant for the primary tumor must be the same as for the secondary, consequently the difficulties are not at all diminished of explaining the production of the first, otherwise than by a pre-existing dyscrasia. For my own part, I do not find myself prompted to anticipate in any manner the coming decision of this question.

§ 121. After having acquainted ourselves with the clinical idea of malignity, let us ask whether there are anatomical characters, by which one may recognize malignant tumors before they have proven themselves such by recurrence and metastasis, and with Waldeyer we answer, that in general, the tumors are subject to metastasis so much the sooner as the soil is richer in blood and juices, upon which they have grown, and the greater the number of mobile cells is, which are either in the tumors or in their nearest surroundings. As for the rest, it will still constantly be our task to increase the treasure of our experience in this so exceedingly important province, by the accurate histological investigation of every tumor coming under our hands, and the most careful inquiries possible, of the future fate of the case. For the present we will content ourselves in specifying, as far as our present experience reaches, the grade of the malignity in every single species of tumor. It will therewith show itself, that before all others, "cancerous" new formations are distinguished by their malignity; that, however, a certain malignity also belongs to several histioid tumors (especially sarcomas and enchondromas), which is not always occasioned by a combination with cancer.

§ 122. Before we leave this important point, it is yet incumbent upon us to place in a correct light several ideas allied to malignity, which must not be mistaken for malignity. This obtains, first of all, for the danger to life in general. A tumor may very easily by its seat, its size, its weight, &c., cause not only the greatest inconvenience to an individual, but may also become the direct occasion of his death, without that on that account alone we should ascribe to it the character of a malignant tumor. A fibroid of the prostate closes the outlet of the urinary bladder, and thereby induces death from retention of urine; a fibroid of the uterus becomes dangerous to life from hemorrhage, but we are not therefore justified in calling the tumor malignant. The multiplicity also of tumor-formations may not in itself be regarded as malig-

nancy. When a formation of sarcoma occurs at the most various points of the skeleton, when foci of irruption are simultaneously found at the cranial covering, upon the tibia, upon the clavicle and the vertebral column, we may indeed conclude that the entire osseous system is diseased; we may conjecture a general disease, like as in skin-eruptions a disease of the entire integument; but it would be erroneous were we to identify this primary generalization of the new formation with that secondary one, which is peculiar to malignant tumors. Both are independent of each other.

a. *Sarcoma.*

§ 123. If one compare the color and constitution of any sarcoma with the constitution and color of muscular flesh, one can scarcely conceive how these tumors could receive the name of flesh-tumors (sarcoma, from σάρξ, flesh). The popular tongue, of course, calls entirely other things flesh besides muscle, above all it also calls granulations flesh; and if perhaps the name was given just in view of this mode of speech, we may also approve of the comparison, and indeed upon more than one ground. Sarcomas, namely, are in so far the most interesting of all histioid tumors, as they undoubtedly repeat that group of tissues which we have learned to know in inflammatory heteroplasia. We find here the round-celled formative tissue of granulations besides its lymphadenoid variety (caro luxurians), the spindle-cell tissue, and the compact fibrous connective tissue of cicatrices. As a rule, we meet several of these tissues together, in such a manner, however, that one of them forms the principal mass of the tumor, whilst the others exist in lesser amounts. The denomination is determined by the principal tissue, *a potiori fit denominatio.* Hence, we distinguish three principal categories of sarcomas, namely: round-celled sarcoma, spindle-celled sarcoma, and fibroma.

The secondary tissues are never co-ordinate to the principal tissue, but stand in relation to it, as either previous stages of its development or as proceeding from it by further metamorphoses. In these metamorphoses exactly the same sequence is maintained as in inflammatory new formation: the round-celled tissue (tissue of granulation) comes foremost; from it is produced in the first place the spindle-celled tissue, and afterward the fibrous tissue. We must not, however, conceal that the series of possibilities of development are not exhausted with the tissues of inflammatory new formation. Cartilaginous, mucoid, osseous, and adipose tissues occur as products of secondary transformation in sarcomas. They naturally always only form subordinate constituents, and give us occasion for constituting varieties; the tumors in which they predominate, or which are even exclusively formed by them, are the further classes of histioid heteroplasms, the myxomas, lipomas, enchondromas, and osteomas. We, however, recognize therein the inti-

mate connection of the collective histioid tumors, and our complete justification in uniting them into one group.

The origin and growth of sarcomas is indeed different in the individual forms; meanwhile we may express, that in general growth by infiltration of the surrounding parts, the so-called peripheric growth, and backward, and therefore central growth, enlargement by interior apposition, occupy the foreground. A peculiarly central growth pertains to fibromas, one more peripheric to the medullary round-celled sarcomas; the spindle-celled sarcomas here, as also in other points, especially in reference to malignancy, maintain the medium between both.

We might set up a large series of kinds of sarcoma and inferior kinds, if we would consider all the modifications which are conditioned particularly by the situation of the tumor. Meanwhile, I regard it more advisable to mention here only a small number of typical recurring forms, to reserve, however, the special sarcomas of individual organs, and systems, for the Special Part. In that place I include the ossifying sarcoma of the periosteum, and the giant-celled sarcoma of the medulla of bone, the glioma of the nervous central organs, the cysto-sarcomas of the various glands, &c. All the finer gradations of the principal forms are also unconsidered here; it has appeared to me as though almost every tumor exhibited something of this kind, and I might assert *that exactly the same tumor can only be again found at exactly the same point of the body.*

Round-celled Sarcoma.

§ 124. 1. The *granulation-like* round-celled sarcoma (sarcoma globocellulare simplex), in its textural and structural relations is allied to the model of the tissue of granulations. To the naked eye, a yellowish or reddish, thoroughly homogeneous, elastically soft mass, at times extraordinarily like the roe of fishes, presents itself from the cut surface; by scraping with a knife-blade, we can obtain a scanty amount of juice, which is almost entirely clear, or contains but few cells. The cells are small, round, and contain comparatively large nuclei, of sharp contour, and provided with nucleoli. The protoplasm, as a rule, is present only in small amount, therewith entirely naked; we must have recourse to hardening the tumor and coloring it with carmine, in order to make it generally distinct, and to convince ourselves that a cell-body actually belongs to each of the apparently free nuclei.*

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* Virchow is disposed to ascribe the phenomenon of the apparently free nuclei to a greater fragility of the cell-bodies, and with this opportunity makes the observation, which is very encouraging to practical histology (Tumors, page 204): "This fragility of the cells is so striking, that for a long time past in every case where a recently investigated tumor appears to consist predominantly of large, naked nuclei, with large, shining nucleoli, until further investigation I suppose it to be a sarcoma."

The structure of round-celled sarcoma deviates only in a quantitative relation from the structure of granulations. The vessels in part are wider, thicker walled; where these, however, break up into capillaries, they are just as delicate, frequently only built of a simple cell-layer, such as we saw in the vessels of granulations. The interspaces between the vessels are everywhere uniformly filled by the round cells and the scanty, soft, and formless basis-substance of the germinal tissue. In rare cases one observes a higher organization of the whole, which reminds of the papillosities of granulations, namely, a radiated striation and a decided disposition of the mass of the tumor for cleaving in radiating directions. We will more intimately speak of this fasciculated round-celled sarcoma, which, by preference, proceeds from periosteum, at the proper time, as sarcoma ossificum.

The simple round-celled sarcoma proceeds most frequently from connective tissue membranes: the periosteum and the sheaths of the nerve-centres are its favorite situations; meanwhile we must also be prepared occasionally to meet it in other parts, especially upon the outer skin, upon mucous and serous membranes, even in glands. The simple round-celled sarcoma is closely allied to the small-celled spindle-celled sarcoma, and through this to fibroma, and manifoldly goes over into it. To this corresponds the relative benignity, which marks just these tumors above all other round-celled sarcomas.

§ 125. 2. *The lymphatic gland-like round-celled sarcoma* (sarcoma lymphadenoides, molle) owes its more limited consistence pre-eminently to the circumstance that its cellular elements are less intimately and immediately combined with each other than the cells of ordinary tissue of granulations. We can here obtain with facility, by scraping the cut surface, a juice with an abundance of cells, whose microscopic observation shows these latter to be round cells, which are distinguished by large, oval, slightly refractive nuclei, provided with one dot-like nucleolus. If we harden the tumor and tease out a thin section of it, we find between the cells a delicate intercellular network, which strongly reminds of the reticulum of the lymphatic follicles, the intestinal mucous membrane and caro luxurians (proud flesh). (Fig. 45.) This network spreads itself among the wide, thin-walled capillaries and gives the whole structure a certain support, while on the other

Fig. 45.

Round-celled sarcoma. *a*. Vascular lumina. *b*. Parenchyma partly brushed out, so that the hardened basis-substance appears as an elegant network. 1-300.

hand it permits the accumulation of an abundance of fluid beside the cells, and favors the isolation of the latter.

The sarcoma under consideration most frequently proceeds from the subcutaneous, subfascial, and intermuscular connective tissue of the thigh. In the next place, the lymphatic glands must be designated as its preferred situation. Here, however, the peculiar case occurs, that the uniformity of structure could cause anatomists to regard sarcoma as a hyperplasia, though ever so monstrous, of lymphatic glands, while yet the clinical character (malignancy of high degree) exhibits a complete uniformity with the soft sarcoma. (See Lymphatic Glands.)

There are several varieties of lymphadenoid sarcomas. The *lipomatous sarcoma* (sarcoma lipomatodes) shows the peculiarity that its cells are transformed into fat-cells by the infiltration of fat. This transformation always affects only a limited number of the existing elements; as, however, the sheen and size which the single cells attain deceive the eye, it may readily have the appearance as though at least the great majority of the sarcoma-cells had become fat-cells. Of any considerable similarity to genuine adipose tissue there can, nevertheless, not a word be said; the want of uniformity of infiltration and the circumstance that we find very small and very large fat-cells confusedly intermingled and never united into little clusters, excludes all mistake for lipoma.

The *mucoid sarcoma* (sarcoma myxomatodes). It is a tolerably frequent occurrence to see here and there small portions of mucoid tissue in round-celled sarcomas. A translucent gelatinously trembling consistency betrays places of this kind already to the naked eye; the microscope, as a rule, exhibits an abundant quantity of mucoid basis-substance, with numerous round, non-anastomosing cells imbedded. The mucoid softening of the basis-substance may properly be regarded as a secondary metamorphosis, to which all round-celled sarcomas are disposed. In as far, however, as this begins at an early period and extends over greater sections of a tumor, is the name "mucoid sarcoma" justifiable. Nay, the mucoid tissue may so predominate, that we might be tempted to think of a completely mucoid tumor, a myxoma, if yet some unchanged places, especially, however, the young developments at the periphery of the tumor, and striking metastases, did not place its sarcomatous nature beyond doubt. An exceedingly rapid growth, which is said to pertain to mucoid sarcomas, may be illusively presented by this, that the mucous, because of its extraordinary capacity for swelling up, occupies a far larger space than does the scanty basis-substance of the sarcoma.

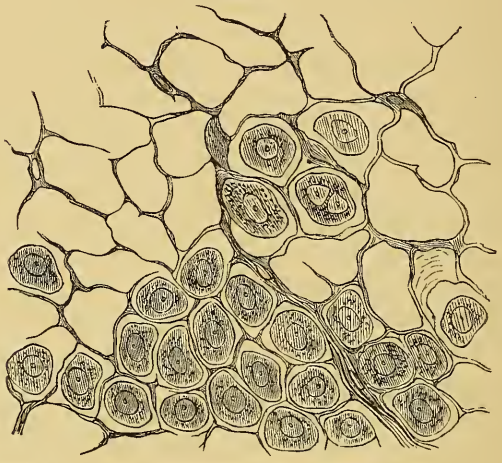
Mucoid metamorphosis and fatty infiltration not infrequently occur side by side, and just these tumors may attain a colossal volume.

Beside the loose connective tissue of the extremities, the subperitoneal connective tissue is also a favorite seat of mucoid sarcoma.

The *large-celled, round-celled sarcoma* shows us an almost epithelial

structure of cells beside a correspondingly large-meshed intercellular net. (Fig. 46.) This tumor is very soft, like the white matter of the brain, and is, therefore, easily mistaken for the following species.

FIG. 46.



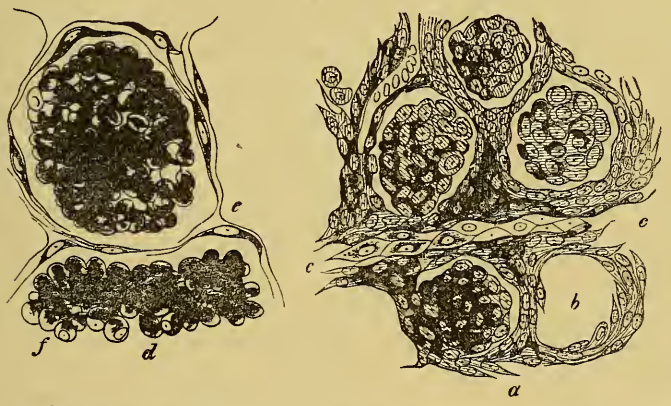
The large-celled, round-celled sarcoma. 1–300. After Billroth.

3. The *alveolar round-celled sarcoma*, Billroth (sarcoma medullare, carcinomatodes) represents a further advance in the independence of the cells, which, upon the one hand, may be compared to the suppuration of an inflammatory texture; upon the other, however, reminds of that sharply defined opposition between connective tissue parts and the cellular apparatus, which we find in cancer. Characteristic of these forms is the occurrence of roundish balls of cells, which are no longer connected together by a proper basis-substance, but are taken up by a correspondingly large cleft in the continuity of connective tissue, like the pus-corpuscles in a small abscess. It is not said therewith, that these cells are also externally like pus-corpuscles; they are rather considerably larger, have vesicular, round nuclei, with bright nucleoli; and in this respect they approach more nearly to the epithelial condition, which, in individual cases, they even deceptively imitate. I esteem this of more consequence than is conceded to me at many hands, because I straightway pronounce the formation as a carcinomatous degeneration of the sarcoma (sarcoma carcinomatodes). According to my judgment, we must no longer hold to the opinion that the carcinomatous structure, which presents the clinical characters of carcinoma, exclusively proceeds from the preformed division between connective tissue and epithelium. "Stroma" and "cellular deposition" may also be produced in other ways, and "epithelioid" is not yet "epithelium," although one might form conjectures as to why those cells, which loosen themselves in a more organic manner, slowly, and not suddenly, like pus-corpuscles, from the mother-soil, always show this tendency to a more

epithelial development. For this is just the difference between an actual suppuration and this imitation, that at the present time we have yet no right to regard the cell-balls mentioned as elements completely separated from the nutrition of the body. Their longer continuance without fatty degeneration gives us security for this.

Sarcoma carcinomatodes occurs at the most various points of the intermediary nutritive apparatus, most frequently in the medulla of bone, in the eye, in the subcutaneous tissues. An exceedingly malignant variety of this, distinguished by the pigment contained in its cells, is the so-called *pigmentary cancer* (sarcoma alveolare pigmentatum). The external nature and the preliminary diagnosis is determined upon the one hand by the great softness of the tumor, upon the other by the dark discoloration. If we examine it microscopically, we find, besides the alveolar structure, which appears as the summit of development (Fig. 47), more or lesser extended parts, which bring to our view former

Fig. 47.



Alveolar round-celled sarcoma, pigmented. *b.* Alveolus from which the ball of round cells has fallen out. *c.* Vessel with pigmented endothelia. *d.* Pigmented round cells. *e.* Spindle-cells forming a stroma.

stages of the development of the tumor. The most common is an infiltration of the connective tissue with pigmented round cells, which is directly transformed by depot-like accumulations into the medullary formation. In other cases a declared sarcomatous structure, and indeed more frequently the spindle-celled than the round-celled, has evidently existed for some time, ere it came to the formation of the characteristic cell-balls. Hence we are led to the opinion, that the melanoses in general are closely allied to each other, a view which we will follow more closely upon the occasion of speaking of the commonly called pigmentary sarcoma.

Spindle-celled Sarcoma.

§ 126. 4. The *small-celled spindle-celled sarcoma* (s. fusocellulare durum) occupies the same position among the spindle-celled sarcomas

that the granulation-like sarcoma does among the round-celled ones. It deviates the least from the model of inflammatory new formations, because it very accurately copies after that spindle-celled tissue of recent cicatrices, which represents the regular intermediate degree between the tissue of granulation and the tissue of cicatrices. The characteristic textural element is a short and narrow spindle-cell with an elongated roundish nucleus, with or without nucleoli. The protoplasm of the cell is finely granular, most dense in the neighborhood of the nucleus; a limitary membrane is nowhere to be perceived with certainty; such a one is certainly wanting in the smaller cells.

In the mass of the tumor, the spindle-cells are very regularly fitted together in such manner that the pointed angle, which remains between the tapering ends of two elements lying side by side, is filled out by the tapering end of a third, which is respectively situated behind and before them. There is nothing to be seen of the intermediate substance; in any event there is no more present than a tissue of granulation; but this minimum quantity, which properly is only a formless, sticky cell-cement, must also not be wanting in the spindle-celled tissue. By its aid and by virtue of the just-mentioned harmonious arrange ment arise lines of cells; there are formed larger and smaller bundles, which furnish the next higher structural element of the spindle-celled sarcoma. Its arrangement in the rarest cases is radiated, so that united bundles go out from a centrally located point; more frequently even a greater number of such points of departure are given, and the various systems of bundles interweave in the various directions determined by the location of these points; generally, however, we are not able to specify any positive principle, according to which the blending of the bundles into a whole is accomplished, and find upon every transverse section (Fig. 48) bundles which are divided longitudinally, others transversely, and yet others in a more or less oblique direction. The determining influence for the course of the cell-rows has been sought in the course of the vessels, yet incorrectly; for although we never fail to find in the larger fasciculi of the tumor a larger vessel running in the same direction, yet this is only the case in the larger fasciculi. More remotely the vessels break up entirely retiform as in other parenchymas, breaking through the cell-rows in all imaginable directions. Withal, the collective vessels, even the larger of a sarcoma, have almost no proper walls, and

Fig. 48.

Spindle-celled sarcoma. Gaping vascular lumina. The cell lines are divided partly longitudinally, partly transversely. 1–300.

present themselves upon transverse sections of a hardened preparation like excavated canals and perforations.

The small-celled spindle-celled sarcoma has a preference for the connective-tissue membranes, fasciæ, vascular and nervous sheaths, the subcutaneous and submucous connective tissues, in short, it has the same seats as the fibromas; it is also often enough (for example, upon the uterus) found beside fibromas. In addition, we can point out in every small-celled spindle-celled sarcoma such places, where the spindle-celled tissue is transformed into fibrous connective tissue; there are tumors which are composed half of the one and half of the other, so that a relationship close to an identity of these tumors must be accepted.

Fig. 49.

Large-celled spindle-celled sarcoma. After Virchow.

5. *The large-celled spindle-celled sarcoma* is anything but simply a variety of the small-celled. The important point in which it is distinguished from the latter, is the excessive development which falls to the lot of the cells in opposition to all the other constituents. The spindle-cells may attain the very respectable thickness of 0.015‴, and so enormous a length, that the two ends in magnifying by 200 diameters are separated by the breadth of three fields of the microscope. The cell is thickest where the large, elongated roundish nucleus, supplied with bright nucleoli, is situated. The protoplasm in the neighborhood of the nucleus is finely granular and soft, more homogeneous towards the circumference; a cell-membrane cannot be shown, only the processes occasionally show so considerable a firmness and so strong a refractive power, that they must be regarded as protoplasm having become rigid. As to the number of processes of the spindle-cell, two constitute the rule; three or more exceptionally occur, which bestows upon the cell the character of a stellate-cell. (Virchow.)

In real typical spindle-celled sarcomas, these cells combine into larger strands, leaves, and fasciculi, which either radiate in straight lines towards all directions from a common basis (radiary sarcoma, foliated sarcoma), or they manifoldly interweave (trabecular sarcoma). These

tumors may attain a very considerable circumference, without a further modification of their texture or structure occurring. The enormous growth of the cells occurs in a certain measure vicariously for the seasonable development of fibrous intercellular substance, and if with Max Schultze we wish to see in the latter only transformed protoplasm, we have here before us the case of a massively produced, but not applied building material.

The large-celled spindle-celled sarcomas proceed from fasciæ and membranes, rarely from the interstitial tissues of glandular organs. They are of limited malignancy, and are, as a rule, once for all removed by a seasonable extirpation. Of course they must not be mistaken for radiating cancers and medullary sarcomas.

As an individual variety of the large-celled spindle-celled sarcoma, there is a tumor to be designated, which is observed upon the skin of the cheek, and essentially depends upon a combination of the round-celled with the spindle-celled type. Broad fibrous lines of spindle-shaped cells go out from one or more points; where these fibrous lines diverge the round-celled tissue fills out the spaces. I have represented this arrangement in Fig. 50. One sees there, how the colossal spindle-cells with their long bodies and still longer processes bound elongated meshes, in which the round-cells lie imbedded.

Fig. 50.

Large-celled sarcoma. A place at which colossal spindle-cells arranged parallel are mixed with round cells. *a*. Round cells. *b*. Vessel. 1–300.

6. The *pigmentary sarcoma* (s. melanodes) by far most frequently proceeds from the choroid coat of the eye, then from the outer integument: both points at which normally a certain pigmentary infiltration of the cellular elements is already observed. We comprehend this phenomenon, as a rule, in such manner, that in the pathological new formation a vital property of those cells is maintained, from which this proceeds. Yet precaution is to be recommended here. The metastatic foci of tumors, also, which are not rare in the pronounced malignity of pigmentary sarcoma, show the same disposition to pigmentary infiltration, although they develop at points where there is not a word to be said of physiological pigmentation. This transfer of an entirely local peculiarity to the secondary tumors has been used as well for as against this opinion. For it, by those who believe that the metastasis is accomplished by the transfer of bodily constituents from the primary foci of development to another spot; against it, by those who believe in a constitutional disease-producing tumor, which wherever it produces tumors, produces black tumors.

I regard it as imperative in this case to keep two things as sharply

defined as possible: 1, the incitation of metastasis by emigrant cells of the primary tumor; and 2, the pigmentation of the secondary tumor. As to 1, I point to the suppositions and doubts expressed in § 120; as to 2, we must constantly remember that all the cells of a melanotic tumor are colorless in their youth. That these are the direct offspring of the emigrant cells of the primary tumor, no one will assert; they are rather undoubtedly local products, and if they yet become colored, we must necessarily refer this coloring to a constitutional disposition, which is independent of the location of the primary tumor. With this the etiological experiences also agree, which point out at least for the outer skin a superfluous formation of pigment as the predisposing cause. This asserts itself either in the production of black warts, which may directly degenerate to melanotic sarcomas, or into now a more diffused, now a more circumscribed brown and black spotting of the skin. The peculiar predisposition of creatures not at all pigmented, as for example, the white horse, to sarcoma melanodes, gives more the impression of a vicarious deposition of pigment, accumulating at one point, and therefore combined with a certain irritation of the tissues.

In all pigmentary tumors the cells are the exclusive carriers of the pigment. We have devoted a particular consideration to the histological detail of pigmentary infiltration in the first principal section, and may now content ourselves with reference to the §§ concerned. At the same place I referred for the case of pigmented tumors the opinion of a pigmentary formation, derived only from hemorrhages, and for this presented the view, that the question here is about the taking up of the coloring matter of the blood from the blood. What inclines me by preference to this assertion, leaving out of consideration the deficient proof of a hemorrhagic production, is an observation upon the first origin of pigment in such tumors, as had existed for some time as simple medullary sarcomas, then to be transformed into melanotic tumors, and as such to form their recurrences and metastases. We can here not infrequently convince ourselves, that the first traces of pigmentary infiltration were visible at the *epithelia of the vessels.* Can this be interpreted otherwise, than that the epithelia have taken up the diffused coloring matter from the blood? that it has been condensed in them and precipitated in granular form? And when afterwards entirely the same formation of pigment shows itself beside the vessels, when finally it occurs in the whole parenchyma of the tumor, according to my judgment we may not doubt that it is also accomplished here in the same manner as upon the epithelia of the vessels, by taking up the diffused coloring matter from the blood.

§ 127. In view of the discussed general pathological relations of melanotic tumors, their anatomical position falls more into the background. That which is commonly called pigmentary cancer, has been already described above (§ 125) as round-celled alveolar or medullary

pigmentary sarcoma. The remaining pigmentary tumors, as a rule, belong to the spindle-celled sarcomas. These are generally of more compact consistency, and of foliated or fasciculated arrangement. In the decided tendency to form superficial elevations, tuberosities, and fungi, which otherwise is also peculiar to round-celled sarcoma, a contrast to be well noticed, is expressed against destructive carcinomas. In regard to color, the above-mentioned principle is the measure of the pigmentless youthful state of the constituent elements. There are pigmentary sarcomas of considerable size, which first of all only betray their true character by a black and brown striation; a spotted or dappled appearance. The deep brownish-black sepia color only represents the highest degree of pigmentary infiltration.

A fibromatous constitution, according to Virchow, only pertains to the above-mentioned black fungosities of the white horse, which also distinguish themselves by their benignity essentially from all other constantly malignant melanosarcomas.

Fibrous Sarcoma.

§ 128. 7. *The fibroids.*—I cannot separate the fibroma from the sarcomas. With the same correctness with which we sought the paradigm of round and spindle-celled sarcomas in the round and spindle-celled tissues of the inflammatory new-formation, will we seek and find the model of fibromatous texture in the completed cicatricial tissue.

Fig. 51.

Transverse section of a fibroma of uterus. 1–300. *a.* Isolated cellular elements. *b.* An unravelled fasciculus of the fibroma. 1–500.

The common fibroid (desmoid) consists of a fibrous, reddish-white, tightly elastic, and so dense, compact, even hard tumor, that in cutting it, it creaks under the knife. The textural elements are those of cicatricial tissue. If we tear off a minute fibril from the cut surface and pull it to pieces, we are astonished at the enormous volume which the fibril assumes, that is to say, the enormous number of more minute fibrillæ into which it may be broken up. The microscope, however, tells us that each of these smaller fibrils is also yet a complication of very delicate, minutest fibrils, only marked by a single but sharply defined line. (Fig. 51, *b.*) Like as a well-braided tress occupies far less space than a dishevelled braid of hair,

although both contain the same amount of hair, so we must also here represent to ourselves, that in the fibroma the fine and the finest fibrils are extraordinarily closely pressed together, until they are loosened by our needles, and then occupy an astonishing amount of space.

Between the fibrils, which are formed of glue-yielding substance, and have the significance of a fibrous intercellular substance, the cells are visible (Fig. 51, *b*), as a rule, small, oval structures, with shining nuclei. I have represented these elements strongly magnified in Fig. 51, *a*, more particularly because Virchow has been induced, by the great similarity of these with smooth muscular fibre, to set up a fibro-muscular tumor as a particular variety of fibroma. I am very far from wishing to bring this resemblance into question; a determination of the histological boundary between spindle-cells and smooth muscular fibres is in fact a very precarious thing; meanwhile, I regard it as conformable, to continue for the present the comparison of sarcoma with the inflammatory new formation, the sarcoma-spindles with the cicatricial spindles. By this we obtain a useful foundation for understanding the collective structural elements occurring in fibroids; for what has been hitherto described, only constitutes the principal mass of the tumor; beside which we find, 1, rows of spindle-cells, which run through the tumor in various directions; 2, roundish foci of germinal tissue, which are here and there sprinkled into the continuity of the fibres. I regard both as transition formations, from which the fibrous tissue is developed in entirely the same way as the cicatrix from the germinal and spindle-celled tissues. I found numerous fibromas upon a uterus, of which the larger principally consisted of fibrous tissue, the smaller ones almost only of spindle-celled tissue.

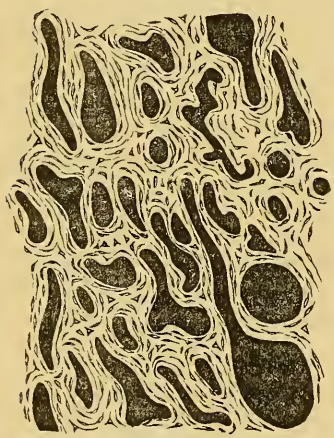
The cut surface of the tumor deserves an especial consideration. The intimate *intertwining and interweaving of the fibrous lines* bestows upon it a peculiar impress. Microscopic examination (Fig. 51) particularizes the appearance, which the naked eye perceives, without acquainting us with the cause of the arrangement. For the arrangement of the mass of some fibromas the circumstance appears of importance, that the new formation particularly localizes itself upon the vessels and nerves of a part. Thus Billroth has described a fibroid of the eyelids, and given it to me for subsequent investigation, which consists of numerous sausage-like cylinders, in whose axes the remains of small nerve-trunks are distinctly visible. Based upon this, Czerny has lately separated a particular group of sarcomas as "plexiform tumors," because beside the nerve-branches he also proclaimed the ramification of the vessels as the occasional cause of these striking structural relations. It must be marked as the most striking formation belonging to this class, when the collective vessels of a tumor, in itself myxomatous, are surrounded by a relatively thick sheath, upon which we can throughout recognize a round-celled nature. An influence of

the course of the vessels upon the course of the fibrous bundles cannot be established in ordinary fibromas. The view is much more probable to me, that in the peculiarly central growth of the fibroma the new tumor-mass is inserted between the existing fibrous rows, pressing them asunder, and thus the incomplete stratified structure of the tumor is conditioned by repeated separation of these fibres, and not by superposition.

Fibroma correctly ranks as one of the benign new formations. We will learn to know the uterus as its preferred seat, and at the same time a series of interesting modifications of the anatomical appearance just sketched.

§ 129. 8. *The cavernous tumor.*—The corpus cavernosum penis gives in its structure, as supposed to be known, the physiological paradigm for the cavernous tumor. We here see the same network of shining, white connective-tissue trabeculæ, which like a sponge contains the blood in wide meshes, visible even to the naked eye. (Fig. 52.) We find the same great elasticity of the network, which makes possible periodically a greater or lesser dilatation with blood, and thereby a corresponding increase and decrease of the new formation. I have at length, by a series of investigations specially directed to this point, convinced myself that the production of the erectile or spongy tissues is the same in both cases.

Fig. 52.



The substance of the cavernous tumor in full development. 1-300. From a cavernous tumor of orbit.

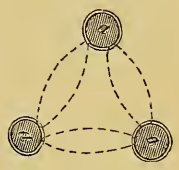
I term this production of the cavernous tumor as the cavernous metamorphosis; for I have come to this conclusion, which might otherwise have been expected from the beginning, that every tissue supplied with bloodvessels is capable of transformation into erectile tissue. The cavernous metamorphosis is in so far to be regarded as a secondary result; upon the other hand, however, the histological process by which the transformation is brought about, is so decidedly a process of new formation, that no doubt can exist concerning the ranking of the cavernous metamorphoses among the histioid tumors. Because however this process exhibits entirely the same transformation of tissues, which lies at the foundation of the formation of fibroma, and because for that very reason the mass of the tumor freed of blood looks just like a fibroid, I think that I should treat of the cavernous tumors at this and at no other place.

§ 130. The mechanism of the cavernous tumor is difficult to discern. When a cavity is reticulated by a network or trabeculæ, the part of

this cavity also, which the network does not fill out, will constantly have the form of a net- or trabecular-work. If we distinguish between network and parenchyma, then each of the two meshes or networks is a parenchyma for the other. The transverse section of each trabecula of one of the networks is at the same time the greatest circumference of a parenchymatous island of the other and *vice versâ*. Fibres, which transversely surround the trabeculæ of one of the networks, would by shortening diminish the parenchymatous islands of the other, whose trabeculæ shorten and thicken. Fibres, which are longitudinally applied to the trabeculæ of the one network, would by their shortening enlarge the parenchymatous islands of the other and attenuate its trabeculæ. We may also divide the whole mass of a trabecular work into proper trabecular substance and tetrahedric or cubic connecting pieces, which belong in common to three or four trabeculæ meeting together. If the trabeculæ of one network become longer and thinner, the whole bulk of both remaining unchanged, upon the one side the proper connecting pieces must necessarily diminish in size; upon the other the trabeculæ of the second network become shorter and thicker; the connecting pieces of this, however, become larger.

If we have made ourselves familiar with these certainly somewhat difficult stereometric representations, we will attain to a very easy apprehension of the mechanism of the cavernous metamorphosis. It is certainly not easy to conceive an ordinary parenchyma penetrated by a vascular network as a network with round trabeculæ. We will most readily succeed if we conceive several vessels in a transverse section (Fig. 53, *a*), then are the circles indicated by the dotted lines, which we at the same time may imagine as the lines of contact of the capillary arches from *a* to *a*, the transverse sections of the parenchymatous trabeculæ. The network of the bloodvessels consequently has long trabeculæ and small connecting pieces; the network of the parenchyma very thick, but taperingly short trabeculæ and colossal connecting pieces.

Fig. 53.

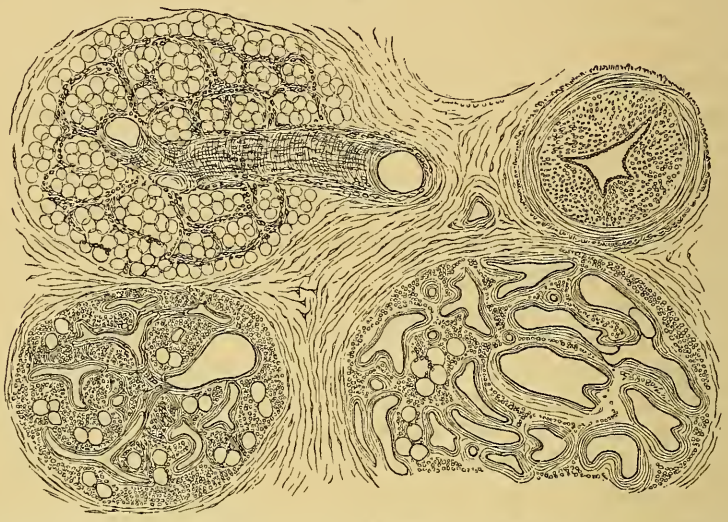


The cavernous metamorphosis then is produced, in that at a circumscribed portion of an organ the transformation of germinal tissue into spindle-cell and fibrous connective-tissue is developed along the vascular walls; from this a retraction vertical to the axis of the parenchymatous trabeculæ, in the direction of the dotted lines (Fig. 53), follows, elongating these, diminishing the connecting pieces, and, as a necessary consequence thereof, dilating the vascular tract; that is to say, shortening the trabeculæ and enlarging the points of intersection of the network, which is formed by the blood.

§ 131. Fig. 54 may serve as illustrating what has been said, which represents the production of the cavernous tumor from adipose tissue. We observe three clusters of fat-cells, which present to us just as many

stages of the cavernous metamorphosis. The cluster least changed shows us the well-known capillary net, which here does not become distinct by injection, but because the vascular walls are covered with numberless round connective tissue cells. That these cells are migratory

Fig. 54.



The development of the cavernous tumor in adipose tissue. Three fat-clusters, representing side by side the stages of development; above to the right the transverse section of an artery. From the panniculus adiposus of the cheek. 1–300.

colorless blood-corpuscles from the blood is very probable, so that in this respect the process presents itself as an exceedingly slow inflammatory process confined to the nearest surroundings of the vessels. In the contiguous cluster it has already progressed so far that only single intact fat-cells yet remain; all the remainder is converted into germinal tissue. The transformation of the germinal tissue into fibrous connective tissue begins along the vessels; the lumina gape, especially at the points of intersection.

The third cluster shows us the erectile tissue in perfection; compare (Fig. 52): the former parenchyma is converted into a trabecular-work, to which the blood-spaces stand in a similar quantitative proportion, as the parenchyma to the vascular net in the least changed cluster.

The cavernous tumor is consequently produced by a fibroid degeneration of the capillary section of the vascular tract; it is unjustifiable to derive it from an ectasy of the veins or arteries. It is not intended to say by this that the larger afferent and efferent vessels of the degenerating district remain unchanged. An enormous thickening of the walls, a more tortuous course, and also an extensibility, such as is normally found upon no vessels except the helicine arteries, especially denote the arterial bloodvessels of the cavernous tumor. Our delineation likewise gives explanation concerning their relations to the blood-spaces of the erectile tissue. They open into these with just as many

outlets as there formerly existed capillaries. The amount of blood contained in the erectile tissue is directly dependent upon the degree of its contraction. In our preparation we see, beside the three degenerated fat-cell clusters, the transverse section of a larger artery. The vessel is strongly contracted; the very much thickened intima has thrown itself into four longitudinal folds; the lumen is small, fissured. We can conceive how a further contraction of the circular fibrous layer must make it entirely disappear. I can give the assurance, however, that this same artery in the state of its greatest dilatation would perhaps occupy twelvefold its present lumen.

The cavernous tumor arises by preference in the adipose layers of the organism. I have once seen the cavernous metamorphosis in the interior of a lipoma. It is possible, as was said, in every organ of the body which has bloodvessels, therefore in all with exception of cartilage, the cornea, and the vitreous humor. There is not infrequently a multiple occurrence of this form of tumor. There are cases on record, where beside a cavernous tumor of the outer skin, there existed cavernous tumors in the muscles and bones.

We may also speak of a malignancy of the cavernous tumor. Yet this malignancy regularly depends upon a distinctly pronounced complication with melanotic sarcoma, whose nodules, and nodes develop in the trabeculæ of the cavernous tumor.

§ 132. The cavernous metamorphosis of fibrous sarcoma itself is of peculiar interest. Billroth was the first to speak of a "cavernous fibroid." I have already remarked in spindle-celled sarcoma, that the vessels of these tumors were almost entirely deprived of proper walls, and that a gaping of the lumina resulted therefrom upon a transverse section. The same obtains of fibromas. Fibromas, with peculiarly wide, gaping, vascular mouths, may have an actually spongy appearance. Billroth found that the peripherally growing polyps of the posterior nares are especially apt to exhibit the cavernous nature, and after my own investigation I can state that the production of the cavernous tissue here depends entirely upon the same histological process, which I have just described more in detail. Fig. 55 gives a vertical section through the periphery of a cavernous fibroid. Externally a vascular germinal tissue, within the known trabeculæ of cavernous tissue, between the two the transitional forms. To whom, therefore, the identity of the histological process does not appear satisfactory,

Fig. 55.

The cavernous fibroid. Billroth. 1–300. (Polyp of posterior nares.)

in order to justify the assumption recommended by me, of the cavernous tumor among the fibromas, he ought to be able to draw a further reason for it from this second intimate relation to the fibromas.

b. *Lipoma, or Fatty Growth.*

§ 133. The lipoma or fatty growth not only pre-eminently contains the characteristic elements of adipose tissue, the fat-cells, but also imitates the structure of the normal fatty cushions of the body in so far as these fat-cells are united into small, roundish clusters, which are separated from each other by connective-tissue partitions. A certain number of such clusters of fat-cells, is comprehended by a stronger connective-tissue membrane into likewise a roundish lobe, and these lobes are they, into which the most of fatty tumors are broken up, as seen by the naked eye. The panniculus adiposus of the body also shows a lobular structure, but never do its fat-lobules (the fat-glandules of authors) attain the considerable size which the individual lobules and nodules of a fatty growth are wont to have. The individual cell of the lipomatous fatty tissue distinguishes itself in a similar manner from the ordinary fat-cell. It is considerably larger, that is to say, more elastically filled with a fat, at the same time, more fluid, and richer in oleine.

All lipomas have a peculiarly central growth. The elementary process herewith, and in the first origin of the tumor, consists in the new-formation contrary to rule of single fat-cell clusters, of a moderate, entirely circumscribed proliferation of connective tissue, which leads to the formation of a cell-depot, and is followed by a fatty infiltration of the newly-formed cells. It appears, however, upon the one side, that the incitation to renewed production is given particularly strong in *the midst* of several already completed fat-cell clusters; upon the other side it is certain that the vessels of the new fat-clusters proceed from the vessels of the old, in a manner similar to what we see in the vessels of the papilloma. Thus it explains itself, that the lipoma, as a rule, is only connected at one point with the neighboring tissues by a larger vascular stem; at its entire remaining surface, however, is bounded by a wide-meshed connective tissue, or even by a smooth connective tissue capsule; thus the peculiar lobular structure declares itself, in a word, the central growth of the tumor.

The same localities at which the physiological fat-infiltration has its seat, are also the preferred situations of the lipoma, namely, the subcutaneous, submucous, subsynovial, subserous, subfascial, intermuscular, and intraorbital connective tissues. From this point of view lipomas appear as partial enlargements of the normal adipose layers, as excrescentiæ membranæ adiposæ (Morgagni); and if we will regard this as a connected system of adipose tissue, and not as any quantity you please of a fatty infiltrated connective tissue, we might esteem the lipoma,

together with obesity, as a hyperplastic tumor. For me, obesity is a fatty infiltration of the existing connective tissue; the lipoma, the fatty infiltration of a new formation, which grows from its own centres.

§ 134. The lipomas like the papillomas grow slowly at the beginning, afterwards always more and more rapidly. They may attain a considerable size. Tumors of the circumference of a man's head, and upward, are even of no rarity. In addition, their central growth necessitates that they very soon press forward out of the surrounding soft parts, and toward the nearest free surface, that they push before them the integumentary covering, and finally project above the surface as tuberosities or polyps.

The larger a lipoma is, so much the more may we expect that the interior of the tumor has progressed to further metamorphoses. There is not infrequently found a chronic inflammatory hyperplasia, and a callous transformation of the interconnective tissue. The fat-clusters in consequence of this process disintegrate in masses; the remaining lobules are separated from each other by broad bridges of fibrous tissue (Fibrous lipoma, steatoma Mülleri). More frequently there are retrogressive processes. The calcification of the fibrous basis-substance of the fat-clusters plays here an important part. Through these there is formed an extraordinarily fine-meshed, sponge-like, calcified framework, which penetrates the entire tumor, or larger sections of it, and bestows upon it an extraordinary hardness and weight. More remarkable still is the mucoid metamorphosis of the lipoma tissue, and the transformation therewith possible of a fatty tumor into a mucoid tumor (myxoma). In very emaciated individuals, debilitated by long-continued disease, we may indeed find the adipose tissue of the heart deprived of its fat, and, instead, converted into a peculiarly puffed out œdematous condition, which upon closer examination proves to be a mucoid infiltration. Just the same occurs in lipomas, and, indeed, particularly in the larger, pediculated lipomas of the outer skin. The mass of the tumor receives from this a colorless, translucent, gelatinously trembling constitution; the fluid flowing from the cut surface contains mucin, so that we cannot avoid acknowledging its myxomatous character, and, if the entire tumor has really degenerated in the supposed sense, no longer to call it a lipoma, but a myxoma.

With the fibromas the lipomas very properly enjoy the reputation of decided benignity. A thoroughly extirpated lipoma never recurs; metastases to the neighboring lymph-glands, or inner organs, are never observed.

c. *Enchondroma, or Cartilaginous Tumor.*

§ 135. When cartilaginous tissue appears in the form of a tumor at a spot where, under normal circumstances, there should be no cartilage, we call it an enchondroma. The substance of an enchondroma is hence

of that peculiarly elastic hardness, of that milk-white, in thin layers translucent color and constitution which pertains to cartilage. Touching the microscopical relations, we distinguish, as is known, the normal histology of several kinds of cartilage, especially, however, the hyaline cartilage, with a homogeneous, and the fibrous cartilage, with a fibrous basis-substance. The cornea, however, also gives in boiling, chondrin, and we may very well term its tissue a cartilage whose cellular cavities are branched star-like (stellate-cell cartilage).

All these textures, then, may be found side by side in an enchondroma. Yet, as a rule, the hyaline cartilage prevails. One of the most characteristic and most frequently occurring arrangements is this, that small, rounded islands of hyaline cartilage at the periphery are transformed into fibrous cartilage or corneal tissue. The *hyaline cartilage at the centre* is distinguished in nothing from the known physiological type. The cells are placed single, or in pairs, or groups, so that one sees that the first foundation has been succeeded by an enlargement by interior growth. The capsules are not always distinct; where they are entirely wanting, this announces a commencing process of softening of the basis-substance. The protoplasm of the cells is of various form. Most frequently we see nucleated stars, a form which either proceeds from a shrivelling of the cells produced by reagents, or is to be explained by the spontaneous mobility of the protoplasm; the latter especially where a transformation of hyaline cartilage takes place into mucoid tissue. The formation of processes then takes place *pari passu* with the disappearance of the capsules and a mucoid swelling up of the basis-substance. Virchow, under these circumstances, has observed quite colossal, long processes of single cells of the enchondroma. (Virchow, Archiv, 28, p. 238.) Towards the periphery of the cartilaginous islands the cells either become smaller, flat, lenticular, the basis-substance becomes striated, there occur in it finer and coarser fibres, which simulate elastic fibres and are remarkable for their rigidity (*fibrous cartilage*); or, again, the cells become spindle-shape, and stellate, they anastomose with each other, and evidently lie in a system of minute canals, provided with points of intersection, while the intercellular substance retains its homogeneous, transparent constitution (*stellate-cell cartilage, corneal tissue*). The contiguous smallest cartilaginous islands are in contact with these fibro-cartilaginous or stellate-cell cartilaginous zones, and are thereby united groupwise into *nodules or lobules* of perhaps the *size of a pea*, into which the whole tumor is broken up, even to the naked eye.

§ 136. As we may deduce from this description of the microscopic appearances, the enchondroma has also a lobular structure; but this is a lobulation which distinguishes itself very essentially from that of a lipoma, or even of a papilloma. The lobules of an enchondroma are co-ordinate to one another; *one was produced beside the other*, and they

are only united into an entity by this arrangement side by side as to space, not by a higher unity; perhaps a common vascular arrangement, a growth by interior development. If it is striking and appears to indicate an organ-like structure, that the individual lobules of the cartilaginous tumor do not exceed a certain size, this has its cause in the simple fact that cartilage in general, even in normal physiology, is not deposited in larger continuous masses and—to express myself teleologically—also cannot be deposited. Cartilage is nourished as a non-vascular tissue, by the conveyance of the nutritive fluid from cell to cell. This possibility of nutrition, however, ceases at a certain distance from the blood-conveying vessels, and if new arrangements for nutrition do not arise by which the central parts are provided, then nutritive disturbances at that place must be the necessary consequence of every further growth. Hence in the formation of the osseous system from cartilage, we find the peculiar arrangement, that with a certain volume of cartilaginous epiphyses, just in their centre, medullary spaces with vessels arise, which then from this point out gives the impulse to the formation of genuine bone (epiphysis-nucleus). The formation of vessels and genuine bone has also been observed in enchondromas. The rule meanwhile is, that the single portions of cartilage never attain so considerable a size that they may not be easily nourished from the periphery.

§ 137. It is herewith naturally presupposed that the connective tissue, which binds together the lobules of the enchondroma into a tumor (stroma), contains a sufficient number of vessels, and that a sufficient quantity of blood flows to and fro in these vessels. In smaller tumors, even at the periphery of the larger, this is the case. Not so in the interior parts of the larger. It rather appears that the vessels here become impervious and are obliterated by the pressure of growth of the tumor. In every enchondroma of considerable size—they have been observed of five pounds weight—we may, therefore, presuppose a more or less complete obliteration of the interior vessels, and in consequence thereof further metamorphoses of the mass of the tumor.

Individual parts of an enchondroma are almost always *calcified.* The cartilage then shows the infiltration, pictured more in detail, at § 49. At one time the basis-substance, at another the capsules and cells, are the first points of attack. For the naked eye we always have an opaque, dark yellow color, and a granular, friable constitution of the infiltrated parts. That occasionally an actual ossification follows this calcification, as in the normal growth of bone, has already been mentioned. We have also already spoken of the transformation of cartilage into *mucoid tissue.* We must not regard this so much a retrogressive process as a change of model; a transformation of a tissue into another tissue, in itself of similar value, whose result may be the partial or entire transition of the enchondroma into a myxoma. It is otherwise

with that softening of the enchondroma cartilage, which begins with a fatty metamorphosis of the cartilage-cells, their transformation into fatty granular cells, &c., where to this a mucoid solution of the basis-substance associates itself, and in this manner, in the interior of the cavities of the enchondroma, form fluctuating spots; in a word, softening cysts, which are filled with a gelatinous fluid, capable of being drawn out to threads and strongly impregnated with mucin. This *cystoid* degeneration of the enchondroma (enchondroma cysticum) might, of course, be conceived as a consequence of nutritive disturbances.

§ 138. Herewith, however, the manifoldness of the anatomical appearances of the enchondroma is not yet exhausted. We must add,—unfortunately not yet exhausted. There yet remains for us to mention the complication of the tumor with alveolar sarcoma (vulgo cancer, because of the analogous structure). Just this complication has bestowed upon the enchondroma that nimbus of a certain malignancy, which does not pertain to the tumor in itself. To the combination tumor, of an enchondroma with a soft sarcoma, those statements refer, where, after the extirpation of an enchondroma, medullary tumors recurred, partly at the same spot, partly made their appearance at other points of the body. In such cases the malignant addition, as a rule, may already be recognized upon the primary tumor. We find smaller and larger nodules of medullary consistency along the vessels in the stroma of the enchondroma. Moreover, it is firmly established, that pure enchondromas may also recur; a creeping onwards of the tumor along the lymph-vessels, metastases to the nearest lymph-glands, nay, even to interior organs, has been several times observed. In reference to interior metastases, the lung is the preferred organ of the enchondroma. Meanwhile, these metastases are, upon the one hand, extraordinarily rare; upon the other, they always remain, but extraordinarily small, although the original tumor is very colossal.

§ 139. Three-fourths to four-fifths of all enchondromas have their seat upon the osseous system, and here again especially at the diaphyses of the long bones. At the proper time we will learn to know the great variety in the manner of the first occurrence and further development, which characterizes the enchondroma of bones; here let us consider but one variety, *osteoid chondroma* (Virchow), because this presents us as its cardinal constituent an essentially deviating cartilaginous tissue.

In enumerating the various cartilaginous textures, as a rule, one tissue is not mentioned, which yet has the best-founded title to be so, in virtue of its anatomical constitution. I mean that peculiar species of connective substance, which after the deposition of the salts of lime has ensued is called genuine bone, previously however consists of a highly refractive, dense, and homogeneous basis-mass, in which the future bone cavities still have a more roundish, let us say a polygonal

form, and very short processes. The trabeculæ of the osteophyte (see Diseases of Bones) are formed of this tissue; in thin layers it lines the medullary spaces of the bone, which is about to pass from the spongy state into the compact. It plays an important part in the union of fractures, as it forms the chief bulk of the so-called callus. Its true cartilaginous properties, however, come to be recognized above all, when as in the osteoid chondromas it produces tumors, and not rarely tumors of colossal circumference.

§ 140. Osteoid cartilage may indeed also form independent of the osseous system, as Virchow also found such beside myxomatous and lipomatous constituents, in a mixed tumor extirpated from the back: this proved itself decidedly as osteoid cartilage. Commonly, however, osteoid chondromas proceed from bone. They begin their growth here between the periosteum and the surface of the bone; in the sequel, however, they proliferate as well through the periosteum as through the compact crust. They mostly present spindle or pear-shaped enlargements of one extremity of a long bone. They have been most frequently observed upon the humerus and femur. Retrogressive metamorphoses are more rare than in all the other heteroplasmas hitherto considered. This is connected with the very complete vascularization, equally good in all parts, which the osteoid chondroma enjoys as well as the osteophyte and callus. The cartilaginous trabeculæ of the osteoid substance form a delicate framework, in whose openings even the most delicate capillaries are safe from the pressure of growth. Only one metamorphosis is indeed generally observed in every osteoid chondroma; I mean the transition into real, genuine bone-tissue. Hence the osteoid chondroma creaks under the knife, or we must even make use of the saw when we would divide the tumor. Upon the cut surface we immediately recognize the ossified parts by their greater firmness and hardness; if the entire tumor has been converted into bone, the osteoid chondroma has become an osteoma.

Concerning the benignity or malignancy of this new formation, there have as yet too few cases become known, for us already to venture upon a certain decision. Meanwhile it appears that the prognosis of the enchondroma also is applicable to this its variety.

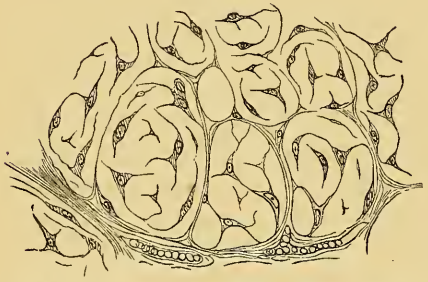
d. *Myxoma or Mucoid Tumor.*

§ 141. If we comprise in a single glance all that has been said in the sections on mucoid tissue, it will be evident that this is indeed to be regarded as a thoroughly independent and vitalized member of the series of connective substances; that, however, it is surpassingly frequently produced by a secondary metamorphosis (§ 42) from other tumor-forming connective substances. We learned to know a sarcoma —a lipoma—an enchondroma—myxomatodes, and understood thereby tumors, which in spots had been converted into mucoid tissue. Herewith, of course from the juxtaposition of anatomical forms, a conclusion

was made as to their sequence; yet numerous and sure observations confirm the possibility of a myxomatous metamorphosis of cartilage, adipose tissue, and the areolar connective tissues, in such measure, that this conclusion commends itself most decidedly against the opinion of a reversed sequence, and that of a simultaneous origin of mixed types of tissues, at least in most cases. This being considered, it at all events appears advisable to call only such tumors mucoid tumors, as absolutely and *in all parts consist of mucoid tissue.* Such indeed do not frequently occur, but still so frequently, that we may maintain the group of myxomas proposed by Virchow.

§ 142. The definition of mucoid tissue, which only requires a mucous-containing or mucoid softened basis-substance, but declares nothing concerning the form and constitution of the cellular parts, admits a certain number of histological subdivisions of myxomas. A number of cells, small in proportion to the quantity of the basis-substance, be they rounded, or be they stellated-branched, most beautifully exhibits the optical and physical properties of mucus. (§ 39.) Hence the myxoma hyalinum (Fig. 56) mostly characterizes itself by its colorless, translucent, gelatinously trembling consistency. If the cells come to predominate in the whole tumor or at individual spots, a whitish medullary condition is presented —myxoma medullare. Fatty infiltration of the cells leads to myxoma lipomatodes.

Fig. 56.



Hyaline myxoma of the subcutaneous connective tissue in the neighborhood of the angle of the jaw. 1-300.

§ 143. A lobular structure, a composition of smaller and larger subdivisions also pertains to the myxoma; these are separated from each other by connective-tissue partitions. But little has as yet been made known concerning its vascularization; injections, which I have myself instituted in a hyaline myxoma of the cheek, of the size of the fist, allow me to conjecture, that the myxoma is poor in capillary vessels, that only vessels of larger calibre occur, which run in the coarser partitions.

The myxoma forms knotty swellings, which grow rapidly, and by this, as well as by the great softness of its tissue, is wont to give occasion for mistaking it for soft carcinoma. Like the lipoma, the myxoma also strives to attain the surface by the shortest and easiest way; here it forms tuberous or fungous elevations, and may even become a pendulous, polypous tumor.

The subcutaneous cellular tissue of the thigh, the back, the external genital parts of women, as well as the intermuscular connective tissue

of the neck and face, are the preferred situations of myxoma; in the next place, it is found in the osseous and nervous systems. Its occurrence in the nervous system, according to Virchow's observations, is not infrequently a multiple, after this manner, that nodes of myxoma are simultaneously found at several points in the connective-tissue perineurium. Prognostically the myxoma, if we know properly to separate the sarcoma myxomatodes, may be reckoned among benign tumors. It does not return after thorough extirpation.

e. *Osteoma, or Bony Tumor.*

§ 144. Somewhat the same obtains of bony tumors as of the mucoid tumors. The osseous tissue is indeed a thoroughly vitalized constituent of the body, even capable of transformation; but, like the mucous membrane, it is a terminal tissue; that is to say, as a rule, it forms the closing link of a chain of other metamorphoses. The stromata of the cancers may ossify. Lücke even described an epithelioma with an ossified stroma. We know a sarcoma ossificans; the enchondroma and osteoid chondroma may ossify; even the connective-tissue partitions of the lipoma are ossifiable. We must, therefore, say here, only such tumors which absolutely and *in all parts consist of osseous tissue*, may be designated as *osteomata*. If, with Virchow, we wish to distinguish a hyperplastic and a heteroplastic osteoma, then of course everything belongs here that we have learned to know of tumefactive hyperplasiæ of the osseous system. Heteroplastic osteomas certainly very rarely occur.

f. *Myoma.*

Under myomas we understand such tumors in which undoubted muscular fibres form the principal constituent. Accordingly, as the muscular fibres belong to the smooth or the striated, do we, according to Zenker, distinguish a leiomyoma from a rhabdomyoma. I have, however, gained the experience, that transitions between smooth and striated muscular fibres occur just in the tumor-like production. Thus a large myoma of the retroperitoneal adipose tissue, which I had the opportunity to examine, consisted of spindle-formed cells which were striated; likewise a myoma of the vaginal mucous membrane which obstinately recurred. Pure leiomyomas show thoroughly the structure of muscular membranes when they occur upon the intestine, the urinary bladder, &c. I assert, that one who has ever examined a tumor of this kind, will be guarded against any mistaking of simple spindle-cells for muscular fibres. The great similarity in the size and constitution of all the cells and nuclei, the tight compression of the cells, conditioned thereby into very elegantly built fibrous lines, has something exceedingly distinguishing. The macroscopic relation, the interweaving of the fibrous lines, certainly reminds me of the fibroma, yet have I never been in the situation to recognize a fibro-muscular tumor in the sense

of Virchow. In a myoma of the testicle I found groups of ganglionic cells and stroma fibres (see Testicle).

g. *Neuroma.*

§ 145. As the term neuroma is used for all histioid tumors inserted in the course of a nerve-trunk, and is particularly frequently applied to fibromas and myxomas, we must separate from these pseudo-neuromas, as genuine neuromas, such tumors as in their principal mass consist of newly formed nerve-fibres and ganglionic cells. A tumor of this sort of the size of a hen's egg has lately been observed in the angle between the walls of the chest and the anterior boundary of the vertebral column (Schmidt, Frankfort-on-the-Main), and so much the more deserves notice as it appears to yield us the first example of a nonhyperplastic genuine neuroma. Of course the supposition that the question is about a hyperplastic ganglion of the sympathetic, is not to be entirely excluded because of the locality of development, and then the case would rank with the frequently observed circumscribed hyperplasiæ of the larger cerebral ganglia (the thalamus opticus, corpus striatum), as well as with the spindle-shaped tumefactions of the peripheral nerves, consisting of nerve-fibres, which Virchow has termed and described as genuine neuromas.

h. *Histioid Mixed Tumors.*

§ 146. In all the histioid new formations hitherto considered, *one tissue* could with more or less certainty be regarded as the prevailing one, and accordingly the name and character of the new formation could be established. There can be no doubt, however, but that there is also a mixed tumor. When beside distinct lipomatous constituents distinct chondromatous constituents are found, when sarcoma nodes and nodules, as we saw, are deposited in an enchondroma, we do not know whether we should name this thing enchondroma lipomatodes or lipoma cartilagineum, sarcoma cartilagineum, or chondroma sarcomatosum. This embarrassment recurs with the question as to the clinical character of this sort of tumor, the prognosis, &c. Meanwhile, upon the basis of several good observations in reference to the latter, we may adhere to: 1, that mixed tumors have a more unfavorable prognosis than each single species represented in the tumor; 2, that the admixture of sarcomatous constituents without more ado places the mixed tumors upon an equality with sarcomas. As a rule, such a mixed tumor already returns after the first extirpation in its true nature as a sarcoma (see the combination of the histioids with carcinoma, under Carcinoma Sarcomatosum).

4. Pathological New Formations, which are Abnormal Productions of the Epithelial Growth, with, and without Participation of the Vascular Connective Tissue System.

§ 147. The exposition of general points of view concerning the nature, the origin, and relationship of the so-called "*carcinoma*," will form the chief contents of this section. By "carcinoma" we understand a new formation destroying the organs of the body, after extirpation commonly recurring and undergoing metastasis, therefore malignant. These properties certainly pertain, as we have seen, also to certain histioid tumors; and it were exceedingly desirable, if there were a positive anatomical characteristic by which we could recognize carcinoma as such, and could distinguish it from other destructive and malignant new formations. We have now become accustomed, and to-day we yet hold fast this custom, of regarding a certain peculiarity of structure, the so-called alveolar structure, as a necessary requisite for the diagnosis—cancer. By this we wish to say that we seek for the substance of the carcinomatous degeneration in a deposition in foci of cells advancing in fixed directions, which necessarily tends to this, that we must grant to the parenchyma of the organ in process of destruction, which remains between these cellular depots, the form of a framework, a trabecular- or net-work (stroma), whose meshes (alveoli) are determined by the form and size of the deposited aggregations of cells. It is manifest that this structure is particularly fitted to lodge large amounts of free cells, which, according to § 121, we must regard as the most effective stimulus as well for the local growth of a tumor as for the infection of the entire organism. The seeming arbitrariness with which we proclaim the alveolar structure as the anatomical criterion of cancer, consequently receives its justification; but a new difficulty arises, when we reflect that then the alveolar sarcomas must also be designated as carcinomas; tumors, therefore, whose "permeation by cellular heaps" ("Durchsetztsein mit Zellenhaufen") we believed we ought to assimilate with the suppuration of inflammatory tissues. I accept this consequence, and thereby place myself upon the platform of those who understand by carcinoma in essentials a clinical character that is anatomically but imperfectly expressed; *i. e.*, only in the obligatory alveolar structure.

§ 148. *The* GREATER *number by far of carcinomas proceed primarily either from the epithelial clad surfaces of the body, from the skin and mucous membranes, or from the secerning glands. They depend upon an abnormal growth of the epithelial tissue.* We may say, that an ingrowing of epithelium into the sub-epithelial layer of connective tissue of membranes or into the interstitial connective tissue of glands forms the fundamental processes in these carcinomas. The nature and manner

of the ingrowing is extraordinarily various. The whole impression made by a carcinomatous destruction, for example, the observation of a vertical section by a low magnifying power, appears to justify the opinion, that in them the question is about a diseased imitation of those histological processes, which precede the development of glands with excretory ducts; namely, here as there we see aggregations of epithelial cells, which proceed from the under surface of the epithelium in the form of cones or strands, and insinuate themselves between the separating filaments of the connective tissue. Active processes of division also show themselves in the elements constituting the cell-aggregations, so that in both of these principal points an undeniable uniformity with glandular growth is present. Nevertheless the view, that the carcinoma formation consists in a subordinate and irregular imitation of the physiological glandular growth (heteradenie of the French), has but a very contracted justification. After having above devoted so much time and space to the consideration of normal epithelial growth, it would ill become us, should we now lose the fruits of that consideration by an ill-timed formation of hypotheses. For the carcinomas of glands with open outlets, of course we may even indicate with emphasis, that all imaginable transitions between glandular hypertrophy and the glandular carcinoma are to be found. We of the latest time have learned to know these intermediate forms more fundamentally, and have invented the name adenoma, to designate a tumor which is neither simple hypertrophy nor carcinoma. This is at least the most comprehensive conception; several authors certainly move the idea of adenoma up and down upon the scale mentioned, in that they now assign it more to hypertrophy, now more to carcinoma; that, however, a motion up and down of this kind is possible, just proves the existence of the scale.

The general comprehension, however, of carcinomas, which proceed from the epidermis or the epithelium of mucous membranes, is much more difficult; namely, here also exists an unmistakable correlation of the hyperplastic and carcinomatous conditions. It is, for example, a well-known experience, that those circumscribed hypertrophies of the skin, which we term warts and papillomas, have the capacity of going over into epithelial carcinoma. This transition is brought about purely anatomically in the following manner: the papillar hypertrophy conditions a more or less great alteration of the level of that plane in which the epithelium and connective tissue come into contact. The steeply raised lateral surfaces of the enlarged or newly produced papillæ bound deep, cleft-like depressions between the papillæ. The epithelial covering of the papillæ is at the same time an epithelial lining of the interpapillary clefts, and as long as this relation remains constant by a sufficient desquamation of the older epithelial cells, the hyperplastic character of the tumor is preserved. It is, however, manifest that a sufficing desquamation is so much the less possible, the more the papillæ

elongate, and especially the richer their dendritic ramification proves to be. The lateral pressure, which the points of the papillæ, widely branched but united to a narrow basis exert, simultaneously closes from above the interpapillary clefts, and causes in them a gradually increasing accumulation of epithelial cells. The epithelium in the deeper parts of the tumor no longer appears as a *lining*, but as a solid *plugging* of the interpapillary clefts. As such it now begins to push forwards against various points of the connective tissue substratum. Oval epithelial cones appear, which first protrude from the under surface of the epidermis into the cutis, then penetrate deeper and deeper. By this the carcinomatous condition is given. We cannot of course avoid comparing these cones with the epithelial cones in the glandular formation; we also observe, as was said, lively processes of division in the constituent cells, although, until proof to the contrary has been shown, I am convinced, that their growth chiefly depends upon a peripheric apposition of young cells, like the growth of normal epithelium, and find this representation just as plausible as perhaps the enlargement of retention-cysts by the secretion from their walls. The processes of division in the interior of the epithelial cones indicate a secondary growth and may indeed contribute the greater part to the thickening of the epithelial cones; to their elongation, however, and their forward progress, upon which the peculiar destruction of organs still depends, they do not contribute. In that I, in reference to the special elucidation of this matter, refer to the considerations following below of squamous epithelial cancers. I content myself, in these preliminary remarks, to have pointed out, that the laws of normal growth are correctly maintained even in these extremest and most dangerous excesses.

1. *Glandular Carcinoma.*

§ 149. Does there actually occur an entirely unequivocal, genuine hypertrophy of glands? If we demand of a genuine glandular hypertrophy 1, an absolute uniformity of structure and texture with the normal gland; 2, a correspondingly increased function; then both of these demands are probably satisfied only in the hypertrophy of the mammary glands during lactation, and those symmetrical enlargements of a kidney and single liver lobules, which is commonly called vicarious hypertrophy, because it is wont to arise in consequence of the destruction of the other kidney or the other portion of the parenchyma of the liver. The renal tubuli are here elongated, the liver-cells of an acinus are increased, and the capillary net has experienced a corresponding dilatation, so that even the naked eye can appraise the increase of volume of the renal tufts or the hepatic acini; the microscope, however, must establish a complete uniformity with the normal. Concerning the hypertrophy of the mammary glands during lactation, I beg to refer to the §§ concerned in the Special Part.

§ 150. All other so-called glandular hypertrophies have their peculiarities. There is in the first place a group, where we constantly remain in doubt as to how much of the enlargement is to be placed to the account of pathological growth of the glandular tubuli, and how much to the account of a simultaneous ectasy of the same. The hypertrophy of the mucous glands in catarrhs of the stomach and large intestine, the trachea and the bronchi, belongs here. The luxuriation of the subepithelial layer of connective tissue, which is wanting in no catarrhs of mucous membranes, conditions a closure by swelling of the excretory ducts penetrating them, and hinders the free emptying of secretion, so that from the beginning a certain ectasy by retention, of the collective internal lumina of the glandular body is joined to this. In addition, the spontaneous growth of the glands brought about by division of the epithelial cells, plays a more or less subordinate part. It may confine itself to a scanty lining of the interior of the gland, gradually degenerating into a mucous cyst. Cases of this kind find an analogue in the atheromas of the sebaceous glands, where we also undoubtedly have more epithelium than is necessary for lining the inner spaces of a sebaceous gland; nowhere, however—unless the atheroma were changed into an epithelial cancer—a centrifugal sprouting of the epithelial layer.

§ 151. To these, in the next place, such cases are joined, where certainly there can be no doubt of an independent increase of the secerning parenchyma, but indeed it may be doubted whether the new tubuli are still to be regarded as genuine, *i. e.*, functionable glandular parts. The sebaceous, as well as the sweat glands, may experience at circumscribed spots of the skin a monstrous development, and, especially the former, form very extensive fungous tumors, without a more abundant secretion making itself observable at the surface. Beside this, in the hypertrophy of sebaceous glands, a decided deviation of structure shows itself, in that an excessive thickening of the connective tissue glandular capsules takes place. A still greater prominence of this cause leads to subepithelial sarcoma of the glands, for example, of the mamma, for which, on that account, the term adenoid sarcoma has been laid claim to by Billroth.

§ 152. With the total emancipation from the physiological purpose of the glandular formation, the sphere of those tumors begins, which I call *adenomas*. The adenoma, apart from its stroma, consists of epithelial cells, which, by their arrangement, immediately remind of the epithelial lining of tubular or acinous glands. The cells are mostly grouped around a central axis, as though they encompassed the lumen of a real tubule; but the lumen is either entirely wanting, or it only exists in spots, occluded by mucous or a colloid mass, and certainly not in open communication with the excretory duct of the gland. It appears that the aim of nature is only to produce in general an unlim-

ited amount of new glandular tubules; what becomes of these afterward appears to be a matter of indifference. That to a regular glandular parenchyma a symmetrical development of the vascular connective tissue system is necessary she appears to have forgotten, and thus, the longer this continues, so much the more a tumor-mass, extraordinarily rich in cells, is produced, which, however, is too poor in vascular connective tissue to be at all points sufficiently nourished, and which, therefore, in itself develops the cause of its subsequent decay.

Up to the present time we know an adenoma of the liver, of the mammary gland, of the sebaceous glands (lupus), of the mucous glands of the rectum. Only in the last-mentioned is the boundary line toward the cylindrical epithelial cancer difficult to be drawn (see below). In the remaining ones the manner of development upon the one hand, upon the other the clinical relations, present us useful distinctive signs from carcinoma. Adenoma forms well-defined, globular nodules, which replace a comparatively small part of the normal glandular parenchyma, from which they have just been produced. The individual nodule subsequently has a central growth; it displaces the neighboring parts more than it infiltrates them. The adenoma of the liver directly capsulates itself. Furthermore, the adenoma must be regarded more as a benign, non-recurring, and non-metastatic new formation, although upon this point the reports have just commenced.

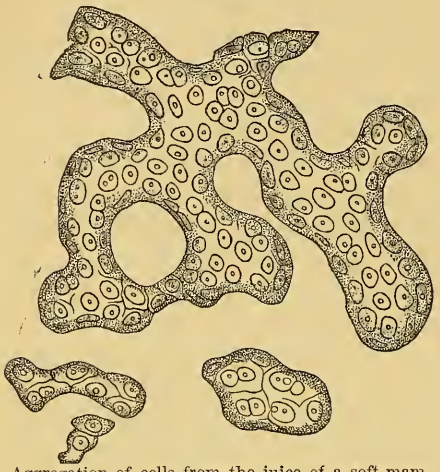
§ 153. The *glandular carcinoma*, with its numerous varieties, forms the natural conclusion to the series of histological developments, which we have hitherto considered. If we imagine to ourselves the independent growth of glandular epithelium still more luxuriant and more general, the regular formation of genuine glandular tubuli, still more neglected in favor of a so much the more rapid proliferation of the interstitial and the surrounding connective tissue, we will, in fact, receive an approximative picture of glandular carcinoma, whose individual features we, of course, must yet subject to a more detailed discussion.

That the new formation proceeds from the glandular epithelium, has of late been established by numerous investigations. The cells multiply by division. First of all, probably the lumen of the respective tubuli and acini always fills up, and instead of them we receive solid cell-groups, which, however, immediately send out outgrowths in all directions, and with these penetrate into the neighboring connective tissue. Here, however, the numerous varieties of glandular carcinoma already begin, of which the most important will follow:

§ 154. The *soft carcinoma* (carcin. medullare, encephaloides, hitherto frequently united with the soft alveolar sarcoma), produces the most, if not also always the largest, cancer-cells. These, by their round, vesicular nucleus, with distinctly shining nucleolus, prove themselves as the genuine offspring of the intestinal glandular plate, and form cylinders manifoldly twisted and beset with knobby appendices, which

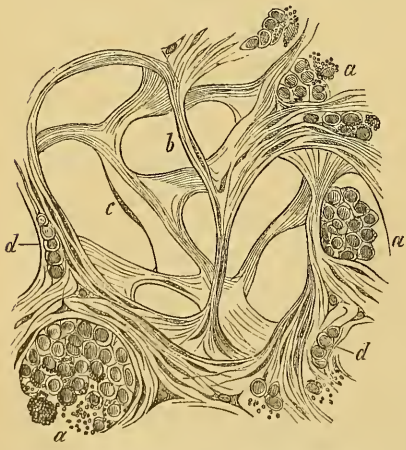
we can get the best view of if we examine in serum the juice (cancer-juice) expressed from a recent cut surface. (Fig. 57.) Upon these cellular cylinders we cannot recognize the limits of the individual elements. This comes to pass, because the protoplasm of the latter is perfectly naked, so that by their immediate apposition an optical continuity of all the protoplasms is produced. It appears that the rapid occurrence of fatty metamorphosis prevents a higher development of the epithelial type, for we rarely meet with a larger cell in whose protoplasm the first fat-globules are not already visible. The more numerous, then, the fat-globules become, so much the better do the outlines of the cells, formerly difficult to be made visible, exhibit themselves. The transformation into granular corpuscles, with a fatty detritus, appears to proceed entirely in the manner known. Of the specific constituents of the cancer-juice, nothing whatever has hitherto been demonstrated, either by the microscope, or by chemical procedure. The clear, colorless serum contains dissolved albuminates and albuminoids, among these probably ferments, which are meanwhile yet entirely unknown to us.

Fig. 57.



Aggregation of cells from the juice of a soft mammary cancer. After Billroth.

Fig. 58.



Brushed-out stroma of soft glandular cancer. *a*. Section of cylinder of cancer-cells. *b*. Trabeculæ of the stroma. *c*. A single spindle-cell, which extends from one trabecula to another, and by the separation of basis-substance along its protoplasm gives the impulse to the formation of a new trabecula of the stroma. *d*. Round-celled infiltrate in the interior of the trabeculæ of the stroma. 1-300.

§ 155. If we examine what remains behind, after the cancer-juice has run out, if we look for the spaces, in which it was contained before flowing out, we will meet with the second factor of every carcinomatous structure, the stroma of the cancer. (Fig. 58.) In order to bring the stroma as completely as possible into view, it is necessary to take thin sections from various places of the tumor, in order to tease them out; then there is presented to us a connective-tissue framework, whose

trabeculæ inclose oval lumina, so large that their shortest diameter exceeds the breadth of the stoutest trabecula by at least twice; that of medium thickness, however, by at least five times. It has already been pointed out that neither the thickness of the trabeculæ, nor the size of the meshes, is the same in all cancers, but that we may speak of a certain proportion between the breadth of the trabeculæ and the width of the meshes. This proportion is of importance for distinguishing from each other individual forms of cancer.

As to what concerns the more minute structure, the thicker trabeculæ of the stroma are, as a rule, formed of a striated connective tissue, in which numerous spindle-shaped cells are imbedded. These trabeculæ are not round upon a cross section, but triangular, quadrangular, and polygonal, the surfaces concave, the edges sharpened. The latter are here and there continued into thin membranes, which partly or entirely stretch over the meshes. Upon the whole we receive the impression of a continued rarefaction of the stroma by the growing contents of the alveoli, and such a one is simply to be accepted also, at least for the first stages of development of the carcinoma, where it is still fastened to the limits of the glandular lobules. Afterwards, when the degenerated lobules and lobes have run together into larger nodes, and these already begin by infiltration to press forwards into the surroundings of the gland, a new formation of trabeculæ of the stroma also arises in the older portions of the tumor, which begins, in that single spindle-shaped cells extend themselves transversely through the larger alveoli, and thus give the central point and the direction for the deposition of connective-tissue intercellular substance.

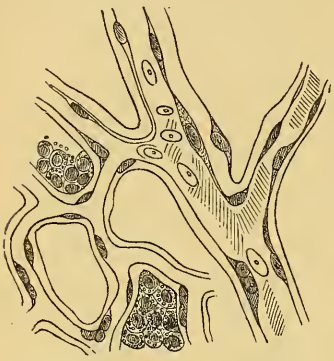
Soft glandular carcinomas have hitherto been observed upon the salivary glands, mammary glands, testicles, ovaries, prostate, thyroid gland, nasal mucous membrane, and liver. Whether and to what extent the soft carcinoma of the stomach proceeds from the glands, yet remains for the present undecided.

The soft glandular carcinomas are exceedingly malignant tumors, particularly in so far as they undermine more rapidly than the others the entire nutrition, and become fatal through cachexy. Metastatic irruptions are, as a rule, only observed in the appertaining lymph-glands.

§ 156. The *telangiectatic carcinoma* (a form of the so-called fungus hæmatodes). In so far as bloodvessels constitute an integral constituent of every glandular stroma, and this, as we have seen, directly goes over into the stroma of the glandular cancer, it is easy to infer, that every glandular carcinoma must at least primarily also be vascular. Now in general these vessels share the fate of the stroma, *i. e.*, they become attenuated, so long as the growth of the epithelial masses is predominant, and even experience a richer development, when this is softened and dissolved by fatty metamorphosis. There are, however, carcino-

mas,—and these correctly deserve to be designated as telangiectatic,—in which from the beginning the vascular development predominates. I found, in a very rapidly growing cancer of the testicle, the stroma entirely formed of vascular ramifications. Fig. 59 represents a fragment of this stroma. I regard the second contour, which accompanies the vascular wall everywhere at a proper distance, as the wall of an ensheathing lymph-vessel, as they have also been found in the normal testicle by Ludwig and Tomsa. Just there I have also most beautifully observed the vascular formation out of "culs de sac" ("kolben") described by Rokitansky, and have convinced myself, that these culs de sac are a competent equivalent of the impervious appendices of the vascular system, which we have learned to know in the tertiary vascular formation (§ 71). The culs de sac, of course impervious, grow towards each other and melt down, when they come into contact into a new capillary loop. (Fig. 60.)

Fig. 59.



Brushed-out stroma of a very rapidly growing carcinoma of testicle. 1-300.

All telangiectatic carcinomas are characterized already, even for the naked eye, by the frequent finding of parenchymatous hemorrhages. Depots of blood of the size of a pin's head up to a hen's egg and over; depots of blood in all stages of retrogressive metamorphosis, blood-cysts and pigmented spots of all forms and sizes characterize the cut surface of this fungus hæmatodes. In reference to malignancy, the telangiectatic unconditionally joins itself to the soft glandular carcinomas.

§ 157. The *sarcomatous carcinoma* represents the second of the possible combinations of cancer and sarcoma (comp. sarcoma carcinomatodes, § 125). If we now imagine to ourselves, that the epithelial system of an open-mouthed gland degenerates in the same manner, as in soft glandular carcinomas, while simultaneously the interstitial connective tissue undergoes sarcomatous degeneration, then we obtain a mixed tumor, which we must leave undecided whether it is to be reckoned with the sarcomas or the carcinomas. I reckon them among the carcinomas, because the sarcomatous admixture only shows itself in the primary irruption, while the recurrence and metastases present themselves as a rule, as pure, soft, glandular carcinomas. Their favorite situation is incontestably the testicle and kidneys. I assert, that the majority of soft carcinomas of the testicle possess a sarcomatous stroma. The trabeculæ of this consist of the characteristic spindle-shaped cells, and are often so thick, that we fruitlessly hunt over several fields of the microscope for the imbedded cancer-cells, if we have intentionally made the section through the more compact portion of the tumor.

In reference to malignancy, this tumor also joins the soft glandular carcinomas. The colossal circumference is worthy of notice, which the carcinoma sarcomatodes may attain. Kidneys of ten pounds weight and testicles of fourteen pounds have been observed.

Fig. 60.

Stroma of a telangiectatic carcinoma of testicle formed by wide capillaries with blind-ending appendices. 1–300.

§ 158. The *hard carcinoma* (simple carcinoma, scirrhus, connective-tissue cancer) distinguishes itself from both the preceding by such prominent peculiarities of structure as well as of development, that probably many experts of my branch, will but unwillingly admit their registration among the glandular carcinomas. As the chosen epithet implies, this distinguishes itself above the allied new formations, par excellence, by the greater consistency of the mass of the tumor. The consistency of a cancerous tumor is conditioned by the quantitative proportion of the cellular infiltration upon the one hand, and by the stroma upon the other. Carcinoma simplex also owes its greater firmness to the circumstance, that the trabeculæ of its stroma are thicker and the interspaces for the cancer-juice smaller, than in soft glandular carcinoma. Still there is a certain scale of degrees of hardness to be established in it, which upon the one hand is conditioned by age and the epoch of development, upon the other by the peculiarities of its situation. There are hard, glandular carcinomas, which throughout are of such firmness, that it requires great force to tear them to pieces ;

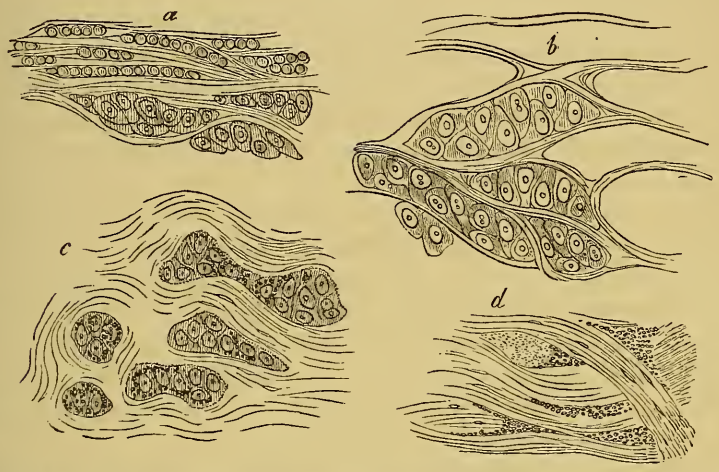
carcinomas, which in cutting creak under the knife (durities eburnea, scirrhus). These carcinomas appear glisteningly white, and show themselves under the microscope to be formed of a dense, finely fibrous connective tissue, which in a few clefts and alveoli contains the nests of cancer-cells.

Frequently *harder and softer parts* are found *side by side*, so indeed, that a central hard portion is encircled all around by a part less hard, up to a directly soft periphery. Observation with the naked eye already leads to the conjecture, that this arrangement depends upon a difference of age between the central and peripheral portions of the tumor. In the tumor always appearing in the form of perfect nodes, the outer border is formed by a zone of the smallest grayish-red depots, which are sprinkled into the contiguous normal parenchyma. Then follow larger and yet larger depots of the same kind, which flow together and thus form the chief mass of the tumor projecting rampart-like upon the cut surface. Further towards the interior, certain white stripes become more distinct, as which the larger trabeculæ of the cancer-stroma present themselves, the reddish-gray infiltrate loses itself or there occurs instead a yellowish marking, which is derived from the conversion of cancer-cells into fatty granular corpuscles (carcinoma reticulatum, Müller). The vessels also of the stroma, of which we perceive but very little in the outskirts of the tumor itself, now become more prominent, and condition beside the white trabeculæ of the stroma, and the yellow points of fatty metamorphosis, a red streaking and spotting. Farther still toward the interior this characteristic also finally disappears, and a glisteningly white, hard, cicatricial tissue shows itself, which from the centre by long radiating lines extends into the tumor. Accordingly we distinguish already with the naked eye four zones, which correspond to just as many stages of the cancer process: the zone of development, the zone of the acme, of the retrogressive metamorphosis, and of cicatrization.

§ 159. The microscope throughout confirms these interpretations of the naked eye. In Fig. 61, *a*, *b*, *c*, *d*, four microscopic views are given, as we get them in examining fine sections from the four zones of the tumor mentioned. Fig. *a* was taken from the periphery of a small nodule of the zone of development, and was formerly so interpreted, that we accepted each of the rows of round-cells here visible as the progeny of a connective tissue cell pre-existing at the same place, and at the same time the first stage of an aggregation of cancer-cells, such as we meet immediately alongside. We have now torn asunder this chain of developments. We regard the rows of round cells as emigrant colorless blood-corpuscles, and are at pains to prove that the nests of cancer-cells are produced from the pre-existing epithelia of the glandular substance. I hold it useless to take such pains, so far, namely, as our aim is to regard the collective cancer-cells as directly the " offspring of the epithe-

lial-cells." On the contrary, I grant, upon the one hand, that in the hard glandular cancer also, the glandular epithelium multiplies by division, and causes thereby an enlargement of the acini or tubuli, though but moderate; upon the other hand, that the first nests of cancer-cells are wont to arise in the immediate neighborhood of the glandular epithelia, so that the opinion of an "epithelial infection" of the round cells ac-

FIG. 61.



Carcinoma simplex mammæ. *a*. Development of nests of cancer-cells. *b*. Fully formed carcinoma tissue (compare following illustration). *c*. Commencing cicatrization; at the same time a representation of the relations of stroma and cells in scirrhus. *d*. Cancer cicatrix. 1-300.

cumulated in the connective tissue is certainly very imminent. According to my comprehension, the question in hard, glandular carcinoma is about a slowly transpiring interstitial inflammation, whose cellular products are converted into epithelial structures instead of pus or connective tissue. The *active* behavior of the glandular epithelium is to be regarded as the first cause of that inflammation and as that force which imparts to the inflammatory products their peculiar direction of development. This is, and remains, therefore, here also the peculiar source of morbid action, although their quantitative performance prove to be inconsiderable. In what manner the communication of the epithelial direction of development to the inflammatory infiltrate ensues, must of course yet remain undecided, still, as has already been pointed out, the view has much in its favor, that individual young epithelial cells penetrate into the interspaces of the neighboring connective tissue, and infect the indifferent cells there existing. We are reminded, in a certain sense, of the method of growth of the epithelia of the outer surface, only that there the migratory connective tissue cells touch the epithelium, and thereby the limit between epithelium and connective tissue is constantly maintained, while here the migratory cells, while

yet fixed in the connective tissue, become infected, and thereby the epithelium penetrates into the connective tissue.

§ 160. Fig. 61, *b*, represents the acme of development. The connective tissue fibres are pressed asunder by the expanding cell-formation, and now present the trabeculæ of a very compact stroma; upon them and in them the bloodvessels of the cancer ramify, by whose size and turgescence the intensity of the reddish tint in the color of the tumor is determined.

That the retrogressive metamorphosis, which cancer-cells fall into, and by which they finally perish, is the fatty transformation, already follows from the examination of the juice scraped off from a cancerous tumor. We find, side by side, therein all the stages of the process mentioned in § 26, from the origin of the first fat-globules in the protoplasm up to the total dissolution of the cell-body. Where, with the naked eye, we perceive yellow striæ and points (carcinoma reticulatum, Mülleri), the microscope, par excellence, shows us granular corpuscles. The thickening of the trabeculæ of the stroma, going hand in hand with the decrease of the cells, becomes more prominent upon transverse sections. In Fig. 61, *c*, we see a carcinomatous structure, which is peculiar to the so-called scirrhus, which, however, is found as a transitional state in every carcinoma simplex. The trabeculæ are extraordinarily thick, formed of a short-fibred connective tissue, provided with spindle-shaped cells. After the complete dissolution and removal of the cellular infiltrate, the connective tissue comes to be sole proprietor. In the cancer-cicatrix, in the oldest part of the cancerous tumor, we see lines of fibres crossing and recrossing one another in all possible directions; here and there a remains of fatty detritus indicates the place where formerly cancer-cells lay; in other respects the cancer-cicatrix has no sort of peculiarities which would distinguish it from other cicatricial tissue (Fig. 61, *d*).

The local productions of cancer end with the cicatricial formation; it is the same event, which in inflammatory heteroplasia we designated as healing; nevertheless, we cannot say, that cancer *heals* by cicatricial formation; for while this healing at the centre proceeds, new sections of the affected glands are continually involved in the destructive metamorphosis at the periphery of the tumor, so that the cicatricial formation constantly remains far behind the infiltration.

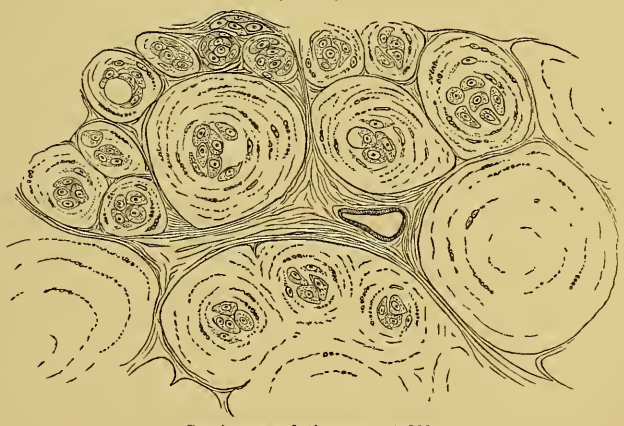
§ 161. Hard, glandular carcinoma occurs most frequently, and in several varieties, in the female breast, then in the glandular layer of the stomach, at the liver, and other glands with open outlets.

Nothing certain can be said concerning the period of the first metastatic formation, still they are regularly wont to ensue within a twelvemonth. Cases are reported, in which a thoroughly extirpated, hard, glandular carcinoma has produced no local recurrence, yet these belong among the greatest rarities.

§ 162. The *colloid* carcinoma (car. alveolare, gelatinous cancer). A soft, gelatinously trembling, perfectly translucent mass of tumor, of a light honey color, forms the gelatinous cancer. According to its nature, a hard glandular cancer, it distinguishes itself from this, its nearest relative, by the invasion of colloid degeneration in the course of development. The colloid degeneration conditions the peculiar appearance, the structure, and the other vital properties of the tumor.

As to what, first of all, concerns the structure, this is, as the frequently-used term alveolar cancer already indicates, the prototype of an alveolar arrangement. A network with the most regular round meshes forms the stroma, and if we trace the cause of this striking regularity, we find it in the circumstance, that every portion of the strongly swelling-out colloid substance, like a collection of fluid in an inclosed cavity, tends to assume the globular form, consequently a parenchyma, which like this cancer, is entirely pervaded with portions of colloid, must *eo ipso* assume the form of a stroma provided with globular meshes. If the colloid globules have attained a certain size, they exert by further increase of volume an atrophying pressure upon the partition walls, which separate them; two or more globules flow together and occupy one cavity, whose original form disappears by the gradual depression of the partitions, in order to strive for the globular form, so that finally a single larger but likewise rounded alveolus is produced. In a thin section (Fig. 62), accordingly, the entire mass of

FIG. 62.



Carcinoma gelatinosum. 1–300.

tumor breaks up into a number of larger and smaller circular surfaces corresponding to the colloid globules, which are separated by connective-tissue partitions.

Answering the question as to the origin of the colloid substance proves a less simple matter. That one portion of it is produced by the retrogressive metamorphosis of the cancer-cells, may for the time being

remain undisputed, as we always meet in all smaller alveoli a group of epithelioid elements, which are wanting in the larger, without anything else having occupied their place, and as we can in fact observe in individuals of these cells the colloid metamorphosis described in § 44. That, however, all colloid substance was produced in this way, cannot be conceded.

If we cast an unprejudiced glance upon the so characteristic histological picture of gelatinous cancer (Fig. 62), and observe how the groups of cancer-cells contained in the alveoli originally adhere to the alveolar wall; then, however, are crowded off from the wall by the ever more numerous layers of colloid substance, without for the time being increasing or decreasing in number, how they finally disappear and vanish when dozens of colloid layers are already deposited; then the conviction entirely of itself grows upon us that the greatest part of the colloid substance is created at the boundary of the connective tissue and epithelium, without that the formed epithelial cells actively participated therewith in any manner worthy of mention. A direct transudation from the blood is naturally not to be thought of, because the endosmotic equivalent of colloid substance is equal to 0. On the contrary, the view of Doutrelepont* would commend itself, according to which we have before us in the colloid substance a metamorphosed formative material of epithelial cells, perhaps an albuminous body, which in other cancers would be consumed for increasing the number of the cells. We cannot avoid in this case, thinking of the manner of production of epithelial cells from amorphous material asserted by Arnold, because the colloid accumulation, if Arnold is correct, would be very simply explained as an accumulation and transformation of those amorphous formative substances. The concentric stratification of the colloid substance points to a certain periodicity of the process of deposition; the fatty granular detritus, which designates the limits of individual layers, must then be regarded as an accessory product of the colloid formation.

§ 163. That vessels ramify upon the septæ and stroma-trabeculæ of alveolar cancer, there can be no doubt; but these vessels are neither numerous nor large, and contribute even in complete injection but little towards coloring the whole, so that colloid cancer constantly makes the impression of a tumor very poor in blood. For the issue of the disease and the dangers which patients undergo from colloid cancer, this circumstance is in so far of importance, as bleedings from the surface of an open ulcerating colloid cancer are neither frequent nor abundant.

In reference to malignancy the gelatinous cancer assumes a peculiar position. It is a cancer which possesses an extraordinary capacity of infection by contact. The infiltration of connective tissue progressing at its limits often takes on actually colossal dimensions. On the con-

* Langenbeck's Archiv. (Despatched for publication in April, 1870.)

trary, metastases to distant points are infrequent, likewise affections of neighboring lymph-glands, which mostly remain inviolable.

Situations—stomach, large intestine, liver, ovary, mammary gland.

2. Epithelial Carcinoma.

§ 164. If we were to take into consideration all the varieties of consistence, color, and texture, there could scarcely be found two epithelial carcinomas taken from different places of the skin and mucous membranes, which could be regarded as completely identical new formations, so great is the influence of the mother soil upon the development of epithelial carcinoma. We must content ourselves at this place in asserting two principal categories which correspond to the two principal kinds of epithelium,—the squamous epithelial carcinoma and the cylindrical epithelial carcinoma. The former occurs par excellence upon membranes clad with squamous epithelium, the latter upon those with cylindrical epithelium, yet the access of the squamous epithelial cancer especially is not debarred from mucous membranes, which bear cylindrical epithelium; for example, from the gastric mucous membrane.

§ 165. The squamous *epithelial cancer* (epithelioma, epidermal cancer, cancroid) forms a white, dense mass of tumor, poor in juice, which upon the cut surface looks either entirely homogeneous or whose minuter structure may still be known only by hints. The palpating finger experiences a considerable, but dull, inelastic resistance. If we exert a stronger lateral pressure, milk-white, twisted filaments press beyond the surface, which have very properly been compared with the so-called comedones, which may be expressed from the sebaceous glands of the skin of the nose. These may be easily diffused in water. There is produced a cellular emulsion similar to cancer-juice; the washed-out cells, however, are altogether genuine pavement epithelium; they might just as well be taken for the epithelial cells of the oral cavity. Certain subordinate peculiarities in the form of the individual cells will more fitly come to be spoken of when considering the transverse sections. The nuclei are constantly very large, ovoid, with double contours, and provided with one or more large and shining nucleoli.

§ 166. When the epithelioma of the outer skin and the mucous membranes does not proceed from warts or cauliflower growths (§ 148), it in the next place always presents itself as a flat, bed-shaped tumefaction and induration. This in continued growth advances as well in depth as it extends superficially. If it has reached a certain maximum at the place of its first origin, then its breaking open ensues here. The surface, from the beginning somewhat tuberous, becomes raw, there arise numerous erosions, holes, and clefts, from which is poured out a white, odorless atheromatous pulp mixed with pus. Hereupon the tumor becomes depressed in the centre, an excavation is produced, which henceforth is covered either by dried secretion, or, if this were

removed, by necrosed shreds of remaining tissues. In this phase of development, therefore, the epithelioma is an ulcer with indurated base and indurated edges thrown up like an embankment. At the periphery of the ulcer we perceive the constant progress of the infiltration into the surrounding parts, at whose indurated edges we may study the acme of development, while toward the interior the decay of the new formation, and, in individual cases, the very distinct reparatory processes come to be perceived.

If, in the next place, we occupy ourselves with the *development* of carcinoma, it will be judicious, in reference to this, to distinguish the first production from its further extension. For the purpose of more accurately establishing the point of departure, vertical sections of satisfactory thinness are most suitable, which we may make through the indurated edge of an epithelioma of the external skin. (Fig. 63.) If

Fig. 63.

From the border of development of an epithelial cancer of the skin. *a*. Tumor-mass in full development; cylinder of epithelial cells, with pearly globules, longitudinally divided. *b*. An enlarged sebaceous gland. *c*. Commencing villiform elongation of the epidermis inwards. 1–150.

we advance in the consideration of this section from without inwards, from *c* to *a*, then the first thing whereby the beginning of the tumor-formation makes itself perceptible, is a striking enlargement of the sebaceous glands (*c*). They become longer, broader, therewith misshapenly knotty, and knobby at their blind ends. Close to the border of the tumor (*b*), an example of truly colossal dimensions is exhibited, and in an impartial consideration, it will appear to us as though the tubuli of the tumefied gland distinguished themselves in nothing from the neighboring projections of the cancroid new formation (*a*). The resemblance is especially caused by this, that in the elongation and thickening of the glandular fundus, the character of a secretory organ

is completely lost; we miss the central lumen, the oil-globules; we only see densely crowded epithelial cells, and indeed epithelial cells of a size which, for sebaceous glandular epithelium, is thoroughly abnormal.

If it consequently becomes credible that the epithelioma of the skin may proceed from the sebaceous glands, still, upon the other side, we must not forget that this "procedure from the sebaceous glands" is only to be regarded as the partial phenomenon of a *thorough derangement of the limits between the epithelium and the connective tissue.* We are indebted to Thiersch* for the communication concerning an epithelioma, which proceeded in a very demonstrable manner from the sweat glands; upon the other hand, we can see in *every* epithelioma that not the glands alone have participated in the formation of the cancroid projections. From the points furthest advanced into the connective tissue, from the projections of the rete Malpighii, which are inserted into the valleys between the papillæ, knobby elongations of the epithelium likewise penetrate deeply, and just this process, to which the elongation of the already existing epithelial involutions of the glands is subordinate, is the universal exponent of all primary epithelioma formations.† Not as glands, therefore, but as appendicular structures of the epidermis, do the sebaceous and sweat glands take part in the luxuriation. They lose their glandular character and change into what they originally were, solid aggregations of cells, which form villiform appendices of the under surface of the epidermis.

§ 167. In reference to the growth of the epithelial shoots and their penetration into the connective tissue substratum of the epidermis, the views of authors are very much divided. According to Thiersch, Billroth, and others, the epithelial shoots exclusively grow by division of the epithelial cells contained in them; according to Köster, the growth is by apposition, and ensues by a corresponding metamorphosis of the endothelia of the system of lymph-vessels, in whose cavities the epithelial projections exclusively extend themselves and advance. I, for my own part, can neither overlook the very striking fact that lively nuclear and cellular divisions proceed in the epithelial shoots, nor ignore the speaking pictures which one receives, if, according to Köster's direction, we cut parallel to the surface and examine the indurated edge of certain flat epithelial cancers of the cutis.

Fig. 64, in fact, shows us the superficial reticulum of lymph-vessels of the cutis in its entirely characteristic configuration, but filled with

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* Thiersch, Epithelial Cancer. Leipzig: Engelmann, 1865.

† Upon epitheliomas of the digestive tract, I have most certainly convinced myself that the tubular glands of the mucous membrane, supplied with cylindrical epithelium, play the same part as the sebaceous glands of the outer skin. They enlarge interiorly, and change their character in such manner that they lose their lumen, and then present solid masses of cells that in the first place are composed of indifferent, then of genuine pavement epithelial cells.

cylinders of epithelial cells. The lymph-vessels here undoubtedly indicate the way and the direction for the progress of the epithelial shoots. It is of course not said therewith that they do this in all carcinomas;

Fig. 64.

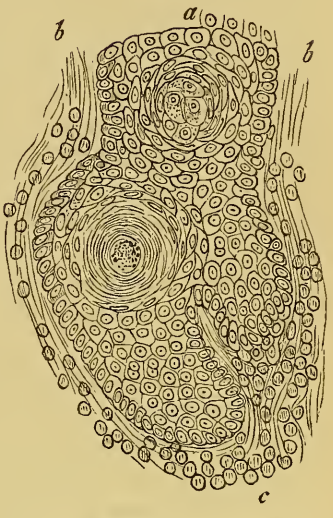
Horizontal section through the zone of development of an epithelial carcinoma of the skin. Extension of the epithelial projection in the system of lymph-vessels. After Köster.

we would probably have to content ourselves to find in the interesting discovery of Köster again only the microscopic expression of the fact already known, that the cancers and sarcomas of glandular organs, for example, the kidneys, the testicles, the lymph-glands, with especial readiness, break into the lumina of the blood- and lymph-vessels, and extend themselves in them. Nevertheless the question here is about a positive observation, which in a very obvious manner explains to us the mode of the penetration and advance of certain carcinomas into the parenchymas of organs. With this part of Köster's representation, the independent growth of the epithelial shoots asserted by Thiersch would also agree. Only the enlargement by apposition of the metamorphosed endothelia of the lymph-vessels would not agree with the latter. In reference to this, I have constantly warned against the one-sidedness of the judgment, and even to-day do not find myself induced to give up the harmonizing acceptation which I have hitherto entertained. I distinguish in epithelium, as, for instance, also in cartilage, a primary and a secondary growth; the former consists in the apposition of young and small cells at the border of the epithelium towards the connective tissue, the latter in an enlargement and multiplied division of the more central cells of the epithelial stratum. Upon the first depends the elongation and widening, upon the latter the suddenly occurring thickening of the young stratum, known to every microscopist. (Comp. the cicatrization of surface of wound, Fig. 39.) Thus it is here also. The peculiar creeping progress of the epithelial shoots takes place by the apposition of mobile cells of the nutritive apparatus (proliferated endothelia, according to Köster) to the most advanced points. The consecutive thickening and transformation into a compact epithelial

projection is for the greater part a consequence of the cell-division in the axis of the epithelial shoots.

§ 168. If we now come to the structure of the tumor (Fig. 63, *a*), we immediately remark that the principal mass of it is formed by just those cylindrical cell-cylinders, the so-called *epithelial projections*. These, upon a transverse section, have a thickness of 1-7 of a line, and as a rule, a considerable length, which indeed we very seldom get an entire view of; they bifurcate once, or several times, up to a complete arborescent ramification. The arrangement of the epithelial cells upon the cross section of the projections is characteristic (Fig. 65), namely, there is found, as at the integumentary surface itself, at the boundary towards the connective tissue, therefore at the periphery of the projections, a layer of small, oval, frequently also brownish-colored elements, to which, towards the interior, the more developed pavement epithelial cells annex themselves. These completely fill out the space; all fit together and into each other. Therewith one remarks everywhere a tendency to a *concentric stratification*.

FIG. 65.



Section of a cylinder of epithelial cells, under a magnifying power of 500. *a* The cylinder itself, with the characteristic stratification of its cells, a younger and an older pearly globule. *b*. The stroma, very rich in cells at *c*, and contributing directly to the enlargement by apposition of the cylinder.

We may well assume that in the constantly exhausting distension of the infiltrated parenchyma, the projections can only attain a certain thickness. Nevertheless if the apposition of new cells does not cease, there must necessarily occur a want of space; there must occur in the interior of the tumor a pressure, which affects as well the projections themselves, as the connective tissue stroma between the projections. I regard this so-called pressure of growth as an exceedingly important energy in the life-history of all infiltrative new formations; namely, in so far as it also acts compressive upon the interstitial vessels, it renders difficult the circulation of the blood, disturbs the nutrition of the parts, and, as a rule, becomes thereby the principal cause for the occurrence of retrogressive metamorphoses. It also comes into consideration in this sense for the epithelioma; beside this, however, I would wish to consider it participative in the tendency to stratification mentioned, which the cells in the interior of the epithelial projections show, and which culminate in the formation of the so-called pearly globules or pearly nodules.

The pearly globules (Fig. 63) are produced, in that, from point to

point in the axes of the epithelial projections, the neighboring elements arrange themselves like the layers of an onion, upon one or two epithelial cells which remain globular, and thereby become so flat, that as with the hairs and nails we can only observe a narrow shaded line as the optical expression of a cell standing upon edge. Large quantities of cells are in this manner compressed into a small, globular space, the whole receives a homogeneous, intensely yellow, luminous appearance, which reminds of the color of hair. The individual pearly nodule may grow to a considerable size, and we will learn to know in the variety pearly cancer (see Nerve-cysts, Brain), a form of epithelioma, where finally the whole epithelioma is converted into a certain number of pearly nodules.

Another interesting, but, as it appears, not exactly frequent transformation, which the cells of an epithelioma experience, is that into serrated cells. We thus call the cells, which are beset at their entire surface with very many serrations, only visible under high powers, added for the purpose of articulating suture-like with the neighboring cells, and thereby produce an exceedingly firm connection of the cells among each other.

§ 169. The second, never-failing structural element of the epithelioma is a *connective-tissue stroma*. With regard to the cylindrical form of those bodies with which it divides the existing space, we must imagine it as a honeycombed framework, whose open ends are directed outwards. The stroma, first of all, is the *displaced* and pressed-apart parenchyma of the cutis, or the mucosa. Inasmuch, however, according to our former deductions (§ 83), without regard to the first origin, the epithelium is in all cases to be regarded as a product of connective tissue, therefore we may presuppose, in the stroma of an epithelioma, a very active participation in the new formation. Now, in fact, we do find a luxurious cell-proliferation (*c*), especially at those points where the epithelial projections grow the most in advance of their tips; the stroma is in general rich in young elements; it is also disposed to self-growth, particularly to papillary excrescences.

The stroma carries the vessels of the epithelioma, and these share its fate in every respect; they become obliterated when the stroma atrophies; they dilate when the stroma displays a productive activity (see below). Fig. 63 shows at the same time a very successful injection of the vessels, which was managed according to the directions of Thiersch.

§ 170. We come to the decomposition of epithelial cancer. The conditions for this are developed with the tumor itself. It has already been pointed out how, by the pressure of growth, the circulation, and therewith the nutrition, may experience disturbances in larger or smaller sections of the tumor. These disturbances, as a rule, will first become influential at those points where unfavorable nutritive circumstances *per se* exist. These are, moreover, the central parts of the epithelial projections; namely, the thicker the epithelial projections

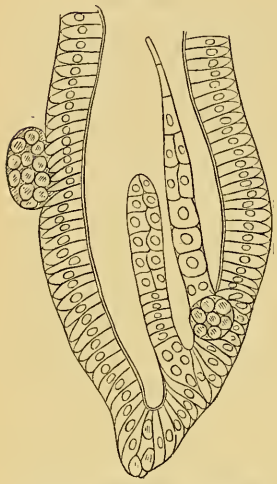
become, so much the further removed are the cells here situated from the soil which has produced and should nourish them. The circumstance, that just these cells are those first produced, and therefore the oldest of all, acts with the same purport, so that we regularly see the phenomena of retrogressive metamorphoses arise in the axes of the epithelial projections. The question therewith is mostly about a fatty degeneration of the epithelia, which leads to the formation of numerous atheromatous abscesses. These are originally separated from each other, but gradually flow together into a single cavity, penetrating the projection lengthwise. We perceive cavities of this sort already with the naked eye, at the surface of the epithelioma, as yellowish-white, comedone-like points. The rupture externally finally ensues, the hollowed projections open and empty their contents at the surface. Hereupon the tumor sinks together, and the ulceration, that separation above mentioned of pus and atheromatous pulp, begins.

Epithelioma does not rank among malignant new formations. At least cases are guaranteed, where a thoroughly extirpated epithelioma, *i. e.*, with the free excision of surrounding parts, never recurred. This is certainly not the rule. The cicatrix, mostly within a twelvemonth, becomes the seat of a new analogous formation of tumor. On the other hand, proper metastases are certainly of comparatively rare occurrence. The nearest situated lymph-glands suffer the soonest; but the interior organs only, when the primary affection has assumed such colossal dimensions, that in comparison with it the insignificant metastatic affections do not at all come into consideration. Metastasis is probably in all cases caused by the migration of young epithelial cells, which cause at the place of their settlement an epithelial infection of the indigenous elements of the vascular connective-tissue system.

§ 171. The *cylindrical epithelial cancer*. We have not been able to agree, up to the latest time, whether the crypts of Lieberkühn of the digestive tract are actually designed as tubular glands, or whether in fact only as crypts, *i. e.*, culs de sac of the surface, and only for increasing the same. The hesitation mainly proceeded from histology, which proved that these so-called glands were clothed up to their fundus with the same cylindrical epithelium as the free surface and the papillæ placed upon it. The facts of pathological histology are in nowise suited to banish these doubts, for the only affection from which we might expect an explanation in this direction, the cylindrical epithelial cancer of the digestive tract, shows such a uniform participation of the epithelium of the crypts and the papillæ, such an elevation and depression of level at the limit of epithelial and connective tissue, going hand in hand, that it is absolutely impossible to draw a sharply defined limit between the two. It is therefore also explicable, that the same new formation might just as well be apprehended as a destructive papilloma (Förster), as a proliferous adenoma (Klebs).

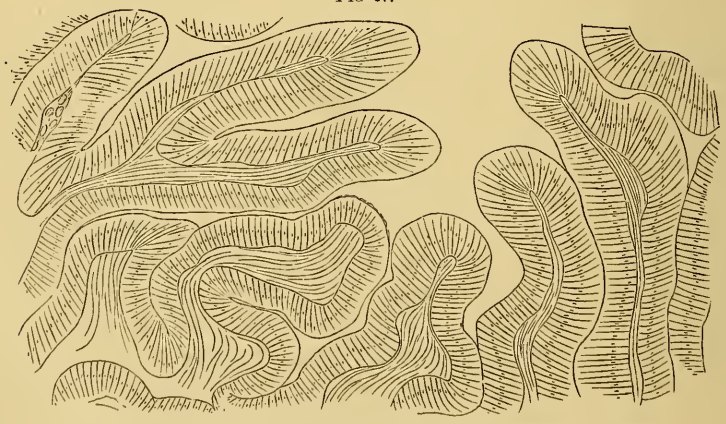
An acquaintance with the minute processes in the development of cylindrical epithelial cancer we owe to both the authors mentioned. The first step of the change is probably always a depression and a more complicated organization of the glandular tubuli. It is, however, important to state therewith, that this from the very beginning, I might say intentionally, exhibits the character of an enlargement of the surface, because the question is never about a solid projection of cells in the sense of a flat epithelioma, but constantly about involutions of the existing glandular lumena, which are clad with a simple layer of cylindrical cells. The new formation, in the next place, proceeds to a positive increase of surface, *i. e.*, to a production of papillary excrescences upon the walls of the cavities. The statements of Klebs in this direction are exceedingly interesting, which prove, that from the fundus of the glandular tubuli, pointed and knobby outgrowths elevate themselves, which in the first place are formed entirely of epithelial cells. (Fig. 66.) Afterwards, we find richly organized papillæ, which grow in all directions, particularly also inwardly, and thereby contribute to the destruction of the parts attacked. The free surface of the mucous membrane has already, at an earlier period, participated in the process by a greater or lesser luxuriant papillary proliferation.

Fig. 66.



From an adenoma of the digestive tract. Copied after Klebs. (Handbook of Path. Anat., Fig. 4.)

Fig 67.



From the section of a cylindrical epithelial cancer of the stomach. 1-300.

In general, however, the free surface is to be regarded as *locus minoris resistentiæ*, in consequence of which the tumor *in toto* constantly pre-

sents itself, as at first, a bed-like, afterwards a fungous elevation of the surface. In order properly to estimate the complicated structure of this, and particularly to distinguish the papillary proliferations from the septæ of the elevations and depressions likewise clothed with cylindrical epithelium, the teased-out preparations or sections of a certain thickness are only useful, because upon very thin sections an uninterrupted contour leads over from hill to valley, from valley to hill, but the concavity or the convexity of the ridges clothed with epithelium do not come into view. (Fig. 67.)

§ 172. I know that almost all mucous membranes, particularly also the mucous membranes of the larynx, the uterus, the bladder, and others have their peculiar epithelial cancers, which distinguish themselves from the principal types of the flat and cylindrical epithelial cancers in the same manner as the transitional epithelium of these parts do from the simple flat epithelium of the skin, or from the simple cylindrical epithelium of the stomach and intestine; still in relation to these finer shades I refer to the discussions of the Special Part.

APPENDIX.

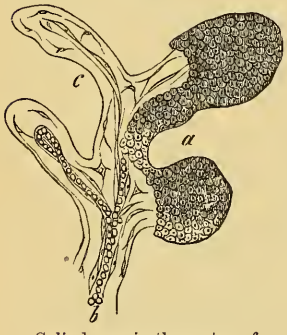
The Cylindroma.

§ 173. As a problem, as interesting as difficult, which accident has presented now to this, now to that investigator, along with all fundamental discussions concerning cancer and sarcoma, the question as to the essence and the nature of a tumor presents itself, which has been called by Henle siphonoma, by Billroth cylindroma, by Meckel tubular cartilaginous tumor, by Friedereich tubular sarcoma, by Förster, however, and the most recent examiner of it, Köster, mucous cancroid. As the great number of names already permits us to anticipate, the opinions of the various investigators concerning the tumor are widely divergent. May we assume that in all the cases examined the question was actually about the same new formation? The uniform situations of development in the face, especially in the cavity of the orbit and its surroundings, speaks for this; while at the same time the circumstance that the former investigators occupied themselves by preference with the most peculiar, not with the most essential products of the new formation, may yield justifying explanations of their difference of opinion.

The most peculiar products are certain larger *hyaline bodies*, which may easily be isolated by teasing-out, and at once impress by their remarkable external forms. Beside perfect globules, we discern more cylindrical, also even club-shaped and cactus-like figures. There is frequently the appearance, as though the hyaline chains strove to separate in various directions from a common point of union, &c. The

numerous hypotheses concerning the origin and further development of these bodies, in which mostly the histogenetic theories from time to time prevailing are reflected, it is impossible that I can go through at this place; I only mention that the apprehension of Billroth, according to which these are to be regarded as perivascular mucous-tissue sheaths or their fragments, has been the most diffused, until of late Köster, upon the ground of a very careful examination concerning the history of production of the whole tumor, has brought forward the hyaline globules, cylinders, &c., as the product of a secondary, hyaline metamorphosis, which the cell-trabeculæ of a cancroid of the lymph-vessels experience. According to this author we have to deal in all cases with a cancer-like proliferation of cells, which makes its appearance in the lymphatic net of the part affected. The endothelia of the lymph-vessels are they which multiply by division and amid obliteration of the lumen produce cell-strands, which of course ramify and anastomose just like the lymph-vessels themselves. Thereupon the hyaline degeneration begins, first of all in the axes of the cell-strands. It can even be demonstrated in individual cells; afterwards, however, the product of the degeneration flows together to those large globules and cylinders, which at the most yet remind of former cell limits by the presence and the stellate arrangement of a finely granular substance. The hyaline degeneration may lead up to a total consumption of the epithelial mantle, whereupon a relatively large hyaline cylinder appears imbedded in the connective tissue stroma.

FIG. 68.



Cylindroma in the cortex of cerebellum.

The state of the bloodvessels in the axes of the hyaline cylinders, which I myself have exhibited in a most complete manner in a progressing tumor upon the brain (Fig. 68), is explained by Köster by the well-known ensheathing of the bloodvessels in the lymph-sinuses.

The cylindroma is a tumor readily recurring, rarely exhibiting metastasis, and may therefore deserve a place near the cancers. To distinguish it from glandular and epithelial cancers, the designation as cancroid, which formerly belonged to all epithelial carcinomas, may even to-day be still continued for it.

SPECIAL PART.

I. ANOMALIES OF THE BLOOD, AND THE PLACES OF ITS FORMATION, ESPECIALLY THE SPLEEN AND THE LYMPH-GLANDS.

A. Dyscrasic Conditions.

§ 174. The blood plays so prominent a part in pathology, that it requires a more detailed discussion, although the anomalies of the blood take up but a comparatively short space in this text-book.

The position of blood in pathology is conditioned by its physiological importance. The blood is the medium of the exchange of material of the organism. It is the nutritive fluid which conveys to each individual portion of the body the nutritive constituents indispensable for its existence, and instead conveys away from the parts the useless and injurious products of the chemical processes associated with nutrition. The latter with the blood arrive at the excretory organs, where they are removed from the organism. Considered from this point of view, therefore, the blood is a place of concourse for the various chemical bodies which have already served, or are yet to serve, in the exchange of material; for bodies, which at all events remain here but *temporarily*, and in this way impart to the blood itself an inconstancy of chemical composition, for which not the blood itself, but the organs of the body are answerable.

But also when we consider the blood as an organ of the body, it is an inconstant element in contrast with the other organs. That generally we are correct in placing the blood among the other organs of the body, is beyond all question. In the first place it arises in the area vasculosa from germinal tissue, concurrently with the other organs, beside this, however, it has its specific cells, the blood-corpuscles, which have the entirely specific function of fixing in themselves the oxygen of the atmospheric air. That these cells have a fluid intercellular substance, that the blood in general is a liquid, must not mislead us in this apprehension. These textural constituents, however, are of a nature but little stable. The blood may very properly be esteemed as that tissue which the soonest again replaces its losses, which in general the soonest changes its morphological and chemical constituents. Withal

it does not prepare its constituent elements in itself, but derives its cells, for example, from the lymph-glands, the spleen, and—according to Bizzozero, Neumann, and others—from the medulla of bones, its albumen from the process of digestion. Therefore, here also, fixed organs are answerable for the constitution of the blood.

The normal constitution of the blood therefore depends in the first place, upon the regular admixture and transformation of the histogenetic constituents of the blood, then upon the regular and unhindered access and exit of the more transitory nutritive and excretory matters, finally upon this, that no improper and hurtful materials from any side whatever be taken up into the blood. Every disturbance in this connection will produce a mixtural change of the blood, *a dyscrasia*, and in fact by far the greatest number of the anomalies of the blood are diseases of this kind of blood-adulteration.

§ 175. Of the manifold dyscrasias of the blood, however, but few are exposed to *anatomical* consideration; namely, only those, which depend upon anomalies of the visible part, floating in the colorless fluid of the blood. As is known we distinguish in this connection, 1, the red blood-corpuscles; round disks with a central depression of both sides, perhaps four times as broad as thick, without a nucleus, without a membrane (?), composed of a colorless protoplasm (stroma) and a reddish-yellow fluid substance (hæmatocrystalline);* 2, the colorless or white blood-corpuscles, which are so sparsely found in the blood of healthy persons, that to four hundred and fifty red ones we find but one colorless. These cells are without a membrane, have a finely granulated protoplasm, and distinct nuclear structures. One either sees a simple, round, relatively large nucleus, or two to five smaller, smooth and shining nuclei. Their form is inconstant, as they possess the capacity of spontaneous motion in a superior degree; in the dead blood they are globular. They are therefore cells, which thoroughly resemble the cells of the germinal tissue and pus, and are scarcely to be distinguished from them by anatomical signs; 3, the elementary vesicles discovered by Zimmermann, colorless, of very ill-defined contour, circularly round structures, which, because of their minuteness and paleness, can only be seen with very high powers, but which occasionally occur in enormous numbers.

1. *Chlorosis.*

§ 176. A numerical decrease of the collective structures mentioned above, is the essential characteristic of the chlorotic blood-deterioration.

* Beside the disc-shaped, red blood-corpuscles, one always sees a certain number which have become globular. These distinguish themselves by their apparent minuteness and their darker coloring, up to brownish-red; peculiarities which are explained, in that the same mass, which was previously extended in a flat disc, is contracted into a globule.

This decrease uniformly affects all the formed constituents, so that the proportional number of the colorless to the colored blood-corpuscles experiences no change.

The blood as a whole appears more thinly fluid and lighter colored, if you will, more watery than normal; in evaporating there remains behind a far smaller percentage of solid residue; all this, however, not because the blood contains more water, but because it contains less cells. Where the color of the blood gives the tint for the color of an organ, for example, the mucous membranes (conjunctiva), in certain regions of the outer skin there a pallor comes to prevail, which has bestowed upon the whole disease the name of chlorosis.

With regard to the etiology of chlorosis, several points are yet obscure. This much is certain, that the chlorotic blood-deterioration does not depend upon a premature decay, not upon an atrophy of the blood-corpuscles, but upon an imperfect and insufficient replacement of the effete and cast out cells, by young vitalized elements. As for the remainder, however, whether we shall accuse a functional disturbance of the organs preparing the blood-cells, the spleen, and the lymph-glands, or a disturbance of the more remote factors of blood-formation, for example, chylification, we know not. The opinion of Virchow deserves especial consideration, according to which the imperfect development of the blood more frequently coincides with a certain imperfect development of the entire circulatory apparatus, especially of the heart and the arteries (see below), so that chlorosis is to be regarded as a congenital, and not as an acquired disease, in such measure, as is commonly done.

2. *Leukæmia.*

§ 177. The leukæmic dyscrasia consists in an alteration of the numerical proportion of the white to the red blood-corpuscles. We have above stated the average proportional number of the white to the red as 1 : 450. A moderate increase of the colorless cells lies within the bounds of health, and among other conditions may be established after every hearty meal. If, however, the number of the white blood-corpuscles in opposition to the red increases to such an extent, that for example, for ten red ones one white one occurs, nay, that finally the red and white corpuscles float in the blood in equal numbers, then this condition becomes perceptible already to the naked eye as a whitish decoloration (Himbeerfarbene, white raspberry colored) and we are correct in speaking of the "white blood" of leukæmia. This exceedingly interesting diseased condition was first simultaneously described in the year 1845 by Virchow and Bennett; to the German pathologist, however, the merit is due of having immediately recognized and explained it in its essential significance. According to Virchow we here deal with an *increased supply of the colorless cells* to the blood, a sup-

ply, for which pathological conditions of the same organs are answerable, from which also in normal circumstances, the colorless cells are conveyed into the blood, the spleen, and the lymph-glands.

§ 178. The spleen has from all time been regarded as an important organ for the renewal of the blood; in our days it has at one time been designated as the grave of the red blood-corpuscles, at another as the birthplace of the colorless; Kölliker has probably correctly ascribed to it both functions. The abundant amount of colorless cells contained in the blood of the splenic vein is undoubted, which exceeds that of arterial blood by from five to ten times. That the *lymph-glands*, especially the mesenteric glands, are a source of the colorless blood-corpuscles, is just as little doubtful. Thus, if we compare the lymph of the ductus thoracicus with that of the peripheral lymph-vessels, before their passage through the glands, we find that it contains a larger quantity of lymph-corpuscles. The afflux of colorless cells from the side of the spleen and lymph-glands, however, is not the same at all times. It is greatest some time after the ingestion of a meal. This increment coincides with that transitory hyperæmia of the whole digestive tract, which is called forth by the reception of food, and which makes itself known particularly in the spleen as a distinct tumefaction of the organ. If we have the opportunity of examining a spleen at this time, we find, leaving out of consideration the considerable hyperæmia of the pulp, the Malpighian corpuscles distinctly swollen. The mesenteric glands also are uncommonly large and rich in blood. It is, therefore, probable, that the increased supply of blood has, as a consequence, a more rapid new formation of colorless blood-cells in the Malpighian corpuscles of the spleen, and in the mesenteric glands. The newly-formed cells mingle with the lymph,—thus the blood current; there occurs a transitory leucocytosis; as soon, however, as the digestive hyperæmia of the abdomen again abates, the lymphatic organs upon the one hand, the blood mixture upon the other return to the ordinary relations.

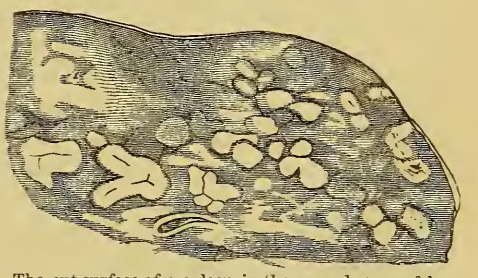
§ 179. Leukæmia is also regularly associated with a tumefaction of the lymphatic organs. The *spleen* stands foremost in this connection. Far more than one-half of all leukæmias are purely splenic; more rarely beside the spleen, the lymph-glands; most rarely the lymph-glands alone are diseased.

The *leukæmic splenic tumor* is originally a pure hyperæmia of the spleen. The more slowly flowing blood accumulates especially in those anastomosing canals of the pulp, which were recognized by Billroth as a part of the blood-tract of the spleen, and because of their easily to be demonstrated connection with the efferent bloodvessels were named "cavernous splenic veins." The lymphoid parenchyma of the pulp (the intervascular strands of Billroth) likewise participates in a considerable

degree; beside the customary colorless splenic-cells, we there perceive unusually many red blood-corpuscles; the Malpighian bodies also are larger than normal, yet their change remains for the present still a less striking phenomenon. A distinctly lobulated, or better, a knobby constitution of the surface of the organ strikes the unaided eye; beside the dark red color, the limited consistency, and considerable increase of volume of the pulp. Each of these knobs corresponds to the area of a splenic arteriole (penicillus); the depressions between the knobs are conditioned by the insertion of the larger splenic trabeculæ, which but slowly follow the enlargement of the whole organ. The capsule also does not bear any too sudden distension. I find, among my notes on Virchow's demonstrative course (Berlin, 1857–8), a case of splenic leukæmia, where the spleen in the stage of pulpous hyperæmia was tumefied to the dimensions of a foot long, two inches thick, and five inches broad, and, in consequence thereof, a rupture of the capsule had occurred. The rent, covered by a blood-clot, was three lines long, and upon both sides presented the first conditions of rupture, a commencing separation of the capsular fibres.

§ 180. In the further course of the disease, a hyperplasia of the Malpighian corpuscles, or as we should say at the present time, of the lymphoid arterial sheaths, more and more develops itself. The question therewith, first of all, is about an increased filling of these with colorless cells, which are developed from those pre-existing by division. A distension of the finely filamented intercellular network follows the cell-formation, and at length upon this follows a corresponding formation of new capillaries, so that the enlargement of the Malpighian corpuscles in fact affects each of the three structural constituents, and consequently is to be conceived as a genuine hyperplasia. The Malpighian corpuscles now present themselves upon a cut surface distinctly as white, compact nodules, offering vigorous resistance to pressure by the finger, and from one to three lines broad; one now perceives upon them much more frequently than under normal conditions, a furcated division, even an arborescent ramification; a proof that they have not only increased in thickness, but have advanced along the vessels to which they are attached, be it upwards or downwards. (Fig. 69.)

Fig. 69.



The cut surface of a spleen in the second stage of leukæmic swelling. Enlargement of the Malpighian corpuscles. Pigmented atrophy of the pulp.

The hyperplasia of the Malpighian corpuscles naturally adds a new one to the existing impulses of the tumefaction. The spleen in thickness, breadth, and length, attains the maximum which it generally can

attain. As, however, notwithstanding all this, the question is about processes within a given space, *i. e.*, determined by the size of the splenic capsule; it is almost self-evident that beside the hyperplastic processes, "room-making" retrogressive metamorphoses also accompany them. The latter especially affect the pulp, which, wedged in between the constantly aggrandizing Malpighian corpuscles, is destroyed in large portions. Herewith an abundant pigmentary formation constantly takes place, and as this is the greatest immediately at the borders of the white glistening Malpighian corpuscles, there results an extraordinarily variegated, granite-like marking of the cut surface. The consistence also of the organ, according to the measure of the predominating constituent, the Malpighian corpuscles, becomes exceedingly compact, leather-like, almost like a board. To this, chronic inflammatory processes of the peritoneal covering associate themselves, partly level or net-like hyperplasias of cartilaginous constitution, partly membranous, very vascular adhesions with the adjacent abdominal organs.

§ 181. In contradistinction to splenic leukæmia, Virchow names that rarer form, lymphatic leukæmia, which from the commencement characterizes itself by a predominant participation of the *lymph-glandular system*, while the splenic tumor falls into the background or is entirely wanting. All the glands do not at once swell up, but the disease begins perhaps in an inguinal or axillary lymph-gland, and in the first place extends to the collective lymph-glands of the region; then those situated farther interiorly, nearer the thoracic duct follow, perhaps the mediastinal and retro-peritoneal groups; thereafter peripheral glandular groups swell up anew, until finally everything, that is called lymph-gland, is more or less tumefied. Individual glands therewith not infrequently attain three to fivefold, even tenfold, their normal circumference. Nevertheless, anatomical examination, in every case, shows a simple hyperplastic process. The circumstance, that even in tumefactions of very high grade the lymph-passages remain free, and one is able to fill up the lymph-sinus of the gland as well from the afferent lymph-vessels, as by piercing it, already points to this. If we examine fine, teased-out sections, we see nothing that might not also occur in a normal lymph-gland: close-meshed nets of fine, shining filaments penetrated by blood-capillaries, and filled up with lymph-corpuscles. Only that the cortical tufts and the medullary channels are much broader, and the capsules and the connective-tissue septa are thicker than normal. W. Müller states, that in hyperplasias of lymph-glands, the delicate connective-tissue-cell-net, which penetrates the lymph-sinus of the cortex and the lymph-channels of the medullary substance, proves itself as the essential histioplastic element, in so far as just here new medullary layers are developed beside those present.

I believe that this is especially the case in the leukæmic hyperplasias (see below).

§ 182. The pathological histology of leukæmia, however, is not yet exhausted with these hyperplastic conditions of the spleen and the lymph-glands. The participation of other organs of the body rather shows that in these we only see the expression of a general disposition to the formation of new lymphadenoid tissue. The presence of a certain quantity of unformed connective tissue appears, in fact, to be the only condition upon which the occurrence of the characteristic changes is dependent. In that the cells multiply by division, they form circumscribed, smaller and larger depositions, appearing milk-white to the naked eye, which only distinguish themselves from depots of pus, in that the cells lie in a finely filamented network formed of stiffened protoplasm, which beside the cells yet presents sufficient space for the flowing through of the nutritive fluid. It is, however, scarcely necessary to say that just this imbedding of the cells, which distinguishes the leukæmic tumor from depots of pus, places them upon a level with the lymph-glands, elevates them into lymphadenoid tissue. (Compare herewith the leukæmic tumefaction of the liver, the kidney, the serous membranes in the appropriate chapters of the Special Part.)

3. *Melanœmia.*

§ 183. In the melanotic dyscrasia among the ordinary floating constituents of the blood, there occur pigment bodies, which, in the best-defined cases, may be demonstrated in every preparation of blood taken from the heart. They are flakes of the most irregular shapes, not to be more minutely described, composed of yellow, brown, pre-eminently, however, of black granules; the most of them are but small, smaller at least, than the red blood-corpuscles; others are larger,—individuals considerably exceed the circumference of the red blood-corpuscles.

Here and there we may distinguish upon the black lumps a transparent, colorless capsule, which equalizes the inequalities of the surface. The capsule is rarely of a thickness worth naming; then, however, there occurs in it a concentric stratification.

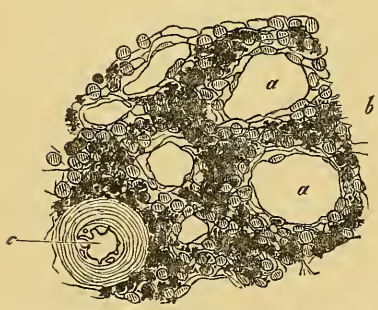
§ 184. I have amply expressed myself in the General Part (§ 56, *et seq.*) on the formation of pathological pigments. What was said there also finds its application to the melanotic pigmentary flakes. They arise from the coloring matter of the blood, are metamorphosed, and condensed into the form of granules of separated hæmatine. The conditions and place of their origin may also be stated with a certain precision. The melanotic pigment is formed under the influence of the malarial cachexy, and indeed especially in the spleen of the person affected.

The pathological anatomy of intermittent fever begins with an active

hyperæmia of the liver and spleen. The intumescence, which, in consequence of this, develops in both organs, may become one of very high degree. Nevertheless, only in longer continuance of the hyperæmia does it come to lasting disorganizations. As such among the diseases of the liver, we will learn to know a diffuse, interstitial hyperplasia of the connective tissue, the induration of the liver. In the spleen there is now observed a kind of softening of the entire parenchyma, now likewise a more indurated condition, with thickening of the capsule, and affecting the trabeculæ. To this is associated in particularly severe cases, as only yet occur sporadically in Germany, thanks to the extensive use of cinchona bark, a formation of pigment, as well in the liver as in the spleen.

We may deduce this directly from the very great and continuing accumulation of blood in both organs. The pigment appears in the liver *beside* the vessels; numerous, but small extravasations of blood in the capsule of Glisson and in the liver-parenchyma give here the first impulse to the formation of pigment. In the spleen, whose peculiar structure excludes the possibility of an extravasation, as here the blood can always only extravasate into a blood-cavity; the pigmentation occurs in the intervascular strands of the pulp, therefore in those regions of the organ *where the blood flows the slowest.* Here already, under normal conditions, the formation of blood-corpuscle-containing and pigment-cells is from time to time observed. In the pigmented spleen the black flaky masses lie so dense in the intervascular strands (Fig. 70, *b*), that even for the naked eye the spleen has from a slate up to a black color (the milza nera of the Italian malarial district).

Fig. 70.



The melanæmic spleen. Cross section from the centre of the organ. *a.* The cavernous splenic veins. *b.* The intervascular strands, with the pigment. *c.* A branch of the splenic artery. 1-300.

From hence the pigment flakes reach the blood. We know that a blood-tight closure of the intervascular strands towards the cavernous splenic veins (Fig. 70, *a*) does not occur; we consider the former as a minutely porous filter inserted between the arterial transition vessels and the venous radicles, which in the spleen is the same that capillaries and parenchyma are in other organs. In this filtration of the splenic blood the pigment flakes are torn away from the places of their formation and pass over into the blood, where their presence causes the melanotic dyscrasia. As far as the blood goes, so far do also the black fragments go. They are found in all organs of the body, mostly, however, in those which are distinguished by the narrowness of their capillaries, for example, in the brain. All the pigment flakes cannot pass

freely here. The larger among them remain sticking. Now comes to pass laceration of the vessels behind the occluded spots, hemorrhage, inflammation, and softening, in short, an array of anatomical changes, which is accompanied by the severest clinical phenomena. The rete mirabile of the kidneys also are not favorable to the free passage of the pigment flakes, at least, next to the brain, we most frequently find a melanotic pigmentation in this organ, black dots and striæ in the cortical substance, which, according to position, correspond to the Malpighian corpuscles and the vasa afferentia.

b. Coagulation of Blood in the Vessels (Thrombosis).

§ 185. One of the most important chapters of general pathology is occupied with the causes and consequences of coagulation of the blood in the vessels. We take from this chapter only that which is necessary for comprehending the histological processes which therewith come into question.

There are two conditions under which the coagulation occurs; a slowing of the circulation, and inequalities upon the inner surface of the vessels, against which the blood chafes in flowing by. In very many diseases of the vessels to be treated of in the following sections we will have to mention thrombosis as a complicating additional phenomena. Moreover, the coagulation by increased friction, can in very many, if not in all cases, be traced back to a coagulation from stagnation; namely, wherever at the inequalities in question small, and the very smallest depressions are found, in which the blood begins to stagnate. We will return to this in speaking of endocarditis.

§ 186. The act of coagulation itself depends upon a separation of the fibrin from the blood. Fibrin is not contained in the blood as such, but is only formed in the coagulation. A. Schmidt has established the interesting fact that in the blood-corpuscles is contained an albuminoid substance (globulin, fibrino-plastic substance), which enters into a firm union with a similar (fibrinogenous) substance contained in the liquor sanguinis, when the hindrances to coagulation are removed, or especially if the conditions facilitating coagulation are given. It is this firm union which we call fibrin.

Recently separated fibrin is a colorless substance swelled out in the highest degree. Two thousandth parts of fibrin impart to coagulated blood a gelatinous consistency. Recently separated fibrin is not visible under the microscope, because it is a perfectly homogeneous, entirely colorless substance. This, however, changes from the moment of coagulation. The molecules of fibrin have so great an attraction for each other that it contracts to an ever smaller volume, and therewith more and more expresses the contained fluid. To the separation into solid and fluid there corresponds an exceedingly characteristic microscopic

process. In the just described homogeneous mass numerous clefts and gaps arise, between which the solidifying fibrin remains behind as a more or less delicate network formed of round filaments.

§ 187. One may observe this transition wherever too great a number of cellular elements do not make the observation impossible. The latter, however, is the rule in the coagulation of blood in the vessels. Enormous quantities of red and colorless cells are fixed here by the coagulated fibrin, and so completely cover the microscopic occurrence of the fibrin coagulation that one can observe nothing thereof, even in the thinnest sections made through a hardened thrombus. We may be thoroughly convinced of this that the separation of fibrin is the cause of the thrombosis; that the subsequent contraction and a peculiar desiccation which the thrombus undergoes are quite dependent upon the described metamorphosis of the fibrin; but for the microscope there is no fibrin present in the vascular thrombus rich in cells, and, we may add, neither does it ever appear.

§ 188. The recent thrombus, constantly has a dark red and gelatinously soft consistency, such as belongs to every blood-coagulum. Its external form is in every case dependent upon the space in which the coagulation ensues. Very commonly they are cylindrical plugs, which fill up the entire lumen of a small or medium-sized vessel, and shut off towards the still open blood-current by a conical point (obstructing thrombi). Other clots do not entirely close the lumen of a vessel, but are only placed upon one side of the wall, and distinguish themselves by a more ribbon-like shape and a tongue-formed end (partial thrombi—wandständige thromben—thrombi attached to the wall). Further modifications are brought about by the already separated clot inducing new fibrinous separations, wherever it is washed over by the blood-current. Layer after layer is deposited, and thus by *continued coagulation* can—1, a partial clot very easily become an obstructing one; 2, the coagulation may pass from one vessel into a neighboring one. In the latter case the advancing clot in the first place is again a partial one, then becomes obstructing, &c. What circumference, what form the thrombus will finally have is entirely incalculable, and only to be predicted with any certainty in a few cases; for example, in the ligation of arteries; thus, the position obtains here that the coagulation, as well in the direction towards the heart as in the direction towards the periphery, does not reach further than to the nearest pervious collateral vessel. As a rule there is not much to be said of peripheral coagulation, because it is wont to turn out always very thin and unapparent, on account of the complete contraction of the vessel.

§ 189. We may now pass to the consideration of the further fate of thrombi. We must, however, begin by bringing into notice several distinctions in their *primary structure*. Much depends upon how rapidly a thrombus was produced, whether a certain portion of blood was sud-

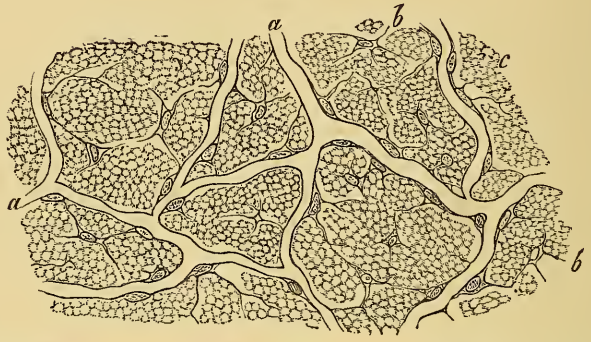
denly placed out of the current and immediately coagulated by any sudden occurrence; as, for example, by ligation, or whether the thrombus forms more gradually. In the first case the mingling of the colorless and red cells of the thrombus is so uniform that we find upon sections the colorless cells dispersed at regular distances throughout the mass of the red blood-corpuscles. It is otherwise where a coagulation slowly arose and slowly became larger and larger. I here allude, for example, to the thrombosis which arises in the vessels of a surface of amputation which has become diphtheritic, and from hence slowly advances into the veins of the part; to the thrombosis in the left auricle of the heart, in stenosis of the mitral valve; to the thrombi in varicose veins, aneurisms. In all these cases, which we will learn to know more intimately under diseases of the vessels, the so-called *viscosity* of the colorless blood-corpuscles asserts itself, and gives occasion to the stratified structure of the thrombus. The colorless blood-corpuscles are sticky, *i. e.*, their protoplasm has a tendency to cling to solid parts, to penetrate into their pores. It is most wont to combine with the protoplasm of other colorless cells; already in the more slowly flowing venous blood we not infrequently find the colorless blood-corpuscles together in pairs, and only to the rapid current of the blood in the arteries, and to the continually repeated pouring into a system of innumerable narrowest tubes, is it owing that under normal circumstances no lasting connection is formed between these structures.

Let it be assumed, now, the thrombus has attained a certain size, a recent layer of coagulated blood has lately been deposited thereon, then of all the blood-cells flowing over it, the colorless ones, because of their stickiness, will first remain clinging to the thrombus, and attach themselves to its outer parts, like as according to Von Recklinghausen's observation in suppurative inflammations, which are produced by the penetration of a finely porous body into the subcutaneous cellular tissue, the pus-corpuscles penetrate into this body and densely infiltrate its borders. Enough, a layer of colorless blood-corpuscles forms, which so long covers the surface, until a new deposition of the red thrombus-mass ensues. In other words, the blood-coagulation ensues interruptedly, and between the intermissions the colorless blood-corpuscles have time to attach themselves in large amounts to the surface.

If we make a transverse section through a thrombus of this kind (Fig. 71), we immediately observe that a system of transparent lines runs through it, which permits the more or less distinct recognition of a concentric arrangement. These lines are the optical expression of transversely divided layers of colorless blood-corpuscles, which alternate with somewhat wider layers of ordinary blood-clot. In regard, therefore, to their primary structure, we distinguish two kinds of thrombi: 1, *unstratified thrombi*, which were produced by the sudden

coagulation of a cut-off portion of blood; 2, *stratified thrombi*, which were produced by interrupted, slow, and repeated coagulations.

Fig. 71.



Cross section through a thrombus by ligation of the crural artery, thirty-seven days old; hardened in alcohol, treated with dilute acetic acid, and then with a little ammonia. *a*. Capillaries. *b*. The cell-net of the colorless blood-corpuscles. In the basis-substance the contours of the red blood-corpuscles.

§ 190. The two principal directions in which a blood-clot may subsequently metamorphose are designated upon the one side as organization, and upon the other as softening.

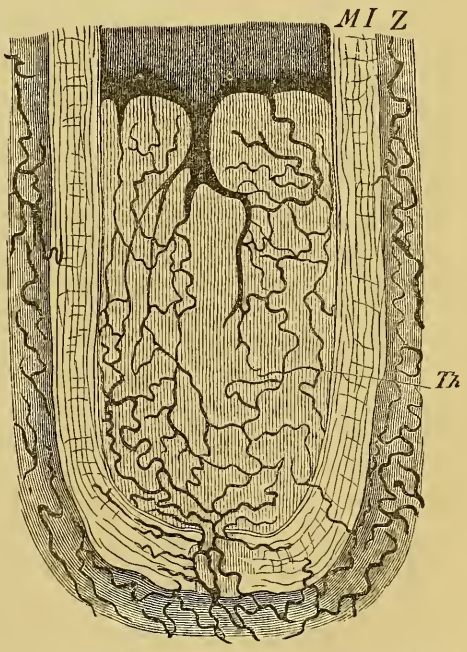
The organization, or connective-tissue metamorphosis, has hitherto been almost exclusively studied upon the unstratified thrombi of larger vessels. Hence the following representation, also, in the first place only takes cognizance of this, and expressly deals with the organization of stratified thrombi as a yet perfectly unknown process. The thrombus is largest immediately after the coagulation, when it also has the dark red color and the gelatinous consistency of a recent blood-clot. From this time it decreases day by day, finally entirely collapses and disappears in several months without leaving behind a trace of its presence. With this continuous diminution a decoloration and condensation of its substance goes hand in hand. It loses its original dark red color until it can scarcely yet be distinguished from the walls of the vessel by a reddish tint; it becomes drier, more compact; while originally it was loosely attached to the wall of the vessel, it afterwards enters into the most intimate connection with it; in short, it assumes the character of a connective-tissue plug, which appears to be more a portion of the surrounding connective tissue as well as of the wall of the vessel than a part of the blood. This course of the changes, as the naked eye determines it, is explained by the microscope in the following manner.

§ 191. It has already been mentioned, that in a recent unstratified thrombus the colorless blood-corpuscles are dispersed among the red at tolerably regular intervals. The opinion formerly prevailed, that the first change went out from these colorless blood-corpuscles. At present also the organization of thrombi has become the office of the migrating cells. Thrombi have been produced in animals by ligation, and sub-

sequently by cinnabar injections into the blood, the colorless corpuscles treated with this finely granular material being easily recognized by the microscope. It was now shown, that those cells from which, upon the second or third day after the coagulation, the organization of the clot proceeds, carried cinnabar, and are consequently to be regarded as being immigrants. They send out in various directions processes, which touch one another, and form a delicate protoplasmatic net, with nuclei at the points of intersection. (Fig. 71, *b*.) We could even now compare the arrangement to a connective substance, in which the cells are represented by the colorless blood-corpuscles, the basis-substance by the mass of the red blood-corpuscles and the fibrinous material. And in fact I might say this is the idea which lies at the basis of the organization, and is thereafter carried out.

Very soon after the first foundation has been completed, the vascularization of the thrombus begins.* It takes place according to the type of the tertiary vascular formation, *i. e.*, by the opening of capillary blood-passages along the filaments of the protoplasmatic net. A more or less complete vascularization can be demonstrated, either by injection or by thin sections, in every thrombus more than eight days old. The vessels are thin-walled capillaries with alternating nuclei (Fig. 71, *a*); they principally receive their blood from the yet pervious lumen of the thrombotic vessel itself, and return it there again, until communications otherwise but still scantily, form with the vasa vasorum. For the accomplishment of this latter, it is necessary that the non-vascular tunica intima, separated from the media by its homogeneous limitary membrane, be broken through, a task which is more difficult to nature than we might suppose. (Fig. 72.)

Fig. 72.



Longitudinal section of the ligated end of crural artery of a dog, fifty days after ligation. Injected by O. Weber. *Th.* Thrombus. *MI* Middle tunic of vessel. *Z.* Cellular tissue tunic.

§ 192. By the vascularization, the guarantee of a durable, organ-like connection with

* See O. Weber, Handbook of General and Special Surgery, edited by Pitha and Billroth. Vol. i, page 143.

the body is given to the thrombus; from this time it enters completely into the series of vascularized connective substances. How are matters, however, with the basis-substance of this peculiar connective tissue?

The red blood-corpuscles together with the fibrinous material form the principal mass of the recent thrombus. Their changes, therefore, are also the principal cause of the changes which we can perceive without the microscope. That the red corpuscles very soon part with their coloring matter, causes the decoloration; that the fibrinous material contracts and expresses the contained fluid, brings about the diminution and the desiccation of the thrombus. As to what remains, there is, 1, a decolored protoplasmatic lump for every red blood-corpuscle; 2, the fibrinous substance, as indeed an invisible but none the less very firm cement of these lumps. Both together form a mass, never fibrous, very difficult to tear, which represents the basis-substance of the thrombus from the first week up to the eighth. Thus their constituents may yet long be recognized for what they originally were. In a thrombus by ligation, thirty-seven days old, I still found the decolored blood-corpuscles retaining their form so well, that at the beginning I could not recognize the vessels and connective tissue cells for the quantity of blood-corpuscles; only after the addition of acetic acid did the contours of the blood-corpuscles disappear under the immense swelling up of the preparation, and the vascular and cellular nets came out distinctly. Only now was the resemblance to a vascularized connective substance not to be mistaken; also because of this behavior towards acetic acid, I do not hesitate in letting the stroma of the blood-corpuscles go directly over into the connective tissue basis-substance. But even after the addition of acetic acid, by the careful neutralization of this reagent by means of ammonia, the contours of the blood-corpuscles can yet again be made to appear, so that we see, side by side, both the vascular and cellular nets and the former blood-corpuscles. (Fig. 71.)

§ 193. All that yet follows of the histological changes may, according to § 154, be designated as the cavernous metamorphosis of the thrombus. It is that which in times past has been described as the sinus-like degeneration. The lumen of the bloodvessels widens more and more, while the original parenchyma disappears, and is replaced by a moderate amount of colorless cicatricial tissue, concentrically stratified around the vessels. The cavernous condition, at a certain period, has been most beautifully represented in Fig. 73. At a later period the lumina of the vessels ever become larger and larger, the trabeculæ constantly thinner, until at last they entirely disappear, and therewith the thrombus ceases to exist.

§ 194. The softening of thrombi forms a similar contrast to their organization, as suppuration does to the organization of inflammatory new formations. This especially obtains with reference to the clinical

significance and the macroscopic peculiarities of the process. Touching the latter, a decoloration of the originally dark-red thrombus here also plays a prominent rôle. This regularly begins in the centre of the thrombus, and from here advances towards the periphery; hand in hand with it goes a certain condensation, which, however, is not as in organization a durable one, but is only a transitory phenomenon, and imme-

Fig. 73.

From the cross section of an arterial thrombus of three months. *a*. Media, only the innermost layers. *b*. Boundary lamella of the media and intima. *c*. Intima. *d*. Boundary of intima towards the thrombus. *e*. Thrombus. *f*. Lumina of vessels. Distinct epithelium. 1-300.

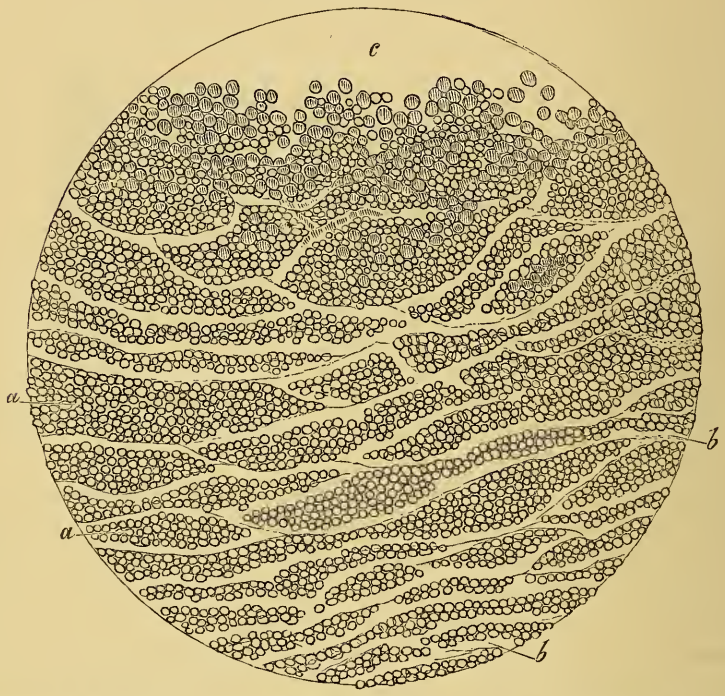
diately passes over into the contrary, softening and liquefaction of the mass of the thrombus, so that at a certain time we find in the interior of the thrombus a yellow, *pus-like* fluid, at the periphery a yet tolerably compact, flesh-colored layer, intimately adherent to the wall of the vessel. The circumstance that the softening generally occurs in thrombi of peculiarly stratified structure, modifies the anatomical picture in a manifold manner. The layers of colorless blood-corpuscles now show themselves as very prone to take part in the process of softening; now they are they which resist decay the longest. In the former case, the connection of colorless cells is dissolved at an early period. Ere yet the red blood-corpuscles have entirely given up their coloring matter, the thrombus breaks down into a reddish-gray pulp, which is now more uniform, like the lees of wine, now has more the appearance of chopped meat.

When, on the contrary, the colorless blood-corpuscles resist longer than the colored ones, there results primarily a caseous consistency and color, afterward a more spongy or honeycombed structure of the entire thrombus concerned in the softening.

§ 195. I have been at pains also to establish the histological detail of the softening of thrombi. The representation given in Fig. 74 is from the transverse section of a stratified, interiorly softened thrombus. The upper border of the picture shows the limits of the exterior part not yet softened, and the central part already softened. Below we see the almost regular alternation of colorless septa, and the interdeposited

layers of blood-clot. At the boundaries of the softening upon the one side, the colorless lines break up into rows of single, colorless blood-corpuscles; upon the other, the compact masses of red corpuscles loosen and mingle with the fluid of softening. They had already previously

Fig. 74.



From the cross section of a softening thrombus. *a*. Layers of blood-clot. *b*. Colorless layers, consisting of firmly united white blood-corpuscles. *c*. Cavity of softening. 1–300.

lost their coloring matter and become cloudy, so that they can scarcely be distinguished from the originally colorless cells; now their stroma also dissolves, and imparts to the fluid of softening a slimy consistence, often capable of being drawn out into threads. The colorless cells also disintegrate into small granules. The fluid of softening therefore contains, as a rule, only a granular detritus and fatty globules; these impart to it the yellowish-gray, puriform appearance; actual pus-corpuscles (even if we will so call the colorless blood-corpuscles) occur in it but sparsely, and nothing may be said of any new formation of cellular elements, so that designating the softening of thrombi as suppuration, characterizes indeed the macroscopic phenomena up to a certain point, but by no means touches the nature of the thing.

§ 196. The softening of thrombi is in more than one respect a dangerous process. Foremost, however, the possibility threatens, that wherever the thrombus touches the free current of blood, parts of it

may be loosened and conveyed onwards. If this has happened, the fragments are carried onward by the blood-current, and reach

a. From the radicles of the vena cava, through the right heart, the lungs;

b. From the radicles of the pulmonary veins, through the left heart, the various organs of the body;

c. From the radicles of the portal vein, the liver. How far they in this migration advance into the ramifications of the vascular region entered upon by them, depends upon the circumference of each single fragment. It is manifest, that only such fragments may everywhere pass freely, which are not larger than the blood-corpuscles. All that exceed this size, remain fixed somewhere and occlude the vessel, whose lumen they cannot pass (embolism).

Much may be said concerning the favorite routes of the migrating plugs (emboli): emboli of the lungs by preference readily go into those long, straight-running branches of the pulmonary artery, which run at the inner surface of the lower and middle lobes of the lung to the borders and the contiguous parts of the outer surface. In the aortic system, *larger* emboli are wont with predilection to seek the popliteal artery, and the artery of the Sylvian fissure. It is probable that the limited curve of the route which the embolus has to pass in the cases mentioned, determines its course. It often appears to happen, that an embolus rides upon the forked place of division of an artery, the spur, and then, like a scale of ice before an ice-breaker shatters into smaller fragments. These divide among a greater number of branches given off. Multiple emboli at a certain region of an organ, with complete immunity of the remainder, for example, at a single Malpighian pyramid of the kidney, a single lobule of the lung, thus find an explanation. Finally, it has been established by the experiments of O. Weber, that smaller emboli can pass the capillary system of the lungs, in order to remain sticking in the narrower capillaries of the kidneys.

§ 197. The *embolic processes*, *i. e.*, the morbid changes which are developed in organs affected by emboli, we will have to study more in detail at another place. Here only the general remark, that anæmia is indeed the first and direct consequence of every occlusion of a vessel (the withholding of blood, ischæmia); that the anæmia, however, as a rule, immediately gives way to an excessive congestion. The more completely the closed vascular region is connected by anastomoses with neighboring regions, so much the more will it present itself as a cæcal appendage, a recess of the circulatory apparatus, which indeed is filled from all sides with blood, but has no sufficient efflux, so that a higher pressure prevails in it than in all other capillaries. This secondary congestion may proceed up to tearing the vessel, to a hemorrhagic infarction, but the blood stagnates, the blood-exchange sinks to nought, nutrition ceases. All embolic processes, therefore,

essentially have the character of disturbance of nutrition, nothing less than necrosis itself. (Compare Metastatic Abscesses of the Lungs, the Liver, the Kidneys, Embolic Necroses of Bones, Yellow Softening of the Brain, &c.)

c. Inflammation and Formation of Tumor.

§ 198. There was a time when one with all seriousness discussed the possibility of an inflammation of the blood, hæmitis (Piorry). The numerical increase of the colorless blood-cells, which we can demonstrate in leukæmia, induced, especially Bennett, to the opinion of a suppuration of the entire blood. Yet all representations of this kind must already be rejected, because for our conception of the idea of inflammation, the contrast of parenchyma and blood, of the thing to be nourished and the nutritive material, is indispensable. Hence we can only in general admit inflammatory and—as we will at once add—neoplastic processes for the forming-places of the blood-corpuscles, especially the lymph-glands, although also upon the other hand, we not only concede, but even expressly emphasize, that through these inflammations the composition of the blood itself can be influenced and changed.

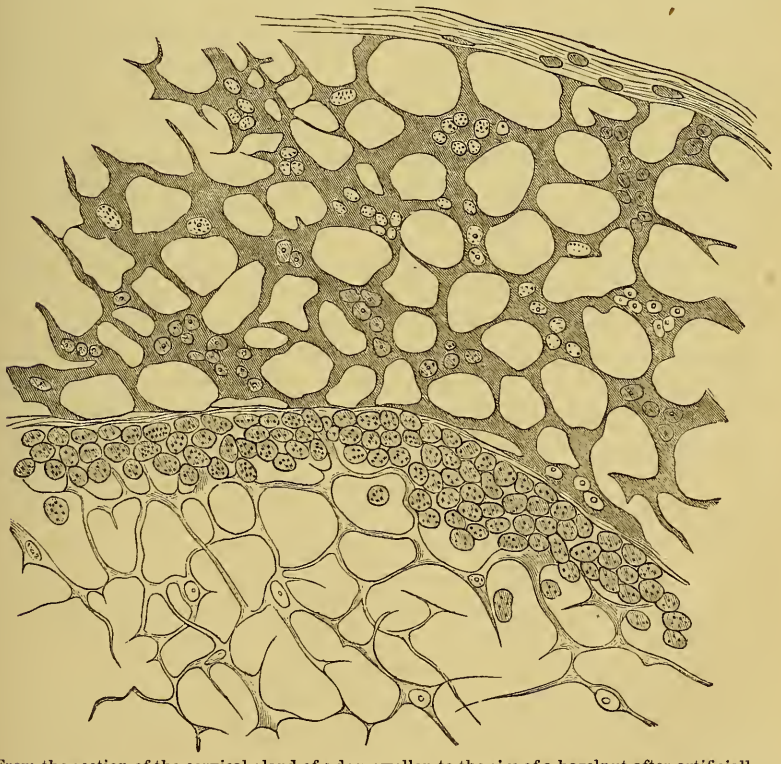
§ 199. We believed above that we could not characterize the lymphadenoid tissue better than by saying, that a youthful state, yet very closely allied to the embryonal formative tissue, had to a certain degree become permanent. We must be mindful of this circumstance, when we perceive how easily lymphadenoid tissue can be determined to enter upon any direction of development whatever, imparted by a corresponding irritation. Inflammatory conditions of the organs from which the lymph-glands received their lymph, cause suppurative, cheesy, and indurative lymphadenites. All specific inflammations reproduce themselves in the appurtenant lymph-glands, thus the gumma syphiliticum, miliary tubercle, typhous new formation; finally, almost all carcinomas, when they begin to form metastases, pass over first of all to the lymph-glands. Therewith the new formation concerned appears upon the lymphadenoid tissue with few exceptions in a purity and exclusiveness, which is frequently wanting at the primary focus of the disease, so that I can very particularly recommend the lymph-glands for the study of the tumor-mass as such. By this it has not been said, that the lymph-glands yield a very fitting object of investigation also, for the development of the new formation, on the contrary just here our knowledge yet shows important gaps, as may become sufficiently distinct from the following summary.

§ 200. 1. *Lymphadenitis acuta.* The internal condition of a lymph-gland, which is moderately swollen and painful in consequence of an inflammation in the region of its lymphatics, is generally thus to be interpreted, that beside a hyperæmic filling of the vessels, an increase of contained lymph-corpuscles has taken place. Whence, however, this

increase of lymph-corpuscles? We can as well think of a migration of the colorless blood-corpuscles from the dilated vessels, as of a division of the existing cells, as finally of a wandering from the inflammatory focus, and unfortunately adduce for each of the three possibilities the most important analogies. I say unfortunately; for how important, also, for the knowledge of the physiological function of the lymph-glands would be the decision of this question. An à priori consideration should incline us to the autochthonous origin of the lymph-corpuscles. It is seductive to accept, that only a quantitative excess of the normal cell-formation was in question here; the same which supplies to the blood its physiological need of young elements, and is probably destined here to cover that greater loss in colorless cells, which by migration result in inflammatory depots. Yet just here, where an erroneous representation may become so injurious, we must only speak of simply what has been observed.

According to Billroth (Fig. 75) a well-brushed-out, or still better,

Fig. 75.



From the section of the cervical gland of a dog, swollen to the size of a hazelnut after artificially produced inflammation of the lips. 1-500. After Billroth. Connective-tissue septum. Sinus terminalis. Border of lymph alveoli.

a shaken section through a hardened gland proves, that that system of soft, protoplasmatic stellate-cells, which is expanded between the

walls of the lymph-sinus, undergoes a very considerable hyperplasia. The cells duly swell up, ramify more abundantly, but the processes also thicken and attain new points of junction. Hand in hand herewith goes a luxurious increase of nuclei, so that finally we receive the impression of polynucleated giant-cells, which are connected with each other by broad anastomoses.

The reticulum in the interior of the lymph-alveoli and strands remains passive in the first place, in the presence of this more abundant infiltration of cells. A large number of more minute connective filaments spread out, and the whole tissue retracts into a smaller number of principal trabeculæ, appearing somewhat larger. Only when the question is about very slowly rising tumefactions, do all the trabeculæ of the reticulum experience a reactive hyperplasia, of which hereafter. Beside the disappearing reticulum, the lymph-corpuscles form larger roundish balls. We find such balls here and there, even in the normal lymph-alveoli; now, however, the entire adenoid substance is penetrated by them. These cellular balls may very properly be regarded as foci of division, although the direct proof is wanting. Whether we may point to the above-described giant-cellular metamorphosis of the cells of the lymph-passages in the same sense, is still a question, though here also, at least, the preliminary stages of cell-division, namely, division of nucleus and increase of the protoplasm, are undoubtedly given.

§ 201. The immediate continuation of the simple tumefaction of lymph-glands is the suppuration of the parenchyma, provided that a seasonable cessation does not occur in the production and accumulation of the lymph-corpuscles. Not only that the reticulum of the lymph-alveoli becomes always more rarefied, finally the capillaries also break down, and the net of lymph-passage cells, rich in nuclei and protoplasm, disintegrates. Then a fluid, rich in cells, which cannot be distinguished from pus, fills up all spaces, which until then were filled out by the lymphadenoid parenchyma. If we are dealing with a single lymphatic follicle, for example, of the intestinal mucous membrane, we call the condition a follicular abscess; if with an entire lymph-gland, the condition is termed a suppurative bubo. The future course completely falls under the considerations of suppurative inflammation and formation of abscess, discussed in § 94.

§ 202. 2. *Lymphadenitis chronica.* Chronic inflammation of the lymph-glands is distinguished from the acute, not so much by the slower movement in which the phenomena are developed, as by the durability of the conditions which are its final results. We can, however, distinguish several well-characterized forms of chronic inflammation. In the first place, there is the *genuine hyperplasia* of the lymphadenoid substance, which is indeed only observed in the tonsils and the follicular glands of the fauces. It depends upon a process of growth uniformly affecting all the histological constituents of the follicle, the

reticulum, the vessels, the lymph-passages, and the cells. The single follicle attains three to five times its normal volume, without any striking changes in its texture becoming visible. To the genuine hyperplasia the *leukæmic* form, considered above (§ 181), is anatomically most closely joined, only that the latter bears more a functional character, and is not produced like the former, by habitual catarrhs of the appertaining surface of mucous membrane.

§ 203. In the next place, we touch upon a condition of persistent tumefaction, which only develops in individuals specially disposed thereto, and is on that account regarded as a pathognomonic sign of the so-called *scrofulosis*.

We term this affection of the lymphatic apparatus as scrofulous in a more contracted sense, in that we comprehend in the general idea of scrofulosis, also the primary affection, nay, the entire condition, the constitution of the affected individuals. These primary affections distinguish themselves in part by their destructive tendency, thus especially in the lungs and in the osseous system; in part they have nothing characteristic. In the latter case, then, the affection of the lymph-glands comes decidedly into the foreground, and is par excellence designated as scrofulosis.

§ 204. The histological process, by which the scrofulous glandular swelling is produced, can in so far be termed a partial hyperplasia of the glandular substance, as with it we are not dealing with a uniform increase of volume of all the structural constituents, but only with an increase and enlargement of the cells, which form the glandular elements. I expressly emphasize beside the numerical increase also the enlargement of the individual elements, because it appears to me that this enlargement not only very constantly occurs, but also stands in a most intimate relation to the increase; namely, in the enlarged lymph-corpuscles it proceeds to multiple nuclear division and endogenous cell-formation, like as we have already learned to know in the tubercle-cells, and as we will yet learn to know in the typhous new formation. It is interesting to follow the course of the changes within the gland. Namely, it is shown that herewith, in the first place, those parts are affected which form the proper boundaries of the lymph-current, and hence are exposed foremost to the pathological irritation conducted from the periphery. At a very early period the stellate cells, which penetrate the lymph-sinus and in a certain measure are expanded in it, begin to participate by nuclear division and the production of new elements; this takes place partly at the periphery of the gland in the surroundings of the terminal alveoli, partly in the medullary substance; in both cases we get a soft infiltrate, appearing to the naked eye faintly or reddish-gray, and which is most strongly represented just where, under normal circumstances, a system of communicating lumina effects the bounding of the single glandular constituents. The result is, that

the borders of the neighboring lymph-alveoli are completely effaced in the cortical substance, the neighboring lymph-trabeculæ in the medullary substance, and that in the same measure as the substance of the lymph-alveoli and the trabeculæ themselves also enter into the pathological luxuriation, every dissimilarity of the cut surface is lost, and everything appears metamorphosed into a homogeneous faintly gray substance.

The acme of the process is herewith attained; the scrofulous bubo is perhaps as large as a walnut, when the unchanged gland had the size of a bean; the consistency is, according to the moisture present, now soft and flabby, now firm, even elastic, springy. Meanwhile just the acme of the process is of short continuance. The newly formed material not only interrupts the lymph-passages of the gland, but also compresses the blood-capillaries in such manner that the circulation completely stagnates. It is impossible, by any method of injection, to penetrate into the most swollen parts of the gland. With the supply of blood, the nutrition also self-evidently ceases, the gland falls into "caseous degeneration." Where this enters in, the gray mass first becomes opaque, then whitish-yellow, non-transparent, dry and friable. If the whole gland has passed into the caseous condition, it appears upon a section "as a fresh potato, only not quite so moist, but just as homogeneously yellowish-white." (Virchow, Tumors, vol. ii, 593.)

§ 205. The future fate of the lymph-glands, which have become cheesy (tyromata), appears to be dependent for the greater part upon their situation; thus, while we observe upon the mesenteric glands almost always a subsequent diminution by the resorption of the fluid constituents yet contained, not rarely also the deposition of lime and petrifaction, the more common issue for the lymph-glands of the neck is into softening. The caseous depot melts from within outwards into a whitish-yellow, whey-like fluid, which holds the fatty granular detritus suspended in smaller and larger fragments. If all the caseous material has softened, the neighborhood of the gland is wont to inflame; this inflammation facilitates the way for the "scrofulous pus" outwards. This is evacuated, we have the "scrofulous ulcer," with its overhanging, bluish, hyperæmic, flabby edges. At length this opening also closes, and a drawn-in, radiated cicatrix marks the place where the evacuation took place. A third possibility of decomposition—of all certainly the most desirable—has of late been described by Virchow. It is the complete resolution of the cheesy material. Probably herewith a peripheral liquefaction of the gland and absorption of the fluid into the bloodvessels of the capsule, widened by the collateral hyperæmia, takes place.

§ 206. Finally, we have yet to mention *chronic induration* as a phenomenon falling into the province of inflammation. It has already been mentioned that only the rapidly growing accumulation of lymph-

corpuscles in the lymphadenoid substance brings with it the breaking down of the reticulum; therein already lies the indication that a slowly increasing multiplication of the imbedded cells does not have this breaking down as a consequence. In this case an exceedingly striking "reactive" thickening and elongation of the collective trabeculæ of the reticulum rather shows itself. The latter by this, finally gains so much in mass that in comparison the cells take up a diminishing small space, and the whole gland assumes a compact, fibrous constitution.

§ 207. 3. *Syphilis.* To the condition of indurated chancre (§ 110), therefore the primary effects of constitutional syphilis, there corresponds in the appertaining lymph-glands the so-called indolent bubo, likewise a chronic induration, but conditioned not so much by an induration and enlargement of the reticulum, as by a very uniform, although by no means luxuriant, production of young cells in all parts of the gland. Every space is tightly filled with cells, and therewith for the time being it goes no further. We can temporarily obtain the same increase of volume and induration of glands by piercing and injecting them. This condition may remain unchanged for months, even years; rarely does any progress show itself, whether by more acute inflammation or by cheesy metamorphosis and necrosis. Finally, a fatty metamorphosis of the cells begins, the detritus is resorbed, and the gland returns to its normal state.

4. The *typhous degeneration* of the lymph-glands will be spoken of as a specific consequence of the analogous disease of the mucous membranes; under the anomalies of mucous membranes, the histological processes are characterized by a cell-form, which has already been cursorily described in § 112.

§ 208. 5. *Sarcoma.* The lymph-glandlike sarcoma finds its prototype in the lymphadenoid substance, and therefore a peculiarly favorable seat of development in the lymph-glands. It presents itself in the first place as a hyperplastic swelling; afterward in its true shape, as an incessantly growing tumor. According to consistence and color, rapidity of growth and malignity, several subdivisions may be formed. The least malignant, at the same time the hardest and slowest growing forms, characterize themselves, in that constantly a whole group of lymph-glands are simultaneously affected, for example, the collective glands situated at the upper or lower cervical region. There arises a numerously lobulated tumor, frequently of considerable circumference; each of the lobules corresponds to a tumefied lymph-gland. The vessels and nerves are multifariously displaced, and from this circumstance the removal by operation becomes almost a matter of impossibility (pseudo-scrofulosis).

A second, very much softer, and at the same time large-celled form, is apt to perforate the walls of the veins, and then to luxuriate in the lumina of these canals (venous cancer). It happens that the collective

veins of the anterior cervical or of the inguinal region are filled with sarcomatous thrombi of this kind, and thereafter have in readiness a very fertile material for embolic processes. Concerning the "how" of this intravascular growth, no authentic observations have yet been presented. Microscopically, it makes the impression as though in the first place a coagulation of the blood were accomplished, and then, in a certain degree under the protection of this coagulum, that the further growth of the sarcomatous mass took place. Others assert a direct metamorphosis of the clot into sarcoma tissue.

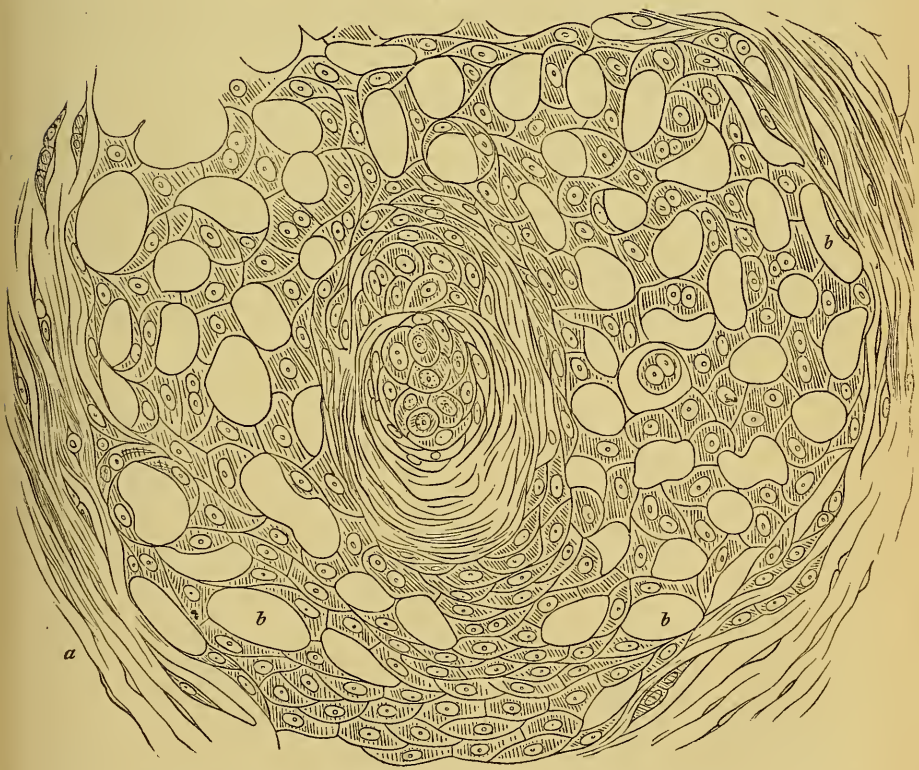
The third group of lymph-glandular sarcomas are characterized by the prominent tendency to forthwith break through the borders of the lymph-glands, in which they arose, and to occasion diffuse infiltrations of the neighboring loose cellular tissue. They are tumors which, touching rapidity of growth and malignity, are excelled by no species of sarcoma, although they never exhibit an alveolar structure. As regards therapeusis, they are in general a noli me tangere, although the experiences concerning fatty degeneration and resorption of sarcoma by erysipelas, which I have stated above (§ 92), relate just to these.

§ 209. 6. *Carcinoma.* It is one of the most interesting histological problems to establish the nature and the manner in which primary carcinoma effects the infection of the neighboring lymph-glands, and if that should be proven, which for the time being is taken for granted, that this is accomplished by means of immigrated cancer-cells, to determine the point at which these cells remain attached, and how they produce the first nests of cancer-cells, either by their own division, or by infecting the lymph-corpuscles. After numerous investigations directed to this point, I can only bring forward that the transformation of the lymphadenoid substance into the substance of a glandular carcinoma is accomplished in an exceedingly simple manner, in that the trabeculæ of the reticulum, like as in chronic induration, experience a considerable elongation and thickening; the meshes enlarge from ten to twenty times, and then, instead of lymph-corpuscles, contain the specific cancer-cells. The structure of the lymphadenoid tissue consequently appears to go over directly into the structure of carcinoma, the reticulum into the stroma, the lymph-corpuscles into the carcinoma-cells.

The epithelial cancer of the lymph-glands presents very much more complicated relations. The general rule, that in metastasing tumors the lymph-glands situated nearest to the locus affectus first become diseased, is maintained with peculiar strictness by epithelial cancer. Therefore, in cancer of the lips we see the submaxillary glands, in cancer of the penis or the labia majora the inguinal, in cancer of the scalp the cervical group, in the first place swollen. Metastases commonly go no further, because the extensive disturbances which the cancer has produced at the place of its origin, intermediately ensuing, bring about the death of the patient at an earlier period.

The tumefaction, as a rule, begins at the periphery of the lymph-gland. This shows several tuberosities, of which one then gradually distinguishes itself by special size, and takes up the other in itself. The gland finally attains perhaps double or threefold its normal volume. As a rule, we can observe upon several neighboring glands, upon one the beginning, upon another a middle stage, upon a third the completed intumescence. The largest nodes (of the size of a pigeon's egg) almost always contain a centrally situated softening cyst. The smaller and the smallest distinguish themselves by their white color and their compact, dry consistency, and sharply and distinctly elevate themselves from the yet normal parenchyma of the lymph-glands. This normal parenchyma, however, at least in the neighborhood of the smallest nodes, is also only apparently normal. The microscope here already shows us very interesting changes, which place us in a situation to obtain an opinion concerning the first origin of the masses of epithelial cells.

FIG. 76.



Epithelial carcinoma. Origin of the smallest nodules in the reticulum of the lymph-tract of the lymph-gland. *b*. Meshes of the reticulum. *a*. Contiguous connective tissue.

Thus, if we trace up the origin of the known epithelial cell-cylinders, we find as the first sign of commencing metamorphosis, small

groups of two to five epithelial cells, lying in an uncommonly large cleft, not of the delicate reticulum of the proper lymphadenoid substance, but of that network which is formed by the nucleated protoplasma cells expanded in the lymph-sinus of the periphery and the lymph-vessels of the medullary substance. I regard these imbedded epithelial cells as migratory, and I conceive the characteristic metamorphosis, which the cells of the reticulum in their neighborhood have undergone, as a result of their epithelial infection.

Now they enlarge, their anastomoses extend, and finally there results an arrangement (Fig. 76), which perhaps reminds of the liver-cell network. The frequent occurrence of double nuclei points to an independent multiplication of the cells by division. Shall we, in the face of this phenomenon and of the fact that the diminution is exclusively found in the surroundings of finished, concentrically stratified epithelial cells, doubt, that here occurs a metamorphosis of the reticular cells into epithelial cells? The reticulated structure moreover yet maintains itself a long time, and can be demonstrated even in cancroid nodules, which have already attained a recognizable size for the naked eye.

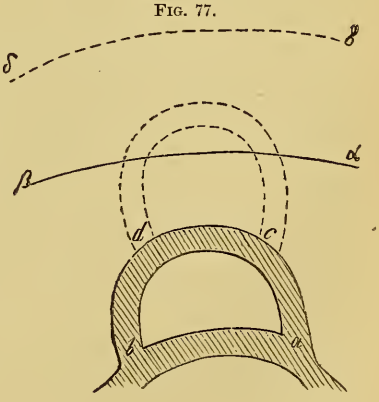
II. ANOMALIES OF THE CIRCULATORY APPARATUS.

1. Diseases of the Arteries and Veins.

§ 210. I will preface the pathological histology of the vascular system with a short consideration of the normal textural relations, particularly because the current representations of these subjects contain several unsolved points of controversy, concerning which, on account of their prominent significance for morbid changes, I would wish to express myself beforehand.

As might primarily have been expected, all the vessels of the body are built upon one uniform plan, and this may best be genetically unfolded. Let *a*—*b* (Fig. 77) be a capillary loop, α—β the limit of a growing organ. The blood flows under a certain pressure, with a certain rapidity, and with a certain tension of the vascular walls from *a* to *b*. We will impute to this pressure, this rapidity and this tension, the value of 1. If, by continued growth of the organ, its limit moves from α—β to γ—δ, the capillary loop *a*—*b* no longer suffices for the nutrition of the enlarged vascular territory. There is produced a new capillary loop *c*—*d*. This grows, like every other vessel of the organism, from a vessel already existing. Let it be implanted, which is very possible, with both its roots upon the capillary loop *a*—*b*, entirely in the same manner as the capillary loop *a*—*b* is upon its own mother vessel. With the enlargement of the tract of the blood, an increase of the blood goes hand in hand, so that the blood in *c*—*d* immediately flows with the same rapidity, the same pressure, and the same tension of the walls, as previously in *a*—*b*. For *a*—*b*, however, these values have changed. If we regard the transverse section *a*, then not only does the blood now flow through this, which filled the capillary loop *a*—*b* with the tension, the pressure and rapidity = 1, but also that, which fills the capillary

Fig. 77.



loop *c*—*d*. There will, therefore, prevail at *a*, provided that *c*—*d* be just as long and wide as *a*—*b*, a pressure, rapidity and tension = 2. Let us suppose this consideration carried further; in the continued growth of the organ let there ever proceed new and new capillaries from the old, then will, in an entirely corresponding manner, the pressure, the rapidity and tension also in the afferent and efferent vessels increase; there will be continually larger demands made upon the capacity of resistance of the transverse section *a* and *b*. We might expect that in consequence of this the vascular walls would become thinner, the lumen wider. The lumen does in fact become wider, the walls, however, not thinner; but here a peculiar law, one presiding over the growth of the entire vascular system, comes into play, by virtue of which the increased demands upon the capacity of resistance of sections of the vessels are answered by a thickening of the walls (hypertrophy and dilatation). The vascular walls become thicker, the one root of our capillary loop becomes the afferent artery, the other the efferent vein.*

§ 211. No one has yet observed the histological process, by which a capillary becomes a small artery or vein. We must draw our conclusions here, as so often from the aspect of that which is being or has been formed. The walls of a capillary consist of a homogeneous, transparent membrane, beset from point to point with nuclei. By treating with nitrate of the oxide of silver we can demonstrate, that this membrane is composed of plates accurately joined to each other, at whose probable central point a nucleus with some soft protoplasm is situated. The plates themselves may be regarded as a thin layer of hardened protoplasm. The capillary membrane stands in uninterrupted connection with a somewhat thicker vitreous membrane, which is found in all arteries and veins, even in the aorta itself, at the boundary between the inner and middle coats of the vessels, and is to be recognized upon a transverse section, beside its greater lustre, directly by a regularly wavy double-contour, as because of its lesser elasticity it does not join the changes of the lumen of the vessel by thickening and thinning, but by folding in and out. (See Fig. 73, *b*.) At the inner surface of this membrane, the intima and the epithelium of the vessel arise; at the outer surface the muscular and the adventitious coats. The formative material is furnished by the capillary cells, which multiply by division, as we can easily perceive upon the so-called transition vessels.

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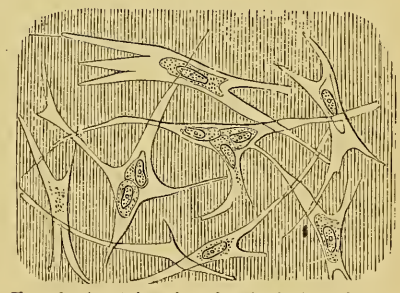
* Strictly taken, our diagram suits only to those vascular arrangements, in which a capillary region only possesses one afferent and one efferent vessel, *i. e.*, *to capillary plexuses*. If this is to be adapted to all vascular arrangements of the body, we must yet add, that by the anastomoses among the neighboring capillary districts the formation of larger, and finally very large capillary regions is made possible, in that perhaps the artery of one region conveys blood for both, the vein conveying back to the heart the blood from both regions. Modifications of this kind cannot of course alter the main points of our consideration.

The intima of the larger arteries and veins shows us, as well upon transverse as upon longitudinal sections, the same picture, Henle's striated lamellæ, which under a power of five hundred diameters (Fig. 78) present themselves as finely striped, wavy layers of connective tissue basis substance, in whose interspaces we find lenticular, flatly-pressed cells. Where these cells lie, the opposing surfaces of the basis-substance are of homogeneous, strongly shining constitution, and doubly contoured in such manner, that thereby the appearance of a real enveloping of cells may be produced. This perception obtains still more probability, if upon a horizontal section (Fig. 79) we observe how very closely the mentioned peculiarity of the basis-substance actually is connected with the lodging of the cells. The intervals between cells with their lining here appear as stellated branched structures, anastomosing with each other. The entire relation reminds very much of the encapsuling of cartilage cells. Still, the question is, whether the star-shaped capsules of the intima are closed depositories; at all events, in new formations, which proceed from the intima, the newly-formed cells also are found without the "connective tissue corpuscles," and must, therefore, either not be produced from *these cells*, or they must have escaped from the capsules. Until further proof we will regard them as migrated colorless blood-corpuscles.

Fig. 78.

From section of the tunica intima of aorta. The explanation in the text. 1–500.

Fig. 79.



From horizontal section of tunica intima of aorta. Explanation in text. 1–500.

Out of consideration for the diseases of the intima, to be treated of hereafter, I have delayed somewhat longer with the structure of this membrane, hitherto too little noticed. In regard to the two outer coats of the vessels I can so much the more compress my remarks. The media formed of smooth muscular fibres furnishes the proper body of all the larger vessels. To the smallest arteries and veins the circular nucleated spindles impart an exceedingly characteristic ringed appearance; in the larger vessels the muscular fibres lie in bundles in a framework of elastic, fenestrated lamellæ. Three to ten, and more main lamellæ, separated by equal interspaces, lie parallel to the surface of the vessel, and are connected by oblique bridges respectively with the next following inner and the outer ones. These bridges are also fenestrated, so that the muscular bundle may continue from one mesh into another. The adventitia, for the greater part, consists of unformed connective tissue,

which is abundantly pierced by vessels and elastic elements (membranes and fibres). Longitudinally running, smooth muscular bundles occur at this place exceptionally (in the larger veins).

a. *Inflammation.*

α. Acute Inflammation.

§ 212. The phenomena of acute vascular inflammation are immediately connected with the history of the coagulation of blood in the vessels, because they make their appearance with the greatest predilection, but also almost exclusively only, where a softening blood-clot is attached to the inner surface of a vein or artery, and irritates the membranes of the vessel by the diffusing products of the softening. This relation is so frequent, that Dupuytren in his time was induced to reverse the sequence of the process, and to accept the acute inflammation of the membranes of the vessel as the cause, the coagulation of the blood as the consequence.

For the unassisted eye, the quite important and very decided textural changes which acute inflammation produces, are but little apparent. We observe a hyperæmia of the vasa vasorum, particularly at the boundary of the media and adventitia, a thickening of the membranes up to three or four times, so that inflamed veins upon a cross section are not to be distinguished from ordinary arteries. The inner surface shows instead of the normal smoothness, a cloudy, opaque, even to a velvet-like constitution. Rarely do we observe small collections of pus, which cause a pustular elevation of the intima. The microscope exhibits much more concerning the condition of a vessel thus changed. The entire walls of the vessel are included in an inflammatory process of proliferation. Thousands of young elements, which without more ado we may regard as pus-corpuscles, are found between the fibres of the adventitia, between all the layers of the muscular coat, between the striped lamellæ of the intima. I have found in the adventitia, beside the cells, occasionally also larger collections of a gelatinous, unformed mass, which I regard as coagulated lymph; there likewise, however, in the outer layers of the muscular coat, also occur extravasations, which follow the course of the vessel to greater or lesser distances. The formation of pus in the outermost membrane proceeds only in single instances to an abscess-like confluence of pus. These abscesses appear as long striæ of creamy pus, which accompany the vessel, and must not be mistaken for vessels, which are filled with the softened mass of a thrombus. The participation of the intima is less constant; I might even assert, that in the majority of cases the intima is the least changed coat of the vessel. In reference to its nutrition, it is so dependent upon the blood circulating in the vessel, that with the occurrence of coagulation, its main source of

nutriment is directly cut off, and it is even exposed to necrosis, if vessels are not immediately developed in the coagulated blood, as in the organization of a thrombus. The passive behavior of the intima must therefore be regarded as a want of vital energy, and nutritive material, and this opinion is confirmed by the observation, that in the further course of the process an actual necrosis and loosening of the intima from the media not infrequently occurs.

§ 213. Beside the thrombotic arteritis and phlebitis, we are rarely in a situation to speak of an acute inflammation of the walls of vessels. Meanwhile, I am reminded, that the vessels are connected by their connective tissue adventitia with the entire connective tissue of the organs, that properly the walls of vessels are a part of this connective tissue, and hence may most intimately participate in the inflammations of organs. We will even see, as in many inflammations of interior organs, for example, of the pia mater, the kidneys, that the adventitia and the parts of the vessel immediately adjacent form the main seat of the changes.

β. Chronic Inflammation.

§ 214. Chronic inflammatory conditions are indeed exhibited upon all sections of the vascular system, yet in this respect no process is so important as the chronic inflammation of the inner membrane of arteries, the *endoarteritis* chronica deformans, as it is called by Virchow. The supposition, that in this disease, which is also called the atheromatous process, we are dealing with an inflammation, is already old. We regarded a peculiar translucent substance, which is elevated above the level of the intima, and which is, as shall immediately be shown, the changed intima itself, as an inflammatory *exudation*, the entire process as an exudative inflammation. The objection that the exudation in its property as liquor sanguinis had no provocation to coagulate just when mingled with the mother-fluid again, of course was very obvious. Rokitansky, therefore, came forward with the assertion, that the substance in question was indeed coagulated fibrin, but not exuded from the vasa vasorum, but that it had been precipitated and *deposited* upon the inflamed place of the wall of the vessel out of the blood flowing by. But this view in the course of time also proved untenable. Lobstein and after him Virchow taught us to seek the essential part of the process in a change of the parenchyma of the intima, and from this to separate that, which is perhaps in consequence of it superimposed from the blood. The fundamental features of our present opinion concerning the disease in question are derived from Virchow.

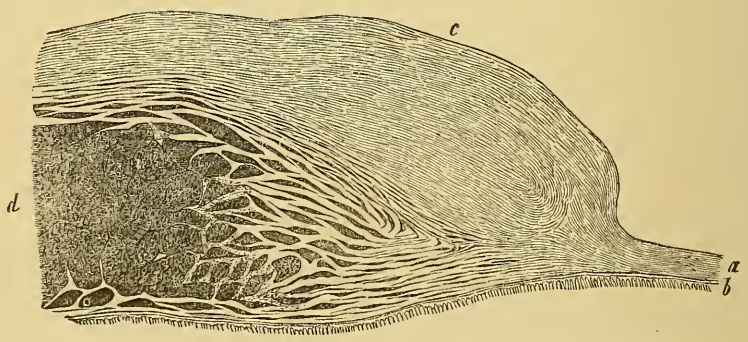
§ 215. We are dealing with a chronic inflammation of the inner membrane of vessels. It is true we do not find all the cardinal symptoms of inflammation, but only swelling, and if you will, functional disturbance; but the more minute changes which the intima

therewith experiences, are thoroughly analogous to those which we see produced in continued states of irritation of the connective tissue. Many things also declare, that a mechanical irritant acting upon the walls, may be regarded as a concomitant cause of the changes. The latter, namely, are found particularly at such places at which the current of blood breaks with the greatest force, at the upper part of the curve of the arch of the aorta, at the points of origin and division of vessels. Still the mechanical injury must be esteemed only as a concomitant cause, especially as the localizing force of endoarteritis. Extreme old age and a rich mode of living, especially the use of ardent spirits, are to be adduced as further etiological relations. Gout and endoarteritis have a similar etiology, and are, therefore, also frequently found together.

§ 216. Certain flat, bed-like, level, rarely tuberous *tumefactions of the inner coat of arteries* form the point of departure for all further metamorphoses. These rarely elevate themselves more than a line above the level of the surface, and are of very irregular outer limits; at the point where the vessels are given off they surround them ring-formed. Their color and consistency are tolerably various, yet in general we can designate them as bluish or reddish-gray and cartilaginous; rarely do we find a more gelatinous or mucoid consistency.

Touching what is found by the microscope, I will once more call attention in the first place, that we can convince ourselves upon sections through the bounds of the morbid swelling, how the outermost, commonly the least changed, lamella of the intima passes over in uninterrupted continuity upon the surface of the swelling, that therefore we have before us not a deposition upon, but an evident thickening of this

Fig. 80.



Endoarteritis chronica. Section through a sclerotic tumefaction of the intima, already fattily degenerated within. 1-25. *b*. Boundary of media and intima. *a*. Intima. At *c*, the same thickened and hyperplastic; at *d*, broken down to an atheromatous abscess. Details in text.

membrane (Fig. 80, *a*—*c*). Furthermore so much is established, that we are here dealing with a process of proliferation in and from the

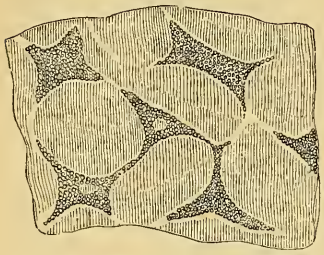
connective tissue of the intima, which has led to an increase of this connective tissue: numberless young cells are everywhere dispersed between the lamellæ; here and there we find larger collections of them. These cell-nests are the points of departure and the central points for new systems of concentrically stratified connective-tissue lamellæ, which are interpolated between those existing, pressing them asunder. With the new formation of cells now a corresponding new formation of fibrous basis-substance goes hand in hand; the number of the cells never so much predominates, that perhaps a purulent condition results. We rather find in *spots*, a soft, even mucoid consistency of the basis-substance, combined with a net-formed arrangement of the cells, therefore, mucoid tissue; upon the whole, however, we cannot avoid emphasizing the great resemblance of the new formation to the normal texture of the intima, consequently to comprehend the first stage of the changes, the so-called sclerosis of the intima, as an inflammatory *hyperplasia*.

§ 217. The inflammatory hyperplasia of the intima at the same time presents the acme of the entire process. As occurs in so many pathological new formations, here also in the course of time a disproportion sets in between the nutritive means and the mass to be nourished. The intima is non-vascular. It derives its nutriment directly from the blood flowing over it. The vasa vasorum, which no larger vessel is without, scarcely penetrate into the media. Hence if the intima becomes thicker, then those of its layers must the soonest suffer the want of nutriment which are furthest removed from the nourishing surface, consequently the outermost, lying nearest the media. Two forms of the retrogressive metamorphosis of tissues are here observed *side by side*. The one the most diffused is a *fatty degeneration of the cells, combined with a solution of the basis-substance*. The unaided eye observes in the interior of the sclerotic elevation, close to the media, yellowish-white opaque stripes, which run parallel to the surface and unite to a more uniform, yellow spot. Instead of this, in more advanced changes, we find a small or large focus of softening, which is likewise filled with a yellowish, smeary, even also crumbly pulp. The abundant admixture of crystalline cholesterin impart to this so-called atheromatous pulp a lustrous appearance. If the focus of softening, by the progressive melting-down of the sclerotic tissues, has attained a greater circumference, for example, if it is only yet cut off by a thin layer of unchanged intima from the blood-current, we call it an atheromatous abscess. This becomes an atheromatous ulcer, when finally the covering tears at its thinnest part, the atheromatous pulp mixes with the current of blood, and thereby the bottom of the focus of softening is laid bare. (See continuation in following §.)

Figures 80 and 81 are intended to explain the histological detail of

atherosis. In Fig. 81 we see by a high power that the fatty metamorphosis of the cells of the intima presents itself as a filling out of the stellated interspaces of its connective tissue with fat-globules. It appears, however, that these preformed gaps become the points of congregation of the entire fatty detritus, even that proceeding from the young, more dispersed cells; for upon the vertical section of an atheromatous abscess, whose one-half is represented in Fig. 80, the fatty detritus appears as an infiltrate, which fills spindle-formed spaces and raises up from each other the superimposed lamellæ of the intima. These spindles, according to their situation, without doubt correspond to those points at which the cells are interpolated between the lamellæ of the intima (Fig. 79). The more the detritus accumulates here, so much the longer and thicker do the spindles become (upon a cross section); the lamellæ, however, become wider and wider separated, and finally perish by softening; hereupon the fatty detritus, without more ado, flows together to a fatty pulp, which fills the cavity of softening. (Fig. 80, to the left.)

Fig. 81.



Fatty degeneration of connective tissue cells of the innermost vascular tunic. 1–500.

§ 218. The form and size of atheromatous ulcers are naturally just as manifold as those of the sclerotic swellings. They are originally sinuous ulcers, *i. e.*, with a probe we pass through a small opening into a cavity, by which the surface is undermined for a greater distance. This space is the former cavity of the abscess; it may be more or less filled by coagulated blood; as a rule, it is not. The thin membrane, which yet covers it, has moreover a tendency, upon widening the vent, to roll up towards the edges; more rarely it is loosened in shreds; in every case the open atheromatous ulcer is so considerable an inequality of the surface, that it readily becomes the seat of the formation of clots, even of longer thrombi, which hang from the walls of the vessel.*

§ 219. The second retrogressive process also, which is observed beside the atheromatous, regularly begins in the deep layers of the sclerosed intima. An impregnation of the basis-substance with lime salts, therefore *calcification*, is its essential phenomenon. There are produced thereby bone-like plates of various form and size, often so large that they, for example, convert the whole arch of the aorta into a single bony tube. A tolerably frequently recurring arrangement is, that numerous smaller

* I observed within a tolerably completely softened atheromatous depot a small button-shaped soft mass, which contained bloodvessels, and had grown out from the media. Upon proceeding, I found under the same sclerotic plate yet an entire series of such buttons. They consisted, excepting the vascular loops, of hyaline mucoid tissue, with fatty degenerated cells. July 20th, 1867.

bony scales, some even only one-half inch long and broad, are here and there imbedded in the intima, which we immediately feel through the coats in touching the vessel. If we peel them out of their encapsulation, the most show a dish-like concavity and sharp edges, corresponding to a curve of the vessel. The latter are they which the soonest penetrate through the covering layers of the intima to the surface, and thus form projecting, rough ridges, by which again an opportunity is given for the formation of thrombi. It tolerably frequently happens that larger bony lamellæ are more or less elevated by the fatty degeneration of the surrounding parenchyma, yet complete separations appear to be infrequent.

I have not been able to convince myself that here an actual formation of bone takes place, to which the customary designation of the condition points as an ossification. The lamellæ of the intima are simply calcified, and by extracting with diluted muriatic acid, may be brought back to their former condition; their cells, however, have perished. I have never found anything which answered to the anatomical dignity of a bone-corpuscle.

§ 220. So far the chronic endoarteritis in the more contracted sense. A sufficient idea of the extended disturbances which this produces, especially upon the aorta, disturbances which, in the instance advanced, scarcely leave intact a square inch of the surface, can only be obtained by personal inspection. If, however, we wish to make the anatomical picture of the disease complete, we cannot yet quit the subject here, but must mention two other processes, which are not so strictly separated by the physician from chronic endoarteritis, because they are in fact very commonly combined with it.

In the first place, there is a fatty degeneration of the intima without preceding inflammatory hyperplasia of the membrane, a simple retrogressive metamorphosis, concerning whose proximate cause nothing is known. The histological process is exactly the same as in the atheromatous process; a fatty metamorphosis of the cells (Fig. 82), with slowly following melting-down of the lamellæ. This "*fatty usure*" (Virchow) begins immediately at the inner surface and progresses (probably very gradually) from within outwards; the intima is destroyed layer by layer. The affection occurs in otherwise always only small, sharply defined spots; upon the aorta and the larger arteries it conditions a delicate marking of the surface, as the affected places appear rough, velvety, and opaque.

The fatty usure is frequently found in individuals otherwise entirely healthy. Nevertheless we cannot deny that by it the firmness of the vessels is directly prejudiced. If the intima has been completely destroyed, although at ever so small a spot, experience teaches that the muscular media, notwithstanding its thickness, cannot withstand the blood pressure. The muscular fibres separate, there is produced a

transverse rent, through which the blood presses forward, and either forms, by elevating the adventitia, a so-called *dissecting aneurism*, or arrives outside by breaking through the adventitia. In this manner is explained the occurrence of hemorrhages in the most various organs, which the atheromatous process brings with it, hemorrhages into the brain, the kidneys, &c.

But the fatty usure of the intima also plays a part in that transverse rent of the aorta which leads to a dissecting aneurism of the aorta. This occurrence is, as a rule, simply regarded as a consequence of concomitant hypertrophy of the left ventricle. The rupture almost regularly takes place a finger's breadth above the semilunar valves, and in the first place affects only the intima and the media; the adventitia is lifted off from the media, the blood forces its way between it and the media on one side down to the heart; upon the other to the aorta descendens, never to the aorta abdominalis. When the aneurismal sac thus formed is stretched to its utmost there occurs a second rupture, either outwards into the mediastinum, or, which is meanwhile very rare, at another place again inwardly into the lumen of the aorta, so that for a short distance two blood-tracks exist side by side. If we now investigate the edges of the rent of the intima at times we find a thorough fatty metamorphosis of them; still further investigations must decide concerning the frequency and the import of this complication.

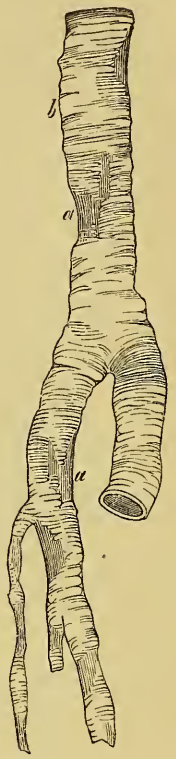
§ 221. A second tolerably constant complication of chronic endoarteritis is formed by the *calcification of the tunica media*. This is found not so much in those regions of the arterial system, which are the principal seats of endoarteritis in the aorta and its main branches, but in the relatively thicker muscular tunic of arteries of smaller and the smallest calibre, in the arteries of the arm, leg, and head, and their ramifications. The question here is likewise about a simple petrifaction; the muscular spindles are filled with the salts of lime, and again appear as muscular fibres, if we dissolve the lime-salts by means of acid. Moreover we are also able, without the microscope, to pronounce an opinion concerning the probable seat of the calcification, as the distinct circular arrangement of the infiltrated parts can only be referred to the circular fibres of the muscular tunic (Fig. 82).

The calcification of the media as a more independent affection occurs much more rarely than in combination with the atheromatous process. As a rule all three tunics of a vessel are uniformly infiltrated in the lime metastasis (see § 51).

§ 222. Let us ask, what influence will the changes of the walls of the vessels hitherto described have upon the movement of the blood in the vessels? They may collectively be traced back—1, to a contraction; 2, to a rigidity of the tube of the vessel. The rigidity, especially represented in the calcification of the intima as well as of the media, causes, that those components of the propulsive force of the heart, which

under normal circumstances, are conserved as tension in the elastic walls of the vessel, and as such always ready to be again converted into vital force, that these components, partly at least in an entirely unnecessary manner, are converted into heat, and are lost to the movement of the blood. The rigidity, therefore, in that it consumes the propulsive force of the heart, indirectly lessens the rapidity of the current of the blood below the rigid place. Tumefaction and narrowing of the tube of the vessel effect the same, and indeed directly in that they produce oblique planes, which oppose the blood-current, and, according to the known law, convert a greater or lesser component of the rapidity partly again into pressure, partly they absorb it as loss by friction. The blood, therefore, will flow more slowly than normal below the rigid and more narrow vessels. This slowing will make itself felt, especially in the remotest parts of the greater circulation; in the toes, the finger-tips, the nose. It may here proceed to a complete stagnation of the blood, and have as a consequence, the so-called spontaneous gangrene of these parts (compare General Part, § 9), which is particularly observed in very old individuals. It is otherwise in the vascular sections on the proximate side of the rigid and narrowed parts. We know that the blood-pressure, which prevails at any point of the vascular system, is proportional to the resistance yet to be overcome. If this resistance grows, which occurs as well by rigidity as by narrowing, then the pressure also increases in the vascular sections situated above. A certain increase of pressure in the entire aortic system will hence be a common consequence of the atheromatous process. This stands in complementary proportion to the decrease of pressure and rapidity below the narrowed and rigid portions. It is, however, self-evident that this increase of pressure cannot be without further consequences. As such we have to designate 1, hypertrophy of the left ventricle; 2, dilatation of the affected vessels. Each of the two forms a kind of compensation of the primary disturbance; hence the hypertrophy retrogrades, when the dilatation takes the lead, and vice versa.

FIG. 82.



Calcification of the media of the femoral artery, together with its ramifications. Not magnified.

b. *Dilatation of the Vessels.*

a. Dilatation of Arteries—Aneurism.

§ 223. The great multiplicity and variety of that which presents itself as true aneurism, *i. e.*, affecting all three coats of arteries, we

formerly sought to overcome by setting up the external form of the dilated arteries as the foremost principle of subdivision, and we distinguished between cylindrical, sacciform, spindle-form, and varicose aneurisms. This attempt has been frustrated. We would be more fortunate, at all events, if we could use the etiology, the manner of production, to distinguish the various aneurisms. Unfortunately, however, just the etiology of aneurism is a very questionable matter, which will probably for a long time yet await its final elucidation. There certainly is no want of hypotheses. We need not go far for examples in seeking the foundation of the disturbance in a deficient elasticity or contractility of the muscular tunic. Of all the constituents of the arterial walls, the muscular fibres are they in which we may presuppose a more active exchange of material, consequently a greater sensitiveness towards its disturbances. For those uniform, cylindrical, or varicose dilatations of all the larger arteries, which we not infrequently meet with in old men, without any visible change whatever of the walls having taken place, I therefore readily take refuge in accepting a diminished capacity of resistance of the middle coat. I also grant, that in other forms it may also play certainly a less important rôle. A bare disturbance of innervation, a paralysis of the tunica muscularis can at all events be less generally cited (Rokitansky). Still here also there is at least also one case in which an explanation of this kind has much that is attractive: I mean the aneurisma anastomoticum. We understand thereby a varicose dilatation, elongation, and meandering of the main trunk and the collective branches of an artery, the ectasy of a limited section of the arterial system. This is found especially in the arteries of the scalp, for example, the occipital and temporal arteries, and strikingly reminds of those dilatations of the vessels of the head which occur after dividing the sympathetic in the neck, so that we would be inclined to think a partial disturbance of the vasomotor nervous system as a co-operating cause of this aneurism. All these, however, are infrequent and less important occurrences.

§ 224. That which in the current clinical language is summarily called aneurism, namely the ectasy confined to a short portion of the aorta or another artery, is at the same time the least evident in an etiological relation. It is regularly combined with chronic endoarteritis. We must investigate in how far this process can lead to a dilatation of the arterial tube. First of all it is to be considered that hyperplasia of the intima as such, brings with it beside the thickening also a spreading in width of the surface of the vessel. The portions of connective substance newly formed in depots not only accumulate above one another, but are also interpolated in the horizontal direction between the original constituents of the intima, and by their growth press them apart with active force. We may certainly regard the horizontal growth of the inflamed intima as at least an assisting energy in the

dilatation of vessels. For if we do not wish to set a high value upon its active participation, yet the intima affected by a molecular change will be less capable of resisting the dilating effect of a second etiological energy, namely, the locally increased blood-pressure, than the normal. I have shown above that in the atheromatous process the blood-pressure must increase above and within the affected section of the vascular system. To this is first to be referred that uniform dilatation of the aorta, which we rarely miss in any diffused endoarteritis. The systolic augmentation of this pressure, however, comes particularly into consideration for true aneurism. This will be a different one than under normal circumstances. The diseased condition of the walls of the vessel hinders that preliminary transfer of rapidity into tension of the walls, which causes that the systolic increase of pressure and its "other condition," the rapidity, are distributed over a greater period of time. Hence both accumulate now to the moment of the commencing systole, in order immediately thereupon to make way for just as large a falling off. The diseased artery receives with every systole a dilating impulse, to which it can no longer oppose an active, but only a passive behavior. The jumping (hüpfende) pulse of diseased arteries teaches us indeed, that in the entire arterial system, instead of the rhythmically accelerated current, a more interrupted movement forwards of the blood takes place. The short, but vigorous impulse, which our finger receives at the radial artery, will, however, be most intensely felt in the aorta itself, because here the loss of impulse does not yet come into reckoning, which necessarily occurs in this kind of movement of the blood. Hence we find aneurismal dilatation by far most frequently (1), in the commencing portions of the aorta; (2), at such places, where by a local narrowing of the arterial lumen a cause is given for a particular increase of pressure *before* the contracted place. I have investigated all aneurisms of peripheral arteries accessible to me for this, and have almost always met with such a cause below the dilated place, in a more or less considerable thickening of the intima. A lasting contraction of those muscles, in which the main branches of an artery ramify, may be found to be the basis for the aneurismal dilatation. Thus aneurism of the popliteal artery is not infrequently the reward of those servants, who for half a day must stand upon the foot-board of lordly state coaches (contraction of the gastrocnemius).

§ 225. In reference to the external form of aneurisms we distinguish the uniform cylindrical, or the spindle-formed dilatation of the arterial tube, from the one-sided, sacciform dilatation. The cylindrical becomes an invaginating aneurism, when the aneurismal sac folds on one or both sides over the contiguous ends of the undilated vessel. Similar modifications also occur in sacciform aneurisms. If the sac only folds over towards one side, its cavity will be separated from the lumen of the vessel by a crescentically projecting ridge; if it folds over above and below

or towards all sides simultaneously, we have the form of an aneurism with a neck.

The sacciform are by far the most frequent, *i. e.*, aneurisms of the aorta ascendens proceeding more from the convex than from the concave side of the vessel. They advance, by their summit, from within against the sternum or the point of union of the manubrium sterni and the clavicle. At the arch of the aorta likewise aneurisms of the convexity are by far more frequent than those of the concavity. We here not at all infrequently observe aneurisms with necks, which subsequently advance above the upper aperture of the chest, and from the beginning attack the œsophagus or the trachea. Upon the thoracic aorta aneurisms proceed by preference from the posterior or lateral circumference of the vessel and press against the vertebral column. All aneurisms of the smaller arteries are much more infrequent, yet the most frequent are aneurisms of the popliteal, carotid, and basilar arteries.

§ 226. The histological interest is especially joined to the question: in the gradual dilatation of the arterial tube, how do its various structural constituents behave; how does the intima behave; how the media; and how the adventitia?

It has already been mentioned, that the intima is regularly put into a hyperplastic condition by endoarteritis, and this causes that the membrane takes part in the dilatation, without experiencing any considerable attenuation. Aneurisms of four to six inches diameter may be lined with a sufficiently thick, nay in places with a more than normally thick inner membrane. The most various stages of the atheromatous process occur in it side by side, yet calcification stands foremost; lime-plates have even been found, which spanned the half, nay the whole circumference of the aneurism, and converted it into a bony drum. More frequently we find a mosaic-like pavement of small lime-plates, which readily loosen at the edges, and then give the first impulse for the deposition of blood-clots. Fatty degeneration, which is wont to be less diffused, is none the less of the greatest importance; thus, by fatty degeneration, particularly by the atheromatous ulcer, the intima finally becomes defective at one or other place; the resistance of the aneurism is compromised in a critical manner.

The *middle* vascular tunic, from the beginning of the dilatation, behaves perfectly passive. The circular bundles of smooth muscular fibre separate, and leave between them interspaces, becoming ever wider and wider. Thereupon they perish through fatty metamorphosis. As soon as an aneurism of the aorta has attained the size of a fist, it already becomes difficult to demonstrate the traces and last remains of the media.

On the contrary, we can say of the *adventitia*, in the true sense of the word, that it gives security against rupture. The pressure of the growing aneurism acts upon this membrane, as a moderately growing

or frequently repeated pressure everywhere acts upon a stratum of unformed connective tissue; it excites in it a chronic inflammatory, or, as we say, a reactive hyperplasia. A compact, dense connective tissue hence surrounds the aneurism upon all sides; upon the one hand it passes into the possible defects of the inner tunics; upon the other, it brings about the growing together of the outer surface of the aneurism with the adjacent organs.

The participation, therefore, of the adventitia has a thoroughly salutary character. But its means are also exhaustible. In the first place, it is not able by its thickening to restrain the growth of the aneurism. It regularly and at all points gives way to the blood-pressure, and can never attain the degree of resistive capacity which is obtained by the combined power of a normal intima and media. How great, however, the demands are which are placed upon the resistive capacity of the walls, is shown in the conflict of the aneurism with the osseous system. If an aneurism of the aorta ascendens presses against the sternum, or an aneurism of the thoracic aorta against the vertebral column, then first of all everything perishes which is found between the bone and the blood. Intima, media, and adventitia, mediastinal connective tissue and periosteum disappear traceless under the pressure of the contending forces. Thereupon the bone gives way, slowly it is true, so that the completely stripped remains often project far into the lumen of the aneurism; but still it disappears. The bony tissue thereby undergoes a peculiar fibrous metamorphosis (Fig. 11), described in detail at § 41. This, however, can also only be regarded as one act of the decay and the solution. The result is a deficiency of bone. Aneurism of the ascending aorta not infrequently causes an entire absence of the manubrium sterni, the upper part of the body of the sternum, and the sternal ends of the clavicle; aneurism of the descending aorta causes half spherical deficiency in one or more of the bodies of the vertebral column.

A second limitation of the salutary effects of the adventitia grows out of the circumstance, that these effects, which for the greater part depend upon a continuation of the hyperplastic process to the adjacent connective tissue, can only reach as far as the connective tissue reaches. Every free surface against which the aneurism advances, can become fatal to the patient, in that it gives occasion for the bursting of the aneurism. The pleural surface is less dangerous in this connection, because the pleural cavity is an inner space of the connective tissue, whose surfaces readily adhere to one another. By the advance of the aneurism upon the lung, the fatal catastrophe is provisionally deferred. This only then occurs when both the pleural surfaces are ruptured, and the air-filled parenchyma of the lung and the smaller bronchi are thereby opened. Much more rapidly does a rupture happen to those aneurisms which advance against the larger air-passages of the trachea itself. Aneurisms of the ascending aorta finally burst through the

outer skin; other points of opening are the œsophagus, the pericardium, the pulmonary artery, rarely the peritoneum and the retroperitoneal connective tissue.

§ 227. The formation of thrombi very commonly comes to pass in the cavity of aneurisms. Inequalities of the inner surface form, as a rule, the point of departure. Still the retardation of the blood-current also plays a part, inasmuch as coagulation takes place with special readiness in sacciform, necked aneurisms. The aneurismal thrombus is constantly of peculiarly stratified structure; the outer layers, which were first deposited, are most completely decolored, fibrous, compact, as every blood-clot becomes, when it is exposed to a continued pressure; never are even but indications of an organization to be observed. Hence the thrombosis of aneurisms also, although it directly diminishes the lumen, yet but in very rare instances leads to a spontaneous healing of the aneurism. This has been observed at most in entirely sacculated aneurisms of the smaller arteries. For the most part, the thrombotic filling of an aneurismal cavity proves insufficient to withstand the blood-current. If the sac bursts, the thrombus is destroyed, and the blood finds its way outwards between the fragments. A softening of the aneurismal thrombus also occurs, whereby the danger of loosening fragments and embolism is produced.

β. Dilatation of Veins. Phlebectasy.

§ 228. Dilatations of veins, spite of their much more frequent occurrence, spite of many peculiarities of the anatomical picture which they present, are yet but a faint copy of the dilatations of arteries. We remarked above, that there could be no question of any endophlebitis chronica in the sense of the atheromatous process of arteries. Thus just that complication is left out of consideration which plays so important a part in aneurisms, especially as an etiological energy. The etiology of phlebectasy is generally very evidently always and everywhere the same, namely, mechanical dilatation by locally increased blood-pressure, and to this etiological monotony corresponds just as great a uniformity in the issue of the anatomical changes. We can indeed find, if we wish, in the ectasy of veins also, those three fundamental forms of dilatation, to which a cylindrical canal is in general prone, we can distinguish cylindrical, spindle-formed, and sacciformed phlebectasies; but this distinction has here a comparatively limited value, simply because in most cases of phlebectasy all these forms occur side by side; because we nowhere deal with a single, very considerably dilated point of a vein, but always with a moderate dilatation of whole plexuses of veins, or also the collective roots of a venous trunk.

Under normal circumstances there prevails in the venous system so limited a blood-pressure, that in the large veins it but slightly exceeds

the atmospheric pressure, and may even become negative in the immediate neighborhood of the heart. Corresponding to this, the veins have comparatively thin walls; they are, so to speak, only arranged for a moderate blood-pressure. If from any circumstance an increase of the blood-pressure takes place, the lumen of the vein dilates, the walls are stretched; if the increase of pressure is continued or periodically recurring, the walls remain lastingly stretched, phlebectasy begins.

§ 229. One self-evidently observes phlebectasy the soonest at such places where the valves are situated. The sinus of these valves widens and causes small, knotty distensions of the venous tube, which we can even perceive through the integuments if the vein runs superficially. The valvular flaps themselves are therewith more strongly pressed up stream; finally they no longer suffice to cover the lumen, and the more this is the case, so much the more does the ectasy extend to the whole venous tube. The vein then stretches in the longitudinal direction, the vessel becomes longer; as, however, the beginning and end are fastened and cannot experience a great dislocation, the elongated vessel must either bend zigzag, or even wind spirally. Both happen, the zigzag in larger, the spiral in smaller veins. The zigzag curving forms the transition to that degree of phlebectasy which we term *varicosity;* namely, since the outer, convex circumference of the curve readily deflects outwards, there finally arises here a sacciform ectasy, which is attached to the vessel, like the sacciform aneurism to an artery. If the same is repeated at each new bend which the vessel makes, this finally appears entirely and altogether to consist of sacciform aneurisms placed alternately in a row. This is the fully formed "varicose condition," which is generally found upon the collective vessels of a venous plexus, or the roots of a large venous trunk. With it in most cases the highest grade of phlebectatic development is attained. As one yet higher can properly be designated the varicose tumor only, which meanwhile is only observed at a certain locality, namely, the hæmorrhoidal plexus.

§ 230. Of all the veins of the body, the venous plexuses of the true pelvis and its outlets are the most disposed to phlebectasy. This depends in the first place, in that these plexuses by their communication with the portal vein (vena hæmorrhoidalis interna) participate in the unfavorable relations of the circulation of this vessel, without sharing the beneficial influences of abdominal pressure, which facilitates its circulation; on the other hand, however, upon the continued and frequently repeated hyperæmias, to which these parts are subjected by sexual activity.

The ectasy of the vesical plexus stands as the basis of those morbid changes at the neck of the bladder (catarrh of the mucous membrane, moderate enlargement of the prostate), which we so frequently find in older persons, and term vesical hæmorrhoids.

The ectasy of the hæmorrhoidal plexus (the proper hæmorrhoidal condition) begins with an injection of the venous transition vessels, which course in the submucous, loose connective tissue of the rectum near to the anal orifice. With this first of all is associated a mucous catarrh of the surface, and, as I find, a slight hyperplasia of the mucous glands. The changes of the mucous membrane afterwards retrograde, the phlebectasy advances to the formation of large convolutions of varicose veins, which elevate the mucous membrane and form a circle of transverse folds around the opening of the anus. Finally, the ectasy concentrates upon one or several points of these folds, which develop to rounded tubers, then to fungous tumors of considerable size.

If we make a section through a large hæmorrhoidal tumor, we already observe with the naked eye, that its principal mass is of a spongy texture. The pores are formed by the lumina, the septa by the melted-down walls of dilated and varicosely degenerated veins. We must imagine to ourselves the production of this structure in such manner, that under the influence of the continued increased blood-pressure, the ectasy of the veins acts atrophying upon the interposed connective tissue, so that finally the walls of the vessels alone remain. In the surrounding of these venous tumors, it not rarely proceeds to inflammatory processes, partly indurative, partly suppurative; in the interior here and there to a coagulation of the blood, which produces partial gangrene.

§ 231. Next after the veins of the pelvic organs, phlebectasy is observed especially in the regions of the greater saphenous vein. Everything which obstructs the circulation in the common iliac vein, for example, the pressure of the gravid uterus or a pelvic tumor upon that vessel, may give occasion for this. In other cases, it is accomplished by a persistent contraction of the muscles of the thigh, for example, in persons, who stand at work; since these compress the deepseated veins of the thigh, it forces the returning blood into the veins of the skin. To this is added the effect of gravity. In general, several etiological forces unite to the common result of varicose veins. Its various stages may already be followed through the integuments. Not at all infrequently do slighter and severer degrees of this stand as the basis of those chronic inflammations and ulcerations of the leg, which because of their stubbornness, so often try the endurance of patients and the physician.

γ. Dilatation of the Capillaries. Telangiectasis.

§ 232. Apart from the hyperæmic, more or less transitory dilatation, there is properly no condition of the capillaries which we could place by the side of aneurism and phlebectasy. That which we expressly term telangiectasis, depends upon an excessive new formation of capillaries at circumscribed spots of the skin. Upon very many paren-

chymas, among others upon the outer skin and its minute structural constituents, the papillæ, the glands, the fatty lobules, the principal details of organization of the parenchyma is everywhere further carried out by the capillary network and subdivided by that anastomosing system of connective tissue interstices, in whose points of intersection the connective tissue cells lie. These connective tissue corpuscles are they, by whose thick, protoplasmatic processes the first foundation of a future vessel is laid in the tertiary vascular formation. (See Kölliker's Handbook of Histology, 3d edit., p. 607.) They trace out a larger or smaller bow, of which both roots are inserted into the walls of a capillary already conveying blood. The lumen of the new capillary opens along this bow. The thread of protoplasm is extended in a thin layer over the entire inner surface, it hardens into a homogeneous capillary membrane; the nuclei of the participating cells move with the remainder of the protoplasm to the outer surface, and from this time figure as capillary nuclei.

Ordinarily in the vascularization of growing organs there is but a small part of the existing connective tissue cells applied to the vascular formation. It is otherwise in telangiectasia. A telangiectasis is produced, in that between the main capillary loops, by the aid of the process which I have just described, a great superabundance of connecting bridges are cast. Telangiectasis is a vascular hyperplasia, not simply a vascular dilatation. Thus, instead of the connective tissue cell-net, an excess of minute, mostly spirally-turned capillaries interweaves the fat-cluster, the sweat-gland, the sebaceous gland, the papillæ of the skin. We can recognize these parts in the numerous lobules by which the telangiectasia is composed, although the specific constituents have been destroyed by the pressure of the growth of the same vessels by which they should have been nourished. The dilatation of the capillary blood-tract in the cavernous tumor was already mentioned in § 129.

2. Diseases of the Heart.

§ 233. We again find the same three layers in the central organ of the circulatory apparatus, which constitute the walls of all large vessels. The endocardium corresponds to the intima, the myocardium to the media, the pericardium to the adventitia. Corresponding, however, to the prominent functional position of the heart, these membranes are here, each in their peculiarity, more highly developed.

The endocardium is a far more delicate membrane than the intima of the aorta. This becomes particularly prominent at the inner of the ventricles, where it only appears as a shining surface, which bounds

the muscular coat inwardly, but in no wise interferes with its color and contour. It certainly becomes thicker where it forms those duplicatures, from which a peculiar firmness is required, at the valves and chordæ tendineæ. At the valves we can even distinguish several different layers in its structure. Thus the lamella of every valvular flap which is turned from the blood-current, is richer in elastic fibres than that turned towards it; and between both lamellæ, at least in the auriculo-ventricular valves, there is found a thin layer of connective tissue, into which vessels penetrate until near the edge of the valve.

The myocardium, corresponding to its physiological importance, the thickest coat of the walls of the heart, solves in its structure that difficult problem, of inclosing a cavity by striated muscular fibre. The muscular fibres are united by acutely angular anastomoses into fenestrated membranes, which by being massively superimposed upon one another and by strong connections inclose the cavity. (Compare § 235, Fig. 85.)

The adventitia is a serous sac, the pericardium, whose visceral layer clothes the heart externally in just as thin a layer as the endocardium does the inner surface, yet it contains its own vessels, which, to be sure, are at many points connected with the vessels of the muscular coat of the heart.

Accordingly, the three coats of the heart, each for itself, appear to us more individualized and independent, than the three tunics of the arteries and veins; and as this greater independence also manifests itself in their diseases, I consider it conformable to have regard to the same also in my description; hence I will treat in succession of the pathological histology of the myocardium and the endocardium, but will defer that of the pericardium to the common chapter "Of the Anomalies of Serous Membranes."

a. *Myocardium.*

a. Hypertrophy of the Heart.

§ 234. Under hypertrophy of the heart we understand an increase of the volume of the heart, which has its foundation in a hyperplasia of the myocardium. A hypertrophy of the heart may uniformly affect both ventricles; far more frequently but one ventricle is hypertrophic, or yet predominantly so. It is not easy to establish the presence of a hypertrophy of slight degree. We are directed to compare the thickness of the walls with the width of the lumen. The proportion of these two changes with the degree of contraction, in which the heart may be. The smaller the lumen, so much thicker the walls, and *vice versâ*. Probably the apparently thickened walls of the heart are only more strongly contracted? Similar considerations will recur in contemplating atrophy of the heart-muscle; we must take care in regarding a dilated heart as

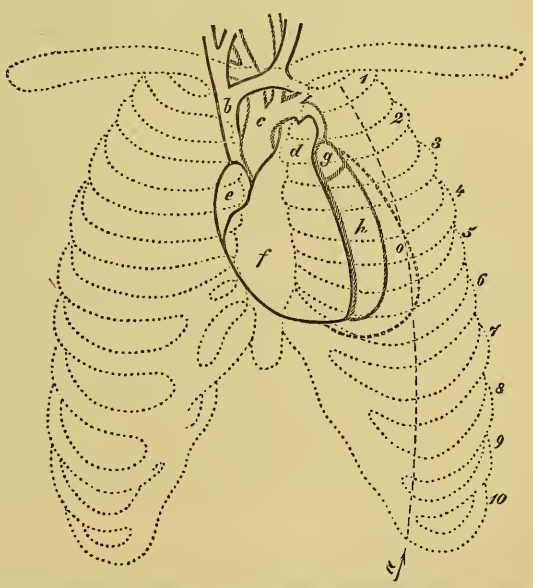
being already atrophic, because its walls are thin. A rapid and correct judgment concerning slight degrees of thickening and thinning of the heart-walls, can only be attained by long practice. On the contrary, it is easy to recognize a hypertrophy of the heart of high degree.

Next to the greater circumference and the frequently very peculiar changes of form, the disproportional weight of the heart already excites our attention. The walls of a hypertrophic heart are of a board-like rigidity and hardness, so that even after being cut open and the blood completely emptied, they do not sink in, and are with difficulty bent in and out. Finally, the considerable thickening of the walls strike us so much the more, as the lumen is wont at the same time to be abnormally large, in that a certain degree of dilatation is associated to every hypertrophy of the heart. A large heart must self-evidently also have large cavities.

The heart undergoes characteristic changes of its external form, when but one of the ventricles is hypertrophic. If to the right ventricle of a child's heart we joined the left ventricle of an older individual, the whole heart would receive more the form of the left ventricle; in the converse case the right ventricle gives the model. The relation in one-sided hypertrophies is entirely thus.

A heart, whose *left ventricle* is hypertrophied (Fig. 83), hence will

FIG. 83.



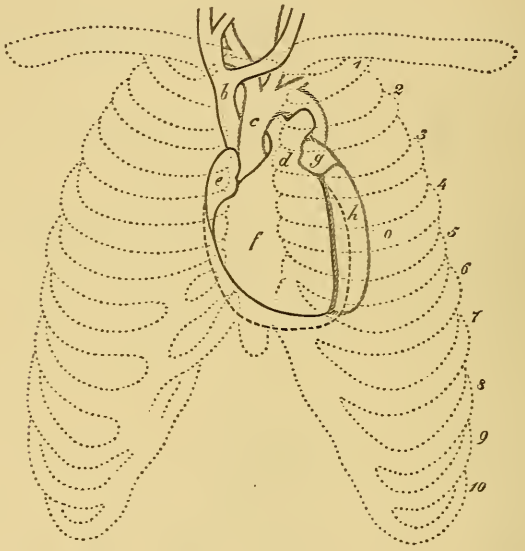
Hypertrophy of left ventricle. Heart in situ. *a.* The mammary line. *b.* Vena cava superior. *c.* Aorta. *d.* Bulb of pulmonary artery. *e* Right auricle. *f.* Right ventricle. *g.* Left auricle. *h.* Left ventricle (normal circumference). *o.* The hypertrophic ventricle.

have an elongated, ovoid, or cylindrical form. The right ventricle still more appears, as is already the case under normal circumstances, as a

mere appendix of the left. The situation of the heart passes more into the horizontal direction, so that the base looks towards the right, the apex towards the left. The apex projects beyond the mammary line, as we perceive by the extension of the heart-dulness in this direction, and the displacement of the impulse of the apex.

On the contrary, a one-sided hypertrophy of the *right ventricle* (Fig. 84) does not cause an elongation, but a widening and thickening of the whole heart. The heart viewed from the front appears quadrate, and

Fig. 84.



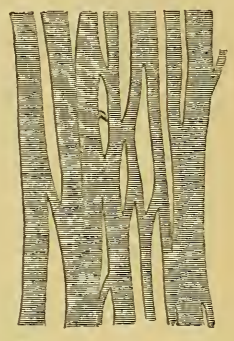
Hypertrophy of right ventricle. Heart in situ. Description as in preceding figure. The contours of the hypertrophic right ventricle are indicated by dots.

as the situation continually tends more and more to the vertical direction, the heart-dulness also extends more to the right; is found at the lower end of the sternum and beyond the right sternal edge. The apex of the heart is no longer formed alone by the left ventricle, the right participates or even entirely forms it; instead, however, of the impulse of the apex, which not infrequently becomes indistinct, there arises, because of the thickening of the heart's base from before backwards, a systolic contact of the conus arteriosus (Fig. 84, *d*) with the walls of the chest,—basic impulse.

§ 235. All hypertrophies of the heart are true hypertrophies from work; they are produced by mechanical obstacles to the movements of the blood. These increase the work of the heart, since they exalt the pressure, which in the beginning of the heart's systole is directed vertically against the inner face of the ventricle, and which is to be.

overcome by the systole. In the atheromatous process of the aorta we already saw a hypertrophy of the left ventricle produced; we will very soon learn to know in valvular deficiency, the by far most frequent cause of hypertrophy of the heart, and yet to recur to them in many other diseases of organs. Touching the histological process of hypertrophy of the myocardium, the opinion is very generally received, that therein the individual muscular fibres thicken. Meanwhile, I have in vain attempted in hyperplastic hearts, to discover a difference in the calibre of the muscular fibres, and have finally been conducted to the opinion, of course suitable only for the heart, of a *partial division*.

Fig. 85.



Network of muscular fibres from the heart. At *a*, interior cleft of a muscular fibre opposite the giving off of a lateral branch, which would produce a new mesh by the gradual enlargement of the network.

The muscular fibres of the heart, as is known, divide forked; we may also say, they unite forked; in short they form nets or membranes with elongated cleft-like gaps. These gaps are of the most various sizes. Beside large spindle-shaped fenestræ we see smaller and the smallest slits and clefts. The latter may straightway be regarded as interspaces in a single muscular fibre. One most frequently observes them at such points of a somewhat thick fibre, where this sends off a lateral branch (Fig. 85, *a*), and it does not appear to me to be doubtful, that the traction of this lateral branch in contraction favors the cleaving of the fibre.

β. Atrophy of the Heart.

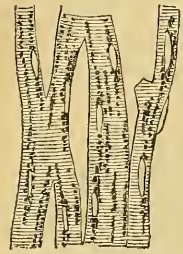
§ 236. As the heart indisputably is the most active muscle of the body, and in consequence thereof consumes more nutritive material than most other organs, so will also disturbances of general nutrition make themselves felt comparatively soon at the heart. Not only the senile involution of the body, but every marasmus, every cachexy, be they caused by acute or chronic morbid conditions, may, in this sense, lead to atrophy of the heart, which then exhibits itself in an attenuation and flabbiness of the entire muscular structure, and hence appears as *general* atrophy. Beside this occur *partial* atrophies, confined to the outermost or innermost layer of the muscular coat; there even occur atrophies in spots, which then also owe their origin to local causes.

In all cases the muscular fibres become thinner, weaker, and even perish. This most important phenomenon of atrophy, however, is met with under various modifications of the histological picture, which permit us to distinguish just as many kinds of atrophy.

§ 237. 1. The brown atrophy, as its name implies, is characterized

by a simultaneous discoloration of the muscle from a rust-brown to a dark ochre-color, together with the decrease of volume. The cause of this peculiar phenomenon is the deposition of a yellow granular pigment into the muscular fibre. This is now very uniformly distributed into the contractile substance; now one sees the granules accumulated in fine rows between the primitive fibrillæ and around the nuclei (Fig. 86); whence it arises, whether it is the condensed proper pigment of the muscular fibre, or whether it arises from the participation of the coloring matter of the blood, is not known. Brown atrophy is always general. It is most frequently found in marasmus senilis, marasmus from inanition, in the tuberculous and carcinomatous cachexies.

Fig. 86.



Brown atrophy of heart-muscle. Fragment of a membrane of muscular fibres, with pigment-granules in the interior of the primitive bundles. 1–300.

§ 238. 2. Yellow atrophy is the fatty transformation of the heart-muscle (compare § 30 and Fig. 7). Accordingly as the deposition of fat-globules becomes more abundant, do the muscular fibres become pale, yellowish, at length whitish, lardaceous. The consistency also decreases. The muscle is tender, friable, and is easily rubbed down between the fingers; on the other hand, the decrease of volume is not always striking. The yellow atrophy characterizes itself in contrast with the brown by the acuteness of its development, and occurs in four forms. *a.* As diffuse degeneration of the whole heart-muscle in febrile diseases of acute course, acute exanthems, typhus, &c. *b.* As fatty decay of the superficial subpericardial layer of the heart-muscle, in consequence of nutritive disturbances, caused by inflammation of the contiguous pericardium (see Pericarditis). *c.* In numerous depots of the size of a pin's head, in the innermost muscular layer, lying nearest to the endocardium of such hearts as have undergone a dilatation of high degree (valvular deficiency). In this case one already perceives through the endocardium, especially at the papillary muscles and trabeculæ of the heart's apex, the whitish sprinkled, that is, the interlaced appearance, which this affection imparts to the heart muscles. *d.* In the form of a large, up to the size of a hazel-nut, fatty depot of softening, which is commonly situated in the centre of the muscle of the left ventricle, towards the apex. The passive behavior and the great brittleness of the fatty degenerated parenchyma, as a rule, leads to a rupture of the heart, which distinguishes itself from other ruptures by very gradual separation, layer by layer, of the muscular structure. An atheromatous degeneration of the coronary arteries, with thrombotic occlusion of a larger branch of them, may in all cases be regarded as the cause of this dangerous condition.

§ 239. *Appendix.*—Fatty metamorphosis of the heart-muscle must

not be mistaken for that excessive fatty infiltration of the subpericardial connective tissue, which is commonly called *fatty heart*. This is found in general corpulence (obesitas), and may become the cause of the greatest disorder, even of death; thus, upon the one hand, the fatty masses from the longitudinal and transverse grooves luxuriate over the heart to that degree, that yet but a small island of the heart-muscle is visible over each ventricle; it is scarcely imaginable that the heart should not be hindered in its movements by this burden; upon the other hand, the infiltration penetrates into the interstitial connective tissue of the myocardium itself. The latter, it is true, occurs constantly only in a limited circumference, but yet it suffices to make a portion of the muscular wall atrophic by pressure, and thereby directly to diminish the functional capacity of the heart.

γ. *Inflammation.*

§ 240. Inflammation of the heart-muscle is one of the most obscure chapters of united pathology; and pathological anatomy, unfortunately, is able to contribute in but an exceedingly incomplete manner towards its elucidation. In the striated muscles of the trunk and the limbs it is conformable to experience that even the slightest degree of inflammation, for example, even that slight tumefaction which we find accompanying chronic rheumatism, and of which it has not yet been decided whether it essentially goes beyond a considerable degree of hyperæmia, is combined with the severest functional disturbances. The muscle rests in a contracted condition. The slightest attempt to stretch it meets with the most decided resistance from the patient, because of its painfulness. If we attempt to transfer these experiences to the heart, it is readily manifest that even the slightest degree of a *diffuse* inflammation must have as a consequence the stoppage of the heart, and therefore the death of the patient, and that only subsequent stages of the inflammatory process would in general be possible in partial affections. We have even gone so far as to reject the occurrence generally of diffuse inflammation; yet incorrectly. I can assure that there is an inflammation uniformly diffused over all parts of the heart. In a man (54 years old) who had been treated for a long time for constitutional syphilis, had thereupon passed through an inflammation of the lungs of both sides, death occurred so suddenly in a few days after leaving the hospital, that the relatives conjectured a stroke of apoplexy. I found, on making the post mortem, apart from several products of syphilis, a condition of the heart, which I believe I can, without hesitation, call a diffuse, parenchymatous inflammation of the heart-muscle.

The heart was half contracted, of strikingly rigid walls, so that it could only be pressed together a little by the greatest force. Even after having made the customary sections for opening it, the organ did not collapse. Immediately, however, a very striking anomaly of the

muscle became noticeable. This had lost its fresh red color, had a shade of violet, the cut surface was iridescent, the cut edges were nearly translucent, the consistence was that of caoutchouc; still the fibres would tear before they stretched. Under the pericardium, as well as the endocardium, were numerous ecchymoses, probably in consequence of a high degree of circulatory disturbance in the muscle, for here no vessel was filled with blood, so that the deficiency of blood certainly contributed its part to the decoloration.

§ 241. Microscopic analysis exhibited everywhere deposits of a finely granular substance in the interior of the muscular fibres; this substance was not uniformly distributed, but accumulated in small spindle-formed heaps, particularly around the nuclei, and might be regarded as "increased protoplasm." Never have I seen a more pregnant picture of Virchow's "parenchymatous inflammation." Beside this the muscular fibres were collectively divided by cross-rents into short parallelograms, a phenomenon which we will yet frequently meet with in the pathological histology of striated muscles. This is in every case to be regarded as a mechanical tearing. I have convinced myself that they can be very easily produced in the muscular fibres of the rabbit by forcible stretching. A reason for the mechanical extension is by no means wanting in our case, and it is to be accepted that the rigid and infiltrated muscular fibre would be more disposed to break into fragments than the normal. That, however, this minute tearing must have the same influence upon the functional capacity of muscles as the greatest transverse rents, is manifest.

§ 242. Apart from the diffuse parenchymatous myocarditis, one is wont to regard certain occurrences in the heart-muscle as the *events of inflammation of the heart-muscle*, without, however, having sufficiently recognized the chain of the phenomena which gradually lead to them; these are abscess and induration of the heart. I will consider abscess of the heart at this place, induration of the heart in chronic endocarditis.

δ. Abscess of the Heart.

§ 243. We find in the muscular substance of the heart a circumscribed spot of the size of a pea, a bean, seldom larger, perhaps of the size of a walnut, at which, instead of muscle, there is found a grayish-yellow, or a generally discolored thickish pulp. This pulp, beside numerous pus-corpuscles, contains par excellence, the detritus of the dissolved muscular fibres, albuminous molecules and fat-globules, it may be also larger fragments of the contractile substance, upon which, however, the transverse striation is no longer to be recognized. The form of the depot is predominantly oval, though ragged abscess cavities, penetrating with long processes into the muscular coat, have also been observed. At the border of the depot we at times see demarcation by a gray-reddish, very soft layer, which, according to Rokitansky, consists

of granulation tissue. If the abscess lies close to the endocardium, it elevates the latter; it may also advance between the lamellæ of the auriculo-ventricular valves.

§ 244. The issue of this condition may be various. Most rarely there may be a thickening or cheesy metamorphosis of the purulent pulp, with a connective tissue capsule and tolerance of the cheesy, afterward earthy, node. At all events, the evacuation of the abscess by bursting is more frequent. Accordingly, as this lies nearer the inner or outer surface of the myocardium, the rupture ensues either into the pericardium, and is then followed by a pericarditis of a rapid course, or inwardly into the heart-cavity itself. In the latter case it then follows that the blood rushes into the cavity of the abscess, and washes out the detritus. Therewith is opened an abundant source for embolia, and indeed especially in the region of the greater circulation, as the cardiac abscess has its seat by preference in the left ventricle. The cavity of the abscess itself appears as an accessory space, as a recess, if you will, an aneurism of the heart's cavity (acute cardiac aneurism). How long this condition may be maintained depends entirely upon the thickness of the portion of cardiac wall not yet destroyed. This and the cardial portion of the pericardium alone restrain the inevitably threatening rupture of the heart and the fatal pouring out of the blood into the pericardium. It is somewhat different when the abscess, as is frequently the case, has arisen in the septum of the ventricles. The bare communication of the ventricles through a small opening appears to have no essential influence upon the circulation; if, however, the purulent destruction advances upwards from the septum, if the pus penetrate into the loose connective tissue between the two lamellæ of the tricuspid, then by the bursting of the abscess, each of the three valvular segments attached to the septum, namely the inner segment of the tricuspid, the left segment of the valve of the pulmonary artery, and the right segment of the aortic valve may be detached, and thereby the condition of insufficiency of the corresponding valvular apparatus be brought about. (Compare Insufficiency and Stenosis of the Cardiac Orifices, § 255.)

§ 245. *Appendix.*—Apart from the large, solitary affections just described, we are wont to consider also those small depots of softening, of the size of a pin's head, which are occasionally found in pyæmia, puerperal diseases, glanders, and similar infections, and then always in greater number in the heart-muscle, as cardiac abscesses. As a rule, several of these lie close under the endo- or pericardium. They are originally grayish-white spots in the muscle, afterward small cavities, which are entirely filled with a thinly fluid pulp. Microscopically we never find actual pus-corpuscles, but generally nothing but vibriones (see § 24). These lie closely crowded in the beginning between the muscular bundles, then they penetrate, under the simultaneous dissolution

of the muscular fibres, into their interior, nay, upon a cross section there is the appearance as though the contractile substance disintegrated into vibriones, because the replacement of the muscular fibres by the masses of vibriones occurs without any increase of volume. Further than to the formation of small, abscess-like depots of softening, the changes cannot be followed, because the whole affection occurs only in the severest, rapidly fatal forms of the infectious diseases mentioned.

ε. *Heteroplastic Tumors of the Heart.*

§ 246. In anomalies of serous membranes, we will have to mention an idiopathic sarcomatous formation at the pericardium. All cancerous, tuberculous, and sarcomatous affections of the heart, are moreover metastatic irruptions. But even these belong to the more rare conditions. Since a few years only do we know that *miliary tubercle* in general occurs in the heart. Von Recklinghausen found them in the muscle; as in general all heteroplastic tumors are met with par excellence in the connective tissue of the myocardium. I have lately found miliary tubercle twice in the endocardium, and indeed near the free edges of the mitral valve. Both times I was dealing with acute miliary tuberculosis of the collective serous membranes, as well as of the pia mater, and indeed in infantile bodies.

§ 247. What was formerly understood by tubercles of the heart, namely the finding of larger caseous nodes in the myocardium, belongs, as Virchow has lately shown, probably not to tuberculosis, but to *syphilis*.

The gummata of the heart-muscle are most frequently found in the partition wall of the ventricles. As a rule, several nodules, up to the size of a pea, are united by a large quantity of inflammatory connective tissue into a tuberous and lobulated tumor; yet individual nodules also attain just here a considerable size, so that they protrude into the cavities of both ventricles.

§ 248. Cancer-nodes, perhaps metastases of soft or melanotic cancer, seldom attain a considerable size in the heart. Tumors over the size of a hazel-nut already belong among the rarities. All proceed from the connective tissue of the myocardium, and according to their situation now advance more inwards, now more outwards; in the former case they occasionally elevate and break through the endocardium, in the latter, the pericardium; thrombi of the heart's cavities (cardiac polypus) also are said to have the capacity of cancerous degeneration, which requires a more exact investigation.

b. *Endocardium.*

a. Acute Endocarditis.

§ 249. It was pointed out above that the endocardium was indeed the analogue of the intima of the vessels, but a far more delicate membrane; it was mentioned, that it contained vessels, at least in places; where these are wanting, the rich vascular net of the myocardium sends its terminal loops close under the thin inner membrane, so that we can throughout ascribe to it an immediate relation to the vasa vasorum. Hence we must not be surprised to find in the endocardium a much more sensitive organ than in the intima vasorum. Various anomalous, mixed conditions of the blood, the pyæmic, the puerperal, the typhous blood adulterations, above all, however, the blood adulteration in acute articular rheumatism, act upon the endocardium as inflammatory irritants. According to Bamberger's estimate, twenty per cent. of all cases of acute articular rheumatism experience the complication with endocarditis.

In regard to the more exact localization of the process, it must first of all be stated, that the endocardium of the left heart is so very frequently affected, that cases of endocarditis of the right heart are actually to be termed rarities. Then the seat of the affection is determined in a very decided manner by the mechanical violence to which certain points of the endocardium are exposed in the heart's action. They are those lines in which the segments of the valve touch in closure of the valve; this is not perhaps the free edge of the valve, but at the semilunar valves an already normally well-marked line, which only touches the free edge at the centre (nodulus Arantii), and at both ends, however, remains one-half to one line removed from the valvular border; at the auriculo-ventricular valves the line of junction everywhere runs a line's breadth from the free edge; it runs, at the upper surface, just where at the lower, the posterior ends of the furcated chordæ tendineæ are attached to the surface looking towards the ventricle. Here, as a rule, we have to seek the first beginnings of the changes. These may from this place extend over a large part of the valve; they may also simultaneously exhibit themselves at another spot of the endocardium, but the lines of junction of the valves are and remain the preferred seats of endocarditis.

§ 250. The histological process in acute endocarditis is composed of three factors of certainly very dissimilar value. First of all, a *participation* of the vasa vasorum can everywhere be established, where such run in the neighborhood of the inflammatory focus. Congestion of blood and a considerable proliferation of the cells of the adventitia can regularly be exhibited upon the transverse section of inflamed auriculo-ventricular valves. (Fig. 87, *b*.) The main stress is of course not to be laid upon this, but upon the *progressive metamorphoses of the non-*

vascular, outer lamellæ of the endocardium. The connective tissue of this experiences, under the new formation of numerous young cells, and the simultaneous softening of the basis-substance, a so considerable intumescence, that even with the naked eye we observe a number of warty inequalities, which are elevated from the level of the valve. (Fig. 87, *c.*)

Fig. 87.

Acute endocarditis. Section through a flap of the inflamed mitral valve. *a*, Upper, *a'*, Lower lamella of endocardium. *b*. Middle layer whose vessels are hyperæmic. *c*. The efflorescence of the upper lamella. *d*. Fibrinous deposition. 1-10.

These granulations are of a very perishable character. Not only, that in the closing of the valves their opposing contact tears and destroys the soft tissue; there also very soon occurs in it a finely granular, not fatty metamorphosis of the entire substance, and therewith so great a friability of the vegetation, that the blood-current washes them away with ease in larger and smaller particles. If this has been accomplished, there results a correspondingly large loss of substance, the endocarditic ulcer, which as a rule extends throughout the whole of a lamella of the valvular flap. The edges of these ulcers are constantly unevenly elevated; they contain, as long as the endocarditis is upon the increase, the initiatory stages of the process which passes over to the adjacent connective tissue. The same occurs, although less frequently, at the base of the ulcer; the other lamella of the duplicature is affected, and when this has also been destroyed, the valve has a hole. Perforation of the valvular flaps is one of the most dangerous catastrophes, for it too easily happens, that henceforth by the force of the blood-current the original opening is widened, or even the valvular flap is detached at one or other side. At the auriculoventricular valves, occasionally, the entire valvular attachment together with the insertions of the papillary muscles is detached. The perforation, like the ulcer, is always surrounded by the described inflammatory excrescences, which, through the fibrinous deposits directly to be mentioned, may become so extensive, that the opening can scarcely be discovered between them.

This most rapid and common course of acute endocarditis is, therefore, altogether without suppuration. The granular disintegration mentioned, a kind of necrosis of the newly-formed materials, prevents suppuration. We do not wish to say by this that suppuration, generally speaking, never occurs in the anatomical morbid appearances of endocarditis. Pus, however, exclusively forms, upon the one hand, in the loose connective tissue between the two lamellæ of the valves; upon the other, in the subendocardial connective tissue; even here it never proceeds to larger collections of this fluid, but always only to small abscesses, at the most of the size of a pin's head, which elevate the endocardium in the form of pustules.

The third factor, which plays a more or less prominent rôle in every

acute endocarditis, is the *deposition of fibrin* at the uneven surface of the affected valvular flap. I expressly emphasize, that here, as a rule, only fibrin, and rarely a sanguineous thrombus is deposited; thus, it appears to me, as though just because of the macroscopic similarity of fibrin with the efflorescence of tissue, the discontinuity of both were often overlooked. The fibrinous deposit (Fig. 87, *d*) fills all the small inequalities of the surface, but increases the entire volume of the efflorescence in so disproportional a manner, that it strikes the naked eye far more than the change of the valve itself. Moreover the thrombosis is just as little to be regarded here as a salutary production, as a first step towards healing, as in aneurisms. The fibrinous material easily breaks up. Hence it hinders neither the progress of ulceration nor the perforation of the valvular flap, but increases the danger of metastatic inflammations by embolia of the broken-off fragments.

β. Valvular Aneurism.

§ 251. The production of the so-called valvular aneurism deserves special mention. We generally understand, under valvular aneurism, every circumscribed projection in the continuity of a valvular flap. Conditions of this kind, as a rule, have nothing to do with endocarditis. They are sac- or pocket-formed projections of the valve, in which both otherwise entirely normal lamellæ participate. The inlet is always found upon that side of the valve upon which, when the valve is closed, the strongest pressure rests, the pocket upon the opposite side. At the aortic valves we reach into the aneurismal sac from the sinus Valsalvæ, at the auriculo-ventricular valves from the cavity of the ventricles. Moreover there also occur in the neighborhood of the cardiac orifices, and at other places, involutions of the wall, which are entirely analogous to those now spoken of, although strictly we cannot call them valvular aneurism. Thus at the points of origin of the coronary arteries, and at the floor of the inner sinus of Valsalva. The latter, by the way the most frequently occurring of these involutions, forms its pocket into the right heart, and indeed now above, now below, and now between the lamellæ of the flaps of the tricuspid valve, fastened opposite to one another. The same three possibilities obtain for aneurism of the membranous, non-muscular spot of the septum ventriculorum. It may advance from the left ventricle above, between the lamellæ and below the left flap of the tricuspid valve into the right heart. I have observed the case, where simultaneously an aneurism, of the size of a cherry, of the sinus of Valsalva existed at the upper, and one of the size of a pea of the septum pellucidum at the lower surface of this flap.

If after this deviation we return to the endocardiac valvular aneurism, then the production of this presupposes a complete destruction of a lamella of a valve. The blood penetrates into the opening made, presses

asunder the two lamellæ, and brings about a more or less strongly marked projection of the one which is unchanged. The endocarditic or acute valvular aneurism is, therefore, essentially distinguished from the form just mentioned, since not the whole valve, but only one lamella takes part in the projection.

γ. Valvular Perforation.

§ 252. In regard to perforation of the valves, it is necessary to distinguish the inflammatory destruction of the proper valvular flaps from a harmless perforation, which is very frequently found at the free edges of the semilunar valves. The latter depends upon a rarefaction of that portion of the valvular flap which lies beyond the proper line of closure, and is according to my conviction, nothing else than an approximation of the type of the semilunar valves to that of the auriculo-ventricular valves.

Namely, if we cast a glance upon the anatomical arrangements by which the blood is prevented from flowing backwards, we immediately distinguish therein a double type, the type of the semilunar valves and that of the auriculo-ventricular valves. I will pass over these typical varieties in two words. The semilunar valves are duplicatures of the intima, of which each projects in a half circle directed with its convexity up stream; the terminal points of their line of attachment come into contact in the same section of the vessel. Thus arise pockets, whose outer surfaces by being filled with blood are brought together, and thus produce the closure. In the peculiarity of its origin here rests the guarantee that the valvular flap can only move in a direction with the blood-current. On the contrary, in the auriculo-ventricular valves we find upon a section of the cavity, movable flaps attached like the leaves of a door, which, if it depended alone upon the line of origin, would turn over towards either side; meanwhile, they can also only give way to the blood-current in one direction, because their flapping over into the auricle is prevented by the fastening of their free edges to the chordæ tendineæ.

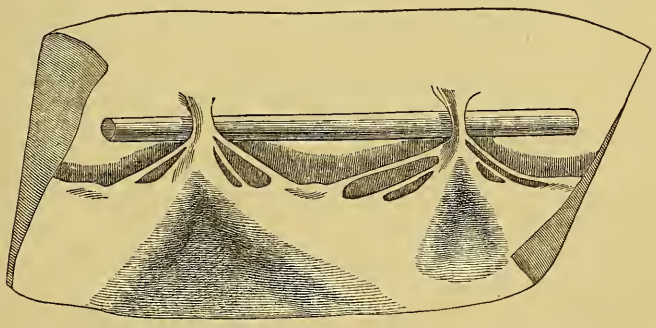
It would certainly be surprising if nature, which is generally so simple in its means, had here actually two valves differing in principle, and if the variety of the anatomical arrangement did not rather depend upon the departure from one and the same principle lying at the foundation. As such appears to me the principle of the semilunar valves, not only because of its far more frequent occurrence (venous valves), but also because, in the harmless perforation in question, we have before us a modification of the semilunar valve, in the sense of the auriculo-ventricular valve.

We may also consider this perforation, as a glance at the adjoining representation shows, as a partial dissolution of the free edge from the nodulus Arantii up to the points of attachment. The free edge, how-

ever, in the closure of the valve has the significance of a check; it prevents a too far return of the valvular flaps. We need only introduce an index finger into a sinus of Valsalva, in order to establish that the valvular pocket is narrower at its entrance than in the line of closure, *i. e.*, that the free edge of the valve presents a shorter and straighter line of connection between the nodulus Arantii and the wall of the vessel, than the line of closure. The free edge of the valve, therefore, acts as a check, entirely like the chordæ tendineæ of the auriculo-ventricular valves. For this function, naturally all of the valvular surface which lies between the free edges and the line of closure is useless. In the disappearance of this intermediate part, except a few connecting bridges, only the functional independence of the free edge is therefore recognized.

In extreme cases, moreover not so infrequent, of marginal valvular perforation, there is produced a yet further approximation of the type of the semilunar valves to the type of the auriculo-ventricular valves in this, that the point of origin of the valvular edge separates from the point of origin of the line of closure. Thereafter half of the edges of two contiguous valvular flaps, together with their thready connecting bridges to the line of closure, arise from a point of the vessel situated beyond the proper valvular insertion. This removal of those points, to which the check-cords of the valvular flaps are attached, from the cross-section through the vessel, to be closed by the valve, and the possibility brought about thereby, that the valvular flaps are always maintained in a more exact direction, and, therefore, always more effectual, is the absolute principle of the action of the auriculo-ventricular valves. In extreme cases of perforations of the semilunar valves (Fig. 88), those bundles of tendinous threads, which arch over a glass

FIG. 88.



Fenestrated semilunar valve of pulmonary artery. Natural size.

rod, that we can pass from one sinus of Valsalva above the point of origin of the line of closure of the valve, into another sinus, represent the papillary muscles of the heart. The point of origin of the valvular

line of closure may now always move further up the wall of the vessel, without endangering the reliability of the valvular closure. The proper valvular flap may always become more level and pointed, since the nodulus Arantii is firmly held at the old place, and the two roots of every line of closure form with each other a constantly diminishing obtuse angle, as is likewise manifest in the preparation represented. In short, the innocuous perforation or fenestration of the semilunar valves, is to me a connecting link between the type of the semilunar valves and that of the auriculo-ventricular valves.

δ. Chronic Endocarditis.

§ 253. In contrast with the acute inflammation and the softening of the valvular tissues caused by it, the chronic inflammation presents itself as a peculiar induration and thickening of the endocardium. The majority of individuals affected with chronic endocarditis state that they have formerly suffered with acute articular rheumatism. This might determine us to admit the possibility, nay the probability of an acute commencement of the endocardial changes; we might conjecture that a disturbance in itself insignificant in the line of closure of the valves, does not heal, because it is situated at a place which is continually exposed to mechanical violence, and just because it does not heal, becomes the point of departure and the central point of a chronic inflammatory process, such as we have the opportunity of observing in neglected ulcers of the outer skin.

Upon the other hand, the identity of this process with chronic endoarteritis must be brought forward. The microscopic changes, as in the former, revolve around an inflammatory hyperplasia of the connective tissue, to which, as a second stage, is annexed calcification; more rarely the fatty metamorphosis of the newly formed material. The very prominent tendency to a retractive shortening at the inflamed parts, can only be adduced as something peculiar to chronic endocarditis. This can naturally only obtain at the duplicatures, whose one-sided attachment permits a contraction of the free edge.

§ 254. Every point of the endocardial surface may at times be the seat of chronic inflammation, yet we find the latter so predominantly frequent at the valves, and at the apex of the left ventricle, that I can confine myself to the description of these two instances.

ε. Valvular Insufficiency.

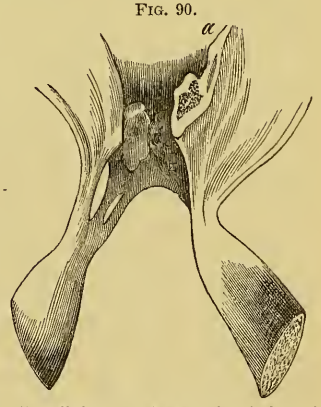
§ 255. We call the coarse deformities which the cardiac orifices experience through chronic endocarditis in general, valvular insufficiencies. They are composed of three anatomical conditions, to be distinguished in every case. 1. Thickening, the immediate consequence of hyperplasia of the connective tissue. At the base of the aortic valves and at the line of closure of the mitral, slighter thickenings are

an extraordinarily frequent condition, which does not disturb the functional capacity of the valves. Higher degrees bring about in the line of closure of the mitral one sided, at the aortic valves commonly on both sides, rough prominences, rigid through lime infiltration. These cover the entire surface of the semilunar valves to the height of several lines, so that, finally, instead of three delicate, crescentic-flaps, three rigid, nodulated bodies are placed festoon-like around the aortic walls. (Fig. 89.) 2. Retraction. It is the consequence of the retractive shortening of the hyperplastic connective tissue mentioned. Taken together with the thickening, it creates the impression, as though the whole mass of the valve were pushed together into a small elongated roll, as though a sail were reefed. At the aortic valves the narrow borders beyond the line of closure not infrequently remain unchanged in a remarkable manner, and float as movable bands at the free edge of the shortened valve. At the mitral, where the process passes to the tendons of the papillary muscle, the shortening presents itself as a dragging down of the valve into the cavity of the left ventricle, as an abnormal stability of that position which the valve should only assume after complete systole. (Fig. 90.) 3. Deformity. The tissue of an inflamed valve is, notwithstanding its rigidity, endowed with a certain intrinsic mobility; it is affected with a kind of inflammatory fusibility, which permits it to grow together wherever like touches like. Of course, as long as a valvular apparatus has its full mobility, there will be two points which come into contact during the closure of the valve, and again constantly separate during the opening of the valve; but on the one part, the inflamed valves, as a rule, no longer have their full mobility; on the other we always see the deformity occurring first of all between two points which are least distantly removed from each other in the opening of the valves. The deformity of two adjacent valvular flaps advances in the line of closure from without inwards. At the semilunar valves of the aorta the deformity occurs the soonest between the right and the posterior valvular flap. If this has advanced to the nodulus Arantii, the wall of partition which divides the two sinuses of

Fig. 89.

Insufficiency and stenosis of aortic orifice. Thickening and shortening of valvular flaps. Natural size.

Fig. 90.



Insufficiency and stenosis of the mitral valve. The valve has been converted into a rigid funnel, cut open at *a*, the papillary muscle separated from the walls of heart. At the section *a*, and in the background, we see the thickening of the valvular flaps. At *a* also a calcified granule. The thickened chordæ tendineæ fused into a few strands, also the apices of the papillary muscle tendinously indurated.

Valsalva is probably lowered, and one valvular flap has been made of the two, which up to a certain degree performs the functions of two, if, however, thickening and shortening do not make this impossible. (Fig. 89.) The deformity is most frequently found, and with the severest effects at the segments of the mitral valve. The auriculo-ventricular orifice is thereby constricted more and more from both sides, so that finally there scarcely remains a small fissure-like opening, and the mitral valve is presented as a rigid diaphragm between the auricle and the ventricle. The melting-down of the chordæ tendineæ (Fig. 90) proceeds from the point of their forked division and their acutely angular insertion at the under surface of the mitral valve. This contributes no little to increase the rigidity and immobility of the valve.

Fig. 91.

Fusion of the right and posterior valvular flaps of the aortic valve, at *a*, the line of fusion. Sufficient valve of two flaps.

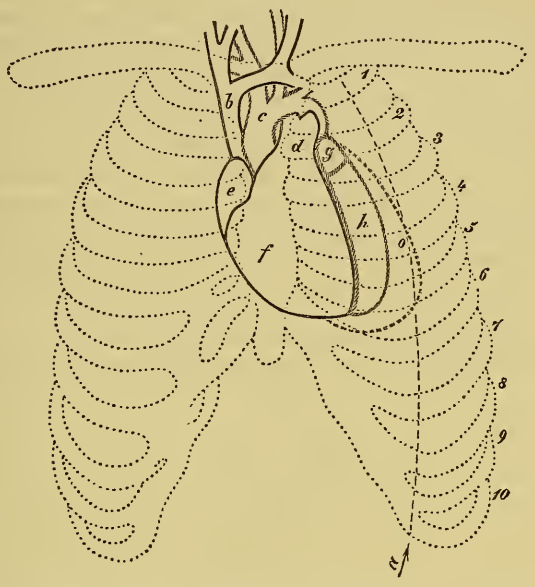
For clinical application: It is manifest, that by the existence of valvular insufficiency, very profound disturbances are occasioned, first of all in the movement of the blood, afterward in the functions of the various organs. We have to group the valvular insufficiencies, and indeed, not only those just described, but also those caused by acute endocarditis, in this connection according to two points of view. 1. The thickening, rigidity, calcification, and the deformity of valves cause, that in the moment when the valves should be smoothly applied (the aortic valves during the systole, the mitral valves during the diastole) that this application does not take place, but the valve forms a projection into the orifice concerned and narrows it. *Stenosis.* The blood breaks against this projection, there arises a murmur, which is best heard where it is conducted to the surface by the shortest route. 2. The retraction, the perforation and partial detachment of the valve, the rupture of the chordæ tendineæ cause, that the valves in the moment when they should oppose themselves by their tension to the backward movement of the blood, are not able to cover the whole lumen, that an opening remains, through which the blood flows back into the section of the heart whence it just came. *Insufficiency.* The act of valvular closure, as is known, is accompanied under normal circumstances by an audible double tone; the first, the systolic tone, is derived from the tension of the auriculo-ventricular valves; the second, diastolic, from the tension of the semilunar valves. If now this tension does not take place, the corresponding sound must also be wanting. On the other hand in its stead a murmur may arise which is produced by the regurgitating blood-current at the abnormal opening; a murmur, which indeed will be very intense, but always only short. Stenosis and insufficiency are always jointly present as the result of chronic endocarditis; acute endocarditis may by perforation and detachment have also insufficiency without stenosis as a consequence.

a. Stenosis and insufficiency of the *aortic valves.* (Figs. 89 and 92.)

The left ventricle of an adult with every systole throws about three ounces of blood (a wineglassful) into the aortic system. The greater resistance, which the ejection finds at the stenotic aortic orifice, will make itself felt as an increase of the systolic blood-pressure upon the inner surface of the *left ventricle*, and according to § 235 cause a *hypertrophy* of the same. At the same time stenosis causes *a systolic murmur, which can be most distinctly heard at the right edge of the sternum* at the height of the second intercostal space, because here the as-

cending portion of the arch of the aorta (Fig. 92 c) lies very close to the thoracic wall. The murmur is continued into the arteries as tones. Another series of phenomena obtains during the diastolic phase of the heart's action. Insufficiency of the semilunar valves causes here, that a portion of the blood just

Fig. 92.



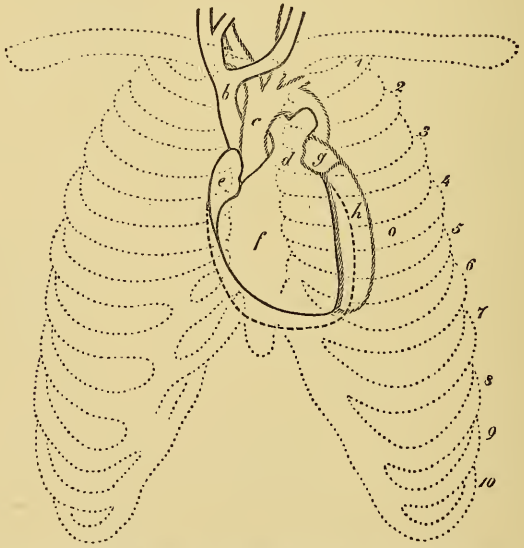
Hypertrophy of left ventricle. Heart in situ. *a.* The mammary line. *b.* Vena cava superior. *c.* Aorta. *d.* Bulb of pulmonary artery. *e.* Right auricle. *f.* Right ventricle. *g.* Left auricle. *h.* Left ventricle (normal circumference). *o.* The hypertrophic ventricle.

thrown into the aorta flows back, because in the relaxing left ventricle the blood then stands under a lesser pressure than in the aorta. We now no longer hear the known diastolic tone of sufficient valves; rather, a second occurs, therefore, *diastolic murmur*, which may be most distinctly heard above the heart's apex, towards which the regurgitating blood is directed. Another effect of insufficiency is the *rapid decline of the pulse* in the arteries, which therefore has here an entirely different cause from that in chronic endoarteritis. The principal danger which threatens the sufferer with stenosis and insufficiency, is undoubtedly the *lowering of the blood-pressure in the arteries*, the equalization of that difference of pressure in the arteries and veins, which alone renders possible the flowing of the blood in the capillaries. From this ensues accumulation of blood in the veins, in the lesser circulation, cyanosis, dropsy, &c.; meanwhile, these extremest occurrences are prevented for a long time, in that the left heart is not alone hypertrophic, but at the same time dilated, consequently contains an abnormally large amount of blood, and is prepared to receive back again a portion of that just thrown out. This dilatation is not perhaps a consequence of the insufficiency, but it is the result of stenosis; it, however, compensates the consequence of the insufficiency, as hypertrophy makes the consequences of stenosis harmless. All of these spontaneous equalizations, however, have their limits. If we supposed that the aortic valves were entirely closed, we would admit, that in such a case even hypertrophy of the highest degree and dilatation would not be able to restrain the threatening lowering of tension in the aortic system. There are stenoses, however, which in fact are not far removed from the complete closure of the aortic orifice.

b. Insufficiency and stenosis of the mitral valve. (Figs. 93 and 90.)

Stenosis of the mitral valve causes, that the influx of blood into the left ventricle during the diastole, is no longer accomplished with the same ease as normally. The blood is dammed in the left auricle. This detention produces a pressure, which is analogous to the increased systolic blood-pressure upon the inner surface of the left ventricle in stenosis of the aortic valves. The *left auricle* is indeed under these circumstances more inclined to *dilatation* than to hypertrophy, yet in all dilatations, a thickening also of the muscle constantly takes place, as of the endocardium. There naturally arises at the contracted auriculo-ventricular orifice in the diastole, *a diastolic murmur*, *which* is most distinctly heard *at the apex of the heart*, towards which the blood-current is directed. Now the systole follows. During this a portion of the blood taken up is thrown back through the insufficient valve into the auricle; therewith a systolic murmur in place of the first sound of the heart, as far as this is derived from the mitral valve. In this partial regurgitation of the blood from the ventricle, we have, however, a second cause for the increase of the blood-pressure in the left auricle. Consequently the effects of insufficiency and stenosis unite to the joint result: *increase of tension* in the left auricle and in the entire lesser circulation. All clinically important phenomena group themselves around this central point. The elevation of tension is in the first place of salutary influence, in so far as it effects,

Fig. 93.



Hypertrophy of right ventricle. Heart in situ. Description as in preceding figure. The contours of the hypertrophic right ventricle are indicated by dots.

that in spite of stenosis, the left ventricle is rapidly and completefy filled in the diastole. It therefore compensates up to a certain degree the existing valvular deficiency. Upon the other hand it causes an immoderate filling of the vessels of the lungs, a passive hyperæmia of the lungs, which leads to the so-called brown induration of this organ (see Anomalies of the Respiratory Organs). The *second sound of the heart*, so far as this is derived from the valves of the pulmonary arteries, appears *strengthened* because of the tighter tension of the valvular flaps. This is best heard at the left of the sternum at the height of the third rib, where the conus arteriosus (Fig. 93 *d*) lies closest to the thoracic wall; afterwards the

work of the right ventricle becomes greater, since in every systole it has to open the tightly stretched valves of the pulmonary artery, and to pour its blood into the already immoderately filled lesser circulation. *The right ventricle* consequently becomes *hypertrophic* (see § 235). Dilatation associates itself to the hypertrophy. The right auriculo-ventricular orifice participates in the dilatation, and finally becomes so large, that the tricuspid valve does not suffice to span over the lumen in the systole. There then happens a relative insufficiency also of these valves, the stagnation is extended to the venous system of the body, and leads to pathological conditions at the liver, the intestinal tract, at the kidneys, &c., which we will consider in the anomalies of those organs. An exceedingly characteristic sign that the relative insufficiency of the tricuspid has occurred, we have in the so-called *venous pulse*, where a systolic blood-wave is continued into the beginnings of the venous system.

The stenosis and insufficiency of the pulmonary artery is almost always a congenital disease, and will be considered in the third section of the chapter. Stenosis and insufficiency of the tricuspid is a great rarity. In its diagnosis the venous pulse plays a principal rôle.

ζ. *Induration of the Heart and Partial Cardiac Aneurism.*

§ 256. Chronic endocarditis leads to entirely different results when it attacks the extended part of the endocardium, the lining of the inner cardiac surface. The hyperplastic thickening of the connective tissue stratum here never produces a perceptible elevation of the level; on the contrary, from the very beginning it produces a certain depression of the affected place, which is very gradually converted into an actual sacculation, finally into an aneurism.

The anterior wall of the left ventricle most frequently becomes the seat of these changes. Here, in the neighborhood of the heart's apex, the endocardium appears, in the circumference of a silver dollar and upwards, milk-white, compact, and tendinous. The surface is smooth, nay, it is smoother than it should be; we miss the complex organization which the system of muscular trabeculæ specially imparts to this region. We cut in and convince ourselves that under the thickened endocardium not only the muscular trabeculæ, but the entire muscle has disappeared. We find a thorough-going induration, one to two lines thick, of white, dense, and stretched connective tissue; in this induration we can no longer distinguish the endocardium from the muscle, nor the muscle from the pericardium. Under these circumstances the question is certainly very pertinent, whether the process, according to its nature, is not to be accepted as a circumscribed indurating inflammation of the muscle (§ 242). That a hyperplasia and shrivelling of the interstitial connective tissue is in fact the process by which the heart-muscle is consumed, there is no doubt. In my investigations at the borders of the depot I could constantly demonstrate, where the myocardium, gradually growing thinner, passes into the induration, atrophic muscular fibres, which lost themselves in a connective tissue rich in cells, although not exactly luxuriantly proliferating. But I hold that this process is to be regarded as a direct *propagation of the chronic endocarditis upon the*

subendocardial and intermuscular connective tissue. Namely, the entire myocardium is not always and everywhere destroyed; however, they are regularly its outer, not the inner layers, which yet exist.

§ 257. As has already been indicated, induration of the heart forms the preliminary condition of a circumscribed dilatation of the heart, the so-called partial cardiac aneurism. Notwithstanding the indwelling tendency to retractive shrinking, the newly-formed connective tissue, which now replaces a part of the heart's wall, is not able to withstand the pressure of the blood. Hence the diseased spot experiences an extension, which now presents itself more in the form of a uniform, shallow depression, now as a rounded sac attached to the heart's apex, whose interior communicates with the heart's cavity through a somewhat narrow opening. The size of the aneurism varies within wide limits, from the size of a cherry up to a hen's egg. There not at all infrequently happens in it a thrombosis; we may expect this so much the more, the more the aneurism has the sacciform shape with a constricted neck. Just in these cases in contrast with the aneurisms of large arteries, at times an obliteration of the cavity takes place, which according to Rokitansky is certainly not effected by the thrombus alone, but for the greater part by connective tissue vegetations, which proceed from the inner surface of the sac. Ruptures have rarely been observed, and only in extreme attenuation of the walls; it was the converse in acute cardiac aneurism produced by suppurative myocarditis.

η. Thrombosis of the Heart— Cardiac Polyps.

§ 258. If we consider the ordinary grounds for the origin of thrombosis (roughnesses of the surfaces of vessels and slowing of the blood-current), we will conclude from the beginning that in diseases of the heart also abundant opportunities are offered for coagulation of the blood. It has already been mentioned, that recent endocarditic efflorescences are wont to be covered with fibrinous deposits of various thicknesses; such are strikingly seldom seen at the surface of indurated valvular flaps, even when they are beset with projections and roughnesses of all kinds. We must, however, remember that each ever so small an inequality of the endocardium may give the impulse to the separation of fibrin. The thrombi produced in this manner are, it is true, as a rule, of but limited circumference, and also do not grow into those large, globular blood-clots which are straightway called cardiac polyps, or with Laennec végétations globuleuses. These probably exclusively arise by a relative slowing or an entire cessation of the blood movement in certain regions of the heart. The case most frequently occurring is, that in consequence of stenosis of an orifice, or in incomplete contraction of the heart, the blood is not entirely emptied from one or other division. Then that portion of blood remains behind which had to pass over the furthest distance to the outlet, the blood, therefore, which exists in the apex of a ventricle, or in an appendix of an auricle. Here

are numerous, often also branched and concealed, pocket-like recesses, from which the blood is generally only removed by very complete contractions. These facilitate coagulation in a great measure, for we always find in them the first foundations of the thrombosis. We frequently enough see numerous small clots, which fill the intertrabecular spaces of the heart's apex in such manner, that the inequalities of the inner surface are in a certain measure thereby equalized.

§ 259. Afterwards, it is true, the various thrombi are elevated above the hidden corners of their first formation; those contiguous to each other melt together, and thus are formed simple, high, and thick blood-clots, which occupy a large part of the heart's lumen. The shape of these plugs is in general accommodated to the shape of the cavity which they partially fill, and with whose inner surface they come into intimate contact in every systole. I have seen how a thrombus coming from the left auricle had grown through the stenotic mitral valve, had here a constricted neck, and again was enlarged in the left ventricle to a thicker body. Their termination is ordinarily globular, so that Laennec could call the cardiac thrombi, végétations globuleuses. The color depends upon the existing phase of their metamorphosis. We rarely find larger thrombi which are yet completely solid in their interior. In this case they exhibit to us a peculiarly stratified structure, and it is not difficult to recognize that the parts nearest the surface of the heart form the point of departure of this stratification, are consequently the oldest, first deposited.

In the further changes of cardiac thrombi, the circumstance obtains, that the peripheral layers can be better nourished than those centrally situated. Hence we find decoloration and softening not in the oldest, but in the most central parts of the whole thrombus, from where they, layer by layer, project to the surface. It may happen that we find a globular vesicle filled with a puriform fluid, which is fixed to the walls of the heart's cavity with thoroughly solid roots (the first intertrabecular clots). It is scarcely necessary to say, that in a probable breaking-up of a cardiac thrombus, the danger of embolia and embolic processes of inflammation and suppuration is very imminent.

3. Congenital Anomalies of the Circulatory Apparatus.

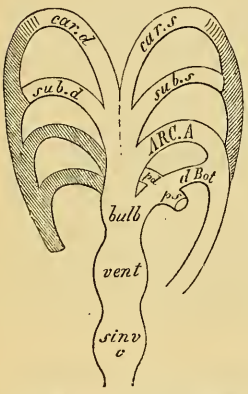
§ 260. As a congenital anomaly of the circulatory apparatus, we first of all must consider the case, where this entire system has remained behind in development in contrast with the remaining organism. This is above all shown in a *too small heart* and the comparative diminutiveness and delicacy of the walls of the aorta and its main branches. More accurately regarded, the collective vessels, even the smaller arteries and all the veins, are formed weaker than they should be. This condition, which occurs par excellence in the female sex, is almost

always complicated with just as deficient development of the blood-corpuscles (chlorosis, § 176) and of the sexual organs; which of these three disturbances however, is to be regarded as the primary and which as the secondary, must remain uncertain. The membranous spot of the septum ventriculorum, which is here always particularly large and disposed to aneurismatic sacculation, deserves a special consideration. (§ 251.)

§ 261. A second group of congenital anomalies depends upon a disturbance of the first development of the heart and the vascular trunks arising from it.

As is known, the heart originates as a straight, contractile tube in the central line of the blastodermic vesicle. We distinguish in it three swellings (Fig. 94), the sinus venarum communis, the ventricle, and the bulbus aortæ, as well as a large number of pairs of vascular arches, which arise from the latter. It is indicated in the accompanying figure by shading, which of these vascular arches wither in the sequel, and which become permanent vascular trunks; also that a wall of partition growing from before backwards divides the innominata from the left carotid and subclavian. The latter vessels then are shifted upon the arch of the aorta until they have reached the points from which they arise in the fully formed animal (Fig. 95). The extent of the arch from the left subclavian to the ductus arteriosus Botalli is called the isthmus of the aorta.

Fig. 94.



Diagrammatic drawing of the first foundation of the heart and large arterial trunks.

Deviations from this sequence in the first origin of the large vessels are not rare. Thus the giving off of the innominata may go further than the arch, it may reach to the bulb of the aorta. In this manner we have a *double aorta ascendens*, whose smaller right branch is of course nothing but an independent innominata. If the separation of the left carotid from the left subclavian was incomplete, there results also a common trunk for these two vessels, a *left innominata*. Thus then it happens, that the third arch from the last of the right side does not become the right subclavian, but the right carotid, the fourth from the last of the right side becomes the left carotid, the fourth from the last of the left side the left subclavian, so that then on the left there is one superfluous trunk, on the right an unsupplied extremity. It is as though the vascular layer and the animal layer had been dislocated against each other. In this case nature helps herself, in that she sends the superfluous vessel behind the œsophagus and the trachea to the right upper extremity; the *right subclavian arises below the left.* Finally, to this early period of the development I already trace the congenital narrowing, that is, *occlusion of the aorta descendens.* At the spot of

the descending aorta where the ligamentum Botalli is attached we find a sharply marked constriction of the whole tube of the vessel. In most of the cases hitherto known the entire lumen was occluded. Instead of this a collateral circulation had been established between the ascending and descending aorta by means of anastomoses between the first intercostal, the internal mammary, dorsalis scapulæ, subscapularis, the thoracica, and the epigastric arteries. I am of the opinion that this obliteration, which is specially designated by Rokitansky as an obliteration of the isthmus aortæ, is produced yet before the division of the heart into a right and left half, therefore at a time when the blood could still reach the descending aorta through the ductus arteriosus Botalli (Fig. 94), because a shrinking of the aorta *in spite of the high blood-pressure* would be contradictory to all experiences which we have gained in aneurisms.

§ 262. The S-formed curving of the cardiac tube proceeds parallel with the partial destruction of the system of aortic arches. This determines the postural development of the heart. For, from the moment when this is completed, we observe the lower curve of this S, the future apex of the heart turned to the left; we see the venous sinus opening in below and behind from the right, and the aorta comes forth above and anteriorly towards the right, in order thereby to pass over with the second curve of the S backwards into the arch. (Fig. 95.)

If we ask after the intimate connection of these phenomena, the answer can only be indirectly given. We must start from this, that every column of fluid which is driven through an elastic tube under strong pressure turns spirally. It is easy to be convinced of this, if to a water-cock, from which the water flows with great force and abundance, we attach a comparatively narrow gum-tube and observe the out-flowing stream. We already perceive the rotation in the simple, cylindrical stream, if we as much as possible regard it from before or behind; as soon, however, as we slightly compress the outlet and thereby elongate it, we observe also the rotation of the flat stream from the side. Moreover, we may avoid the trouble of the experiment, as we have the same results every time we pass urine. If now the force of the detrusor urinæ is not sufficient to force the urine under the ordinary pressure through the urethra, the spiral turning of the stream of urine disappears, and this disappearance is, therefore, designated as a symptom of commencing paralysis of the bladder. All that has been said, moreover, finds its full application to the blood-current in the vessels. The column of blood turns spirally, or, which is the same, it behaves like a cylindrical body twisted to one side, and imparts

FIG. 95.

The embryonal heart after the completed S-formed curvature. The vascular branches of the arch in their permanent arrangement. Ductus arteriosus Botalli.

this peculiarity as giving the turning-point and a principal constituent to the whole vessel.

Among other things, it is shown by the approximation in a straight line of two points, not too far distant, so that they form a curve, towards which side the body was twisted, whether it was strained in a right or left spiral; for example, if we fold together a pocket-handkerchief longitudinally, twist it tightly from left to right, hold it vertically before us, and holding the two ends of the twisted kerchief, one in each hand, attempt to approximate them, it immediately falls into a loop, which looks with its curve to the left. Exactly like the pocket-handkerchief does the cardiac tube behave in the approximation of the aortic bulb to the venous sinus. The loop turned to the left corresponds to the heart's apex, while the vena cava corresponds to the lower, the aorta to the upper piece. The cardiac tube, therefore, does not bend like a flat body, but like a cylinder twisted from left to right. We may, therefore, accept that in most individuals the spiral of the blood-column turns from left to right, and that therefrom results the ordinary situation to the left, of the heart.

Meanwhile, there are cases where this rotation is accomplished in the opposite manner. Then the cardiac tube curves like a cylinder twisted from right to left, the heart's apex points to the right, and the consequence is a complete reversal of the asymmetrical viscera, which are formed only after the heart, the *situs viscerum inversus:* the liver lies to the left, the spleen to the right, the cardia to the right, the pylorus left, the right lung has two, the left lung three lobes, &c. We may, at the same time, deduce from this that the asymmetry of the heart is answerable for all that is asymmetrical in the animal body.

§ 263. A new phase of the development of the heart is accomplished with the sinking down of the common trunk of the pulmonary artery at the anterior circumference of the aortic bulb and the simultaneous origin of the septum of the ventricles. This act also may experience a disturbance; namely, it happens that the main trunk of the pulmonary artery, instead of at the anterior, is given off at the posterior region of the aorta. Consequently it happens that the *aorta* is placed *over the right*, *the pulmonary artery over the left ventricle*, a monster, which naturally can only exist so long as the circulation of the fœtus makes the function of the lungs unnecessary.

§ 264. Finally, we yet have to mention the *congenital stenosis of the right heart*, particularly of the conus arteriosus and the orifice of the pulmonary artery. This most probably owes its origin to a fœtal endocarditis. Just the same hyperplastic indurative conditions meet us here which we have learned to know in chronic endocarditis. The entire impression of the changes caused by it is that of a cicatricial stricture of the lumen. White, shining threads of connective tissue are put upon the stretch when we attempt to unfold the divided conus arte-

riosus. The valves commonly appear curled, laid into folds, as though the base were diminished to which they are attached. Moreover, this entire part has remained behind in development, dwarfish and small.

The constriction of the lumen is commonly one of so high degree that but little is wanting to a complete closure, and its effect is very complicated, since it interferes at a time in the process of development of the heart when the division of the heart into a right and left half is not yet fully completed. In the next place, we consider that the right ventricle cannot empty its blood through the pulmonary artery, and we ask ourselves, where does it empty itself? It empties into the aorta. The septum ventriculorum has not yet been completed; growing up from the apex, it has not yet reached the junction to the base. It is now pressed over toward the left ventricle, so that the dilating aortic orifice comes to stand as well over the right as over the left ventricle, consequently takes its origin from both ventricles. If we further consider that the main afflux of the lesser circulation is cut off by the obliteration of the trunk of the pulmonary artery, and ask ourselves, whence do the lungs obtain their blood? In the first place, they receive less blood than they should; the blood accumulates in the venous system of the greater circulation, the main cause of that permanent dyspnœa with which these individuals are afflicted. The blood, however, which the lungs do not receive through the stenotic pulmonary artery, they get from the aorta, and indeed partially through the patent remaining ductus arteriosus, partially through the bronchial arteries, whose anastomoses with the lesser circulation are considerably enlarged in this case. Meanwhile, it is manifest that all these arrangements, even if they grow to the greatest possible completeness, can yet only bring about a scanty equalization of the disturbance. For as in the single-chambered fish-heart, so here the arterial will be mingled with the venous blood in the aorta. The lung only receives half-venous blood, and can contribute so much the less toward the removal of the carbonic acid from the entire blood. The blood, therefore, becomes more venous, colder, and darker than the normal. To this comes the already mentioned accumulation of blood in the venous system of the greater circulation, the never-failing, but here particularly prominent consequence of every disturbance which the blood movement experiences in the heart. The veins of the remotest parts of the body, the lips, the eyelids, nose, ears, the hands and feet, are continually exuberantly filled, so that the blue, livid color of those parts, blue disease, cyanosis, belongs to the pathognomonic signs of this disease.

III. ANOMALIES OF SEROUS MEMBRANES

§ 265. The correct recognition of the normal structure and of the physiological significance of an organ, has from all time been the most authentic basis for judging of its pathological changes. This obtains also especially for the anomalies of serous membranes. It was formerly universally, and is yet at this time occasionally the case, that in an anatomical description of the serous membranes, one was satisfied to designate them as membranes which were distinguished from the remaining membranes of the body, in that they possess a very thin connective tissue stroma, and a single layer of pavement epithelium. This making of a parallel with other membranes of the body, especially with the mucous membranes, has manifoldly misled our judgment on the pathologico-anatomical conditions of serous membranes. It is, according to my conviction, perfectly inadmissible.

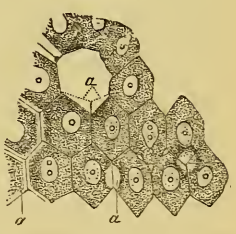
In order to arrive at a correct representation of the nature and significance of serous membranes, we recall a former statement (§ 72), according to which the unformed connective tissue of the body forms a continuous whole, in which the muscular and nerve fibres, the osseous and cartilaginous tissues, epithelial structures, &c., are set in and built up. A higher structural unity of these constituents of form with the connective tissue belonging to them, forms the organs, muscles, membranes, bones, brain. Between two adjacent organs, however, as a rule, there remains a somewhat wider insertion of connective tissue, and if in their functions these organs are to be movable, they can only be so when this insertion is divided into two layers, which oppose smooth surfaces to each other. The visceral and parietal lamina of *serous sacs are such layers of connective tissue, whose membranous existence therefore does not indicate the independence of an organ*, but is directly to be derived from the continuity of the connective tissue of the body in general. In the serous membrane, a layer of the connective tissue of the body presents itself to us, whose continuity is disturbed by no interposition of other formed constituents. *The serous cavity, however, is an inner space, if you will, a fissure of the connective tissue of the body.*

§ 266. This difficult definition is of an importance not to be under-

valued, for judging all pathological conditions in serous membranes. In the next place it may serve us to a correct limitation of the task to be accomplished in this chapter. It indirectly tells us, that the connective tissue of serous membranes stands in uninterrupted connection with the interstitial connective tissue of organs, which are clothed by them. Accordingly it is self-evident, that the serous membranes can participate and actually do participate in all changes which attack the interstitial connective tissue of organs. Hence if we will not tear asunder without necessity what belongs together, we will incidentally treat of a great number of changes of those organs, in which the serous membranes participate, especially processes of chronic inflammation and new formation. For the present chapter there only remain for us the superficial affections actually confined to the serous membrane: abnormal secretions, excrescences, and parenchymatous changes, as far as we can here speak of a parenchyma.

§ 267. Let us now pass to a short repetition of the normal anatomy of serous membranes. Herein also will our definition prove useful and indeed, especially, in reference to the epithelium. As is known, the surfaces of serous membranes are clothed with a single layer of pavement epithelium; flat, nucleated cells of polygonal shape form a mosaic; after treating with nitrate of silver, the borders of the cells come out most distinctly. (Fig. 96.) In all histology is there a simpler texture than the stratified pavement epithelium? At least thus it appears. However, it also only appears thus. The question, where in these flat cells does the nucleus exist? already prepares difficulties. Is the nucleus contained in an interior space of the plate, as in the flat epithelia of the outer skin, or has the plate a hole, in which the nucleus is contained, as a pane of glass in its frame. Neither of the two. It is attached to one, and indeed, the lower side of the cell.* A larger or smaller quantity of finely granular protoplasm forms the cement. The cell, apparently so simple, accordingly consists of two parts: a homogeneous and polygonal plate, clear as glass, and a nucleated protoplasm. The quantity of the latter is mostly so small, that it just suffices to fasten the nucleus in its situation under the central point of the plate; it may, however, be so considerable, that the protoplasm forms a continuous layer, which is correspondent to the homogeneous plate. In such cases the cells, observed from the surface, have a finely granular appearance. We

Fig. 96.



Serous epithelium. (Endothelium, *His.*) Each cell formed by an anucleated polygonal plate and a nucleated layer of protoplasm. The latter retracted at *a*, *a*. After Münch. 1–500.

* This obtains without limitation only for adult creatures. In embryos, the homogeneous plate, which is here spoken of, has generally not yet been developed, and the large, future endothelial cells, rich in protoplasm, frequently engaged in active division, lie naked upon the connective tissue surface.

must, however, carefully observe the places where the adjacent cells touch each other; for it not infrequently happens here, that the protoplasms retract a little from each other, and then are produced round, clear gaps in the granular layer, over which the homogeneous lamella passes uninterruptedly. (Fig. 96, *a*.)

This duality in the structure of the epithelia is most simply explained by the significance of serous sacs as inner spaces of the connective tissue. The epithelial cells of serous sacs are not epithelial cells in the ordinary sense. They do not unite an independently defined form with a just as independent exclusive function, as do perhaps the epithelia of mucous membranes. The epithelial cell of a serous sac is essentially an endothelial cell. It is produced, in that the protoplasm of a soft connective tissue cell partially indurates, and thereby forms the homogeneous plate, while the remainder of the protoplasm and the nucleus remain unchanged. This remainder of the protoplasm, however, belongs just as well to the homogeneous plate as to the intercellular substance of the contiguous connective tissue; it is the vital focus for both. The peculiar structure of the omentum gives us an excellent opportunity to convince ourselves of this double significance of serous epithelia. The fully formed omentum is also, as is known, in its more minute texture a network, whose larger and smaller trabeculæ are formed of wavy connective tissue fibres. Only the larger trabeculæ convey bloodvessels in their axes. The smaller and the smallest are only round bundles of connective tissue fibrils, which not only do not contain any bloodvessels, but also no cells in their interior. We ask, where are the cells of this connective substance? We must either admit, that there is present here a connective substance without cells, or we must accept, that the nuclei of the superimposed epithelial cells at the same time function as connective tissue cells. The latter is undoubtedly the more correct acceptation. For if we, perhaps, with the aid of diluted acetic acid and a moderate mechanical violence, strip off the epithelial layer, it very commonly happens that the nucleated lumps of protoplasm remain attached to the connective tissue, and the anucleated plates are alone taken off. The same occurs, as we will hereafter see, in the beginning of acute inflammations; generally, also, other new formations take their departure from these cells, so that the pathological histology of serous membranes is a continual proof, that the epithelial cells of serous membranes are at the same time the most external of the connective tissue cells.

Of the stratum of connective tissue of serous membranes it is only to be observed, that it is almost everywhere extraordinarily thin, and that it contains rich nets of fine elastic fibres, especially in the visceral layers of those organs which are subjected to more considerable variations of volume. These elastic fibres, because of mapping out the ex-

tent and the limits of serous membranes in transverse sections, are very welcome to the anatomist.

a. Inflammation.

§ 268. We will, in the first place, occupy ourselves with the anatomical changes which an inflammatory irritant calls forth at the surface of serous membranes.*

I can here only, in passing, point to the great multiplicity of *inflammatory irritants*, which always, according to their intensity and quality, condition the different course of the inflammatory process. Most of them are of a chemical nature in the simplest cases; at some place an exudation of heterogeneous fluid takes place into the serous cavity: perforation of the stomach or intestine, the gall-bladder, opening of an abscess or depot of mortification, outpouring of morbid secretions of the uterus and fallopian tubes into the cavity of the abdomen, &c. The etiology of peritonitis, pleuritis, and pericarditis in infectious diseases and in rheumatism, is less evident. We must here remind ourselves that the serous cavities are to be entirely accepted as inner spaces of the connective tissue. Hence the liquid of serous cavities takes part in all the abnormal changes of the blood. Since Von Recklinghausen found resorbing stigmata of the lymphatic vessels upon the serous covering of the diaphragm, we may even advance to the opinion that the fluid in the interior of a serous cavity is subjected to a certain renewal, a change. So much the more rapidly will also an irritating body from the liquor sanguinis appear in the serous cavity. Here, however, like as in the joints and the endocardium, there is yet added to the—shall we say fermentative—irritants from the infecting body, a second auxiliary force: the movement of the opposing layers of the serous sac against each other. In virtue of this friction the one layer rubs the infectious body straightway into the other, and I have no hesitation in perceiving an auxiliary force for the development of the inflammation.

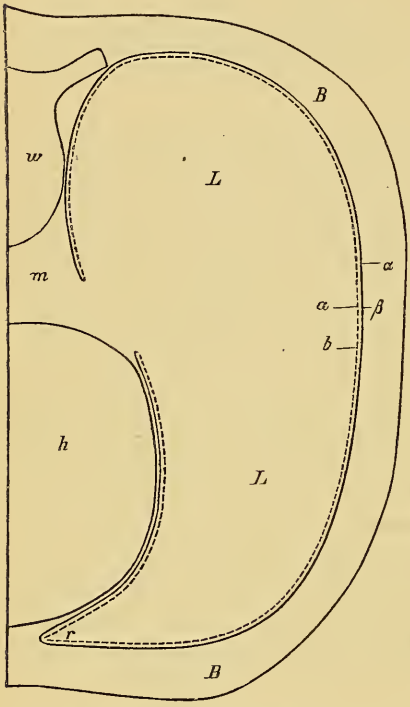
For the *diffusion also of local inflammatory irritants over the whole serous surface*, the physiological change of place of the viscera, and the friction of the opposing layers of the serous sac occasioned thereby, is of the utmost interest, as will yet shortly be shown.

Because of the greater simplicity and perspicuity of the relations, we will, in the first place, direct our attention to the movement of the lungs in respiration, and the friction which the pleura pulmonalis experiences from the pleura costalis. During inspiration the lung is enlarged in all its diameters, and is diminished during expiration. The size and shape of the respective thoracic cavity is at all times correspondent to the size and shape of the lung: it adjusts itself to it; but how do the pleuræ behave therein? While the pleura pulmonalis joins in the dilatation and contraction of the lung, the pleura costalis effects, even by folding together at the borders, the diminution of surface with the thoracic walls required by expiration. Thus it happens that both pleuræ are in contact with their entire surface only at the moment of deepest inspiration. (Fig. 97.) If expiration begins, the borders of the lung (*r*), and with it the most extreme point of the pleura pulmonalis, glides out of the fold of the pleura

* In many points in the following representation I will keep to the excellent investigations of Dr. Münch, of Saratow, undertaken under my superintendence in the Pathological Institute of Bonn, from which also the figures marked *Mch* are derived.

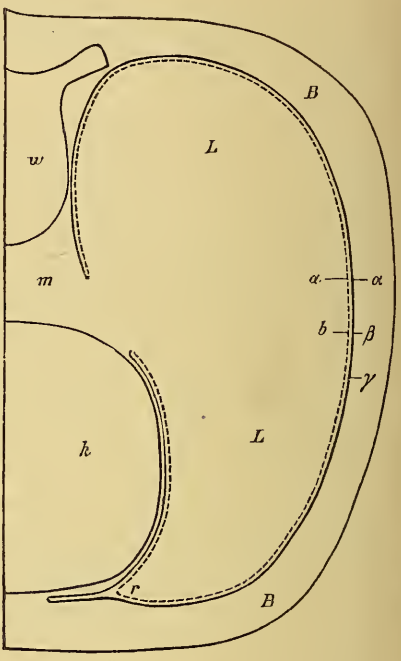
costalis, and slips backward at its folding surfaces until a new inspiration commences. (Fig. 98.) Like the free border of the lung, every other point of its surface, according to the measure of its distance from the stationary apex, on the

Fig. 97.



Diagrammatic section through the left half of the thorax during deepest inspiration. *L.* Lung. *B.* Thoracic walls. *h.* Heart. *w.* Half of vertebral column. *M.* Mediastinum.

Fig. 98.



The same during complete expiration. Description same as in preceding. α, β, γ, see in text.

one hand, and the likewise stationary posterior border on the other hand, will in inspiration be pushed for a certain distance forwards and downwards, in expiration for the same distance backwards and upwards. Suppose now, any given spot of the pleura pulmonalis (a) is wet with the irritating fluid, then this place is pushed forward in commencing inspiration, and for its part moistens a yet intact part of the opposing pleura costalis (α, β). In the subsequent expiration, in the gliding back, a part of the pleura pulmonalis, which lies anterior to the primarily affected spot (a, b), is infected by this. If it lies before the primarily affected spot, it will also be pushed further onward than this in inspiration, and accordingly infects a further part of the yet free pleura costalis (β, γ); in short, in every new respiration, a new zone, as well of the costal as of the pulmonary pleura, is infected. The diffusion of the irritant in this way, however, ensues in the various regions of the pleural sac with various rapidity. The latter is almost nothing in the neighborhood of the apex and the posterior border, and increases with the distance from these points, so that it is greatest towards the free borders.

The relations spoken of assume a somewhat different appearance in the peristaltic movement of the intestine. In the moment when a segment of the intes-

tine undergoes a continuous contraction from above downward of the circular muscular fibres, it forms with the adjacent, in its turn extending section of intestine, a ring-shaped, oblique plane; upon this the pressure prevailing in the abdominal cavity is divided into two component parts, of which one—directed vertically to the axis of the intestine—compresses the section of intestine, while the other moves it away in the direction of the axis, but against the direction of the wave of contraction. The recoil which the intestine experiences in pressing downwards the contents, acts as an auxiliary force in this change of place. That as the root of the mesentery is to be regarded as a fixed point, will therefore be able to bring our segment in contact with so many more points of the peritoneum, it will be able to contribute so much the more to the diffusion of a local pathological irritant, the longer the mesentery of the segment is.

From these considerations, which I will carry no further, since they belong more to pathological physiology than to pathological anatomy, it is evident that a perforation of the very movable small intestine is much more dangerous than a perforation of the fixed vermiform appendix; a perforation of the stomach more dangerous at the anterior surface and at the greater curvature than at the posterior surface and the lesser curvature; that a pleuritis which arises at the apex of the lung remains circumscribed, while a pleuritis of the free edge soon passes beyond the original limits, and so forth.

Inflammations of serous membranes are divided upon the one hand into acute and chronic; upon the other into adhesive, purulent, and probably also the indurative forms. In fact the most manifold transitions occur, hence I prefer a mixed but practical division.

§ 269. *The Recent Inflammation.*—The epithelial stratum is self-evidently exposed, first of all, to every inflammatory irritant acting from the surface. Hence, among the inflammatory phenomena everywhere we find changes of the epithelium foremost. This, in common with the simultaneously occurring exudation from the congested blood-vessels, forms, therefore, the first stage of every acutely setting-in inflammation, and the anatomical foundation of what we are wont shortly to term a recent pleuritis, pericarditis, or peritonitis.

The serous membrane is reddened; with the naked eye we can establish the increased injection of the subserous vascular branches. That in the serosa itself the capillaries are congested and dilated, and that in consequence of this the parenchymatous islands appear somewhat smaller than normal, we perceive upon every stripped-off fragment which we place under the microscope, under a low power and treated with iodized serum. At the same time the surface is less smooth and glistening, this is caused because the epithelium is wanting, and the migration of colorless blood-corpuscles has already commenced. We perceive in moderate amount a pale red, soft, elastic substance, which now membrane-like lies loose upon a part of the surface, now is stretched thread- or ribbon-like between the opposing layers of the serous sac, or glues them together. The latter especially occurs, where two serous surfaces are in apposition without extensive movement; thus between the adjacent lobes of a lung, between the liver and the diaphragm, spleen and

stomach. If a larger quantity of free fluid is present, as is the rule in recent pleuritis, a portion of the "recent inflammatory adhesive mass" is wont to swim therein in shreddy flakes. If we take some of the substance and examine it under a high power, upon the one hand we find large masses of cells and cell-nuclei, upon the other a loose, finely-filamented web, which in chemical examination proves to be a coagulated albuminous body.

a. In Fig. 99 I have rendered a large selection of various cell-forms, which exist in the recent, inflammatory adhesive mass, as also free in

Fig. 99.

Cells and nuclei from a recent inflammatory adhesive mass. *a.* Loosening of same from the homogeneous plates of the epithelia. 1-500. *Mch.*

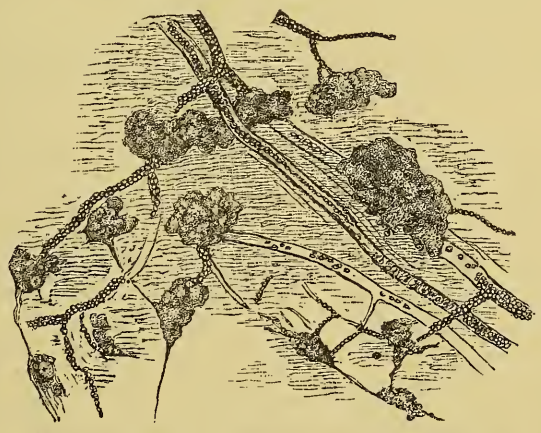
the exudation, upon the first day of an artificial pleuritis (produced by the injection of iodine). We there see free nuclei with one or more nucleoli, nuclei in division up to breaking into small globules, round cells with large nuclei and very little protoplasm, the same in division, cells with much protoplasm and divided nuclei. I will not assert that all these structures are derived from the epithelium; the great majority of them have probably migrated from the vessels, in the manner described by Cohnheim (§ 89), but I must persist therein, that at least a part of them are of epithelial origin. The cell-mosaic (Fig. 96) has broken up; the nuclei, instead of their original flattened, have assumed the globular form, and have separated from the homogeneous plate.

I cannot, without more ado, ignore positive observations, as those rendered in Fig. 99, *a*. In these cells the connection of the nuclei, that is, of the protoplasm with the homogeneous plate, is not yet completely severed, but the moment of separation is evidently very near at hand. Upon one of the cells the plate has already tipped over to the opposite side; upon a second, the nucleus is only held fast yet by a thin thread of protoplasm; a third shows us the simultaneous increase of the nuclei by division. The liberated cells continue to increase by division, as we have already seen above; in short, the epithelial cells first affected by the inflammatory irritant, react to this irritant in this, that the nucleated protoplasm at its lower surface behaves just like an irritated connective tissue cell, in that it forms new nucleated lumps of protoplasm by division. The anucleated homogeneous plate is therewith thrown off; is, however, yet found as such in the serous cavity a long time afterward.

b. The coagulated albuminous body, which we meet with beside the

cells and nuclei of the recent inflammatory adhesive mass, has nothing to do with the epithelium. It is rather an essential constituent of the inflammatory exudation. The considerable pressure, under which the blood in the hyperæmic vessels of the serosa stands, has the pouring out of the fluid of the blood as a consequence. In every artificially produced hyperæmia, be it a hyperæmia from irritation or stagnation, we can convince ourselves of the great ease with which this exudation can be produced and continued. In a chemical relation the exudation contains the same bodies which are peculiar to the liquor sanguinis, although never in the same proportional composition. The amount of albumen especially is very varying, which is now found above, now below that of the liquor sanguinis. Pathological histology directs its attention exclusively to the portion of the exudation in question, and which soon becomes solid, which we straightway term *fibrinous exudation*. This term is based upon the supposition that with the liquor sanguinis the fibrin of the blood also penetrates to the surface of the serous membrane, and having arrived there, is poured out in a solid form. Is this supposition correct? Virchow has set up the opinion that the fibrinous exudation, like fibrin in general, is a product of tissue activity, and is only produced upon the spot; therefore, here in the parenchyma of serous membranes. Nevertheless with this I cannot agree. If we observe the surface of an inflamed membrane by reflected light, a keen eye here and there observes closely standing, small, point-like elevations, the smallest buttons, of transparent aspect. If we carefully strip off the serous membrane and observe it under a weak power (Fig. 100), we immediately recognize that the seat of these nodules is

Fig. 100.



Inflamed peritoneum. Hyperæmia and exudation. *Mch.* 1–100.

everywhere determined by the course of the bloodvessels. They now appear as rounded lumps of a formless, homogeneous substance, which appear to have swollen out at numerous points directly from the capil-

laries and transition vessels, like the gum from the pine tree. I regard this picture as full of significance. I believe that it brings to our immediate view the source of the fibrinous exudation. The fibrinous exudation is, in fact, the fibrin of the blood.

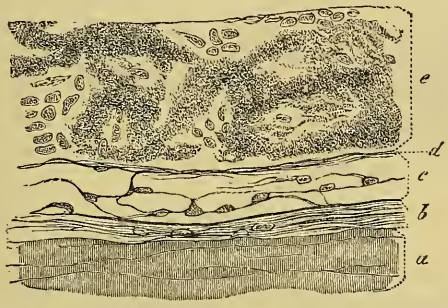
The microscopic forms in which fibrin hardens are not always the known, fine, felted threads of the thrombotic coagulation, but frequently a less split up mass, formed of broad, wavy fibres, which is distinguished from the areolar connective tissue by the disordered heaping together of the fibres. In general it is just as easy to distinguish fibrin by its irregular exterior from every other constituent of the exudation, as it is difficult to give a description of this deviating appearance. It is just neither a crystal, nor a cell, nor a fibre; it is a clot, so that I will content myself with a reference to Figs. 100 and 101.

§ 270. *The adhesive inflammation.* The issues into organization upon the one hand, and into suppuration upon the other, which in general are peculiar to the inflammatory process (§ 91–106), recur in the inflammations of serous membranes. They, however, afford here a double interest, because they are modified by the given anatomical foundation, and hence have, in common with those models, only the actual essentials. This much preliminary. We have to deal with two opposing connective tissue surfaces. If these surfaces produce a homogeneous material and one fitted for organization, an intimate fusion of this material may very readily occur, nay, it would be surprising if such a fusion did not here and there occur. Consequently it is a very common final result of organization, that more or less extensive connections of the opposing surfaces occur through connective tissue bridges. We call these connective tissue bridges "adhesions," and those inflammations which are accompanied from the beginning with *organization of the inflammatory new formation "adhesive inflammations."*

§ 271. The histological processes of adhesive inflammation assume very different appearances, according as the inflamed layers of a serous sac are separated from the beginning by a larger amount of free fluid or not. If the separation does not occur, if the layers remain in continued intimate contact with one another, then, as a rule, the *recent inflammatory adhesive mass already suffices to produce by its own means connective tissue, that is, adhesions.* This fact could, in some measure, appear mysterious, as long as we saw in this substance nothing but fibrin, which, as a cell-less exudation, had to be judged incapable of organization. We now know that the fibrin constitutes only one portion of the inflammatory adhesive mass. Fibrin forms a spongy framework (Fig. 101), in whose numerous pores the youthful cells, probably also increased by division, exist (Fig. 101, *e*). These young cells do not lie so densely that we could exactly call the mass filling up the

fibrinous trabeculæ germinal tissue; rather a certain quantity of homogeneous, clear intercellular substance holds the cells apart in such interspaces as we perhaps find in mucoid tissue; there can be no doubt but that this substance passes over immediately into connective tissue, that in it and through it vessels form, in a word, that it

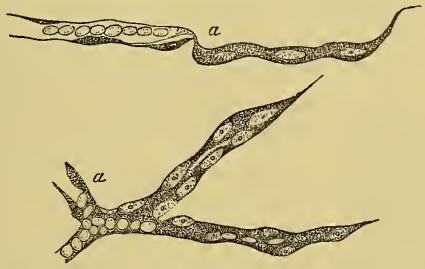
Fig. 101.



Adhesive inflammation. Diaphragmatic pleura. *a.* Contiguous muscular structure of diaphragm. *b.* Subserosa. *c.* Serosa. *d.* Boundary of the serosa and the exudation. *e.* Exudation. 1–400. *Mch.*

possesses the physiological dignity of germinal tissue. Thus we see, then, how the originally round cells become spindle-shaped; the processes come into contact, fuse together, and scarcely has in this manner, even externally, a greater resemblance to the known connective tissue textures been established, especially to the inflammatory spindle-cell tissues (§ 93), when also the second

Fig. 103.



Vascular formation and opening of blood-track. A strand of fused cell-protoplasms as foundation. The blood-corpuscles have already in part advanced into the protoplasm. 1–500.

act of organization, the formation of vessels, already makes a beginning. Nowhere has one a better opportunity of learning the histological procedure of the secondary and tertiary vascular new formation than here.

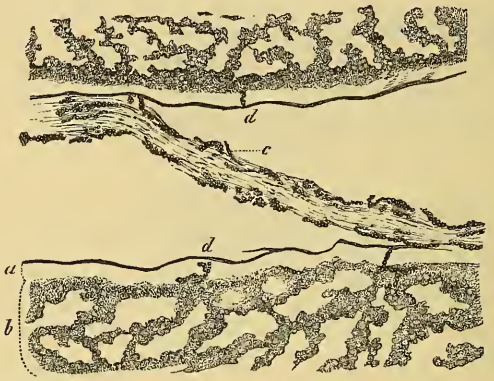
The preparations (Figs. 102 and 103) are taken from a pseudo-membrane, which, at the fifth day of an artifi-

Fig. 102.

Vascular formation in a pleuritic layer of adhesion 5 days old. An enormously long nucleated thread of protoplasm as the foundation; the mother vessel at *a*. 1–500. *Mch.*

cially produced (by iodine injection) pleuritis, glued together the opposing lobes of the right lung of a dog, and elucidates the creation of vessels in a perfectly unequivocal manner, their foundation in the form of nucleated threads of protoplasm, which have arisen by the fusion of cells ranged behind one another, the opening of the blood-track, entirely as I described it on a former occasion. Figs. 104 and 105 teach us

Fig. 104.

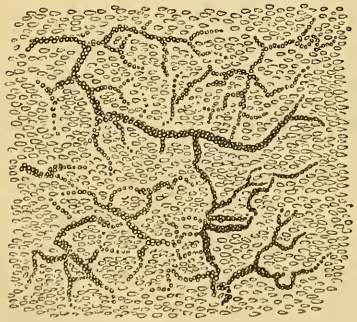


Pseudo-membrane between two lobes of the lung, permeated at both sides by a vascular net. *a*. Serosa. *b*. Lung. *c*. Vascular net of the pseudo-membrane. *d*. Limited number of afferent and efferent vascular branches. 1–100. *Meh.*

that this vascular formation, first of all, spreads superficially. At only a few places (at *d*, *d*, Fig. 104) do the afferent and efferent mother vessels advance from the serosa, while upon shreds of the membrane stripped off and observed from the surface, the most elegant vascular network is exhibited. (Fig. 105.)

In primary adhesion, whose accomplishment we are considering, every serous membrane in the first place forms its own vascular net; hence upon the cross-section (Fig. 104) we see in one and the same pseudo-membrane two vascular nets, which are separated by a layer of tissue not yet vascularized. This, however, changes afterward; namely, if the fusion of the products of the surfaces of both sides is not disturbed, the central part of the connective tissue is also gradually vascularized, and finally, the vascular nets of both sides enter through exceedingly numerous anastomoses into immediate connection.

Fig. 105.



Vessels of a pseudo-membrane seven days old. 1–100. *Meh.*

Consequently, without the exuded fibrin having therein appeared

in any way active, and without, thus far, the subepithelial connective tissue having entered into a considerable proliferating process, there has been formed a thin, indeed, but very richly vascular layer of connective tissue between the serous layers. We can take hold of this and strip it off from its substratum, the serosa, on both sides. Herewith, the ease with which this is accomplished reminds us involuntarily of the ease with which the epidermis is occasionally stripped off from the inflamed cutis, and impressively reminds us that hitherto the weak and few afferent and efferent vascular trunks are the only actual connecting bridges between the serosa and the pseudo-membrane. At a later period this is changed. The connection between the serous membrane and the pseudo-membrane becomes firmer, and finally so firm that scraping or stripping it off is no longer to be thought of, and the pseudo-membrane appears as a very intimate, completely indissoluble gluing of the opposing surfaces. Adhesion is accomplished.

§ 272. We meet with far more complicated displays of forms, as already indicated, when the opposing walls of a serous cavity are separated from the beginning by a larger quantity of exuded fluid, and are continuously maintained in this separation. If we regard the adhesion not only as the result, but at the same time as the cure of the inflammation, and in a certain degree as the final object aimed at of every product of the surfaces, which thereby attain their purpose, then we must say, that with the primary adhesion the expedients of serous membranes are far from being exhausted. There are here not only a first and a second, but also a third intention. The first we have considered; the second is analogous to the healing of wounds by second intention, organization after suppuration, which will occupy our attention farther below.

The third intention is a peculiarity exclusively belonging to serous membranes; it is a medium between both the others. Not pus, not atmospheric air presses between the opposing surfaces striving for union, but a fluid, which, indeed, according to its quantity, is abnormal; in regard to quality, however, does not essentially deviate from that which is also normally contained in the interior of the serous cavity. This, it is true, does not irritate; but yet it hinders union, and gives room for very extensive productions of the surface. The latter do not proceed from the epithelium, but from the connective tissue parenchyma of the serosa, and altogether and entirely have, as Rokitansky has already shown, the character of a proliferation of germinal tissue, a granulation. Meanwhile I will not anticipate.

§ 273. The question, therefore, is about that, by far the most frequent form of pleuritis or pericarditis, which being mostly produced from rheumatic causes, is attended with the abundant exudation of fibrinous serosity. A decided, scraping, friction-sound, is in the beginning to be heard everywhere, afterwards only in the upper part of the serous sac,

while the lower has been filled by fluid. We can determine the degree of filling by the pleximeter. The fever was high, and owing partly to this, partly to the hindrances and disturbances which the lungs or the heart experienced in their movements, the patient died at the height of the disease. We open the pleural sac (the pericardium), and find it more or less filled with a clear yellowish fluid, in which whitish-yellow, soft shreds and flakes swim. A pale, yellowish-white or reddish, now translucent, now opaque, at one time coherent, elastic, then brittle, even a soft friable substance, covers the walls, and is sharply defined from them, partly by the color and consistency mentioned, partly it is more or less easily peeled or stripped off. The external appearance and the whole disposition of this substance excites the impression, as if here a soft, plastic material had chanced between the layers of a serous sac, and had then been modelled by the movements of the lung or the heart; namely, a portion of it is found where it least injures the movements of the viscera mentioned; it fills all the folds and angles; it fills the fold of the pleural sac between the diaphragm and the thoracic walls; it fills the sulcus of the heart and the pericardium, where this is reflected backwards upon the great vessels. Where, however, the substance covers the free surface of the heart or the lobes of the lung in a thick layer, the surface shows a peculiar net-formed or villous condition, as we would expect from the repeated application and tearing asunder of the serous layers; if we place soft putty between two glass plates and then tear them asunder, we receive the same figures.

We see that the whole of these peculiarities betrays a great resemblance to whipped fibrin of the blood, and there has been an inclination, from all time, to take this substance simply for exuded fibrin of the blood, and to let the adhesions proceed from it. Meanwhile, already at an early period, a protest was entered against this acceptation. Especially did Reinhardt strive against the organizing capacity of pure fibrin, and first described its metamorphosis into a slimy, fatty, opaque material, which finally terminates in solution or the cheesy metamorphosis, not, however, with a transformation into connective tissue. Notwithstanding, however, it was a long time before the already indicated teaching of Rokitansky broke the ice, and received its present import by Buhl.

According to this we have to distinguish, in the loosely deposited stratum of exudation, two layers. 1. *An upper*, during the acme of the inflammation irregularly thick layer, which in fact consists of fibrin, and which everywhere covers the lower. The greater part of the fibrin is commonly attached to the most movable parts of the organs, for example, at the free borders of the lobes of the lungs, like as also in defibrinizing the blood, the flakes of fibrin remain hanging to the instrument used for beating (a glass rod, &c.). The microscopic relations of the fibrinous exudation have already been described in § 269.

It forms the same large meshed framework as in the primary adhesion, only it is not of a uniform height, but varies in this respect from one-fourth to six lines and over. 2. A lower layer, which is a production of young connective tissue from the connective tissue of the serous membrane. We must probably accept, that already immediately after the denudation of the surface of its epithelium, the inflammatory new formation was also excited in the stratum of connective tissue of the serosa; this, however, only attains a considerable height from the third to the seventh day of the course of the disease. Upon sections we find numerous young connective tissue cells in the parenchyma of the serosa, cells which toward the surface crowd together more closely, and are here cast off. Beyond, they appear to be imbedded in a mucoid, clear basis-substance, together with which they represent the layer of germinal tissue in question. Both, cells and basis-substance, are to be regarded as a genuine efflorescence of the serous membrane; they are the true plastic exudation, not the fibrin, as was once falsely asserted.

§ 274. Concerning the external form of the young connective tissue efflorescence, it is only to be observed, that from proximate causes this for the present can attain no independent existence. From the analogy with the appearance, in other places, of young layers of germinal tissue, we may indeed accept, that the form to which the efflorescence tends is that of a membrane with small tuberosities. But upon the one hand, the continually repeated mechanical violence is in the way of such a formation; upon the other, it is made impossible at almost all places by the superimposed layer of fibrin. Hence the tissue of granulation penetrates from below into all the interspaces of the fibrin, grows around and through it layer by layer, and thus raises it more rapidly to a considerable thickness than would otherwise have been the case. But even in this most intimate permeation, in which the fibrin plays the rôle of a supporting framework, we must yet deny to this body all active participation in the acts of organization.

Vascularization follows in the footsteps of the formation of germinal tissue. In a short time an extraordinarily rich capillary net permeates the young pseudo-membrane. The new vessels are characterized by a strikingly large calibre, and, as is so frequent in young vessels, by delicacy of the walls. The afferent and efferent vessels of the serosa are, on the contrary, narrower and less numerous. There consequently results an arrangement, similar to the rete mirabile, where the blood-pressure in a corresponding manner is increased by the interposition of a broad bed for a stream between an afferent and efferent vessel. The same result is also to be expected in this case; and that in fact the blood does, in the newly-formed vessels, stand under a far higher pressure than in the vessels of the serosa, is proven by the numerous extravasations which now ensue, partly in the interior of the pseudo-membrane, partly at its surface, and which give it a reddish spotted

appearance, a red color likewise to the free fluid. The vascularization of the pseudo-membrane leads therefore foremost to a very critical arrangement for the whole course of the case, an arrangement which offers the most possible favorable chances, not alone for the continuance of the exudative process, but also by the abundant conveyance of nutritive material, favors in the highest degree the productive processes in the pseudo-membrane. There is added, therefore, just at this moment, the danger also of a *too abundant* cell-formation, the danger of suppuration, to the patient. The physician observes the unfavorable turn; he says, the disease is becoming protracted, the resorption of the exudation is stagnating, &c.

§ 275. Meanwhile, this danger of suppuration will occupy us further on. Let us, in the next place, consider the course of the inflammation when it remains true to the last to its original adhesive character. We may reasonably ask, how, then, under the conditions described, it can be possible that the exudation in general ever comes to a stand-still. The cause lies, in the first place, in the transformation of the young proliferation of germinal tissue into fibrous connective tissue. The transformation, as we stated more in detail in § 93, is constantly connected with a certain shrinking, and this in turn leads to the obliteration of the great majority of the newly formed vessels, so that in regard to vascularity the completed adhesions represent but a very small fraction of the original vascular net. Upon the other hand, we must remember that the fibrin, which, being not only deposited upon the young connective tissue, but also projects into it with numberless processes, does not indeed organize, but yet contracts vigorously and from all sides. The contraction begins immediately after the separation of the clot, and if circumstances are otherwise favorable—and where could they be more favorable than just here?—advances constantly until it has either attained the smallest possible volume, or until a further metamorphosis robs the fibrin of its most characteristic peculiarity. Is it to be expected that this contraction of the fibrin should not act compressive upon the covered and inclosed tissue of granulation and its vessels, and thereby put a stop to the transudation? Enough, the transudation finally ceases and gives way to resorption. The free fibrin, which swims in the exudation in shreds and flakes, then at first tends to a mucoid fatty metamorphosis; we find numberless fat-globules in the soft, swelling substance, which may, moreover, also be derived from a fatty metamorphosis of the cells which were contained. To the naked eye this degenerating fibrin appears whitish opaque, and if the resorption of the free fluid goes on with exceptional rapidity, a portion of the fibrin, probably yet before its complete dissolution, dries up in some recess of the serous sac, becomes cheesy, and remains for years as a caseous substance. The rule certainly is, that before the disappearance of the fluid, all the fibrin, as well the free as that which covers

the connective tissue efflorescences of the walls, dissolves completely in this fluid, in order, then, to be simultaneously resorbed with it into the blood. The opposing layers of the serous sac approximate to each other, they finally touch, and the products of the surfaces of both sides fuse. The bridge is soon formed, upon which the vessels of the visceral and parietal layers anastomose with one another.

The final result are the known *false ligaments* between the pleura pulmonalis and costalis, between the heart and pericardium, between the individual abdominal viscera among each other and with the abdominal walls. They have frequently been investigated in reference to their histological qualities; they bear upon their surface a single layer of pavement epithelium, like the serous membranes themselves; in other respects, they consist of wavy connective tissue bundles, between which run long extended, thin bloodvessels; also nerve fibres of new formation were once found in an adhesion (Virchow). What appears to me the most important in the whole affair, is the circumstance that here, where by the continual mutual friction of the surfaces, by the continually recurring approximation and withdrawal of both the points connected by the adhesion, the organization of the germinal tissue is influenced, the ordinary cicatricial tissue, with its short, stretched, and rigid fibres, does not form, but a connective tissue, which comes much nearer to the normal type of loose connective tissue.

It therefore appears that the final result of the inflammatory organization depends very essentially upon the external conditions under which it is accomplished, and that especially a repeated extension and relaxation of the cicatrix must belong to it, in order to produce a genuine loose connective tissue, instead of the rigid cicatricial tissue.

§ 276. *The purulent inflammation.* We distinguish a primary and a secondary suppuration. In most of the inflammations of the abdomen, especially in those which are produced by perforation of the intestine, or by infection on the part of the female organs of generation (puerperal fever), we have superabundant opportunity to study the former. If the inflammation has but just arisen (so-called fulminant peritonitis), we most distinctly convince ourselves that, like in the adhesive form, so here also a stage of recent adhesion opens the series of phenomena. In fact, the histological transformation of the recent adhesive mass into pus appears just as easy as that into connective tissue. The indifferent cell-forms present, are pus-corpuscles as soon as they are suspended in a serous fluid, and therewith continue in their luxuriant proliferation by division.

The formation into the so-called specific pus-corpuscles, *i. e.*, young cells with manifoldly divided nucleus, is entirely unessential; meanwhile, it is likewise very frequently observed. This transition so presents itself to the naked eye, that the known reddish membranes and membranous shreds become yellowish-white at their borders and melt

off; finally, however, more instantaneously they dissolve into a purulent fluid. I have been able to establish this more than once in artificial peritonitis; at the same time, however, made the experience that this stage of recent adhesion generally lasts but a very short time in primary purulent inflammations, and very soon gives way to the most essential phenomenon of purulent inflammations, viz., purulent exudation.

The question herewith is foremost about an exudation in the most proper sense of the word. From the dilated vessels numberless colorless cells migrate and then infiltrate the connective tissue, in order thereafter—as I for the time being yet accept for explaining the frequently enormous masses of pus—to multiply by division. As we see in Fig. 106, a vertical section through the serous covering of the uterus,

Fig. 106.

Purulent inflammation upon the serosa of the uterus. *a.* Serosa infiltrated with colorless blood-corpuscles. *b.* Surface secreting pus corpuscles. *c.* Muscular structure. 1–500.

all the interspaces between the somewhat thicker layers of fibres are literally filled with cells. In the frequently occurring flask-shaped and similar forms, we also see that these cells do not lie quiet, but are engaged in amœboid locomotion. To what point this locomotion is directed, there can scarcely be a question; upwards, towards the exterior. We must imagine that a mighty exudative current of liquor sanguinis passes through the membrane thus infiltrated. This also will, by preference, move in the interstices of the fibres and carry with it the cells existing here in great quantities; afterward, when as a quiescent fluid it fills the serous cavity, it will hold them suspended as pus-corpuscles. The exudation thus becomes purulent upon its way from the bloodvessels to the free surface of the serosa; thus we receive the purulent exudation.

In the beginning, as long as the separation of cells is yet limited, the exudation is also yet clear and throws down gelatinous, translucent flakes of fibrin in large amount; afterward, it is pure greenish-yellow, thinly fluid pus. In post-mortem sections of cases of puerperal peritonitis, we not infrequently find, in the upper regions of the abdominal cavity, in the surroundings of the liver and stomach, yet the recent inflammatory adhesions; further downwards, around the kidneys and between the mesenteric folds of the upper loops of the small intestine, a tolerably clear exudation intermingled with flakes of fibrin, which towards the true pelvis becomes purulent streaks; in the true pelvis, however, is completely purulent. The serosa appears to the unaided eye, hyperæmic, but in such wise, that the red of the vascular injection is subdued by a milk-white shade, which overlays it like a veil. This is derived from the purulent infiltration of the membrane.

§ 277. We must place by the side of primary purulent inflammation, those cases where an adhesive inflammation passes over into the purulent. We stated above, that this transition is anatomically prepared and favored by the luxuriant vascularization of the young pseudo-membrane, which, especially when a new injury acts upon the inflamed membrane, furnishes the material for a yet more luxuriant production of cells, *i. e.*, for suppuration. This unfortunate turn, as a rule makes itself known to the physician by a violent chill and a hectic fever following thereupon. The new formation of cells starts very suddenly—thus it appears—into a more rapid movement. All cells, be they in the exudation, in the pseudo-membrane, or in the serosa itself, participate therein. The clear serum becomes cloudy. Large shreds of the pseudo-membrane are loosened and detached from their resting-place, then to liquefy into pus; bare places of the serosa themselves suffer loss of substance. Such ulcers are not infrequent in the pleura over the individual ribs, and penetrate into the subserous connective tissue, more rarely to the periosteum or even to the bone, which is then exposed and becomes necrotic. Apart from this event, however, the suppuration, even in the most violent inflammations, retains the character of a surface-secretion. The suppurating serous membrane is not to be compared to a destructive ulcer, but to a productive, granulating surface of a wound. As the latter shuts itself out from the exterior, so this soon shuts itself off from the cavity of the serous sac by a roughened membrane of young connective tissue, the pyogenic membrane of authors. The same occurs, when a primary purulent inflammation disposes to healing.

Meanwhile, frequently enormous quantities of pus have collected in the serous sac; and can we be surprised thereat, if we consider, how large a quantity of pus is yielded even by small ulcers; that here, however, an ulcerative surface is present, which is not measured by square lines, but by square feet? It is not at all a rarity that by para-

centesis, or at the post mortem, a half bucket of pus is emptied from a pyothorax. The diaphragm is depressed, with it the liver or the spleen, the intercostal spaces are effaced, the lung becomes smaller than it could become by its own retraction, hence it is compressed and hangs as a narrow strip of scarcely a hand's breadth, devoid of air and of leather-like consistence, in the pus. Finally the pus, like that of abscesses, seeks an outlet. If it is a pyothorax, as a rule, the interspace between two of the lower ribs is chosen for the point of rupture; moreover, just at this period, medical skill is wont to interfere, interrupts the natural, but somewhat slow course of the phenomena, and decides by the trochar the point of outlet.

§ 278. As to the further course—*i. e.*, the gradual *healing* of the condition—we can apply our experiences of the second intention, with the restriction, that here, corresponding to the colossal ulcerating surface, the cicatricial formation also ensues in colossal dimensions. There occurs the known sequence of germinal tissue, spindle-cell tissue, and the stretched, short-fibred cicatricial tissue; the second proceeds from the first, the third from the second, as has been described more in detail in § 93, *et seq.* The cicatricial tissue does not appear in insignificant quantity, but it forms a shining *white induration* from one-half to three lines thick, which clothes the serous membrane and covers the contiguous organs. The mechanical effects of cicatricial contraction, which obtain here as well as in every cicatricial formation, are frequently immense. One can very distinctly see in this instance, how nature accomplishes mighty events by the simple addition of small, uniform effects. Yet in the healing of a pyothorax opened externally, the only question is about nothing less than the resistance which the arch of the bony framework of the chest opposes to a complete retraction inwards, therefore, to that change of form, contrary to which it is the purpose of its existence to contend. It has most erroneously been supposed, that the induration spoken of could lend a helping hand towards again distending the compressed lung. Experience, however, teaches, what simple reflection must also teach, namely, that the lung must first be directly and forever compressed by the induration. Sooner would the other thoracic viscera, especially the heart, be drawn over as much as possible, in order to fill the space which the compressed lung formerly occupied. But the doctrine of Toricelli cannot be brought into question at all. The stress lies upon the drawing together of these contiguous organs. The indurated sac, into which the pleura was converted, must and will contract, like as a urinary bladder contracts. The force, however, with which this is accomplished, is so great, that not only the soft, yielding thoracic organs must follow it, but that the ribs also are drawn downwards and together, until they have the form of a steep roof and are curved inwards; the vertebral column is correspondingly curved. Thereby the lumen of the serous cavity also disappears

more and more; but few drops of pus are yet evacuated through the fistula; finally obliteration, and complete healing take place.

B. Non-inflammatory New Formations.

§ 279. Were I at this place to mention every *occurrence* of cancer, sarcoma, chondroma, lipoma, &c., in serous membranes, I would not only have to repeat the collective pathological new formations, but also have to anticipate a good portion of the diseases of the intestines, the lungs, liver, &c.; namely, to the heteroplastic new formations, which have their point of departure and seat in the parenchymas of those organs, the serous membrane behaves quite like the adjacent connective tissue, and in this peculiarity takes part in the new formations. In the face of this, I will here only speak of such new formations as are diseases of the serous membranes, proceed from them, and run their essential course within their parenchyma.

§ 280. In the first place a *hyperplastic development of connective tissue* is to be mentioned, which comes to pass in continued dropsical effusions, in the walls of the serous sac. As a rule a *milky cloudiness* is the first that we see. This is derived partly from a moderate increase of thickness of the serous membrane, chiefly, however, from a different constitution of its fibres. Virchow has introduced the name of sclerosis for that condition of the connective tissue fibres, where they have increased it is true but little in circumference, but so much the more in contents, *i. e.*, in solid substance. Fibres of this kind are more rigid, less capable of swelling out; particularly less accessible to chemical reagents than the normal, and are far more refractive. To the latter circumstance, the sclerotic places of serous membranes owe the milk-white color. Just as many doubts prevail concerning the nature of sclerosis, as concerning the position of the process in whose company it originates. There the question is, whether its purport is a simple or an inflammatory transudation: here, whether a simple or an inflammatory hyperplasia. Now according to my opinion, we must distinguish as strictly as possible between active and passive hyperæmia, and accordingly seek the point of departure of the disease either in an inflammation, or in a static anomaly of the circulation. We will also generally be successful in this. We must, however, acknowledge, that a static hyperæmia predisposes just as well to inflammation, as conversely also in every inflammatory hyperæmia, a static element is developed in the actual partial dilatation of the bloodvessels. Hence both of the phenomena frequently go hand in hand and mingle in such manner with each other, that it is afterwards uncommonly difficult to say, what belongs to the one and what to the other. Instinct and custom play a great part. As a rule we regard the dropsy of the pleural cavity in cardiac diseases as a purely static transudation, while we put down the

dropsy of the tunica vaginalis propria testis, hydrocele, as a prototype of inflammatory dropsy. Between them, dropsy of the pericardium and of the abdomen stand nearest to hydrothorax; dropsy of the ventricles of the brain to hydrocele; dropsies of the bursæ, sheaths of tendons and joints, form the disputed border-land. That which is ambiguous and discretionary of this entire doctrine depends upon the want of useful, distinctive criteria for the point, where we shall begin to call the transudation upon the one side, and the new formation upon the other, inflammatory. Julius Vogel has wished to take the amount of spontaneously coagulating albuminous bodies in the transudation as characteristic of inflammation (Hydrops fibrinosus = inflammatorius). But we now know, that also the transudation, certainly not inflammatory, which collects during the death agony in the pericardium, contains fibrinogenous substance. Touching, however, the new formation, which indeed at present especially interests us, it has been desired to set it up as the inflammatory element, par excellence, a procedure, which appears to have found so much accordance and hearing, only because by one blow it relieves us of all further scruples concerning the doubtful determination of the limits between hypertrophy and inflammation. Now according to my judgment, there is generally no sharply defined limit between these two things. Inflammation is a caricature of normal nutrition, and hypertrophy is only a lesser grade of the same distortion. It naturally cannot be my intention to withdraw from further discussion by a sounding phrase. I rather readily confess, that I by no means feel myself mature to pronounce finally concerning this point; I was only concerned to justify myself, when I simply designate the things which are to be described here, as hyperplastic, without finding in their form a prejudice for their cause and origin.

§ 281. The above-described *milky cloudiness* especially strikes us where it affects the serous covering of an organ of dark color; thus, especially, the capsules of the spleen and liver, and the visceral pericardium (tendinous spots of the heart). Were the brain not of a whitish color, without doubt the sclerosis of the ependyma in chronic hydrocephalus would likewise present itself as a milky cloudiness. Sclerosis, as was said, is only the lowest grade of hyperplasia of connective tissue, of which it has not yet been decided, whether therein, there has in general taken place a new formation, or whether there is only a strengthening of the old connective tissue through intussusception.* Besides sclerosis, however, we know an entire series of very different proliferations of connective tissue, which are collectively characterized by their more circumscribed appearance. The formation of sharply defined, flat elevations of *cartilaginous texture* stands nearest to sclerosis. These are most frequently found upon the capsule of the spleen, where they are of jagged contour, and yellowish-white translucent color, and

[* Molecular addition.]

may attain the height of a half or entire line. They are wont to be circularly round, lentil-shaped, and of greater transparency upon the pleura, while upon the thickened tunica vaginalis propria testis, they are characterized by their often very considerable circumference and hardness. The *fibromatous* are allied to the cartilaginous eminences, which in their histological organization are most similar to the corneal cartilage. The former are above all characterized by their tendency to polypous development. Likewise in the dropsical tunica propria testis, but also in the peritoneal sac, we occasionally find *free* fibrous bodies, of the size of a cherry up to a hazel-nut, of round or roundish form, and concentrically stratified structure, which are nothing but the severed heads of polypous excrescences of this kind, of the walls. Of the *softer dendritic vegetations*, occurring less frequently upon serous membranes than upon synovial membranes, Rokitansky gives the following description: "They originally arise as a hyaline, club-shaped vesicle (a tuber of germinal tissue of the smallest size, Rindfleisch), which expands into a dendritic structure, and produces in its interior connective tissue. The clubbed ends of the branches and twigs commonly undergo a flattening to lenticular or melon-seed-shaped corpuscles, at times also receive manifold facets. Sometimes the primitive club grows into a bag-shaped cyst, filled out with serum or an œdematous fibrous meshwork." We might term this condition a pendulous myxoma. But in fact it forms the transition to a complete liquefaction of the interior of the club, a pediculated *softening cyst.* The latter are found, by far, most frequently upon the peritoneum, and here again upon the serous covering of the female sexual organs, upon the broad ligaments, the ovaries and tubes.

§ 282. *Lipoma arborescens* (Müller) is a special peculiarity of serous and synovial membranes. How very analogous the central growth of lipoma in general is to the dendritic growth, has already been amply discussed by me in § 133. Lipoma arborescens might be regarded by us as unfolded lipoma tuberosum, if we did not prefer to see in it simply a hyperplastic development of the known villous and polypous fatty appendices of serous and synovial membranes, the appendices epiploicæ, glandulæ Haversianæ, &c.

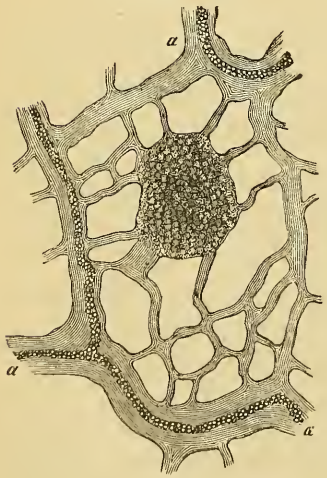
§ 283. For the *heteroplastic tumors* (sarcoma, tubercle, cancer), which are found partly protopathic,* partly deuteropathic,* upon serous membranes, the question proper is only one of special histological interest; the question as to the origin of the embryonal tissue, which, as we know, forms the foundation for all. Namely, all these new formations strikingly distinguish themselves, when they actually originate upon the serosa, and have not broken through from an adjacent organ, per

[* Of primary and secondary formation.]

contiguum, into the serous sac, by their entirely *superficial seat.* Scirrhus appears as a "soft mass, poured out uniformly upon the serous membrane" (Rokitansky); medullary cancer the same, or as a roundish, flat elevation; gelatinous cancer "in the form of knobs, which at times grow to an astonishing volume, and vegetate almost *free* in the serous cavity, *i. e.*, confined to the scanty, inconsiderable vascular adhesions;" sarcoma fuso-cellulare as a fungous vegetation. Miliary tubercle, finally, is apt to figure as a miliary gray vesicle. The most of these tumors may be scraped off from the serosa with a knife, whereupon the latter remains somewhat rough indeed, but yet without any considerable loss of substance. There has evidently but exceedingly little of the connective tissue of the healthy serosa been taken up in behalf of the new formation, and in the tumors of serous membranes we have just the most possibly pure representation of their essential textural relations. And whence is this superficial situation derived? It is derived from the fact that these tumors collectively, at least primarily, arise *from the epithelium* of serous membranes. Nothing, indeed, prevents them from afterward penetrating deeper, not only from the surface of the serosa into the parenchyma, but also through the parenchyma into adjacent organs. Wherever there is connective tissue, the road is open to them. But we must also not forget, that the serous epithelial cells are connective tissue cells.

§ 284. One example will suffice to give us an idea of this exceedingly peculiar mode of origin. I make choice of that of miliary tubercle in the omentum. Fig. 107 shows us a very small, not yet fully grown nodule, by a low power (100). It is attached as a globular, cellular structure to nine delicate connective tissue fibrils, which run from its periphery radiating to the larger, partly vascular trabeculæ, of a larger meshwork. Let us now examine one of the nine points of connection of the connective tissue fibrils with the nodule under a higher power (800). Here, at the border of the new formation, we must surely, provided the nodule were yet engaged in growing, find phenomena which elucidate the detail of its origin. We find what I render in Fig. 108 by a copy. The nodule grows by a proliferation of the epithelia. The homogeneous lamella has been elevated upon one side of the connective tissue fibril, thrown off upon the other, and instead of the nucleated protoplasm we

Fig. 107.



Miliary tubercle of the omentum. 1-100. *Mch.*

see smaller and larger groups of young cells, which have manifestly been produced from those by division. The substance of the fibril itself is intact up to the nodule. Here the fibril vanishes; will, however, probably be connected retiform with the other eight fibrils in the interior of the nodule, in the same manner as it was before the tubercle formation. It evidently takes no part in the proliferation itself, and we have as yet the right to regard the whole new formation as a product of the serous epithelia. If at a later period the thicker connective tissue trabeculæ (Fig. 107, *a*) have been reached by growth at the periphery, then will also non-epithelial connective tissue cells contribute their mite to the enlargement, by apposition, of our nodules. The considerable volume, however, which the nodule must already have, ere this can happen, shows at the same time how far also the means of epithelial growth reach.

Fig. 108.

Production of miliary tubercle by proliferation of the serous epithelium. 1-800. *Mch.*

IV. ANOMALIES OF THE SKIN.

§ 285. For the study of the histological processes, by which the numerous affections of the skin are accompanied, it is very advantageous to divide the organ into epidermis and papillary layer upon the one side, the corium and subcutaneous connective tissue upon the other, and to append to these subdivisions yet a third, which is concerned with the anomalies of the glands of the skin and the hairs.* The papillary layer, apart from its other physiological functions, is the matrix of the epidermis. Both form a *vegetative whole*, and this correlation becomes especially prominent when in most of the diseases the question is about disturbances of the vegetative relations. The glands also have their proper diseases, as well as the hairs and nails. Herewith it cannot and must not be denied, that we frequently meet with simultaneousness, homogeneity, and all sorts of transitions in the diseases of the various constituents of the skin. No subdivisions in things belonging to natural history are of any absolute value; it is for us to make choice of such a one as best suits the actual relations. In mucous membranes, for example, a disjunction of this sort of the structural constituents would be very injudicious.

I. Diseases of the Epidermis and the Papillary Layer.

a. *Inflammation.*

§ 286. The general covering of the body is as such exposed primarily to all the injuries which the organism encounters from without. We must, therefore, not be surprised that a long series of pathological conditions of the skin owe their origin to external irritants. Herewith violent actions happening but once, a shock and a blow are not to be thought of; but those insignificant, it is true, but continuous or frequently repeated irritations of the surface, such as are produced by dirt, vermin and scratching, injuries from the weather, unsuitable clothing, working among chemically or mechanically irritating materials.

* The nails will be treated of among the hornlike hyperplasias of the epidermis, the keratoses, in the Appendix.

These inconsiderable irritations are none the less strong enough to affect the exceedingly sensitive papillary layer rich in vessels and nerves, through the epidermis. The papillary layer answers by hyperæmia and inflammation; its anomalous condition is shared by the epidermis, and thus we obtain a group of changes, which, at least primarily, are confined to the papillary layer and the epidermis.

To this is added a second. It is known, that in infectious diseases, after the general affection has arrived at a certain height, that an affection of some organ is apt to be superadded. We say, the disease localizes itself, and joined therewith is the obscure notion of the infectious matter passing to the exterior. In fact, this disease-focus is very commonly found in actual secretory organs. In small-pox, measles, and scarlet fever, the skin is selected as the seat of the disease; we are, however, of the opinion, that also nettle-rash, erysipelas, certain forms of herpes, and a large portion of chronic skin diseases depend upon the localization of a general affection. Now, in all these cases, the question is not, perhaps, about anomalies of secretion, as the humoro-pathological notion might permit us to conjecture, but about hyperæmia and inflammation, and, indeed, these do not affect the whole skin, but in the first place at least only the most superficial layers. The papillary layer proves in a wonderful manner to be the part affected by preference, also in these diseases of the skin from within, arising from the blood. May we now here also, as in external irritations, appeal to the greater sensitiveness of the papillary layer? Scarcely, indeed. We must seek the cause of the localization in other circumstances, and I cannot refrain, in this connection, from ascribing a peculiar influence to the distribution of the vessels.

The vascular distribution in the papillary layer of the skin is known from normal histology. (Fig. 109.) Each individual papilla has an afferent and efferent capillary; both pass into one another by a simple loop, or—what is more common—they are connected with one another by a larger number of vascular arches. All these vessels are strikingly winding; it is particularly striking, that the roots of the simple capillary loops wind corkscrew fashion around one another, until they unite at the apex of the papilla. The points of union or of curving are constantly dilated. Everything indicates that a certain increase of the pressure and retardation of the circulation must occur in the papillæ of the skin. The vascular apparatus of the larger papillæ, with more than one terminal loop, may straightway be regarded as a rete mirabile.* They are related to the vascular nets of the cutis as appendices,

* I have often convinced myself upon injected kidneys, that the Malpighian corpuscles also present themselves as a congeries of two or three vascular ramifications, of which each completely resembles a papillary ramification. Are the Malpighian corpuscles, in their origin, papillary excrescences in the fundus of the renal tubuli? (Compare Henle, Handbook of Sys. Anatomy, Braunsweig, 1862. The viscera, page 310, *a*, *b*, Fig. 237, 238.)

like the branches of a stream, in which the water, with the same fall, meets greater resistance. This arrangement may have its physiological significance; it may be of great importance to the skin as a respira-

Fig. 109.

Vertical section through the skin of the lower lip, after Thiersch. *a.* Horny layer of epidermis, which is continued into the hair-follicle as inner root-sheath. *b.* Body of sebaceous gland. *c.* Sweat-gland. *d.* Vascular branch. *e.* Papilla of root of hair.

tory organ; apart from that, however, it is to be ascribed to it, that all occurring hyperæmias of the skin attain a peculiar intensity, duration, and consequence, just in the papillary layer.

That which obtains of the papillary layer in general, obtains also particularly of the somewhat smaller, it is true, but also the so much denser crowded papillæ in the circumference of the outlets of the hair-follicles. (Fig. 109.) Here also, therefore, in hyperæmias which affect the entire integumentary organ, the dilatation of the capillaries, the retardation of the blood current, and all the consequent results, will become particularly prominent. In one word: the vascular arrangements of the subepithelial connective tissue of the skin are so constituted, that thereby the more special localization of so many inflammations of the skin upon the epidermis and papillary layer can be brought into connection.

§ 287. We designate the large group of these superficial inflammations of the skin as eruptions, *exanthems*. All exanthems begin with a hyperæmia of the papillary layer. This first betrays the condition of irritation, and is the source of all the following immoderate and anomalous nutritive processes. Already in the first stage, however, the great multiplicity of the pathologico-anatomical pictures of disease shows itself in glaring contrast to the monotony and simplicity of the microscopic appearances. The greater part of collective dermatology may be fitly regarded as pathologico-anatomical material. For what prevents the anatomist, in the description and distinction of various macroscopic forms, sizes, and positions, which the spots, pimples, vesicles, pustules, &c., present, from going just as far as the dermatologist? Pathological histology, however, knows nothing of such a multiplicity; it exhibits here also, with what simple means nature advances to the most different performances, and properly knows only two series of changes, which, combined together, or even each for itself, compose the various forms of exanthems. We may term these elementary series simply inflammatory and inflammatory hypertrophic, and by the second group obtain, at the same time, a convenient transition to the simple hypertrophies of the papillary layer, warts, &c. This division would thus tolerably coincide with that according to the time in which the disturbance runs through the various phases of its development, so that we could designate the inflammatory processes at the same time as running a rapid course, or acute; the inflammatory hypertrophic as running a slow course, or chronic; the non-inflammatory hypertrophic, however, as those which, if left to themselves, seldom heal. Herewith, however, we must at present constantly maintain, that this acute and chronic are not equivalent to the chronic and acute of the dermatologists; that the question here is only about elementary forms, and that an affection, which in dermatology would be termed a chronic exanthem, can very well be composed of frequent repetitions of inflammatory processes run-

ning a rapid course. It is better to avoid misunderstandings of this sort from the commencement. Even at the risk of repetition, we will take the fundamental forms of exanthematic inflammation as wide or as narrow, as is the custom in pathology of the skin, and leave at the pleasure of the reader the further-going simplification by abstractions, as we indicate them.

§ 288. 1. The *erythematous* exanthem. Simple *redness of the skin*, even the exuberant congestion of the capillaries of the skin with blood, would scarcely furnish a subject for histological consideration, if the lately made observations of R. Volkmann and Steudener (Centralblatt, 1868, 36) upon erysipelas did not prove, that in this essentially erythematous inflammation of the skin, a very diffuse migration of the white blood-corpuscles takes place, as well in the cutis as in the subcutaneous cellular tissue, which certainly disappears again upon the second or third day (by decay and conveyance away of the cells), but which may always serve as a proof, how easily the redness of the skin advances to those higher grades of inflammation, as whose never-failing first stage it figures in dermatopathology. We will further mention, that even transitory reddening of the skin is apt not to be entirely traceless. Commonly, a shedding of the outermost epidermic layer follows afterward, be it in the form of scaling (desquamatio furfuracea), or in the form of peeling (desquamatio membranacea). This phenomenon is explained only by the intimate relation in which the nutrition of the epidermis stands to the processes in the papillary layer. Every hyperæmia involves a disturbance, a discontinuance of the nutrition of the epidermis. The detail is not known. This much however appears certain, that through this disturbance a separation of the epidermis occurs in a badly nourished external, or a better nourished inner part. This separation manifests itself in an actual, although imperfect cleaving, let us say in a loosening of the epidermis between the horny and the mucous layers, without exudation. If then it progresses in the further growth of the epidermis to a shedding of the oldest parts, then a premature shedding also of the deeper, younger layers of the epidermis, shows that these have prematurely died, and been separated from their mother soil.

We distinguish diffuse and circumscribed reddening of the skin. Not infrequently a primarily diffuse redness of the skin concentrates more and more in the course of time upon one or more points of the surface of the skin situated within its extent, and the more this occurs, so much the more we may expect at this point an advance to the higher grades of inflammation.

§ 289. 2. The *papulous* exanthem. We call the smaller inequalities of the surface of the skin papules, which present themselves to the finger feeling them as solid nodules seated upon the skin. The papule arises, in that the inflammatory hyperæmia, in a circumscribed region

of the papillary layer, advances to exudation. The exudation is not seated in the epidermis. This is drawn unchanged over the enlarged papilla; it is only tighter and more tense, since it has to cover a greater surface. The exudation is seated in the papilla itself. The question is about an abundant saturation of this with nutritive fluid, not with cells, at least not in recent cases. That in the longer continuance of the papule, especially in its eventual further development into a pustule, productive processes are added, we will have to report further below.

The individual papillæ are considerably enlarged. It has been asserted, that they therewith experienced not so much an elongation and thickening of their apex as a broadening of their base, so that a kind of equalization of the level occurred within the infiltrated area. This will be difficult to decide, as a direct investigation is as good as impracticable; because, the papular infiltration, like so many inflammatory infiltrates of the connective tissue, vanishes immediately after, or even during death. The elastic counter-pressure of the stretched epidermis effects, that the exuded blood-fluid returns into the vessels as soon as the slackening blood-pressure permits it. We find quite normal places of the skin, where the distinct exanthem but just stood. I mean, however, that the sharply-defined, distinct prominence of the papule above the surface of the skin points more to a tumefaction of the outermost slightly clubbed papillary apices. Moreover the papular formation affects with peculiar frequency the mentioned ring of small and crowded papillæ at the neck of the hair follicles. The papule is then perforated at its centre by a hair, circularly round and tolerably large. Hebra presupposes, in this case, a small amount of exhaled fluid between the mucosa and the horny layer of the epidermis. I found here, no fluid in the epidermis, but do not wish to lay any great stress upon this dissent.

Most of the papules are redder than the surrounding skin surface; a greater concentration of hyperæmia upon this one point has even brought about the advance to the formation of the papule; but with the exudation itself there arises also a force for the limitation of the hyperæmia; namely, because the exudation demands for itself the space which the papilla affords, and drives out the blood which alone is able to give way. Thus it happens that the papules are not always redder than the surroundings, but often of the same color, not infrequently even paler.

The papular exanthem is most constantly found in measles.

§ 290. 3. The *wheal*-exanthem is in an anatomical relation very closely allied to the papule. Wheals are flat and broad elevations of the skin-surface, hard to the touch, as we best observe when we pass the hand lightly over them. The smaller wheals, up to the size of a lentil, are round; the larger, often very large, arise by the confluence

of the smaller, and are in that degree variously contoured. The smaller wheals have the color of the surrounding skin; rarely are they intensely reddened. The larger, especially the higher they are, so much the more does it seem as though the red of the wheal were pressed aside and had concentrated upon a narrow border at the edge of the wheal, while the wheal itself becomes paler and paler. Finally we have white wheals with a red area. These are to be regarded as the highest stage of development of the urticarial exanthem.

The wheal (pomphus) is an acute inflammatory œdema of the papillary layer. The exudation is probably more thinly fluid, more of a serous constitution than in the papule, and it may be in connection with this, that just the eruption of wheals is of such an extraordinarily fugitive nature, that it is easily increased by scratching, while without it, it disappears rapidly and traceless. The place of the infiltration has already been mentioned. In the higher grades of pomphosis, the papillary layer is swelled out in such measure, that the blood-tract in its interior is completely compressed; the blood arriving there is detained at the boundary of the inflamed parts, and here accumulates. The red border around the white wheal indicates therefore a collateral hyperæmia, called forth by the impermeability of the capillary region within the swollen place.

Pomphosis, as a transient œdema of the papillary layer, interferes less deeply in the nutritive process of the skin than all the exanthems; it is never the forerunner of diseases of a higher grade; even scaling is rarely apt to occur after it.

Of external irritants, stinging the skin with nettles, as well as stings of insects, most readily call forth the urticarial exanthem; of internal irritants, the ingestion of certain articles of food (strawberries), and the nettle fever.

291. 4. The *vesicular* exanthem. The papule and wheal show us an exudation at the first station of the track from the capillaries of the papillary layer to the surface of the skin; they show it to us in the connective tissue which immediately surrounds the vessels. The vesicular eruption leads us a step further. The exudation exists in the epidermis; it has collected between the rete mucosum and the horny layer; the latter is raised up and arched outward, knoblike. The expressions, bulla and vesicula, which refer to this condition, denote only a quantitative difference. We say bullæ and vesicles; vesicles are of the size of a millet-seed and smaller; that which is larger than a millet-seed, is perhaps called a bulla.

Touching the origin of bullæ, this in general depends upon a transudation, pressing upwards from the very much dilated vessels of the papillary layer, and passing the rete mucosum of the epidermis, but is retained by the horny layer. The cells of the latter, through their intimate apposition, partly also by the suture-like connection of their

serrated surfaces, are so firmly united, that they form an entity, a compact membrane impermeable to fluid, which is well suited to retain and extend over even larger quantities of fluid. The behavior of the rete mucosum is not the same in all cases. In very rapidly forming blisters, for example, from burns, the soft cell-bodies which are seated sod-like upon the surface of the papillary layer, are elongated in an entirely mechanical manner by the force of the transuding current of fluid and drawn out into fine threads (Biesiadetzki). If the transudation ensues less rapidly, as in herpes and erysipelas bullosum (Haight), the lowermost cellular layer of the rete Malpighii remains unchanged, while the cells in transition are partly elevated, partly, as the miner says,—"dislocated." The transuding fluid swells out more prominently at the apices of the papillæ than in the depressions between the papillæ; consequently, the cell-layers spoken of are lifted off from the papillæ, while they remain attached in the interpapillary furrows. There arises a system of cell-trabeculæ and cell-membranes, which are more vertically erected in the space between the horny layer and the papillary layer; thus, indeed, that the largest among them rise up out of the interpapillary clefts, in order, further outwards, to become finer and finer. All these trabeculæ are formed of nucleated transition-cells, which are stretched and flattened by mechanical force; the finest consist of individual cells, often drawn out into several processes. If the transudation becomes more bulky, the trabeculæ, large and small, tear apart at the centre; one part remains upon the elevated horny layer, the other is attached to the papillary layer.

Only the miliary vesicles show us the accumulation of fluid between the plates of the horny layer (Haight), yet the intimate connection of this exudation with the secretion of sweat, forbids us from directly reckoning the miliaria with the vesicular exanthems.

The future changes of the vesicles are various. In the first place we have the possibility that the vesicles will burst and pour out their contents, or that they remain so long unchanged, until, with the decline of the hyperæmia, a resorption of the exuded fluid into the blood becomes possible. The pressure of the elevated, recognized, elastic horny layer may contribute its share to this. That such a one is in general to be taken into account, is evident from the occurrence of vesicles with hyperæmic area. Here the vesicular contents exert so strong a pressure upon the vessels below it, that the affluent blood is prevented from flowing in, and stagnates at the limits of the vesicle. Meanwhile a reunion of the once separated epidermic strata never happens. Even when the horny layer has applied itself perfectly flat and apparently all is as before, there will afterwards still occur a premature desiccation and shedding of these lamellæ. In the meantime, a new horny layer has formed from the rete Malpighii. This remains thin for a long time and lets the vessels of the papillary layer shine

through to such an extent, that yet after weeks a red spot delineates the form and size of the previous vesicle. Concerning the histological detail of this reparation, what places of the papillary layer are the specially producing ones, how the stratification takes place, &c., normal histology has to give information, but as yet owes us an answer.

We call this issue the "desiccation of the vesicle," and distinguish therefrom a second, less favorable transformation, which, in short, is termed the purulent. This, meanwhile, leads us to a new province.

The vesicular eruption is one of the most frequent; it occurs from external and internal irritations of the most various kind; of the former the best known are: heat, blistering plasters and fomentations, mechanical violence, scratching, and repeated pressure; of the latter are to be named: herpes, pemphigus, morbilli, &c.

§ 292. 5. The *pustular* exanthem. Pustule, purulent vesicle, is in the language of dermatology a summary designation for every circumscribed collection of pus under the epidermis. The pustule is accordingly a sharply defined, straw-colored elevation, and if we add that it is constantly round, often with a central depression, umbilicated, and surrounded by a red area, we will have pretty much exhausted the general characteristics. Now, it is of course manifest, that purulent collections of this kind may be produced in very different ways, and the value of the definition just given is to be estimated accordingly. We at this time set aside those pustules which are caused by the formation of pus in the deep layers of the skin (for example, around the hair follicles), and will occupy ourselves entirely with those two forms, in which the place of formation of the pus does not extend below the level of the papillary layer.

a. As we have just pointed out, *pustules* may proceed from *vesicles;* this is the case in the skin diseases: eczema, impetigo, herpes, pemphigus, and ecthyma. One can even with the naked eye establish the gradual clouding of the vesicular contents, and be convinced by letting out a drop of the fluid, that this is produced by the presence of cast-off epithelial cells, as well as numerous pus-corpuscles. Afterwards the pus-corpuscles exceed, and finally nothing prevents us from exactly designating the vesicular contents as a somewhat thinly fluid pus. If we examine the skin in a section (Fig. 111), we find the papillary layer well preserved in its outlines, but penetrated with a great number of young cells, which accumulate at the apices of the papillæ in such masses, that an uninterrupted layer of such cells forms here the transition to the lowest stratum of the rete Malpighii. The latter is yet easily recognized at the lateral parts of the papillæ, and in the depressions between them, if we make use of the yellowish color and the upright position of its cylindrical cells as means of recognition. It is otherwise at the summits of the papillæ. Here all distinction between connective tissue and epithelium ceases; only by having recourse to separating them

with the needle, can we say: this is the limit of the papillæ, and here the epidermis begins. For me there is no doubt, that just here is the main source of the young cells, which we find in the vesicular contents. The irritated papillary layer is in the condition of the most luxuriant internal production; the young cells migrating, push towards the surface, and are here separated, before their complete formation into epithelia, as germinal and pus cells. Herewith some probably press through between the cells of the rete Malpighii; the greater part emigrate out at the apices of the papillæ, where the rete is broken through; and exactly the same relations exist between the thing secreting and the thing secreted, as at a granulating wound-surface.

The whole is accordingly an *acute purulent* catarrh of the skin, and if we add the previous vesicular formation, we may thus express ourselves, that a primary serous catarrh had afterwards become a purulent catarrh.*

The healing of this condition may ensue in various ways, according to the treatment. If we allow things their course, by the desiccation of the purulent vesicular contents a crust is apt soon to form, under which the secretion gradually becomes slower, and finally ceases with the production of a new epidermal covering. The crust has frequently been regarded as a protective covering, under which, according to the plan of nature, the new formation of the epidermis could proceed undisturbed. This, however, is just as convenient as incorrect. The scab is an entirely desiccated, dead, organic substance, which is further decomposed and decays, as soon as it finds moisture enough for this. If we now reflect that the catarrhal papillary layer yields fluid enough to develop this process of decay, and that in consequence of this, decaying, and hence irritating matters are continually developed at the lower surface of the scab turned to the papillary layer, we will soon come to the opinion, approved also by medical experience, that on the contrary, very peculiarly favorable circumstances, a very rapid decline of the hyperæmia, a very complete desiccation, &c., must exist, for the catarrh to heal under the scab. Reparation of the surface moreover follows entirely in the same manner as in the desiccation of vesicles. I have, indeed, observed, that just here in the new epidermis, with striking frequency, concentrically stratified globules occur, the so-called pearly nodules, but this is certainly only a transitory irregularity in the processes of stratification.

§ 293. It is otherwise, when we are dealing with an exanthem, which from other causes has no disposition to heal, when vesicles and pustules only denote the acute setting-in of a chronic catarrh. There are, for example, eczemas of the leg, which have their proper foundation not

* We designate by the word catarrh, par excellence, the analogous conditions of the mucous membranes. Hence, I will treat of the special histology of catarrh under the anomalies of the mucous membranes.

in an external irritation, but in a chronic disturbance of the circulation, a venous hyperæmia and phlebectasy. These give the most frequent opportunities for observing *chronic catarrh* of the skin. Their phenomena are dependent upon a continuance and further increase of the hyperæmia of the papillary layer. This, in the first place, and quite directly, guarantees the continuance of secretion of the surface. Abundant quantities of transudative fluid press to the surface; the more abundant, however, the secretion becomes, so much the more does it lose the purulent character, as the production of pus-corpuscles does not increase, while the transudation increases very considerably. Finally, we obtain an almost clear fluid, rich in salines and albumen, whose enormous quantity bids defiance to all bandages (salt rheum). In the skin itself, the longer it continues so much the more there is developed a condition, which we may directly designate as inflammatory hypertrophy. This also depends upon the hyperæmia of the papillary layer; in the first place, at least, they are always the papillæ which thereby experience an enlargement, in that they, as we see this in the growth of granulations, use a part of the germinal tissue produced at their apices for their own enlargement. Even with the naked eye we cannot infrequently see small red buttons shoot up, which have quite the histological characters of granulations, but are nothing else than the enlarged—if you will, the degenerated—papillæ of the skin themselves.*

§ 294. In the further course, the irritative condition of the surface is apt to be communicated also to the deeper layers of the skin, the cutis and the subcutaneous connective tissue, so that to the chronic catarrh conditions are joined which are described in the second section of this chapter as elephantiasis. It is difficult to establish what share in this the catarrhal irritation of the surface, what share the predisposing cause of eczema itself, the disturbances of the circulation of the blood and lymph have, in how far they are to be regarded as a reactive hypertrophy, in how far as diseases for themselves; hence I will here let fall the thread of the representation, in order to take it up again at that place (elephantiasis).

Only about the efforts at healing and the actual healing of chronic catarrh will I permit myself to go into the subject more minutely. As

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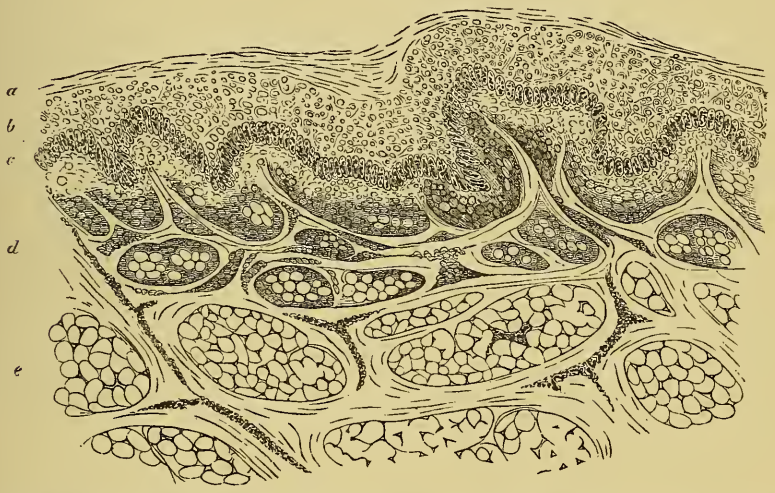
* How nearly hyperplastic and heteroplastic development come together here! Particularly will he, who has wished to be too exact in the conceptions, not only of hyperplasia and heteroplasia, but also of inflammatory heteroplasia and the heteroplastic tumors, finally of simple and imflammatory hypertrophy, be better taught just in diseases of the skin. We should, and may serve ourselves with these designations, in order to become lucid concerning the existing conditions, but we must not regard them as rigid formulæ. All-accomplishing nature knows nothing of this kind. In our case the formation of germinal tissue at the limits of the epidermis and the connective tissue belongs, up to a certain degree, in the plan of development of the skin; the excess, however, immediately makes a granulation surface of the surface of the skin.

the catarrhal papillary layer was found to be not unlike a granulating, wound-surface, so also its return to the normal state resembles healing by second intention. The processes in the corium must of course be regarded as the analogues of *cicatricial formation in deeper parts*, which, as we will remember, plays so great a rôle in second intention (Fig. 39, *c*; § 104). These present a wonderful union of two powers opposed to each other, namely, formation of cicatricial tissue and increase of volume instead of decrease. We will speak of this more specially in elephantiasis. It is not to be doubted that these processes have their reaction upon the condition of the surface; upon vertical sections (Fig. 110) we very commonly find obliterated vessels, known by stripes of

FIG. 110.



Vertical section through the skin after chronic eczema. *a*. Horny layer. *b*. Mucous layer of epidermis. *c*. Pigmented stratum of cylindrical cells. *d*. Papillary layer. *e*. Cutis pervaded by stripes of pigment.

pigment, running obliquely to the surface of the cutis, and we may accept that their obliteration limited the supply of blood to the papillary layer. We would, however, go very far wrong, if, upon these processes in the cutis, we place the same hopes for the healing of the surface as in the second intention. On the contrary, here is a case in which all depends upon the treatment to which the diseased part is subjected. Astringent and desiccating means, before all a systematic compression must here come to the aid of nature. Under these circumstances, the healing proceeds with a gradual diminution of the proliferated papillary layer and with skinning over of the whole surface. The papillæ especially lose in volume, partly by the return of the infiltrated fluid to the mass of the blood, partly by fatty degeneration and resorption of the numerous cellular elements; basis-substance shows itself between the cells. Of hairs, glands, and nerves, there is nothing any

longer to be found; these evidently perished in the tumult of the new formation, which proceeded from the connective tissue surrounding them, yet nothing is known concerning the nature and the manner of their destruction. The papillæ finally become less elevated than normal, only that the boundary between connective tissue and epidermis, presenting upon cross-sections a flat wavy line, reminds of their existence. (Fig. 110.)

The formation of epidermis at the surface, in contrast to a granulating wound-surface, begins simultaneously at many points; it proceeds just as well from within outward as from without inwards, and what is probably connected therewith, that here everywhere there yet exists a portion of the old rete Malpighii, which, without further change, may pass over to the formation of a new horny layer. The horny layer, however, for a long time yet remains very thin, and it is known how easily a renewed pressure of transudative fluid splits the delicate membrane and re-establishes the scarcely healed affection. We will yet mention that in cases of permanent healing the deepest cell-layer of the rete Malpighii betrays a striking tendency to pigmentary infiltration (Fig. 110), which makes itself perceptible to the naked eye as a brownish discoloration, or brown spots of the affected part of the skin.

§ 295. b. The second form of exanthematic pustulès, the *pock*, is indisputably the one among the efflorescences of the skin which presents the greatest histological interest. The pock is, up to a certain time, a pus-vesicle, a pustule, yet upon the one hand, with this stage the acme of the development has not yet been attained; upon the other, the way to this stage is so peculiar that the pock is thereby sufficiently characterized as an exanthem for itself.

The pock arises as a papule upon a strongly hyperæmic base. This proposition, which is found in all the books, is correct if we will call every hard nodular elevation of the surface of the skin a papule. But the pock-papule distinguishes itself very essentially, for example, from the above described (morbilli)-papule. The pock-papule is a swelling, which, for the greater part, at least, has its seat *in* and *not under* the epidermis; namely, the formation of pocks begins, apart from the hyperæmia of the papillary layer, with a circumscribed parenchymatous inflammation of the epidermis. I use this expression with all due restriction. That peculiar clouding and swelling of the cells, which we learned to know in §§ 36, 37, and which we here find again, has, in my judgment, yet no established place in general pathology. The circumstance that upon the swelling fatty degeneration just as often follows as does endogenous cell-formation, makes it doubtful whether we should regard it as a progressive or retrogressive cell-metamorphosis. In our case the question is decidedly about the inception of a productive, therefore probably correctly named, inflammatory process.

The swelling affects neither the innermost, nor the outermost cell-

layer of the epidermis; it affects the central layer, which we above designated as transition-cells and have reckoned with the rete mucosum. These cells are no longer naked, as those smaller elements seated immediately upon the papillary layer; they have a membrane, which is here and there characterized by the elegant serration of the surface discovered by M. Schultze. The membrane renders them unable to answer to the inflammatory irritant simply by division; the division must present itself as an endogenous cell-formation; the first stage, however, of the endogeneous cell-formation is just that cloudy swelling, which follows after the segmentation of the enlarged protoplasm and the conversion of the segment-globules into pus-corpuscles. (Compare herewith the representation of the subject in the General Part, § 68, Fig. 30.)

§ 296. The individual pock is constantly round; only by the confluence of adjacent papules do more complicated forms arise. As the cause of this peculiarity, there can be demonstrated upon many pocks, the concentric arrangement around the outlet of a hair-follicle or a sweat-gland. We can distinguish these pocks from the others with the naked eye. We recognize them by an exactly central depression of the surface, the so-called *umbilicus*. As is known, the epidermis is not only continued into the hair-follicle by its rete Malpighii, but also by its horny layer. If now the swelling spoken of, but especially that directly to be mentioned, the more extensive serous saturation of the rete Malpighii in the surroundings of the follicular outlets, interfere, then the horny layer of the epidermis of the hair-follicle (the inner root-sheath) will behave towards this enlargement like a central check, which restrains the centre of the pock from elevating itself even as high as the periphery. The epithelium which lines the excretory ducts of the sweat-glands is less tenacious than the inner root-sheath. It owes its greater coherence probably to its peculiar stratification, which cut vertically or obliquely the plane of the strata of the epidermis. However, the nearest surrounding of the excretory ducts remains unmolested. At all events I have numerous preparations, in which the excretory duct of the sweat-gland presents itself with its surroundings as the "check" of a pock-papule. (Fig. 111, *a*.)*

§ 297. The next following stage of development can be termed the conversion of the papule into the pustule. This is in all cases introduced by a serous infiltration of the epidermis. A clear fluid presses forward from the papillary layer, elevates the horny layer of the epi-

* Auspitz and Basch (Virchow's Archives, xxviii) demonstrate the production of the umbilicus in a manner not very plausible to me: "While the swelling of the cells continually extends outwardly, and thus the volume of the whole efflorescence constantly increases, as a rule there is in the beginning a but slowly forming pus inclosed by these peripherally collected swollen cells, as in a capsule, which gradually enlarges; without that, the formation of pus at the centre, can in every case keep pace with this increase of space."

dermis, but not as in the production of blisters of the mucous layer, but it forces its way in between the lamellæ of the epidermis, forces them apart, and displaces them in such measure, that they pass from a horizontal position into one oblique or vertical (Fig. 111, *b*). The

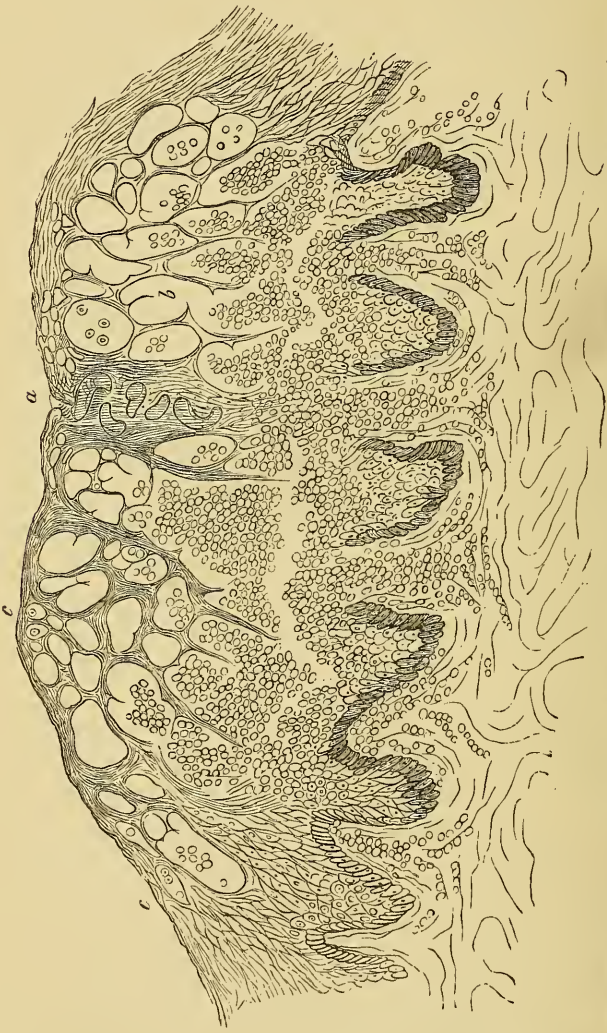


Fig. 111. Vertical section through the centre of a pock, at the transition of the papule into the pustule. *a*. Umbilicus with duct of sweat-gland. *b*. Compartments in the epidermis, formed by the separation of the lamellæ, and filled with lymph. *c*. Smallest compartments, containing single pus-corpuscles. The papillary layer in the state of purulent catarrh. 1-200.

upper part of the pock receives hereby a peculiar organization, which already at an early period attracted the attention of observers, and gave occasion for ascribing to the *whole* pock a cellular [compartment] structure. This is decidedly incorrect. Only the upper part of the pock, the *roof* of the pock, is divided into compartments in its interior. From this, we can now by numerous punctures or by a quite flat cut,

shaving off only the horny layer, obtain that clear lymph, which plays so important a rôle in transferring the cow-pock.

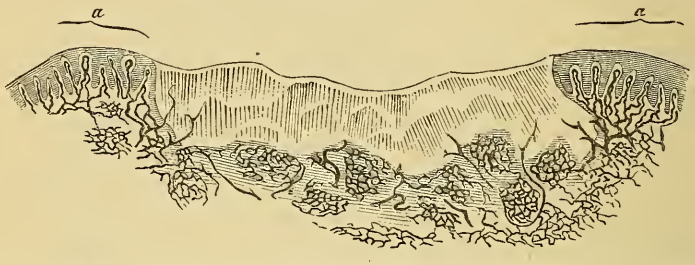
§ 298. The formation of pus begins thereafter in the deeper layers of the epidermis. It here first of all enters at the place of the parenchymatous inflammation. From each of the swollen cells there proceeds a host of pus-corpuscles, and soon the compartments of the hood of the pock are filled with a yellowish cloudy purulent fluid instead of with clear lymph. With this purely epithelial production of pus, the process may go no further. The pus dries up, and yet ere the pock has fallen off, under it has been formed a new epithelial covering for the cutis.

Commonly, however, to the epithelial suppuration there is superadded a suppuration on the part of the papillary layer. Here two cases are possible. We can distinguish a catarrhal and a diphtheritic formation of pus. In regard to the catarrhal form, I will content myself by referring to § 292 and Fig. 111. The suppuration here is a secretion of the surface; the papillary layer remains intact, and in the healing covers itself with an epithelial covering, which for some time only is distinguished from the normal by its greater delicacy. This pock heals without leaving a scar behind. It is a far slighter affection than the destructive pock, not only according to its anatomical, but also according to its clinical course. In the destructive pock, the production of pus on the part of the papillary layer is no secretion but a melting down of its own substance, and hence followed by a loss of substance, by the formation of ulcer and cicatrix. Bärensprung has very well described the macroscopic relations of the diphtheritic pock in the following words: "In the second stage (of the pock-formation), it comes to exudation, which appears wherever hitherto only hyperæmia has been perceptible; the formerly vividly red spots of the corium now appear white down into the subcutaneous cellular tissue, saturated with a soft exudative mass, and only yet bounded at the edge by a red border; the papillæ also are decolored." "In the third stage the vesicles are converted into pustules. If we examine the pocks now, we are convinced that the entire previously infiltrated part of the corium with its papillæ is destroyed by suppuration. The pocks have a half-globular, arched form, and beside pus also contain shreds of the dead tissues. In a fourth stage, finally, the summit of the pustule has burst, the contents have flowed out, and in its stead, small open ulcers exist, which heal, leaving behind the known, net-formed cicatrices."

Microscopic investigation furnishes to this conclusive and lucid description, a very simple commentary, elucidating the affair in every respect. The exudation of Bärensprung is not a formless something; it is no coagulated albumen or fibrin, but it consists of cells, pus-corpuscles. We are reminded, that in the catarrhal suppuration also, the papillary body is pervaded richly with young cells, which partly

migrate and are separated. This infiltration now becomes excessive; the cellular elements accumulate *in the interior* in such enormous amounts, that they not only hide from view everything else, connective tissue fibres, vessels, nerves, but also compress them and cause them to atrophy. The access of the blood is prevented, hence the pallor of the infiltrated part. The annexed engraving (Fig. 112) gives of this a

Fig. 112



Diphtheritic pock. *a*. The normal and well-injected skin of surrounding parts. Further description in text. 1–50.

good representation. The vessels are injected with carmine glue. Where the blood could not penetrate, the injection could also not penetrate; consequently, we here see to the right and left of the pock (*a* }) the capillary loops of the papillæ completely filled, while the pock itself has remained free. It is as though a half circular piece of the cutis with the papillæ belonging to it, were cut out of the capillary net. This whole piece is infiltrated with pus-corpuscles in the manner spoken of, and may be regarded as dead; only the question yet is, how long the connective tissue fibres and the obliterated vessels which are in it, and which bring about the connection with surrounding parts, how long these resist dissolution. In older individuals they are wont to maintain themselves longer than in the younger. In the former case, a close and imperfectly separable *scab* forms upon the cutis; in other cases, the infiltrated piece soon melts down into pus, which by drying furnishes a scab; in both cases, however, there remains behind a superficial deficiency of the cutis, an ulcer, which heals by second intention and leaves behind a lasting scar.

§ 299. 6. The *squamous* exanthem. I have upon more than one occasion pointed to the difficulties attendant upon the separation from each other of the ideas, inflammation and hypertrophy, as etiological categories of the pathological new formation. The squamous exanthem without doubt takes its origin in a chronic inflammation of circumscribed spots of skin. These are reddened, slightly swollen and endowed with the other attributes of an inflammatory hyperæmia; as the consequence of this hyperæmia, however, there appears not an exudation in or under the epidermis, but only a more abundant formation of otherwise normal epidermal cells. This primarily presents itself as an in-

creased scaling off of indurated cells, the so-called epidermis-scales, from the hyperæmic, slightly elevated parts of skin (squamæ, desquamatio, squamous exanthem). Soon, however, the separation becomes more abundant, and there are formed white heaps, from the size of a millet-seed to a lentil, also disc-formed plates, which consist of scales heaped on each other, and are moderately firmly attached to their foundation. (Psoriasis.) The question, why in the increasing disease, instead of a simple separation of epidermis-cells, a heaping up of these occurs, pathological histology explains as follows: the more luxuriant the cell-formation at the surface of the inflamed cutis becomes, so much the more incomplete is the formation of the individual cells. The average height of development which is attained under these circumstances, is that of transition cells between the cylindrical elements of the rete mucosum and the lowest cells of the horny layer. Hence, that systematic hardening ceases, which we call becoming horny, and in its place occurs the simple desiccation of the yet soft protoplasm. In this desiccation the cells naturally agglutinate, and, as we see, thereby preserve a longer, although purely mechanical connection with the surface of the body.

The white, often silvery white color of the psoriasis-scales arises from the combination of the desiccation of those cells with a simultaneous entrance of air into the interior of the whole heap, whereby this moreover receives a peculiarly spongy, porous feel. If we remove the scaly heap, which, as a rule, is possible without exerting much force, we find the papillary layer under it almost bare. The epithelial layer which covers it is so thin, that they come off even by the lightest touch, and a slight bleeding may be produced; but the epithelial layer is nevertheless yet present in full continuity; there is absolutely nothing to be found of an exudation. Everything considered, our judgment concerning the nature of the squamous exanthem can only go so far, that here upon a decidedly inflammatory basis a new formation is progressing, which indeed presents a very considerable quantitative, but—apart from the non-completion of the horny process—no qualitative excess of the normal formation of epidermis. The squamous exanthem is an inflammatory hyperplasia, and forms consequently the transition to the following section.

b. *Hypertrophy.*

§ 300. All that was said above (§ 83) concerning the physiological growth of the epithelium and the participation of the sub-epithelial connective tissue in it, can without change be applied to the epidermis and the papillary layer. The papillary layer furnishes the epidermis with young cells; these aggregate at the rete Malpighii, and gradually grow into epidermis-cells. A morbidly increased activity of this process is the common basis for a great number of hypertrophic conditions, which we have to consider in the sequence. I say "a great number," and seek

the ground of this multiplicity of the pictures of the disease in the circumstance, that the embryonal formative cell, which becomes the epithelial cell, is before its migration out of the connective tissue a homologous constituent of the latter, and may serve just as well for the enlargement of the papillary layer when it is produced in an abnormal quantity. The same process which afterward furnishes epithelial cells, if interrupted at an earlier stage, must yield connective tissue. Hence, if I have united in one and the same chapter, the hyperplasias of the epidermis and the papillary layer, this was done not alone because they are in fact almost always found together, but because this relationship is declared by the unity of the fundamental process underlying them. We place those forms at the top, in which the epidermis alone, at the end those in which the papillary layer alone is concerned, and arrange the medium forms accordingly as the one or the other predominates, or both are equally present.

§ 301. The *induration* (callositas) is a circumscribed thickening of the horny layer of the epidermis. It accordingly forms a flat elevation of the surface, gently sloping towards all sides, of horn-like translucent constitution. The consistency is dependent upon the degree of moisture at the time, and varies from elastic flexibility up to hornlike brittleness. The microscopic structure characterizes itself from the normal horny layer only by the number of layers of flattened horny epidermis-cells superimposed above one another.

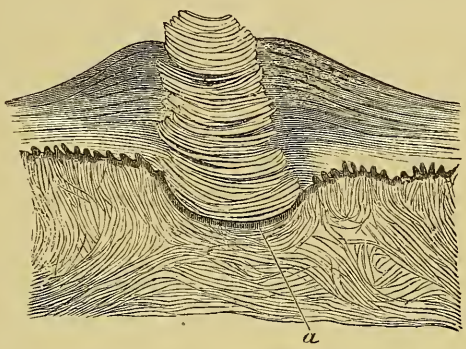
If we ascribe to the epidermis the function of protecting the surface of the body as a covering, fine indeed, but yet very capable of resistance towards external actions, then as a logical consequence we may receive the induration as a functional hypertrophy—similar to the hypertrophy from work of muscles. For experience teaches, that indurations exclusively form at such places where the surface of the skin is exposed to a frequently repeated strong pressure, in the hollow of the hand and the sole of the foot. The circumstance, that these regions are already provided by nature with a very much thicker horny layer, would then have to be placed to the account of natural design. The idea is more simple, that by the outer pressure a hyperæmia of the papillary layer has occurred, and from this a more vigorous nutrition of the epidermis, an idea moreover which would not be opposed to the one first mentioned, but explanatory.

§ 302. *The corn* (clavus) is a modified induration. Here as there, a hyperplasia of the horny layer is the essential part of the anatomical condition; here as there, external pressure is the inducing cause of the hyperplasia. Another, however, is, whether the point, at which the forces acting against each other are cancelled, falls exactly at the place of contact of the parts pressing and pressed, or whether it falls within the part itself pressed; in other words, whether the part pressed can

move or not. In the former case there is formed an induration, in the latter a corn.

In Fig. 113 there is represented under twenty diameters a vertical section through a corn. Here also we have a slight swelling of the surface; it is, however, much smaller, and directed more upon one point than in the induration. At all events the swelling, which the under

Fig. 113.



Clavus (corn) in section. After Simon. At *a*, the depression of papillary layer under the pressure of the central parts of the induration. 1–20.

surface of the thickened horny layer presents just at this point (*a*), is more important. This forms a blunt cone, which is directed vertically towards the cutis, and has apparently penetrated into it for some distance. The collective elevations of the papillary layer have already been levelled by this extending pressure, the skin itself begins to attenuate, and the cases are not infrequent, where in fact the cutis is completely perforated. If we consider the epidermis itself, where the clavus is thickest, it presents to us a striking displacement of the planes of the layers; namely, corresponding and perfectly parallel to the curve of the cone mentioned, projecting against the cutis, the collective layers of the epidermis arranged over them are also curved inwards, so that the central part of the induration contrasts itself to the surroundings as something peculiar. This curve inwards is also produced by the outer pressure; the outer pressure has, therefore, in a certain measure prepared for itself an instrument from the materials of the epidermis, with which it operates against the deeper parts of the skin.

§ 303. A group, not indeed frequent, but so much the more interesting, of thickenings of the horny layer are presented by the KERATOSES (Lebert). Quite monstrous accumulations of horny substances are rendered possible in the keratoses, by the stratification of the horny epidermis-cells ensuing according to another than the normal law of stratification.

It is known that under normal circumstances the plane of the strata of the corneous epidermis-cells is parallel to the surface of the body as a whole, and that herewith the more minute arrangement of the integ-

umentary surface by the papillary layer is disregarded. Only the lowest cell-layer of the rete Malpighii consistently follows every elevation and depression, and considered in itself would present a perfect mould of the papillary layer. Between it and the horny layer, the thick cushion of the transition cells mediates, which, as an unstratified, and in this respect an indifferent material, fills out all the inequalities of the substratum, and makes possible the transition to the horizontal plane of the strata. These cells are wanting in the keratoses, or are yet present only in very small amount. I believe they indurate too rapidly, and regard a "too rapid" induration as the essential physiological foundation of the whole disturbance. With the transition cells, however, the transition also from the one plane of the strata to the other is lost; the horny layer of the epidermis must thereafter follow all the elevations and depressions which the papillary layer presents, just as the rete Malpighii does. Consequently, every layer of indurated cells extends into the layer situated next above it with just such projections as the one situated next below into it, and as finally the papillary layer projects into the lowest stratum of the horny layer. All are inseparably united with each other, and hence it comes that all the horn which is formed remains attached; thus those extraordinary thickenings of the horny layer by which the keratoses are characterized become possible.

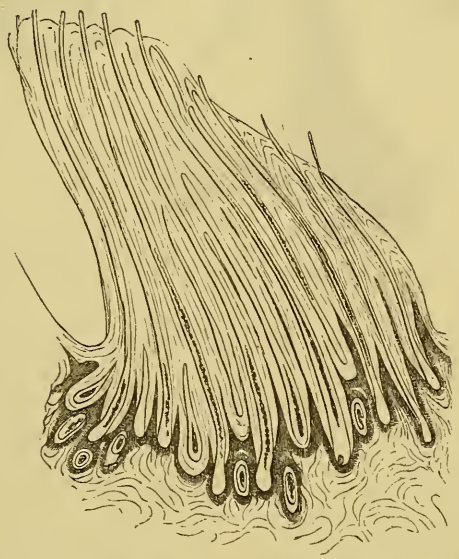
§ 504. According to Lebert's precedence we distinguish a diffuse and a circumscribed form of keratosis. In the former we deal with the formation of flat, indurated crusts, which often cover the skin for a great extent. They not infrequently resemble flat scales, hence the name *ichthyosis;* at times, however, they are more prominent tubers, or prismatic cones, and bring into view in this form their intimate relation to the circumscribed keratosis, the cornu humanum. It is perfectly certain that in fact these crusts, in their principal mass, consist of indurated epidermis-cells; when, therefore, some authors state, in unravelling macerated crusts, to have isolated fibres and lamellæ, these fibres and lamellæ were likewise formed of epidermis-cells. Their being found explains itself by what follows.

If we break through an ichthyotic crust, we observe upon the broken surface a vertical striation; here and there probably also it is as though rigid fibres were loosened. By a suitable maceration with weak alkaline solution and subsequent very careful manipulation with needles, shaking, &c., we at times succeed in breaking up the whole crust into prismatic bodies—if you will, into short and thick fibres—from the top down. Each of these fibres then consists of a certain number of lamellæ of horn concentrically stratified around the axis, which may be counted upon a cross section like the rings of a tree. In the axis itself, in the outer two-thirds of the pseudo-fibre, we find nothing; in the inner third either nothing likewise, or a small cavity, which had been occu-

pied by a more or less elongated papilla of the skin. From this it follows that the papillæ of the skin furnish the determining force for the peculiar stratification of the lamellæ of the horn. The axis of our stratified cylinder is the continuation of the papillary axis, and the whole obliquity of the arrangement of the lamellæ is nothing but a repetition of the steeply sloping sides of a papilla.

Meanwhile this does not yet suffice for all cases of ichthyosis. We must consider that the surface of the cutis presents also vertical surfaces at the involutions of the hair-follicles, and that not only do these surfaces directly pass over into lateral surfaces of the papillæ, but that the epithelial lining of the hair-follicles also is the immediate continuation of the epidermis. Hence there is nothing more common than that the ichthyosis is continued to the hair-follicles upon hairy places of the skin. The lamellæ of horn formed here will naturally be casts of the hair-follicles, and upon cross sections will form rings, which are placed concentrically around the lumen of the latter. When this lumen is filled out by the hair, and thus the hair in a certain degree appears as the axis of the stratified body, we may use this circumstance indeed for information, but we may not believe that to the hair as such any determining influence upon the stratification of the lamellæ of the horn appertains. The hairs also at the diseased spots are constantly thin and disposed to fall out, which indicates that they have been disturbed in their vegetation by the horny metamorphosis of the hair-follicles. This

Fig 114.



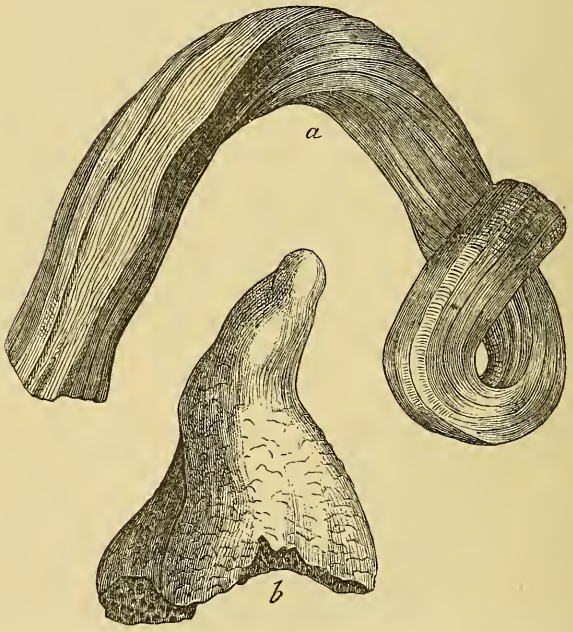
Ichthyotic crust in section. From an ichthyotic calf. 1-30.

also, as a rule, reaches deeply into the fundus of the follicle, so that only the actual hair-bulb remains free. Fig. 114 gives the vertical

section of an ichthyotic crust, and its connection with the skin lying under it. The preparation is derived from a calf born ichthyotic, which is preserved in the Physiological Institute of Breslau,* and is peculiarly fitted for giving information concerning the relations of ichthyosis to the hair-follicles.

§ 305. The cutaneous horn of the human being (cornu humanum) may be placed by the side of ichthyosis as a circumscribed keratosis. A true monster among cutaneous horns (9 inches long) exists among the collection of the Pathological Institute of Bonn. As the representation (Fig. 115) shows, it is, upon the whole, a roundish prism, but provided with several longitudinal ridges; it is spirally curved after

Fig. 115.



a. Cutaneous horn nine inches in length, from the collection of the Pathological Institute at Bonn. Natural size. After O. Weber. *b*. A second cutaneous horn from same place, natural size.

the manner of a ram's horn. By far the greater number of cutaneous horns, while of lesser length and thickness, yet present the same exterior as this. A more searching analysis assigns to each of the longitudinal ridges visible at the surface, a single, not always elongated papilla of the skin, to the whole horn a correspondingly large group of papillæ as of mother soil, so that in this regard a complete uniformity can be established with ichthyosis.

There are, however, also cutaneous horns which, instead of the gen-

* Compare Harpeck, Description of the skin of a calf born with an ichthyotic cornea. Reichert and Du Bois-Reymond Archiv, for the year 1862, Part III, p. 393.

eral uniform thickness, exhibit a tapering point upon a broad conoid basis. The collection of Bonn has also a very perfect example of this species (Fig. 115). The tolerably sudden broadening of the base (at *a*) ensues by the application of new lamellæ of horn, which cover each other from without inwards like the shingles of a roof. Each of the lamellæ, however, again breaks up into elongated prisms, always belonging to a papilla; only at the outermost circumference do we get in maceration actual lamellæ which give us the papillary casts with a somewhat slighter curving. The question here apparently is about a process, which was originally confined to a smaller group of cutaneous papillæ, and which first gradually extended to the surroundings, then, however, more and more rapidly.

If we observe a detached cutaneous horn from below, there are not infrequently small conical prominences there exhibited, which have been recognized by Virchow as indurated casts of the hair-follicles. The process is, therefore, also continued into the hair-follicles in the cornu humanum. Of course that which the hair-follicles produce of the horny mass can neither now, nor at any time, contribute to the elevation of the surface, and we will never be able to say in this sense that the cornu humanum proceeds from the hair-follicles. But there is, indeed, brought about by this combination a thickening at the base of the cutaneous horn, which, because it lies in the cutis itself, gives rise to the appearance as if the cutaneous horn sprang from a pocket-like depression, a dilated follicle of the skin. A part of what was said about the follicular origin of cutaneous horns may be applied to this. For the production of a cutaneous horn a group of papillæ is necessarily required as a base, and when horns project from the fundus of an atheromatous cyst, the question in the first place is, whether the atheromatous cyst was actually such formerly, and secondly, whether these cutaneous horns do not also spring from a base of proliferated papillæ. How often have I found whole beds of small pointed cutaneous papillæ at the inner surface of atheromatous sacs which had evidently only sprung up subsequently.

§ 306. *Appendix.*—The structures appended to the epidermal horny layer, the hairs and nails, which under normal circumstances present the most compact collections of the horn-substance, are, when once built up in the known form, subjected to no considerable change. At the most they may become atrophic, *i. e.*, prematurely split up and fall off, which, however, is also not to be referred to a disease of the hairs and nails, but to an anomalous condition of the places of formation of both. The same is the case with the opposite conditions, hypertrophy of the hairs and nails. What is of histological interest in this respect, we will impart, for the hairs, in the chapter, Hair Follicles and Sebaceous Glands; for the nails, at this place.

The onycho-*gryphosis* (Virchow), the talon-like deformity of the nails

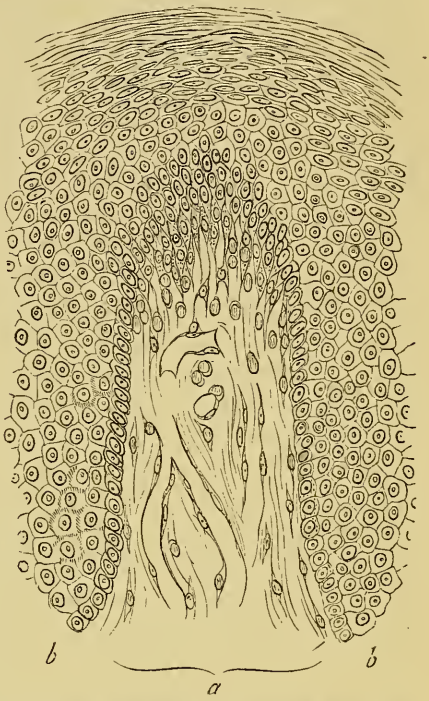
with the simultaneous upheaval from the nail-bed, depends upon a hyperplastic condition of the entire nail-matrix. As such that part of the nail-bed comes foremost into consideration, which is bounded from below by the furrow of the nail. Almost the whole material for the body of the nail is furnished by the long, horizontally situated papillæ of this region, as the nail at the edge of the finger is not thicker than at the limits of the so-called lunula, just up to which the papillæ reach. Hence the nail is also longitudinally ridged, as we readily observe by reflected light, in that each ridge corresponds to a papilla in similar manner as do the upright fibres to the ichthyotic scales. Transverse rolls and furrows are produced by disproportionate, sometimes more rapid or slower growth. I have repeatedly observed that the decrease and increase of nutrition in febrile conditions of a subacute course makes itself known at the nails by a furrow and a small bulge behind it. The ridged portion of the bed of the nail furnishes a thin layer of loose epidermic cells, upon which the body of the nail glides forward as upon a cushion; that these cells at the same time contribute, although but little, to thickening the nail, is indeed to be concluded with great probability from the firm adherence of the nails to the bed, but it has not been proven, and is straightway denied by Henle.

If now the nail-matrix becomes hyperplastic, the anterior part of the nail-bed furnishes layer upon layer of those loose epidermis cells; these layers are heaped up on one another, the nail-body is raised up by them from the bed, and placed more or less upright; upon the other hand the posterior part of the nail-bed yields a deformed, thick nail, several inches long, twisted talon-like, even rolled up like a cornet. Both, as we see, intimately related conditions occur side by side; more frequently, however, but one is present.

§ 307. In the structures designated in the most extended sense of the word as *warts*, we are presented with hyperplastic conditions, in which, beside the epidermis, the papillary layer also participates in a greater or lesser degree; hence it may be imperative, at this place, to go more in detail into the mode of growth of the papillary layer. We said above, that the same cells, which after their migration out of the connective tissue become epidermis-cells, by contact with the intact epidermis, may just as well serve before their migration for enlarging the connective tissue. A thin section through the apex of a rapidly growing cutaneous papilla (Fig. 116), is very well fitted to elucidate to us the detail of this process. As one sees, the boundary between connective tissue and epithelium becomes very distinctly prominent at the lateral parts of the papillæ, since here the small yellowish cells of the rete Malpighii are inserted, quite in the manner known from normal histology, upon the fibrous texture of the papillary layer. Towards the apex the boundary completely disappears, since upon the one hand the roundish cells of the connective tissue accumulate, at the expense

of the intercellular substance, upon the other, the cells of the epithelium, by quite gradual changes of form, pass over from these round elements into more spindle-formed, and finally into regular pavement cells. We consequently find at the apex of the growing cutaneous papilla, an accumulation of embryonal cells, which towards the exterior become epithelium, towards the interior connective tissue, a kind of cambium, as we find it between the wood and the bark of stems of plants.

Fig. 116.



A hyperplastic papilla of the cutis, together with epithelium, from the environs of a cancroid of the lip.

§ 308. In the *common or hard wart* (verruca) there is a circular group of elongated cutaneous papillæ, their free ends slightly clubbed, their vessels ectatic and advanced close under the epidermal covering. The latter, in contrast to ichthyosis, shows the normal threefold division, in that a thick layer of transition-cells fills up all interspaces between the enlarged papillæ, and the horny layer forms the common uniform covering. Afterward, it is true, when the wart projects to the height of a line above the level of the skin, the horny layer exhibits rents and clefts, which correspond to the interspaces of the enlarged papillæ, and gradually penetrate to the bottom of the wart. Thereafter we can count with the naked eye how many papillæ compose the wart spoken of. They consist of from three to twenty, and over; corresponding to this the size of a wart varies from that of a pin's head to half a bean. It moreover appears as though the exfoliation spoken of opened the way to a kind of natural healing, in so far as through the entrance of the air into the interior of the wart, the soft cells existing here, together with the papillæ, are exposed to desiccation.

In an etiological relation it may not be without interest to demonstrate, that the circular limitation of the hyperplastic spot of skin corresponds to the region supplied by a larger or smaller vessel. I can allege from my own experience, that the so-called verrucæ planæ of Ascherson, very small, flat, sharply defined warts, which are especially found on the faces and hands of adults, often very distinctly exhibit a ramification in their grouping.

§ 309. The *cauliflower growths*, the papillomas of the external skin, which in their smaller forms are called porrum or acrothymion, are distinguished from common warts by having no common covering for the cutaneous papillæ contributing to their formation, but remain isolated from the beginning, and each of them in a certain degree grows independently. The mode of growth is indeed the same, upon the whole, as in the common wart, but to the terminal there is also added the lateral apposition of young connective tissue, dilatation and elongation of the capillary loops. Thus arises an arborescently ramified connective tissue stroma, whose contours are repeated in a wider extent by the epidermal stratum.

§ 310. The *pointed condylomata*, at least at their exterior outlines, are very closely allied to the smaller papillomas, especially to the porrum. Here also a common covering is wanting for the hyperplastic papillæ of the skin, standing side by side. The method of growth is identical, only, as Biesiadetzki has proven, in the pointed condylomata, a histological force comes into the foreground, which plays a subordinate rôle in the regular epithelial growth. I mean a certain division of the epithelial cells, which is exclusively observed in the more central, not yet indurated layer of the epidermis. The effect of this secondary epithelial formation is almost nought upon the normal epidermis; in the cicatrization of granulating wounds we can refer to it the peculiar tumefaction of the epithelial border (Fig. 39, *e*); it becomes very important in the increase of thickness of the epithelial cones of the epithelial cancer; in the pointed condylomata the great softness of the epidermal covering comes particularly into consideration, which results from the predominant development of the rete mucosum. The flesh color of condylomata, and their almost mucous membrane-like delicacy, when touched with the finger, is explained, in that no thick, horny layer exists here, which prevents us from perceiving the color and consistency of the young connective tissue rich in blood.

The *broad condylomata* (condylomata lata, plaques muqueuses) are, in a histological relation, strictly to be distinguished from the pointed. The hyperplasia of the papillary layer has here a more superficial character, and is not concentrated at the apices of the papillæ in the measure that it is in the papillomas hitherto described. The hyperplasia of the connective tissue predominates over the formation of epidermis. Thus arise flatly roundish elevations of perhaps one line high, and two to five lines broad, upon whose surface the papillæ appear as tuberosities of the second order. The broad condylomata are of a pale red or a more dirty red color; thus, in them the epithelial layer is very thin, and only in the folds between two adjacent tuberosities, a cheesy epithelial matter has perhaps accumulated, which by its subsequent chemical decomposition develops a repulsive odor. Very commonly a catarrhal secretion of cells arises at the summit of the tuber, probably also a deeper-reaching suppuration of the connective tissue.

§ 311. In the *soft* or *flesh warts* (verruca carnosa, mollis) the connective tissue part of the new formation predominates so decidedly over the epithelial, that the epithelium is only alluded to by most authors, because it not rarely distinguishes itself just here by a deeper pigmentation of the rete Malpighii. Many of the soft warts are congenital, and go by the name of mother marks (nævi materni); others only develop in advanced years, especially upon the face and trunk. "The skin therein forms very gently sloping tumefactions, with flat, at times also uneven, hilly or directly warty surfaces. The epidermis and the rete Malpighii, which pass over the tumefaction, are, as a rule, but little changed; sometimes the covering is somewhat thicker, never, however, does it attain the thickness as in hard warts. If we make a section, we see the layer of epidermis as a uniform, rarely hilly layer, running across the tumor. According to this, the tumor is essentially in the cutis. They commonly include the papillary layer proper and a certain piece of the derma tissue; but rarely do they extend through the entire thickness of the cutis or even into the corium. They always, however, contrast, even for the naked eye, with the more compact and whiter tissue of the cutis, in that they show a more translucent, light gray or light yellow, sometimes gray-reddish, softer, more juicy, at times gelatinous constitution, and not infrequently they possess a coarser vascularity. If we examine this tissue, we find that it is commonly very rich in cells; nay, sometimes consists almost entirely of relatively small cells with very little and soft intercellular substance." Virchow, from whom I take the foregoing description of soft warts, furthermore calls attention to the histological identity of the tissue described with granulation (germinal) tissue, and explains therefrom the close relation in which the soft warts stand to sarcomas of the skin. (See below.)

§ 312. Let us delay yet a moment with the pigmented flesh-warts. In the abnormal pigmentary conditions of the skin we must, according to Virchow, in general, distinguish four cases: 1. Simple pigmentation of the rete Malpighii without considerable change of the cutis; freckles, liver-spots, &c. 2. Pigmentation of the cutis without considerable change of the rete Malpighii and the epidermis. 3. Pigmentation of the rete above an uncolored hyperplasia of the papillary layer. 4. Pigmentation of the rete with simultaneous pigmentation of the hyperplastic cutis. The last three categories furnish the various forms of pigmented marks; the last two are pigmented warts. Touching the deposition of the pigment, this occurs in the form of yellow, brown, or black granules, partly into the cells of the rete Malpighii and the connective tissue, partly outside the cells, free into the connective tissue of the papillary layer. The mass of pigment here is often so large that it is absolutely impossible to discover beside the pigment granules any other peculiarity of texture or of structure. It reaches down into the

cutis in long stripes, and accompanies the larger afferent and efferent vascular trunks. It must be regarded as a rarity, when in the epidermis besides the rete Malpighii also the nuclei of older epithelial cells are colored uniformly black, while yet again in the pigmentation of cells just the nuclei remain uncolored. I have once observed this case, but do not find it otherwise mentioned.

c. *Heteroplastic Tumors.*

§ 313. Of the heteroplastic tumors occurring in the skin, two of the most important proceed respectively from the papillary layer, and the epidermis and the papillary layer, while the others have their seat in the corium proper. The former are the epithelial carcinoma and the sarcoma.

The so-frequent *epithelial carcinoma* of the skin was throughout used as the foundation of our description in § 164 of the General Part. Hence I will at present confine myself to the discussion of several points, which were passed over above, in reference to the description. First of all, one word concerning the local etiology of the tumor.

The epithelial carcinoma of the skin is by far most frequently found at the points of transition of the skin into mucous membrane, therefore, at the lips, at the prepuce, at the anus and vulva. If it occur elsewhere, it is, as a rule, a secondary condition, *i. e.*, it forms at such places as have been for years in a certain pathological vegetation, yet without being cancerous. In this connection there come into consideration, 1, several of the just considered hyperplasias of the epidermis and the papillary layer, and, indeed, especially such in which from the beginning the epidermal part of the new formation is predominant, the cutaneous horns, the hard warts, and the papillomas, so that our subdivisions in § 300 attain thereby a very serious clinical consequence; 2, hypertrophic and ectatic hair-follicles and sebaceous glands, atheromatous cysts, and, 3, cicatrices, especially of the scalp.

The change into epithelial cancer is produced, as we have already seen above, in that the border of the epidermis, therefore the epidermis itself, shoots inwards towards the connective tissue, and that thereby the tumor assumes a destructive, ulcerative character.

§ 314. We may then establish, partly according to the seat of development, partly according to particular prominent anatomical tokens of the tumors, the following varieties of the principal epitheliomas.

a. The *warty epithelioma.* One of the most interesting and frequent complications of the anatomical picture, which we considered in § 165 *et seq.*, is that with papillary excrescences. That the cauliflower growths become epitheliomas, and how, has already been detailed at another place (§ 148). To this is in the first place annexed the phenomenon, that also at limits of development of the epithelioma, in that region where the enlargement of the sebaceous glands also begins, not infrequently warts, and even small cauliflower-growths spring up—therefore

a displacement of the epithelial connective tissue border outwardly, which reverses the picture of that which at the same time takes place inwardly. Beside this, however, papillary excrescences not at all infrequently occur upon and in the epithelioma itself, so that the epithelioma is primary, the excrescence secondary. It is scarcely necessary to state, that in the production of the papillæ, the stroma participates foremost. It however appears, that especially the disburdening of the stroma, which occurs after the decomposition, softening and removal of the epithelial villi, contributes to this peculiar change in the direction of the development of the epithelioma. It is certain, that just at the softened spot, the vascular loops are extraordinarily wide, and project in numerous and densely crowded loops towards the lumina, which correspond to the former villi. The secondary papillæ, as a rule, do not attain any considerable size; instead, however, they are extraordinarily numerous and cover either the whole ulcerative surface or placed in groups, a greater portion of the same, as turf does the marsh. A larger cauliflower growth has never, according to my knowledge, been met with upon a cancroid ulcerative surface.

β. The *cicatrizing epithelioma.* This variety of epithelioma is also conditioned by the behavior of the stroma, and indeed of the stroma after infiltration; namely, upon the integument of the faces of elderly persons an epithelioma occurs, in which the infiltration never attains a considerable degree, and leaves behind, at the place over which it passes, no actual ulcer, but only a smooth, cicatricial surface. As this extends exclusively by the surface, and therewith advances from one point, more or less uniformly, in all directions, there results all the appearance of a tree-lichen, so that the popular voice very suitably terms the disease by the name of "corroding tetter" ("fressende Flechte").* That which is histologically interesting and also distinctive for the macroscopic form is the circumstance that the stroma remaining behind, which otherwise produces pus or papillæ, here furnishes, without further change, a tightly stretched, vigorously retracting cicatricial tissue, which remains covered with a thin epithelial stratum.

§ 315. The *sarcoma* of the skin, in its history of production, shows peculiarities which themselves invite to a comparison with the epithelial cancer of the skin. It is not Virchow's smallest merit which he has acquired concerning the doctrine of sarcoma, to have proven that the sarcomas of the skin very commonly proceed from such places as are disposed thereto by their other anatomical conditions. Among the local predispositions the soft, fleshy wart occupies a like prominent place, as the hard warts, the cauliflower growths, the porrum and the cutaneous horns do for the cancroid. Those hyperplasias of the surface of the skin, therefore, in which the connective tissue portion pre-

[* Flechte, in the German, means both lichen and tetter.]

dominates, threaten to pass over into sarcoma. Above all they are the colored soft warts, nævus pigmentatus, of which this untoward tendency has been known for a long time. These, then, do not yield white, but pigmented sarcomas, so that the local predisposition prevails, even in an accessory circumstance. The tumors which develop from soft warts are wont also for a long time to betray their origin in their larger outlines, since they present themselves as genuine *fungi*, *i. e.*, actual fungiform proliferations, with a broad basis and overhanging edges. But the more minute examination also frequently exhibits the derivation from the papillary layer, even in very large tumors. The cutis proper passes unchanged under the tumor, although it may be diverted from its course and dragged into the pedicle.

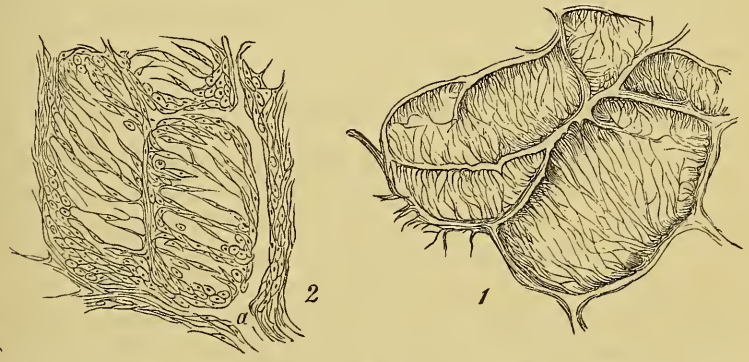
A second predisposing tendency for the development of sarcoma presents itself to us in cicatrices. The cicatricial sarcomas are also called spurious keloids. According to Alibert, a "cicatrix-like tumor" of the skin is designated by the expression *keloid*. It forms elongated, often aborescently ramified elevations of red color, smooth surface and compact consistency, and is wont to develop at previously quite healthy points of the skin. The tissue may be designated as sarcomatous, and the arborescent ramification, according to Collins Warren (Sitzb. d. k., Acad. d. Wissensch., bd. lvii, 1868), is derived from the localization of the new formation about the smaller arterial trunks of the cutis. It is otherwise with the spurious keloids. These are sarcomas not so much from cicatrices, as instead of cicatrices. The round and spindle-celled tissue must only arise transitorily in a salutary cicatricial formation, and soon gives way to the fibrous tissue. If the one or the other hold out beyond the time pertaining to it, if at the same time it accumulate in a disproportionally great amount, instead of a cicatrix we get a tumor which belongs to the sarcoma series. The fungous granulations (§ 105) may already be considered from this point of view; from them, moreover, there are all the transitions to the most luxuriantly proliferating, most malignant sarcomas.

A local etiology has, moreover, yet been proven by Virchow for very many cases of cutaneous sarcoma. A repeated irritation and inflammation most frequently gives the impulse for sarcomatosis, one indication more that our parallelizing the sarcoma with the inflammatory new formation is based upon deeper grounds, not simply taken from the form of the cells. (Virchow, Morbid Tumors, ii, page 246, *et seq.*)

§ 316. The *fibroma* of the papillary layer, which distinguishes itself from the fibromas of other organs by its greater softness, and hence has received the name molluscum, deserves a particular consideration. The fibroma molluscum (Virchow), as a rule, is a multiple tumor, so that we are in the position to learn to know upon one case the most various stages of development. (Compare Virchow, Morbid Tumors, i, 325, and frontispiece.) A small group of papillæ, perhaps but a single

one (this point is not yet decided), furnishes the material for a roundish nodule, which, of miliary circumference, may pass through all the degrees of size up to the circumference of a man's head and over. In its interior the stages of the fibroma formation follow therewith in such manner, that the younger nodes and the younger part of the older nodes consist of round and spindle-cell tissue, the older of fibrous tissue. Yet the circumstance is striking, that the fibrous stage of the tumor never exhibits that compact constitution which is peculiar to old cicatrices, or to the corps fibreux des uterus. The molluscum constantly remains soft, and this is derived, as I can assert from my own investigation, from a peculiar modification of the maturation of the connective tissue, which is brought about by the complication with œdema. Moreover, instead of the maturing connective tissue contracting from all sides the whole mass to a smaller volume upon one point, it here contracts upon certain lines penetrating the mass tree-like, which are essentially determined by the course of the vessels. This modification of the formation of fibres becomes evident wherever any other metamorphosis of the parenchymatous islands requires the development of greater space; it occurs, for example, in the formation of fat-clusters, in enchondromas, myxomas, and colloid carcinomas. The connective tissue stroma of these tumors represents the *greatest* part of the original germinal tissue foundation, which in the specific unfolding of form and the simultaneous disproportional increase of volume of the smaller part, changes into a narrow frame for just these cartilage-islands, gelatinous granules, fat-clusters, &c. In our case the question, as was said, is about a simple dropsical condition, which probably sets in in consequence of a disturbance of circulation, already at an early period in the nodules of the molluscum. The water of the œdema must have room. Hence already

Fig. 117.



Fibroma molluscum. 1. Completed tissue, after Virchow. 2. Immature condition. Formation of clefts in the parenchymatous islands. 1–200. At *a*, the lumen of a vessel.

during the round-celled condition, elongated gaps occur in the parenchymatous islands of the tumor. (Fig. 117.) These clefts, which con-

tain the œdema-fluid, become larger; we may soon speak of connective tissue bridges, which pass over from one vessel to another, and when finally the fibre formation is complete, the whole is a network of stronger connective tissue lines, whose meshes are bridged over by thin bundles of fibres. (Fig. 117.) That this structure must be as soft, nay, even softer, than the ordinary tissue of granulations, is manifest. Hence, if molluscum is derived from mollis, as can scarcely be doubted, a more suitable designation could scarcely have been chosen, for "softness" is, during the whole existence of this tumor, one of its most conspicuous and distinctive tokens.

2. Diseases of the Corium and the Subcutaneous Cellular Tissue.

§ 317. The position which the corium assumes in pathological histology is self-evidently determined by the important circumstance that in it we have before us the greatest continuous collection of connective tissue and of bloodvessels which in general occurs in the organism. Hence we may à priori expect less a series of new and peculiar phenomena than a very clear, I might say, paradigmatic display of the known histological capacities of the intermediary nutritive apparatus. We will not be deceived in this expectation. With the exception of miliary tubercle and enchondroma, there is directly no production of the vascular connective tissue system, which does not appear in the greatest perfection upon the corium; a number of these, namely, the leprous, glanderous, and syphilitic new formations, have their favorite seat in the skin. Lupus occurs exclusively in the skin, yet I see myself necessitated, upon the ground of later investigations, to designate this as one of the new formations proceeding from the sebaceous and sweat-glands, and to deny it the place among the diseases of the corium which it has with most authors.

a. *Inflammation.*

§ 318. The corium proper, according to an investigation of Rollet, very worthy of notice, is so formed that stouter bundles of connective tissue fibrillæ rise obliquely upwards from the subcutaneous cellular tissue; in rising upwards they branch out and cross and interlace with their neighbors in such fashion that there is produced therefrom an extraordinarily dense plaited work. In addition, the fibrils themselves are in their substance very compact, and long resist softening and dissolution. Both, however, the density of the felt, and the compactness of the material, make the corium proper little fitted to furnish the arena for such processes which in a short time take up much room, particularly for purulent inflammations. In the inflammations proceeding

from the hair-follicles (acne and furuncle), we will see how indolently in the given cases the corium behaves in presence of the active inflammatory movements. It is quite different with the subcutaneous cellular tissue. Here there is nothing that could limit a suppuration once excited. The fibres of areolar connective tissue, soft, easily melted down, leave between themselves meshes and gaps (the so-called cells), which are smooth within and filled with fluid or fat-clusters. In these meshes, in the surroundings of the fat-clusters, there is space enough to take up three times as much fluid. Hence it comes that just here, between the skin and muscles, a very active interchange from place to place is maintained by the lymph- and bloodvessels, in short, everything is favorable to give the greatest possible help to the extension of a subcutaneous suppurative process.

We must constantly keep before us these circumstances in the *acute* inflammations of the skin. We thereby comprehend the course of phlegmons, in which the corium proves to be only a too durable barrier, which opposes itself to the efflux of the subcutaneous pus. Nothing new of importance is turned up for pathological histology in the study of this inflammation. They are the most extensive models of suppuration and abscess formation, as we describe them in the General Part (§ 94, *et seq.*).

Touching the *chronic* inflammations of the cutis, the so-called sclerodermia adultorum (to be well distinguished from the sclerema neonatorum and the elephantiasis directly to be described), is esteemed to be a most perfect example of such a one. According to Rasmussen (Hospital-Tidende, 1867), a small-celled infiltration of the vascular sheaths forms the central point of the histological changes. Since this, however, extends to the surroundings, it leads to a more diffuse development of young connective tissue, which secondarily contracts vigorously and causes a peculiar shrivelling of the integument. The skin becomes smooth, shining, and is most intimately applied to the underlying parts; for example, to the condyles of the humerus at the elbow-joint; deformities and disfigurements occur just as though the sclerosed parts of the skin were cicatrices. We will learn to know quite analogous conditions, especially at the liver and kidneys, and at that place to term them cirrhoses, that is, granular atrophy.

b. *Hypertrophy.*

§ 319. We have to regard one of the most peculiar and interesting of skin diseases, the so-called *elephantiasis* arabum, as hypertrophy of the corium and the subcutaneous cellular tissue. The name refers to the striking resemblance of a lower extremity affected with this disease to the foot of an elephant. Thus the immensely enlarged cutis hangs

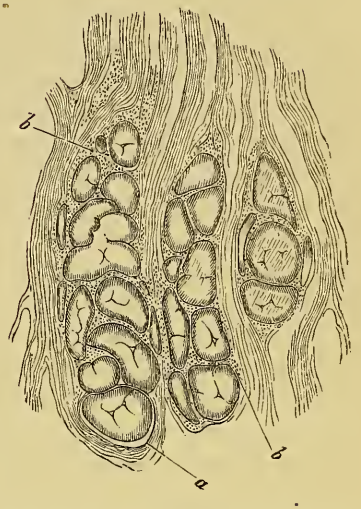
down in broad, swollen sacs at the leg and over the dorsum of the foot, so that the toes only just peep out. A section shows the known structure of the cutis, only on a large scale. In relation to the etiology of the process, I will here only remark that many reasons might determine us to consider it likewise as a chronic inflammation. We broke off above from the representation of eczema rubrum, as we came to speak of the chronic inflammatory thickening of the cutis. We could keep this for the chapter on elephantiasis, since no essential anatomical difference exists between the two cases of skin-hypertrophy. Furthermore, in the countries where elephantiasis occurs endemically (the tropic and subtropic regions), it is a known fact that the disturbance regularly begins with such processes which in themselves bear the character of erysipelas (see § 288). In the course of these inflammations the lymph-glands swell up, which, in the first place, receive the lymph of the inflamed part; in erysipelas of the leg the inguinal glands, in erysipelas of the arm the axillary glands, in that of the face the row of cervical glands. This tumefaction does not again subside. The lymph-passages in the glands remain permanently occluded. There ensues a stagnation of lymph, a non-efflux of the nutritive fluid, and this is to be regarded as the most proximate cause of the occurring hypertrophy.

§ 320. The histological process of elephantiasis is, according to existing investigations, only to be sketched in its most general outlines. It is stated by Teichmann that the ectasy of the lymph-vessels just mentioned can be traced up to their beginnings in the papillary layer of the skin. Virchow adds that from the beginning an irritative condition can be demonstrated in the parts affected with elephantiasis upon the elements of the connective tissue, so, indeed, that nuclear proliferation and increase of cells by division were found, especially in the beginnings of the lymph-vessels. The small lymph-passages are lined with a very abundant, uncommonly dense epithelial stratum. This would point to an immediate connection of the new formation with the chief etiological force, the ectasy of the lymph-passages.

I am, unfortunately, not in a position to be able to speak of the commencement of elephantiasis from my own experience. I have only had the opportunity to subject the later stages to a more exact histological analysis. The blood- and lymph-vessels here also play a great rôle; what, however, is the most striking is the *increase of volume* and *simultaneous condensation of the existing connective tissue bundles.* How, let us ask, is this produced? The cutis is a woven work. Upon a section we meet the connective tissue bundles, partly in transverse, partly in longitudinal, partly in all possible oblique directions. If we now seek a place where accidentally a bundle of longitudinal fibres meets with its one end a bundle divided transversely or ob-

liquely (Fig. 118), we find that the longitudinal fibres deviate at such places and receive the transversely divided ones into their middle. They form a framework whose trabeculæ are elegantly interwoven with the fibres of the cross-cut bundles. This framework, however, is of a very much softer, more delicate constitution than the main fibres. It is less refractive, takes also the carmine coloring less readily than that. A quite gradual transition from the one to the other quality is self-evidently found; in other words, the connective bundles of the skin affected with elephantiasis, break up at both their ends into a number of more minute and softer fibres, which form a framework for the more central parts of other bundles running transversely or obliquely towards them. *In my investigations I have not been able to detect a trace of germinal tissue.* If, therefore, I must give my opinion upon how the increase of the cutaneous connective tissue ensues in the later stages of elephantiasis, I cannot deny the probability that, first of all, the elongation of the fibrils proceeds at their ends out of the soft material, which gradually condenses for this purpose. The main support of this view is, of course, the not finding of any other productive process within the hyperplastic cutis, but yet it explains in a very plausible manner what is found by the unaided eye. The growth in thickness of the fibres ensues primarily from the same material from which the growth in length ensues. This, indeed, sounds somewhat as a paradox. We are reminded, however, that the soft ends of the fibres form at the same time an adhesive cement for such bundles as run in other directions. Why should not the same building material enlarge the one fibres in length, the others in thickness? The growth in thickness is, however, a limited one. As soon as the fibre has attained the average diameter of $\frac{1}{2}$ millimetre, it is sharply defined from the surrounding cement; then an actual interspace forms, which, in a longer or shorter distance, completely isolates the fibre. These spaces are certainly connected with the system of lymph-vessels, and contain those large quantities of clear coagulable lymph which flow from the recently cut surface of a skin affected with elephantiasis. They are most beautifully developed, constantly at the border between the cutis and the subcutaneous connective tissue.

Fig. 118.



Elephantiasis. Longitudinal and cross-sections of cutaneous connective tissue bundles. *a*. Lymphatic spaces visible in the circumference of the transversely divided bundles. *b*. Protoplasm from which the bundles are elongated and thickened. 1–500.

Here also the thickest bundles of fibres exist. Upwards, in the more external layers of the cutis, the fibres are thinner; there is nothing to be seen of interfibrillar clefts; just as little of ectatic lymph-vessels as one would suppose, according to the experiences of Virchow and Teichmann, concerning the beginnings of the process. The relation of the capillary vessels is, at all events, much more striking. The capillary net of the cutis is not denser and richer than normal; on the contrary, it is evident that the old capillary net is stretched over a greater space, but the single vessels are wide, gaping, their walls are fused with the surrounding connective tissue. Like the passages of the boring worm in old wood, so the vascular lumina characterizes themselves in the compact substance of the cutis. I might designate this condition as the first degree of the cavernous metamorphosis, and remind that Hecker has described a congenital elephantiasis where the tissue quite distinctly bore the cavernous characteristics. Meanwhile, in all fibromas the same relation of the bloodvessels is found, and there is yet required a quite peculiar process of shrinking, extending along the vascular lumina, in order to make a cavernous fibroma out of an ordinary fibroma. (Compare § 120.)

The hyperplasia of elephantiasis advances from the cutis into the subcutaneous cellular tissue; the fasciæ participate, finally the intermuscular and periosteal connective tissue. The inclosed higher organs, as muscles and nerves, perish atrophied; so also the adipose tissue. The periosteal growth leads to appositional enlargement of the bones. Numberless exostoses cover the surface, and just here one may be convinced, that not only the periosteum, but also the intermuscular connective tissue lying nearest the periosteum is able to produce genuine bone. Upon the other hand, the hypertrophy of the cutis is imparted to the papillary layer. The papillary layer is, indeed, only the outermost layer of the cutis; hence the skin of elephantiasis is very commonly covered with hyperplastic papillæ, among others often with pointed prickles which bestow upon the surface the appearance of a beef's tongue. The process, however, in the deeper layers of the cutis, is constantly further extended than in the papillary layer; the latter is only secondarily drawn into sympathy.

§ 321. An interesting variety of common elephantiasis, the *pachydermia lymphangiectatica*, occurs especially at the scrotum, penis, mons veneris, and the anterior part of the perineum. The hypertrophic skin is covered upon its entire surface with numberless small vesicles; but some as large as a pea; the first glance, however, shows that the question here is not about an elevation of the epidermis as in the bullar exanthem, but about cavities, which have their seat in the uppermost layer of the cutis itself. The covering of the supposed vesicles, thus, is comparatively compact; the contents, a clear fluid, may be removed by external pressure, returns however, immediately and in

the same measure as the pressure diminishes. If we puncture a vesicle, not only the contents of the vesicle flow out, but with a simultaneous subsiding of the swelling of the skin and all the vesicles, there is often an enormous amount of genuine lymph evacuated.

If from this there is evidence already of the connection of the supposed vesicles with the lymphatic system, histological investigation, especially vertical sections of the diseased parts of the skin, proves that it is the superficial subpapillary lymphatic net which has here experienced a partial ampullar dilatation. The covering of the vesicles is formed by the epidermis and the papillary layer. As a rule one sees four to six papillæ in the elevated part of the papillary layer, which in the smaller vesicles are yet tolerably long and narrow, in the larger, however, broad and low; that they fade so as to be quite unrecognizable, I have not observed. The inner surface of the vesicles is everywhere clothed with the known endothelial cellular mosaic, so that the origin of the vesicles from dilated lymph-vessels is raised above all doubt. The question only is, to what etiological force the peculiar modification of the anatomical change is to be referred. I cannot forbear seeking such a one in the participation of the organic muscular structure of the skin in the hyperplastic process. It is known that the cutaneous region the most threatened with the pachydermia lymphangiectatica, is at the same time the richest in organic muscle, that this structural element forms in the tunica dartos a proper membranous organ (compare Neumann, on the Diffusion of Organic Muscular Fibres. Vienna Sitzungsberichte, 1868, p. 651). Now in the case which I had the opportunity to examine, and which presented in the most pregnant manner the anatomical picture of the disease in consideration, a special hyperplasia and neoplasia of the organic muscular structure extended through the entire corium in well-characterized, thickly placed bundles, radiating in all possible directions obliquely from below upwards. The corium consisted of nearly as many muscular, as fibrous parts. If now we say nothing of the possibility, that through the possible contractions of this superabundant muscle, the lymphatic trunks, which penetrate the cutis in a straight direction and connect the superficial with the deep lymphatic net, were compressed, and that the ampullar ectasy of the superficial net might be conditioned thereby, yet it is not to be denied that a similar effect must also be produced by the simple elasticity of the muscular parenchyma, when this as here develops in a region, which shows the least possible pliancy towards all space-requiring new formations. Hence, I believe, that the hyperplasia of the muscular fibres, by rendering difficult the circulation of the lymph in the corium proper, must be regarded as the principal cause of the lymphangiectasy.

c. *Heteroplastic Tumors.*

§ 322. Touching the heteroplastic tumors of the skin, we may condense our remarks by referring to the elucidations of the General Part. This, especially obtains of myxoma and lipoma, which proceed by predilection from the subcutaneous cellular tissue, likewise of the cavernous tumor and the subcutaneous sarcomas and fibroids, that may perhaps be observed.

The various species of carcinoma exist upon the skin mostly secondarily; it may be that a carcinoma of a deeper-lying part, for example, a lymph-gland, a muscle or a bone, extends by contiguity to the skin, it may be that an actual metastasis ensues in the later stages of the carcinomatosis, to the skin. They are then mostly flat nodules, from the size of a pea to a hazelnut, which occupy the skin of the trunk particularly, in greater numbers. A scirrhus or gelatinous cancer of the mammary gland, when it extends in smaller, densely placed nodes over the skin of the whole anterior chest-wall, and has changed the latter into a rigid, board-like, whitish, translucent, superficially smooth and shining rind, is called ivory-like cutaneous cancer (Alibert), or cancer en cuirasse (Cruveilhier).

§ 323. The leprous, syphilitic, and—if I am correct*—also the lupous new formations, form in reference to pathological histology, a natural family of disease, which, as we have seen, is characterized by a peculiar hybrid position between inflammation and tumor formation. The final aim of the form-development of the tissue, the highest point which is attained, forms a germinal tissue, which stands so near to the known inflammatory proliferation of connective tissue, that Virchow directly terms it granulation tissue, the entire group, indeed, as granulation growths. Notwithstanding that no one will think of reckoning these simply with the inflammatory new formations, they will at least be called specific inflammations. This specificness, however, does not alone lie in the etiological relations, but certainly also in demonstrable anatomical characters. The manner of the accumulation of the germinal tissue already deserves to be noticed. The germinal tissue appears as nodular (tuberous) depositions into the connective tissue of the cutis. The individual nodules attain the size of a pea, even of a cherry and over. The like would scarcely occur in the history of the inflammatory new formation, and deserves rather the designation of a sarcomatous tumor. More important than the peculiarity mentioned is the *longer persistence of the new formation at the boundary between organization and decay.* Quite gradually—so it appears—there takes place either a formation of connective tissue or suppuration, or fatty degeneration of the cells with mucoid softening of the basis-substance. There happen

* Compare § 317, the concluding sentence.

a series of very characteristic intermediate stages, which may be used by us for distinguishing the individual members of the group.

§ 324. We have already treated in detail of the *gumma syphiliticum* at another place. The partial fatty metamorphosis of the formed granulation tissue, the production of cheesy depots within a greater continuity of newly formed connective tissue, was here the most prominent sign of anatomical specificness. The cutaneous gumma deviates herefrom by a somewhat more rapid course and other results. The cutaneous gumma rarely occurs individualized; there are mostly several present, which, placed in groups, occupy a certain portion of the cutaneous surface (lupus syphiliticus). The nodes are seated in the parenchyma of the cutis itself, and although they bring about no visible elevation, we can so much the better appreciate them by the touch. The peculiar hardness which primarily characterizes them, is wont at a tolerably early period to pass over into the opposite condition. It is known that just the cutaneous gumma softens rapidly. Fatty degeneration and suppuration herein go hand in hand, since they prove, as is so often the case, to be links of one chain, in which the formation of pus denotes a loosening of cells out of the organic connection, and the fatty degeneration, the immediate consequence of this isolation, namely the atrophy and death of these elements. In the next place the depot of softening bursts, empties its contents, and there remains behind a sharply defined loss of substance. Its floor and walls are infiltrated with young cells to the thickness of a line and over, and hence have a whitish shade of color, and a compact, lardaceous consistency. A thin transudation containing a few cells and fatty detritus is secreted; the contiguous connective tissue bundles slowly dissolve, and thus the ulcer continually enlarges until the enlargement is checked by an active antisyphilitic treatment. Then first a permanent layer of germinal tissue arises at the floor of the ulcer; then only does the formation of a cicatrix begin.

The syphilitic cicatrix is characterized by its considerable retractibility. Whilst it distorts the healthy surroundings in the highest degree it itself melts down to almost nothing, and after a longer time often makes it quite impossible for us to conclude, from the presence of a scar, upon the former existence of a syphilitic ulcer. This peculiarity also can as yet not be explained by what is microscopically found. The syphilitic cicatrix shows exactly the same constitution, the same sequence of stages in its production, as any other cicatrix. The bloodvessels, of course, perish; in injected preparations, the syphilitic scar appears as a gap in the vascular net of the skin, but the question is, whether the vigorous contraction of the connective tissue is not the cause of this complete obliteration of the vessels.

So much for the development of a single syphilitic cutaneous tubercle. The production and decay of numerous nodes of this sort side

by side, forms the foundation of syphilitic lupus. At one time the nodes are small and superficial, again they are large and deeply seated. In the former case they are wont to be placed concentrically around a point first affected, there arise oval ulcers which become ring-shaped, when the centre heals and forms a scar (lupus syph. serpiginosis). In the latter case are produced deep ulcers reaching into the cellular tissue (lupus syph. exulcerans). A hypertrophic lupus syph. also occurs, namely, when a very extensive new formation of connective tissue is the basis in which the comparatively small and individual nodes form.

§ 325. The pathological anatomy of *lepra* was but a short time ago a tolerably unknown land to us. Only in the year 1848 a work appeared in Paris, by Danielsen and Boek on the Norwegian spedalsked, which was distinguished by excellent representations. Since then Virchow has taken the affair in hand, and has most exhaustively discussed it in his often-quoted work "On Morbid Tumors." In all affections which are observed in the course of lepra, the histological study deals with a fundamental, everywhere-recurring change of the connective tissue, which leads at the skin to the known leprous cutaneous nodes. After that for some time spots of redness and boil-like swellings of the skin have preceded, there are developed in the thickness of the cutis, or even in the subcutaneous connective tissue, numerous nodes, from the size of a hazelnut to a walnut, hard, and more or less prominent according to their seat. These nodes give the skin a tuberous surface, and, as they by preference come to development upon the face and hands, lead to the most repulsive deformity. The microscopic analysis everywhere gave Virchow the same result. The nodes throughout consisted of a granulation tissue very rich in cells. This reaches from the rete Malpighii to the subcutaneous adipose layer; it surrounds the hair-follicles and sebaceous glands, and since it disturbs the nutritive process of these parts it causes their atrophy. Thus it happens that the nodes of lepra, although they are seated upon the hairy part of the head, constantly appear hairless upon their surface. The following representation is a copy of Fig. 178 from Virchow (Morbid Tumors), and presents the lepra tissue highly magnified. Virchow adds that he had nowhere seen the progressive development of a simple spindle or stellated connective tissue cell, through all the stages of nuclear and cell division, so characteristically as here. By division the cells at the same time become smaller and more numerous; the intercellular substance disappears to quite narrow stripes, clouding granularly by acetic acid (therefore probably mucus-containing). Finally, there results the texture represented in Fig. 119, *a*, which may be regarded as germinal tissue in its best form.* Up

* According to Hansen (Nordiskt Medicinskt Arckiv, i, 13), in older lepra nodes cells occur, in which, beside the nucleus, a brownish pigmented, fat-containing globule is found, beside peculiar formless and very large bodies, which appear to be composed entirely of this sort of globules.

to this time, therefore, the lepra node is indeed characterized by its size and the multiplicity of its appearance from the syphilitic new formation, but in the formation of granulation tissue there is a uniformity present than which no greater could be imagined. In this relation the differences first begin in the decomposition. The lepra tissue, indeed, is destroyed likewise upon the one hand by fatty degeneration, and suppuration upon the other; the long continuance, however, of the precarious condition is characteristic. For we can properly call the condition of a tissue precarious, which contains numerous elements requiring nutriment, and together with these has taken the place of a very much smaller parenchyma and poorer in cells, without a simultaneous vascular new formation having increased the nutritive means. We expect retrogressive metamorphoses or the occurrence of suppuration. Both are remarkably slow to make their appearance. Finally, after the lapse of years, the node becomes softer, the basis-substance liquefies somewhat, the cells partly undergo fatty degeneration, but only if the new formation was very limited can a complete decomposition occur. The transition to suppuration and formation of ulcer only takes place when the nodes are exposed to natural injuries and other irritations in an extraordinary manner. Then a moderate increase of cell production effects the transformation of the lepra node into pus, which is evacuated externally, and after its evacuation leaves behind a corresponding loss of substance. The leprous ulcer after this furnishes a thin sanious pus, which is wont to dry to brownish crusts.

Fig. 119.

a. Lepra tissue, after Virchow. Cells in division.

In the remaining disturbances also peculiar to lepra, the described new formation plays a prominent rôle. Anæsthesia of the skin, for example, is produced by the formation of nodes upon the nerves, the spontaneous disarticulation of limbs by the gradual deeper penetration of the infiltration upon the one hand, upon the other by a painless suppuration of the joints, which finally leads to separation.

§ 326. The *glanders*, which is transferred from horses, likewise discloses itself by the production of nodular deposits in the subcutaneous cellular tissue, which consist entirely of germinal tissue, but are characterized from syphilitic and leprous nodes by a considerably more rapid, and indeed constantly purulent metamorphosis.

3. Diseases of the Hair-Follicles and Sebaceous Glands.

1. *Retention of Secretion.*

§ 327. The hair-follicle, with its attached sebaceous glands, is one of the most ingenious anatomical arrangements of the body. The whole manner of the insertion of the hair into the skin, the ingenious care which is yet bestowed upon it within the hair-follicle, all is so lucid for comprehension. But it happens with this also, as with so many very ingenious apparatuses of man's invention. Both are easily deranged. It is certainly wonderfully elegant and practical, how the growing hair pushes forward in its sheath and just at its narrowest place grazes the outlets of the sebaceous glands, which oil it with their secretion and fortify it against injuries, which immediately thereafter befall it from the air. But this narrow inclosure of the hair by the neck of the follicle has also its drawback. But little is wanting to completely occlude the follicle. A slight tumefaction of the subepidermal connective tissue, a moderately increased separation of epidermis cells suffices to curtail the remainder of the interval which is yet present at the outlet of the follicle. Upon the occlusion, then, of the excretory duct follow the retention of the secretion; there follows a whole series of *diseases of retention* of the hair-follicles. These will first of all be observed here.

§ 328. To continue a moment longer with the causes of retention, an external occlusion of the hair-follicle by dirt and uncleanliness may probably but very rarely come into question. That must already be a very peculiarly penetrating and withal tough and smeary substance, not to be raised and pushed aside by the vigorous growth of the hair. The already pointed out increase of separation of epidermis with the simultaneous swelling of the subepidermal connective tissue at the neck of the hair-follicle, is at all events far more important. In one of the diseases to be spoken of here, namely acne, both of these phenomena are co-effects of a subinflammatory condition, and it appears justifiable to accept also the same etiology for other forms complicated with inflammation. But all this vanishes in the presence of a circumstance which exhibits the question as to the kind and manner of the occlusion in general as quite a secondary and unimportant one, I mean in presence of the favorable chances which the anatomical structure of the hair-follicle presents to a deposition and accumulation of secretion, even without occlusion of the excretory duct.

The hair-follicle—if we will cast but a glance at Fig. 109—is club-shaped; it is wider at the fundus than at the excretory duct; its walls are somewhat inclined towards the fundus; especially, however, that portion of the follicular wall which surrounds the bulb, has a position directly turned away from the surface of the skin. *From this it follows that the secretory products of the follicular walls find in this it-*

self a hindrance to their evacuation. To the energetic growth of the hair alone is it to be ascribed, if, notwithstanding this the cast-off cells of the epidermis of the hair-follicles do not remain in the fundus. The growing hair carries them along with it, and hereto the upwards and outwards directed scales of its cuticula may yet peculiarly fit it. The hair, so to say, sweeps out the recess in which it stands. But it is manifest that self-cleansing of the apparatus is only arranged for a very moderate degree of epidermal scaling on the part of the follicular wall. Every, even the smallest increase of the latter, must lead to its retention. The question, what occludes the follicle? is quite idle. We rather should have considered how, in the peculiar structure of the hair-follicle, it is possible that under normal circumstances no retention of secretion occurs. This, according to my judgment, is the only correct standpoint that we have to occupy in the otherwise so problematical etiology of the retention of hair-follicles. We find the beginning of the disturbance in an increase of separation at the inner surface of the follicle, which suffices to explain also the retention.

In most of the cases the increased separation from the hair-follicles is an affection of the whole cutaneous surface, in which the recesses after their manner take part. Persons who throw off much sebaceous matter, whose hairs and nails grow peculiarly rapidly, and who constantly have the head full of dandruff, and young persons at the period of puberty, are hence particularly disposed to the diseases of retention of the hair-follicles. Moreover we are apt to find them in the surrounding of epidermic cancer, warts, wherever an epidermal proliferation is the essential constituent of the anatomical change.

§ 329. Let us suppose now we are dealing with a hypersecretion in the interior of the hair-follicle, the question in the first place will be, whether this affects the follicle in its totality or only a section of it. The former is the case in the *comedo.* We thus call a condition, in which the hair-follicle is uniformly distended in its entire length by accumulated epidermal masses. The skin at this place is slightly elevated, and if we exert considerable pressure from two sides, there springs out a whitish plug, which looks black at its free end, and hence has occasioned the comparison to a living creature, for example, a fruit worm (comedo, mitesser). In fact this end protruded from the hair-follicle, and was colored black by dirt. If we diffuse the plug through a drop of water for the purpose of microscopic examination, we find nothing but epidermis scales, which here and there appear darkly punctated by flat globules. Besides these, fat-globules which were yielded by the sebaceous glands. According to Gustav Simon there also occurs, just here, more frequently than in normal hair-follicles, a very small six-legged mite with a long body, an acarus folliculorum. I do not know it from my own observation. Comedones are, par excellence, found at the alæ of the nose, the bridge of the nose, then upon

the back, therefore, wherever the skin is only covered with downy hairs. The follicles of the hair of the head and beard remain free of them.

§ 330. Another anatomical picture results, when not the whole hair-follicle is the seat of hypersecretion, but only the fundus. The epidermal masses then, without more ado, stratify themselves around a central point formed by a round cell-heap; there arises an epidermal globule, which can only be distinguished from the pearly globule of the epidermal cancer by its considerable size. If the globule has attained the size of a millet-seed, it glistens with a yellowish-white color through the covering epidermis, and is then called *milium* or *grutum*.

§ 331. A third form is called *meliceris*, from the honey-like consistency of the follicular contents, which is produced by a more abundant admixture of oil from the sebaceous glands to the epidermal masses. If the elevation of the surface becomes greater, if the distended hair-follicle projects more and more above the level of the latter, and if at the same time the connective tissue of the papillary layer participates in the process by hyperplasia, there arises the *molluscum contagiosum*. This is thus a wart upon the surface, of the size of a pea, which conclusively distinguishes itself from other soft warts, otherwise of quite the same constitution, only in containing in its centre a dilated hair-follicle, secreting fat and epidermis in abundant amount. A primary occlusion of the hair-follicle, by the way, can be demonstrated the least in the molluscum contagiosum. In the larger tumors, the outlet not infrequently gapes so wide that the contents may be pressed out with the greatest ease. These contents are said to have the capacity of producing the same disturbance upon the skin of a healthy individual. It is a legend with a doubtful historical background; it has, however, given occasion to the suspicious epithet "contagious."

§ 332. The acrochordon is a small, often very long, pediculated polyp of the skin. It looks as though a small, wrinkled, brownish-colored wart hung from the skin of the neck or trunk. If we examine the body of the tumor, we find therein one or two very dilated hair-follicles, filled with sebaceous matter, &c. It is, therefore, probably to be accepted, that this retention has given the impulse to a warty elevation, then to a polyp. External circumstances, especially the habitual dragging and playing with such little tumors, occasion the frequently so striking elongation of the pedicle.

§ 333. Further on we then come to the *atheroma*, the highest stage of development which a simple hair-follicular retention can attain. The hair-follicle is distended by the accumulated secretion to the size of a pigeon's egg, even of a child's fist. We have before us a retention-cyst, upon which we can distinguish a secreting cystic wall and secreted cystic contents. The first consists of a connective tissue very rich in cells, and is lined with two or three layers of pavement epithelium. The

larger the atheroma so much the thinner the cyst; it may finally compare in delicacy with a serous membrane. Nevertheless we must regard it as something hyperplastic, when we are reminded that the connective tissue sac from which it proceeded, is the most invisible of all the layers and sheaths of the hair-follicle. It has also gained very considerably in extent as well as in thickness, and although I am very far from setting up this enlargement as perhaps the cause of the increase of secretion and retention, yet it appears to me very important to establish, that with the gradually increasing epithelial production not only the epithelial layer itself has gained in extent, but also the organ which I regard as the matrix of the epithelium. Moreover, it is evident that the increased epithelial secretion is at the same time the cause and the consequence of the distension of the follicle, that we here have to do therefore with one of those circles of cause and effect, so frequent in the pathology of the physiological cysts, the urinary and the gall-bladder. The cystic contents are at one time a crumbly, smeary mass, then more honey-like, then stiffly gelatinous, translucent, and concentrically stratified. Once I found contents, which the customary designation in German of grits-bag tumor best explains. In a thin fluid, like the yolk of an egg, a number of gray, translucent lumps swam, which resembled boiled grits. Large amounts of cholesterin are wont to be found in all the larger atheromas, and to give the atheroma pulp a glittering appearance. Microscopic examination teaches that everything that looks like boiled grits or jelly, everything that is crumbly and white, consists of epidermis-cells partly in fatty metamorphosis. The yellow parts are granular globules and fatty detritus; the glittering parts, as was said, tables of cholesterin. What is more rarely found is a certain number of downy hairs, which were evidently formed by the original, or by secondarily formed hair-bulbs. The hair, moreover, in all diseases of retention is very strikingly affected. In the beginning of the retention it is nothing but a plug, which completely closes the excretory duct of the follicle. The larger then the accumulation of the epidermis masses becomes, so much the more does the hair in their midst atrophy; its growth either ceases entirely, or it yet continues for a time in a scanty manner.

§ 334. But before we leave the atheroma, we will mention a phenomenon which is wont to become peculiarly prominent just here, it is, however, of general interest for the pathology of the hair-follicle; I mean its *change of place.*

The normal hair-follicle, that is to say that of normal histology, is imbedded in the substance of the cutis; only the particularly strong and long hairs by their roots reach into the subcutaneous adipose tissue. This proposition is to be taken *cum grano salis.* That upon a section of a healthy skin the great majority of the hair-follicles actually do not extend beyond the lower border of the cutis, is correct. But so

soon as a considerable enlargement of the hair-follicle occurs, it regularly moves out of the cutis and becomes subcutaneous. Hence even the smaller atheromatous sacs, without exception, do not lie *in* the cutis, but *under* it. An analogous sinking down is found in lupus, in the hypertrophy of the sebaceous glands, &c., so that in fact it will be worth the trouble to search out its cause. Now herein an old observation comes to my aid, which I made in the examination of a colossal myxoma of the skin of the back, of twelve pounds weight. This tumor had developed in the subcutaneous cellular tissue, and the covering integument was stretched to a high degree. If now we cut out any piece you will of this integument, and observed its under surface by a strong lens, we remarked that everywhere the hair-follicles with their sebaceous glands projected from its level. Several were quite free, others were fixed in shallow, infundibular depressions, which were formed by the connective tissue bundles of the cutis parting asunder. It quite gave the impression, as if pre-existing recesses were opened from below by the distension, like as the outlets of the uterine glands open infundibuliform, when in pregnancy the uterine mucous membrane is stretched from within. Hereupon I subjected the healthy skin to another examination, and found that wherever in the cutis a hair-follicle of medium and of larger calibre existed (I only except the smallest downy hairs), it was imbedded not so much in the cutis as in a *continuation of the subcutaneous connective tissue.* If such a hair-follicle enlarges, the fasciculi of the corium part asunder just as well as if they were pressed apart from below, the recess opens, and that continuation of the loose connective tissue becomes a gubernaculum, by which the hair-follicle descends into the subcutaneous tissue.*

2. *Inflammation.*

§ 335. That the conditions in the interior of the hair-follicle, especially the retention of its secretion, do not remain without reacting upon the surrounding parts, we have seen as well in the molluscum contagiosum as in atheroma. There they were hyperplastic conditions of the surrounding connective tissue, which being excited by the retention of secretion, had tumefaction and thickening as a consequence. *The inflammations* of the hair-follicles, or better, the inflammations which proceed from the hair-follicles, show us, however, that this reaction of the surroundings towards the conditions of the follicles may assume an acute and heteroplastic character.

§ 336. In the so-called *acne* or pimply eruption, an anatomical pic-

* Wertheim had already demonstrated, in 1864, the implanting and the transition of the hair-follicle into a connective tissue bundle coming from the deep parts. (On the Structure of the Hair-Follicle in Man, &c. Reports of the Sessions of the Imper. Academy, vol. l. April.)

ture of disease meets us, which is essentially composed of the retention of secretion upon the one hand, and of perifollicular inflammation upon the other. Hence the pimply eruption is very commonly met with as an intercurrent affection in such persons who suffer much with comedones and milia. The question therewith is probably about an irritation of the cutis from the products of decomposition of the stagnant contents. Another more improbable version would be, that the perifollicular inflammation causes a swelling of the subepithelial connective tissue at the neck of the hair-follicle, and this occlusion first causes the accumulation of the secretion in the hair-follicle. Anatomically, in every acne-pustule we have to distinguish the changes of the centrally located hair-follicle from the changes of the surrounding connective tissue. The hair-bulbs and their sheaths, apart from the fact that between them a large amount of fatty degenerating epidermis-cells are accumulated, are affected throughout. So much the more actively does the connective tissue sac participate in the inflammation. It appears that this entirely melts down into pus, for in the evacuated contents of a mature acne-pustule I find no trace of it, but beside the hair only pus-corpuscles and epidermis-cells, although the loss of substance remaining behind exceeds the hair-follicle in size perhaps two to three times. The vessels of the hair-follicle are macerated by the dissolution of the connective tissue which carries them; the cells of the walls also appear to participate in the inflammatory proliferation, and the walls thereby to lose in tenacity, for they regularly burst, when by the evacuation of the pus they are relieved from the pressure resting upon them.

The surrounding connective tissue must be regarded as the proper focus of the inflammation; here hyperæmia, plastic infiltration, and the formation of pus in an area of from one-half to two lines, succeed each other. The pus collects around the follicles, and already, long before we see it shining through the epidermis, there exists a drop of pus in the depth of the corium, which may be evacuated by making an incision. (G. Simon.) Only at a later period the abscess advances outwardly. The orifice of the follicle opens slowly, the connective tissue bundles, which surround it, separate unwillingly. Between the latter and the epidermal parts of the hair-follicle the pus-corpuscles slip through, and by elevating the epidermis collect circularly around the shaft of the hair. Finally, a sharply elevated, straw-colored pustule rises up very rapidly; the condition has attained its climax.

If we puncture the pustule and at the same time prevent desiccation, all the pus gradually flows out by itself. By a vigorous side pressure, the pus with the hair-follicle is commonly evacuated. Hereupon the morbid vegetation in the skin very soon ceases, the connective tissue bundles draw together again, the small cavity, which previously contained the follicle, is filled by a little cicatricial tissue.

Sycosis only presents a variety of acne. While the latter visits in general such regions of the skin as are only clothed with downy hairs, sycosis affects the hairs of the head and beard, the eyebrows, &c. A preceding retention of secretion cannot be demonstrated in the affected follicles. Köbner seeks the pathological irritation in a vegetable parasite of the hair-follicle, though such a one is rarely found, and I can corroborate this view of Hebra.

§ 337. The opinion that the *furuncular inflammation* also constantly proceeds from a hair-follicle, has, indeed, been not at all generally received; that, however, it may proceed therefrom is conceded, and if it is an accident, it is at least a very singular accident, that no other case has hitherto occurred to me. In the abundant occurrence of furuncle we cannot fail of frequently and readily obtaining the so-called "cores" (Eiterpfröpfe) for investigation. They, however, by no means suffice to decide the question as to the point of departure of the inflammation. For this, more recent cases with the whole surrounding skin are required, and this material is of course much more rare. Wherever I have had the opportunity of examining this material, as the central points of the inflammatory depot, I found those funnel-shaped processes of the subcutaneous connective tissue into the cutis, which we have learned to know as the bed of the hair-follicle. (§ 334.) Bardleben makes a similar statement. (Bardleben, Text-Book of Surgery and Operative Procedure, vol. ii, p. 17.)

The furuncle distinguishes itself from acne and sycosis, in that the inflammatory process does not limit itself to the thickness of the cutis, but that it indeed attains in the cutis its highest intensity, at the same time, however, passes over into the subcutaneous connective tissue. In this exceedingly irritable region the inflammation soon attains a disproportionately great extent. Now hyperæmias, combined with extensive lymphatic saturation, condition here those nodular tumefactions, sometimes as large as a pigeon egg, which one feels through the extensively reddened and stretched skin. In contrast to this wide extension of the preliminary stages, the inflammatory new formation in fact confines itself to a small space. It extends circularly but little beyond the cone of subcutaneous connective tissue mentioned and into the substance of the cutis. Within these limits, however, the plastic infiltration becomes so considerable, the accumulation of pus-corpuscles so dense, that the bloodvessels are compressed. In a certain form of the furuncle, the *anthrax*, in consequence of this the infiltrated part actually dies, becomes black and dry as sole leather; in ordinary furuncles it remains in necrobiosis; the cells frequently show fatty degeneration. Here, as there, however, the infiltrated part is gradually loosened from the adjacent connective tissue by a separating suppuration—and commonly somewhat sooner by our treatment than by itself—is cast out of the skin. This is the already mentioned well-known "core," in whose un-

ravelling we certainly find nothing but disintegrating cells and some connective tissue fibres, beside a large amount of detritus. After the casting out of the core the sinuous ulcer heals by second intention and leaves behind a radiating scar.

3. *Hypertrophy.*

§ 338. We must distinguish the active enlargements of the hair-follicles, depending upon new formation, from the passive ones by retention of secretion. Among the former then again it is necessary to separate the genuine hypertrophies from the spurious, since, in the former, the original anatomico-physiological character is preserved, while in the latter, a specific change in the texture and structure, which at the same time excludes the normal function, is combined with the enlargement. The hair-follicles and their sebaceous glands thereby become something foreign to the organism; they become heteroplastic tumors. Hence the discussion of the spurious hypertrophies will follow in the next section.

§ 339. We can by right only find a genuine *hyperplasia of the hair* in the hairy mother's marks, the so-called moles (nævus spilus). These at times tolerably large, brown, half-spherical or flat elevations of the skin appear in fact to furnish a very favorable soil for the most luxuriant formation of hair. Not alone that the hairs become exceedingly coarse, but if we are the possessor of such a mole, we make the observation that these hairs change and fall out much more frequently than the hairs of the head and beard. If we make a vertical section through a nævus of this sort, we find in a fourth part of the collective, otherwise very densely packed hair follicles, an accessory diminutive hair-follicle, in which a new hair has been already more or less developed; we find those pictures which Kölliker gives in Figs. 79 and 80 of his Handbook. I cannot avoid seeking the essential nature of the nævus spilus in this hyperplasia of the hair. The sebaceous glands are entirely unaffected.

§ 340. I have only once seen a genuine *hyperplasia of the sebaceous glands*, and I doubt whether the new formation designated by Förster as "glandular tumor" of the sebaceous glands, is a genuine hypertrophy, as a corroding character is attributed to it, which pertains only to the spurious hypertrophies in cancroid and lupus. In the case investigated by me, which was given to me by Prof. Wernher, of Giessen, there was a tumor of the size of a pigeon's egg, that was seated by a broad base, but perfectly movable, upon the hairy scalp. The covering skin was provided with numerous openings, visible even to the naked eye, the outlets of the hypertrophic sebaceous glands; hairs were wanting. A cross section reminded very much of the cross section of a normal mammary gland. Acini of from three to five terminal vesicles, with a common excretory duct, beside transversely and obliquely divided wider excretory ducts, are imbedded in a very compact stroma with thick trabeculæ. The individual acinus shows very small, round epithelial

cells; the lumen of the excretory duct contains solid and fluid fat. The whole presents a thoroughly homologous new formation, a further development of the sebaceous gland type, like to that which is carried out in the mamma.

§ 341. By way of appendix I will at once mention here the genuine *hypertrophies of the sweat-glands*, since I do not intend to devote a particular chapter to the sweat-glands. The same obtains of the spurious hypertrophies of the sweat-glands as of those of the sebaceous glands; they are to be regarded either as epithelial cancers or as lupus. The genuine hypertrophy of the sweat-glands occasions a flat, fungoid elevation of the skin, which being smooth and hairless, appears not unlike a soft wart. A section, however, convinces us, that not only the papillary layer, but also the entire cutis, is non-participative. The sweat-glands, as is known, only lie at the boundary towards the subcutaneous connective tissue; here, then, is also the proper body of the swelling,—a cushion of sweat-glands, from three to four lines thick and correspondingly broad. The circumference of a single gland may have risen to the diameter of a line; the adipose tissue appears to be partly displaced, the connective tissue trabeculæ between the glandular bodies are thickened.

The finding of small cysts, with clear, mucoid contents, must be designated as a retrogressive metamorphosis. They arise by the total mucoid dissolution of individual glandular bodies, and fill the cavities in which they were imbedded.

4. *Heteroplastic Tumors—Lupus.*

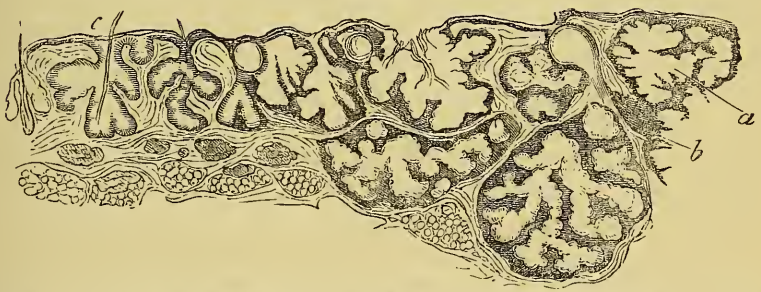
§ 342. The quite evident participation of the hair-follicles and the sebaceous glands in the formation of epithelial cancer was duly estimated in the detailed consideration of this tumor. Herein the hair-follicles and the sebaceous glands appear to be upon a line with all other projections of the epidermis into the cutis, with the sweat-glands as well as with those prominences of the rete Malpighii, directed downwards, which fill up the depressions between the papillæ. There is, however, also an adenoma of the sebaceous and sweat-glands, a tumor which, like all adenomas (§ 152), stands very near indeed to epithelial cancer, but like all adenomas is also to be distinguished from it, partly by structure and texture, partly by the more local, non-metastatic character; I mean *lupus* or skin-wolf.

§ 343. If, in relation to the lupous new formation the views advanced by me correspond more to the older than to the quite modern representations of the subject, this probably lies in that lately one has avoided more than is right, seeing in lupus something peculiar, something deviating from the common schema of the inflammatory new formation. In truth, however, not only the production, but also the

structure and texture of the lupus node present so much that is characteristic, that I will readily obligate myself to diagnose, from the microscopic analysis, the lupus just as certainly as carcinoma. It is true, the cells of the lupus node are upon the whole small and round; they are densely packed, a mucoid cement unites them, and if it were required to find a name for this tissue, that of germinal tissue might probably be the most suitable. But can we, and dare we on that account neglect the great diversity of the inner structure, the quite peculiar production of this germinal tissue?

As to what in the first place concerns the structure, every lupus node, whether this lie in the cutis or the subcutaneous connective tissue, has a very decided acinous structure. Make a section through a lupous infiltrated portion of skin hardened in alcohol, lay it for eighteen hours in a strong carmine solution, and then treat it with means to render it transparent (best of all with Canada balsam), and without more ado, you will confirm this proposition. We distinguish upon the smaller lupus nodes, two to three, upon the larger, perhaps of the size of a hemp-seed, seven to ten oval bodies, twisted to and fro, beset all over with roundish humps, which have a clubbed and a tapering end, and converge with the latter collectively towards a common central point. (Fig. 120, *a*.) These bodies are formed of larger cells, whose proto-

FIG. 120.



Lupus. Section showing the transition of the healthy skin into the highest degree of infiltration. *a*. Acinous alveoli. *b*. Germinal tissue of the lupus nodule. *c*. Metaplastic hair-follicle and sebaceous gland. 1–10.

plasm has not taken the carmine coloring, so that they appear white, and thereby contrast themselves very distinctly with the remaining parenchyma of the node, in which they are imbedded. This remaining parenchyma (Fig. 120, *b*) consists entirely of genuine germinal tissue; the cells are small, quite round, shining, and greedily take the carmine coloring. Here the vessels also of the lupus node, mentioned by several authors, run; these, therefore, surround the first mentioned alveoli, like the bloodvessels do the terminal structures of an acinous gland, so that the acinous structure of the lupus node is undoubtedly established.

§ 344. It is necessary now to ascertain the cause of this so exceed-

ingly characteristic condition, and therewith the conjecture probably will of itself impress us, that the acinous structure of the lupus node might have arisen by the degeneration of a pre-existing acinous structure, perhaps of the sebaceous glands. If now we make vertical sections at the boundary of the advancing lupus, which reach from a completely healthy portion of skin into a completely diseased one, we observe at the first glance, that in fact the sebaceous glands take a very important part in the lupous process. It has been long known that they tumefy in an extensive circuit, and shine through the epidermis as white nodules. Now this tumefaction is partly brought about by the increased formation of glandular elements, partly because the cells do not undergo fatty degeneration (disintegrate), but instead of this become large and vesicular, and distend the body of the sebaceous gland probably to five times its normal volume. Even the bulb-sheath of the hair joins in this degeneration, since they produce, instead of the ordinary flat epidermis-cells, the same large vesicular structures as the sebaceous gland. As, however, this production need not uniformly affect the whole of the bulb-sheath, but at one time the fundus alone, at another, this and a point situated higher up are implicated, the hair-follicle proper soon attains a varicose, knotty constitution. The hair is destroyed. The glands and hair-follicles can no longer be distinguished; either may be mistaken for the other. Nevertheless as yet the condition has nothing characteristic of lupus, since the large-celled metaplasia occurs also in similar manner in the neighborhood of leprous, syphilitic, especially, however, of epithelial carcinomatous affections of the skin. That which follows upon this metaplasia first becomes characteristic.

§ 345. Lupus has been regarded by various persons (Berger, Diss. Inaug. Greifsw.; and Pohl, Virchow's Archiv, vi, B) as a proliferation of the elements of the Malpighian mucoid net. I can join in this view in the sense, that I likewise seek the places of the proliferation at the boundary between the connective tissue and the epithelium, of course not absolutely in the rete Malpighii, not therefore at the boundary which the connective tissue makes with the epidermis in the narrower sense, but quite specially at the glandular continuation of the epidermis. The process begins with a luxuriant cell proliferation in the interstitial and encapsuling connective tissue of the sebaceous and sweat-glands. This proliferation extends into the surrounding parts for variable distances; one can beautifully see how it advances into the adipose tissue, encapsuling the deeper situated sweat-glands, how small, round elements appear there between the contiguous fat-cells, and first surround them in the form of a wreath, ere they entirely cover them and hide them from view. Upon the other hand, the proliferation follows the afferent vascular trunks, often deep into the subcutaneous connective tissue; within the gland itself, the massive newly formed

germinal tissue likewise groups itself in the form of an arborescent ramification, which has its trunk in the place of entrance of the afferent vascular trunk.

Quite proportional to this abundant cell-formation at the periphery of the glandular tubuli and acini, grows the volume of the glandular tubuli and acini themselves; they become deformed therein, clubbed and knotty, as we described them above; the lumen also is destroyed, only the fundamental plan remains, the grouping of the parenchyma about a central point, corresponding to the excretory duct. The cells of which the degenerated acini consist, are no longer those large vesicular elements of the first enlargement, requiring immoderate space. They are perhaps of twice the size of the germinal tissue cells, concentrically rounded therewith in smaller groups; one sees, as it were, the attempt at a higher epithelial organization; the cell, however, remains in the developmental stage of the rete Malpighii.

§ 346. I meet the objection, that one by no means always finds the lupus nodes superficial, but often deep enough in the subcutaneous connective tissue, by reminding that particularly the sweat-glands may already normally be very deeply seated, and that in the enlargement a further sinking down of the glandular body might take place in a manner similar to what we saw in atheroma. Finally, I will not leave unmentioned, that the formation of granulation tissue in the so-called hypertrophic lupus, passes very far beyond the boundary of the glandular bodies, that from this granulation tissue, mature connective tissue may also be developed, and in this manner indurations may arise, which are similar to the hypertrophies of elephantiasis. But the real lupus node is the adenoma of a sebaceous or sweat-gland.

The fate of the lupous new formation, as a rule, is, fatty degeneration of the parenchyma proper, combined with purulent melting-down of the granulation tissue. The small abscesses burst and empty. Tumors and cicatrices form as with lepra and syphilis.

5. *Atrophy.*

§ 347. The falling of the hair of the head *in extreme old age*, depends upon a complete involution of the formative places of the hair, *i. e.*, the hair-follicles and bulbs. The former widen and shorten, the latter become smaller, and either disappear entirely, or yet only suffice for the production and nutrition of downy hairs.

The *premature* falling of the hair constantly depends upon a disproportion in the production of epidermis-cells on the part of the hair-follicles on the one hand, and on the part of the hair-bulb on the other. If too many cells are formed upon the wall of the hair-follicle, the lateral pressure, which the hair experiences in the interior of the hair-follicle, disturbs the nutrition of the shaft of the hair and causes its

desiccation and spontaneous separation from the hair-bulb. This is the case in that defluvium capillorum, which develops as a symptom of constitutional syphilis, or after acute diseases, for example, typhus abdominalis.

The second very much more rare case is, that the formative activity of the hair-bulb sinks below the normal measure. We then have a quite normal hair-follicle; the normal lateral pressure, however, which the shaft of the hair experiences at the narrowest place of the hair-follicle, namely, close below the outlet of the sebaceous glands, is too great to be overcome by the pressure of growth of the hair. The hair, therefore, is held fast at this place, and undergoes a finely granular metamorphosis of its cells, which prepares the solution of continuity in so far, that a moderate pull upon the hair-shaft (in combing) suffices to complete it. The lower very soft section of the hair undergoes a peculiar knotty distension, which is derived from this, that the formative material furnished by the hair-bulb, although insufficient for the development of a regular hair, nevertheless in the course of time grows into a deformed cellular body of considerable dimensions (alopecia areata, area Celsii).

V. ANOMALIES OF THE MUCOUS MEMBRANES.

§ 348. THERE begins at the mouth and ends at the anus a system of membranous canals, which, because at its free surface it is constantly moist and covered with a thin layer of mucus, bears the name of the mucous membrane system. The membranous walls of these canals are an immediate continuation of the outer skin; like these, they present the boundary of the organism towards external nature, the ego towards the non ego; they must constantly be so regarded that, for the sake of example, what a person has taken into the stomach does not yet, in this sense, exist in the organism, but only before its gateways. In accordance with this, not only does the outer skin in general at the oral, nasal, ocular and aural orifices, at the anus, the outlets of the urethra and the vagina, pass over into the tract of mucous membrane, but also each individual layer of the skin may be traced in a corresponding layer of the mucous membrane, the epidermis in the epithelium of the mucous membrane, the cutis in the mucosa proper, the subcutaneous in the submucous connective tissue.* Each layer herewith also retains its significance in general; the epithelium remains here, as upon the outer skin, a protective covering, which shuts off the organism towards without; the mucosa represents the proper connective tissue body of the mucous membrane; the submucosa is a loose cellular tissue, which accommodates the moving about of the mucosa upon the muscular coat. But within this general definition the structure and function of each individual layer alters correspondingly to the physiological office of the various subdivisions of the tract of mucous membrane.

In the first place, concerning the epithelium, everywhere at the gateways of the mucous membrane system, the horny layer of the epidermis is thrown off, so that its antechambers, the oral cavity, the pharynx and œsophagus, the conjunctiva, vulva, preputial sac, the bladder and urethra, are only lined with the mucous layer of the epidermis, the so-called stratified pavement epithelium. The stratified pavement epi-

* The fourth layer of the mucous membrane tract, which no longer belongs to the mucous membrane proper, the muscular coat, corresponds to the complete animal apparatus of motion, to the muscular and osseous systems of the body; the fifth layer is on both sides formed by the serosa, which appears here as the visceral, there as the animal layer of the same serous sac.

thelium, like the rete, consists of a simple layer of small cylindrical cells and a more or less thick stratum of larger pavement cells, which flatten towards the exterior and are then cast off.

No doubt can reasonably exist as to the significance of this decrease of thickness of the epithelium in the anterooms of the vegetative tract. It is the first step towards facilitating the osmotic exchange between fluids and gases in the lumen of the tract upon the one side, and the blood upon the other. Where this exchange, as resorption or secretion, becomes more active, where it forms the foundation of entire nutrition, the last layer of pavement epithelium also disappears, and the cylindrical cells alone remain. Thus the intestinal canal, from the cardia to the anus, thus the respiratory passages, thus the female sexual organs from the external orifice of the uterus, carry a cylindrical epithelium. Its cells are, of course, larger than the cylindrical cells of the rete Malpighii; they have also been subjected to manifold modifications of external form, as the function of the respective mucous membrane requires; but they, like those, are seated immediately upon the connective tissue and between their bases, here and there, only single reserve-cells are visible for replacing their loss, which are probably also not wanting in the rete Malpighii. I see in this modification of form and size no obstacle to regarding them as anatomical equivalents of the cylindrical cells of the rete.

The body proper of the mucous membrane adjusts itself in the same manner as the epithelium to the peculiar functions of the individual subdivisions of the tract. Where such only serve for the conveyance and preservation of contents, at the œsophagus, at the biliary and urinary passages, at the vagina, &c., we find a plain stratum of compact connective tissue fibrils, which limits itself smoothly and evenly towards the epithelium; passes over continuously, however, upon the other side into the bundles of loose submucous connective tissue. It is otherwise where the tract resorbs or secretes. Here, upon the one hand, the mucosa becomes the purveyor to the most important glandular organs; upon the other, its surface, and histological quality alters, in a manner corresponding to those functions. For resorption, for example, the most possibly extended surface of contact of mucous membrane with the chyme is of importance; accordingly, we see the intestine, from the jejunum downwards, is beset with the known intestinal villi, of which each contains at its centre the beginning of a lymphatic vessel; and still more to facilitate transit, the connective tissue coat, which is inserted between the vessels and epithelium, shows here in the most decided manner the peculiarities of lymphadenoid connective tissue, that formation which we first learned to know in the stroma of the lymph-glands. To the apparatus of resorption belong also the numerous follicular (conglobate, Henle) glands, the solitary follicles, the plates of Peyer, the tonsils and follicular glands at the base of the

tongue. These, in a certain measure, present the first station, which matters, arriving at the lymph tracts for resorption, have to pass. If, at the same time, these matters are pathological irritants, hyperæmia, inflammation, and new formation mark their passage; hence, in so many affections of the whole tract we can establish a predominant implication just of the follicular glands.

Only the smaller, simply tubular of the secerning glands find a place in the thickness of the mucous membrane, while the larger, especially the acinous mucous glands, lie with their bodies in the submucosa. Notwithstanding, the abundance of glands in certain mucous membranes is so enormous that, for example, the mucosa of the stomach is formed up to five-sixths of its volume of glandular substance.

Of the submucosa there is less to state. In the pathological new formations we will have to mention it as a peculiarly favorable domain for their development and extension.

A. Inflammation.

1. *Catarrhal Inflammation—Catarrh.*

§ 349. The greater part of all the diseased conditions of man are catarrhs of the mucous membranes, or are complicated with such. The name "catarrh" emphasizes but one, certainly the most prominent phenomenon of the disease, the hypersecretion of the mucous membrane. It must, however, be remembered that the hypersecretion never exists without a simultaneous hyperæmia of the mucous membrane, and that this hyperæmia is the proximate cause of the hypersecretion; at the same time, however, also the more or less remote cause of yet other disturbances, of tumefaction, hemorrhage, pigmentation, hypertrophy, &c., which, taken together, first make out the anatomico-pathological picture of catarrh of mucous membranes.

Hyperæmia is, consequently, to be regarded as the anatomical foundation of catarrh. The hyperæmia may be active or passive. In the first case, it is the immediate consequence of a pathological irritation having taken place; in the second case, it preceded the catarrhal inflammation for a longer time, and has the significance of a predisposing cause; herewith I think of the bronchial catarrhs of persons suffering from heart disease, of gastric and intestinal catarrhs in difficulties of the portal circulation in the liver, of hæmorrhoidal, rectal, and vesical catarrhs. Whether we are justified in these cases, upon the occurrence of the catarrh, in assuming yet a peculiar increase of the existing hyperæmia, or even a transformation of its static character, we will let pass. The discussion of the question, to what degree and where the normal structure of the tract of mucous membrane favors the occurrence or continuance of a hyperæmia, appears to me of more profit. We will, in the first place, point out, that because of the delicacy and

the penetrability of the epithelial stratum, the access of external irritants to the irritable elements of the mucous membrane is far more easy than in the case of the outer skin; furthermore, that here no elastic envelope, as is presented by the horny layer of the epidermis, opposes a barrier to the distension of the congested capillaries, but the softness of the parenchyma permits an almost unlimited dilatation. The relation in which the contractions of the intestinal muscular coat stand to the distribution of the blood in the covering mucous membrane, appears to me of peculiar interest. As is known, the trunks of the arteries and veins, which supply the blood to the vascular nets of the gastric and intestinal mucous membrane, pass through the muscular coat in an oblique direction. They are there surrounded by a sheath of loose connective tissue, which is tolerably strong in the arteries, so that there remains a wide space between the vessel and the muscular bundles; in the veins, on the contrary, very insignificant, so that the lumina of the veins are easily compressed by a contraction of the muscular coat. In consequence of this arrangement, with every contraction of the intestinal muscular coat an obstacle occurs to the return of the blood from the intestinal mucous membrane; there takes place an increased congestion of blood, which continues as long as the contraction lasts, and may assume a more permanent character by the more frequent repetition of the contractions. The great significance for the digestive process is manifest. The peristaltic contractions, apart from the locomotion of the contents, have also, by means of the hyperæmia of the mucous membrane, which they excite and maintain, a favorable influence upon secretion and resorption; upon secretion, since they supply to the open-mouthed glands a more abundant raw material; upon resorption, since they effect that squeezing out of the capillaries of the villi, which according to Kölliker plays so important a rôle in the filling up of the central lymph-space. Meanwhile every physiological hyperæmia is a Danaen* gift for the organ subjected to it; the slightest disturbance of the mechanism turns the benefit into a calamity. Thus it is here also. At no mucous membrane does the catarrhal disturbance of the circulation attain so high a grade as just at the gastro-intestinal mucous membrane, because the pathological irritant which affects the mucous membrane awakens the peristaltic action just as promptly and in yet stronger measure than the physiological irritation by ingesta. Dysentery and cholera present us with examples, on the largest scale, of the injurious effects of this mechanism; the enormous œdema of the mucous membrane of the large intestine, the hemorrhages, secondarily, diphtheritic destructions in the former, also develop under the influence of very severe tonic contractions of the muscular coat; and if we accept that in cholera also an enormously increased peristalsis

[* Timeo Danaos et dona ferentes.]

contributes its share to the immense transudation on the part of the gastro-intestinal mucous membrane, we have thereby established only a causal connection between two known phenomena of this disease. Meanwhile we need not turn to dysentery and cholera; what occurs there upon a large scale, is repeated upon a lesser in the slightest catarrhs; especially, however, in considering hemorrhages of the mucous membrane and the round gastric ulcer will we have to return to this.

Only the vesical and uterine mucous membranes exist under similar relations as the gastro-intestinal mucous membrane. Menstruation is connected with a contraction and relaxation of the muscular structure of the uterus.

There are, however, also mucous membranes which are formed unfavorable to the production of a hyperæmia. The richer a mucous membrane is in elastic fibres, so much the greater resistance will it oppose to a distension and increase of volume through hyperæmia and œdema, so much the more vigorous, during the distension itself, will be the effort to the return to the normal volume; this lies in the nature of elasticity. Diverse phenomena upon the mucous membrane of the respiratory tract, which is rich above all in elastic fibres, are to be referred to this. An acute and more considerable increase of thickness is only observed at those places which possess a very lax submucous cellular tissue, at the duplicatures of the laryngeal entrance, especially at the aryteno-epiglottic ligament, and at some parts of the nasal mucous membrane. These swellings, however, do not have their seat in the mucosa, but they are œdematous infiltrations of the submucous connective tissue. And even they very rapidly disappear, when the elastic force of the constantly stretched mucous membrane gets the mastery of the counter-pressure of the œdema-fluid maintained by the blood pressure; thus especially after death, where it is often absolutely impossible to demonstrate an œdema, which could undoubtedly be established during life, and which was probably the cause of death (œdema glottidis).

§ 350. That the *swelling* of the catarrhal mucous membrane, the second anatomical element of this form of inflammation, is partly at least to be directly derived from the hyperæmia, is self-evident. It is, in so far as it depends upon the increase of the volume of the vessels, and upon a more abundant saturation of the mucous membrane with serum. The latter plays an important rôle in congestive catarrhs, and is characterized by the lardaceous gloss of the swollen membrane, as also by the clear serum which is poured out from an incision. The swelling is many times more considerable when the submucosa participates in it, which is more frequently the case especially at the cæcum.

The active intumescences, *i. e.*, tumefactive conditions of the *lymphatic follicles* depending upon cell-formation, interest the pathological histologist more than these passive ones. It is probably without doubt

connected with the intimate relations of these glands to the resorptive processes, that in almost every catarrhal affection of a mucous membrane we perceive a more or less extensive coaffection of the lymphatic apparatus which takes up the lymph of the diseased mucous membrane. The follicles imbedded in the mucous membrane itself are the most frequently and rapidly diseased; the proper lymph-glands lying without the tract only follow secondarily, and indeed for the catarrhs of the nasal, faucial, and oral cavities, the lymph-glands at the neck; for the respiratory tract, the glands about the roots of the lungs, and the bifurcation of the trachea; for the digestive tract, the mesenteric glands; for the urino-genital apparatus, the retroperitoneal and inguinal clusters of lymph-glands.

Concerning the process itself, it is essentially that acute lymph-adenitis suppurativa, as it was more minutely described in § 200 *et seq.* This presents itself most purely and simply in the *follicular suppuration of the gastric and intestinal mucous membrane.* The severe intestinal catarrhs of midsummer occasionally manifest the collective stages of the process, while its beginnings are found as intercurrent or initial phenomena also in tuberculosis, in typhus, Asiatic cholera, and dysentery. As a rule, simultaneously with the commencing swelling one observes a stronger, denser injection of the bloodvessels in the surroundings of the follicle; it appears as though the general hyperæmia had concentrated particularly about the follicle; partly, however, this hyperæmia may also be collateral, depending upon the entrance of the blood being impeded into the follicle itself. The solitary follicle presents itself as a faintly gray bead of the size of a pin's head, which is encompassed on all sides by a vascular circle. A Peyer's plate affords in this stage the most elegant picture, since the hyperæmic rings of the adjacent follicles touch one another. With the occurrence of suppuration the follicle swells up to the size of a small pea; in its place one perceives a yellowish, fluctuating spot, above which the outer layer of the mucosa passes moderately stretched. If we let out the pus the cover collapses and the place sinks in somewhat. The cavity may be again infiltrated by pouring water over it, and one has the opportunity of admiring its comparatively great extent. The latter is only explained by the participation of the surrounding connective tissue in the suppuration; namely, as long as the pus is contained in the parenchyma of the mucous membrane as an abscess, it acts—if I may use the comparison—catalytic all around upon the connective tissue. Hence at Peyer's plaques it not at all infrequently proceeds to a subcutaneous communication between adjacent follicular abscesses, whereby the mucous membrane is undermined for great distances. Finally the covering necrosis is loosened from the edges, and shows us a loss of substance, which was produced by the ulceration, in the form of a sharply defined round or roundish ulcer. As a rule cicatrization probably ensues

without difficulty, though I have myself once observed a perforation of the intestinal wall close above the ileo-cæcal valve.

The follicular swellings and ulcerations of the stomach presuppose the presence of follicles in the gastric mucous membrane. As is known, there are stomachs in which we seek in vain for even one single follicle. Probably, however, it is to be taken into consideration just with the stomach, whether a formation of follicles may not take place *ad hoc*, in the manner perhaps that Henle imagines the production of "conglobate" glands in general. The formative irritation which the connective tissue of the entire mucous membrane experiences, concentrates itself in a certain measure upon a number of foci, as an exanthem of the skin distributes itself upon a certain, although often very large number, of circumscribed depots; according to what law we know not. The circumstance is characteristic for the stomach, that all follicles are constantly found in the same stage of transformation, whether as gray beads, as abscesses, or as ulcers.

§ 351. The analogous conditions of the *tonsils* present somewhat more complicated relations. The half-spherical surface of this organ, as is known, shows a certain number of pocket-like depressions. The pavement epithelium of the oral cavity lines the depressions; not infrequently we find, especially at the neck of the pockets, small papillæ, which resemble the papillæ of the tongue in miniature. Round about the pockets lie the lymphatic follicles in the parenchyma of the mucous membrane. They are separated from the surface by a thin layer of connective tissue, and do not touch it (as in the sheep, Frey). If, now, we have a catarrh of the pharynx, with angina tonsillaris, an increased shedding off of epithelium takes place, not only upon the tongue (coated tongue), but also at the surface of these involutions. In consequence of which a large amount of pavement epithelium accumulates in the pockets; a white, smeary mass, like the vernix caseosa, forms an extensive plug, which indeed projects from the outlets of the pockets, but is not thrown out, so that already this filling contributes not inconsiderably to the enlargement of the whole tonsil. To this the inflammation and formation of abscess of the follicle associates itself. One after the other, (as it appears all do not simultaneously enter into the process) tumefies and softens. The adjacent abscesses here and there flow together; finally, that is to say, when the maturation of the condition is not disturbed by premature medical interference (scarification, nitrate of silver, &c.), the entire tonsil is penetrated by a sinuous abscess, which becomes a sinuous ulcer, if the pus has emptied itself at the surface. As a rule, this occurs simultaneously at several points. The gland thereafter suddenly collapses, provided always that a complete confluence of all the purulent follicles had taken place. If this is not the case, the follicles yet unopened, as well as those which in general have been spared, remain in their present condition, and ex-

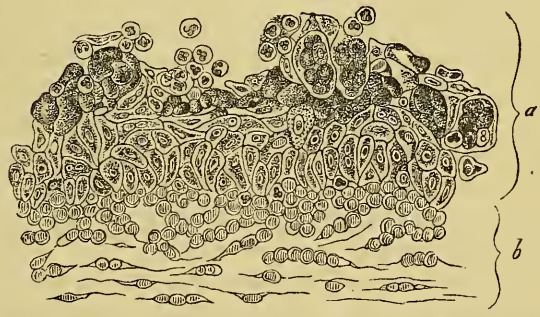
hibit what yet remains of the tonsil. The filling up of the ulcerated cavities with cicatricial tissue, as a rule, proceeds rapidly, and without dangerous complications. If the healing is retarded, should even the floor of the ulcer take on a gangrenous, putrefactive character, the neighborhood of the internal carotid becomes a source of danger, because it may lead to uncontrollable hemorrhage if the vessel is isolated by the suppuration, and then corroded from the side. (Hemorrhagia per diabrosin) [from ulceration.]

§ 352. The changes, which the *secretion* of the mucous membrane experiences by catarrhal inflammation, are so striking, and present points of support so important for clinical decision, that it has been here and there believed that we could define catarrhs immediately as anomalies of secretion. This is not correct, for the anomaly of secretion is not the essence, but the consequence of the catarrhal inflammatory condition. But it would be completely erroneous, did we see in catarrh only an increase of the normal secretion. There is a difference between secretion and secretion, and this difference prevails here. The physiologically most important secretion of the mucous membrane tract, the gastric and intestinal juices, are by no means secreted in greater quantity from the catarrhal than from the healthy mucous membrane; on the contrary, a decrease of this secretion is constantly to be expected as a functional disturbance accompanying catarrhal inflammation. It is already different with the physiologically less important mucus, which also covers the normal mucous membrane. We know "mucous" catarrhs, in which mucus is furnished in increased amount. They occur, par excellence, at such places of the tract, as are distinguished for their greater abundance of mucus-preparing glands, as the pharynx, the respiratory passages, the stomach and large intestine. Yet we know that the preparation of mucus does not exclusively belong to the acinous glands, but that the mucous metamorphosis is the same for the protoplasm of the epithelium of the mucous membrane, that the horny metamorphosis is for the cells of the epidermis (compare § 40), and hence we do not wonder at finding mucous catarrhs and mucous admixtures to catarrhal secretions, also from mucous membranes without glands, for example, at the urinary bladder.

A somewhat more intense irritation than the simple mucous catarrh presupposes the increased secretion of "cellular" elements. We distinguish in this connection *epithelial* and *purulent* catarrhs, according as the secreted cells are predominantly epithelial cells or pus-corpuscles. I say, predominantly, because as a rule, we find both together. A purely epithelial catarrh is, for example, observed upon the mucous membrane of the tongue, where the so-called coating of the tongue is nothing else than a massy separation of pavement epithelium, such as is characteristic for this point of the mucous membrane tract. In relation to the production and separation of the cells, I content myself

with pointing out the detailed representation which I have given above in § 83. We have no grounds whatever to assume that the epithelial cells produced in excess, are formed according to any other than the normal principle of development, and in this connection, we may conceive the epithelial catarrh as a simple hyperplastic process. But what, if we find pus-corpuscles in the catarrhal secretion, if we have to do with a purulent catarrh? It is a question, whether the catarrhal pus-corpuscles are also to be regarded as emanations from the subepithelial connective tissue. Against this formerly universally received opinion, the circumstance especially testified, that we could always demonstrate an epithelium, either by scraping the surface or by vertical section, upon mucous membranes which were completely in the condition of purulent catarrh, and that this epithelium presents not any or but unimportant deviations from normal relations. In fact later investigations, in which I myself have participated after Remak and Buhl, have taught, that the pus of mucous membranes *can* arise by endogenous formation of the superficial epithelial cells themselves. I have already anticipated the details of this production in the preliminary considerations to this section (§ 68). The arrangement of the brood cells upon a section can only inform us as to the place of their production. Fig. 121 is a true representation of the relations

Fig. 121.



Catarrh (purulent) of conjunctiva. *a*. Epithelium. *b*. Connective tissue stratum of the mucosa.

as they present themselves at the conjunctiva bulbi. One sees the mother cells in their natural position, in the *outermost* layer of the epithelial stratum; below and to the side of them, partly normal epithelial cells, partly such as have already entered upon the pathological process; towards the exterior, the pus-corpuscles and the catarrhal secretion becoming free.

It is by no means intended to prove herewith that all the pus-corpuscles of the catarrhal secretion, and that all the pus-corpuscles in every catarrh, are formed in this manner. On the contrary, if we reflect that all young cells possess spontaneous mobility, and that the strong, transudative current of fluid can certainly only be promotive

of the migration of these cells, we cannot set aside the possibility, nay, the great probability, that the elements of the subepithelial germinal tissue just mentioned penetrate between the epithelial cells, and thus come to be thrown off.

§ 353. Mucus and cells are productions of the mucous membrane; they represent the supplied nutritive material in increased amount, after it has already been subjected to a certain alteration into secondary products. The relations are different in very many catarrhs of the gastric and intestinal mucous membrane. The ordinary diarrhœa stool depends upon a "serous" transudation in the region of the small intestine. The blood-serum, with albumen and salts, has passed from the vessels of the villi directly to the surface, and is carried down the intestine by strong peristaltic movements so rapidly, that resorption in the large intestine cannot keep pace with it. The cholera-catarrh distinguishes itself from ordinary diarrhœa, on the one hand, by the exclusion of albumen from the transudation; the choleraic transudation consists entirely of common salt and water (Schmidt); upon the other, by the participation of the whole tract, from the cardia to the anus; finally, by the enormous quantity and the rapidity with which the transudation ensues. The rapidity, especially, is so great, that the epithelium of the small intestine, together with the epithelial lining of the glands of Lieberkühn, is lifted off and washed away in larger and smaller shreds. (Meal soup, or rice-water stools.) If we observe these shreds from the one side, we see the long, glove-fingerlike epithelial coverings of the intestinal villi; if we observe the other side, we are aware of the more globular and short linings of the crypts of Lieberkühn. The intestinal mucous membrane is thereupon in a, so to say, "flayed" condition, and is relentlessly exposed to the hostile actions of the intestinal contents, a circumstance which must not be forgotten for explaining the superficial gangrenous sloughs which the intestine is wont to present in the second stage of cholera.

The "hemorrhagic" catarrh distinguishes itself from the "serous" exudations by this, that here the blood does not appear upon the surface of the mucous membrane in its individual constituents, but as blood. The exit from the vessels regularly ensues at the most prominent points; at the stomach, upon the connective tissue ridges which surround the outlets of the glands; in the small intestine, at the apices of the villi, and, indeed, by preference, from the apices of those villi which beset the edges of the valvulæ conniventes; in the ileum and colon, the surroundings of the follicular glands are preferred, in the colon, especially the plicæ sigmoidæ. The process itself is a so-called diapedesis. The blood passes in the smallest portions from correspondingly small vents at the curves of the vascular loops, first of all into the connective tissue parenchyma, from here to the surface. If afterward the hemorrhage ceases, a portion of the poured-out blood-

corpuscles remains in the parenchyma, and gives occasion for the formation of a brown, to a black pigment. Accordingly, the mucous membrane appears *in toto* brown, yellow, gray, or even black, whereby the dissemination of the pigment follows the laws just discussed, and is only in rare cases of high grade a more uniform one, so that, for example, the stomach looks as though ink had been poured over it.

§ 354. A peculiar series of phenomena are developed by the possibility that serous transudations may also occur upon mucous membranes with stratified pavement epithelium. The outer well-articulated cell-stratum then for a time resists the passage of the serum, is raised from its position, and this gives rise to the formation of a vesicular eruption. Accordingly we see in catarrhs of the oral cavity, the mucous membrane of the lips, the gums, the tongue, and the cheeks, not infrequently beset with watery, clear vesicles, up to the size of a pea, but mostly miliary, which burst after about twenty-four hours, and empty their contents. The affair is either concluded herewith, or subsequently the elevated portion of the epithelium is entirely cast off, and there is left behind a small, round deficiency of the epithelial stratum, an *excoriation*. The exposed mucous membrane then, for the time being, produces pus, the contiguous *edges of the epithelium* are macerated, and appear to the unaided eye like sharp, white contours; the whole is surrounded by a hyperæmic area, and this condition of a circumscribed purulent catarrh lasts as long as the catarrh in general continues. The so-called "ulcers" may not inconsiderably enlarge therewith, so that finally the greater part of the oral cavity is sore, the lesser part normal. (Stomatitis, scorbutus.)

Analogous conditions are found in all antechambers of the tract of mucous membrane (see § 348). The best known are those of the os uteri externus and the glans penis.

§ 355. *Complete and incomplete decomposition, chronic catarrh*, and *hyperplastic conditions of mucous membranes*. What has hitherto been stated concerning catarrhal inflammation characterizes one course of the process, acute catarrh. After this the mucous membrane may return completely to the normal state. The behavior of the connective tissue parenchyma of the mucous membrane is herein the most important. We saw in § 352 how actively the subepithelial connective tissue participates in the catarrhal inflammation. Not in the slightest degree was the thickening and puffing up of the catarrhal mucous membrane to be laid to the account of a cellular infiltration of the subepithelial connective tissue (Fig. 121, *b*). All these cells must completely vanish ere the restitution can be called complete. They partly undergo fatty degeneration, partly they may be taken up into the lymph-vessels. Until this, however, has occurred, weeks may pass by, and so long also the mucous membrane remains a locus minoris resistentiæ to new irritants; for the greater the number of irritable ele-

ments, so much the greater the irritability of the whole organ. This point of view is not always properly valued by physicians and patients. The latter are in a situation similar to those whose mucous membranes are predisposed by a static hyperæmia to catarrhal inflammation. The danger is that the catarrh will return upon the slightest occasion to just the place which it seemed to have left. The relapse then is wont to be more stubborn than the primary disease. The vulnerability of the mucous membrane, and with it the danger of a new relapse, is constantly increased thereby, and always lasts longer. Each relapse increases the number of cells in the connective tissue of the mucosa; the epithelium and the glandular apparatus also gradually participate in the persistent enlargement; the mucous membrane passes over into the condition of hypertrophy. The hypertrophy, therefore, viewed from this side, is a production of the catarrh; upon the other hand, it may be regarded as an anatomical predisposition to catarrh, since the phenomena constituting catarrh, hyperæmia, swelling, hypersecretion, are already developed up to a certain pitch and have become stationary there, so that it requires but a slight excitement to increase this to a catarrhal inflammation. (Chronic catarrh.)

§ 356. Let us now consider the anatomical peculiarity of *hypertrophy of the mucous membrane*. *a.* The hyperplasia of the connective tissue becomes particularly striking where, under normal circumstances, it only appears in sparse amount as the cement of the densely crowded tubular glands upon the mucous membrane of the stomach. The small partitions between the glandular outlets, as the most superficial layer of this cement, become here the place of exhibition of often a very luxuriant production of young connective tissue; they are elevated in the form of villi and lamellæ up to one line above the level of the mucous membrane, and may then be already recognized by the naked eye. In other respects, the connective tissue hyperplasia is very much in the background beside the hyperplasia of the glands, as well in its microscopic as in its macroscopic effects; one even forgets to say that the connective tissue which surrounds the enlarged glands, which forms the pedicle of a polyp, &c., is in good part only newly formed.

b. The *epithelium* covers the hypertrophic mucous membrane just as completely as the normal, hence we may assume a growth of this in surface, which is proportional to the enlargement of surface of the mucous membrane itself. Moreover, it appears to be peculiarly firmly attached to the connective tissue, for without its continuity being in the least interrupted, without that even but a single cylindrical cell were wanting, for example, at the respiratory mucous membrane, it not only allows considerable amounts of transudative fluids to pass through it from the deep parts to the surface, but also a large amount of young cells, which mingle with the secretion as mucous and pus-corpuscles.

c. The increase of volume of the *open-mouthed glands* is, as a rule,

regarded as a functional hypertrophy. As the muscle by exercising its power increases in volume, so here the glands are said to enlarge by the continued more abundant secretion. In opposition to this view, I would place a greater value upon the retention of the secretion and the passive dilatation of the gland conditioned by it. In the hyperplasia of the subepithelial connective tissue, we have a very plausible force for a mechanical obstacle to the outflow of the secretion. By it the excretory duct is compressed, narrowed, distorted, and occluded, while the body of the gland, especially if it lies beyond the mucous membrane in the submucous connective tissue, can enlarge unimpeded. Meanwhile, I am very far from declaring glandular hypertrophy purely as a glandular ectasy. In most hypertrophic glands we can too distinctly observe an elongation or increased convolution of the tubuli, an increase of the acini, as also a luxuriant cell-proliferation in and about the glands. But I as little overlook the quite constant phenomenon, that the tubuli and acini of the hypertrophic glands are wider and contain more accumulated secretion than they should, and I seek the irritant for the new formation in the pressure of the secretion acting from within outwardly, which probably cannot be soon enough evacuated, because of the contraction of the excretory duct; at all events, is not soon enough evacuated.

§ 357. From this point of view we find it conceivable that under proper circumstances even the ectasy attains the predominance over the hypertrophy, and that we so often meet also the *cystoid degeneration* of glands beside hypertrophy, upon chronic catarrhal mucous membranes. Both conditions complicate each other in the most manifold manner, and thereby give occasion to a series of coarser deformities of the mucous surface, which we will shortly discuss.

The so-called *état mamellonné* of the gastric mucous membrane is produced in that the gastric mucous membrane, hypertrophic in its glandular layer, no longer finds space upon its substratum, and is hence necessitated to throw itself into hills and valleys. Up to a certain degree this corrugation, especially in the pyloric region, is physiological; hence the état mamellonné in the first place appears as only a quantitative excess. The determination of the boundary is only possible by microscopic analysis. The for the most part very striking dilatation of the hypertrophic glandular tubuli gives a sure qualitative criterion for the pathological character of the condition. Higher degrees of the état mamellonné lead directly to polyposis ventriculi. We commonly find all transitions together upon the same gastric mucous membrane. By a crossing of the folds, which is most distinct especially at some distance from the pylorus, towards the centre of the stomach, smaller fields are produced, upon which the hyperplasia of the glandular layer attains an ever higher grade. At one time a flat, roundish tubercle rises from the surface. The higher this becomes, so much the

more by the disproportional increase of volume of the projecting part does it become a fungus, finally a polyp, with a globular head somewhat above the size of a pea, and a quite thin pedicle. Such polypi, which otherwise contrast themselves very strikingly with the remaining gastric mucous membrane by their dark red color, we find upon the gastric mucous membrane occasionally to the number of thirty; often four to six of them are attached in common to a somewhat broad base. Next to carcinoma, it is the most considerable, and at the same time, the strangest deformity of the gastric mucous membrane that we have. In the interior of the head of the polyp we find, beside the ectatic glandular tubuli, actual cysts here and there, which are filled with a fluid clear as water, or with mucus. The connective tissue between the tubuli, with the epithelial-bearing walls of the latter, present a system of septa which, beside the degenerated tubuli, occupy perhaps as much room as the septa of an inflated lung beside the lumina of the alveoli. Apart from this, it is distinguished, at least in the cases examined by me, by the great amount of peculiar, oval, strongly shining and almost reactionless bodies, whose histological significance has for the time remained doubtful to me.

§ 358. To the état mamellonné of the stomach, upon the one hand, the gelatinous or cystoid degeneration of the mucous membrane associates itself, upon the other, the formation of mucoid polypi. The gelatinous degeneration, which up to the present time has only been found upon the intestinal mucous membrane, is produced, in that at a circumscribed place, up to the size of a silver dollar, according to an observation of Virchow, the glands of Lieberkühn fill up with mucus, and become cysts of retention of the size of a millet-seed. Contiguous cysts by atrophy of their partition walls fuse together, whereby larger cavities arise; finally, the mucus in the entire structure predominates to such an extent, that the affected part of the mucous membrane attains a gelatinous consistency and color. Upon mucous membrane where the open-mouthed glands are not so dense, as especially at the neck and external orifice of the uterus, the analogous condition does not develop into the gelatinous degeneration; the glands filled with mucus have rather a decided tendency to project individually above the level of the mucous membrane and to form vesicular elevations, probably also pendulous vesicles (so-called ovula Nabothi), which taken together with the hypertrophic and largely secreting mucosa, permeated by dilated vascular trunks, present the anatomical picture of the chronic catarrh of this organ, chronic metritis.

§ 359. By *mucoid polypi*, in the more contracted sense, we understand gelatinously soft tumors permeated by delicate vascular ramifications, and hence reddish, which are attached to the surface of the mucous membrane by a more or less distinct pedicle. The external form is either perfectly smooth and roundish, or lobulated, divided by

fissures. Upon the surface of a section, which in other respects presents quite the color and constitution of the surface, we observe milk-white fibrous lines, which radiate from the periphery of the polyp to the point of insertion, as also larger mucoid cysts, which before being opened feel elastic and hard. Microscopic examination, in the first place, demonstrates a perfectly continuous epithelial layer consisting of cylindrical cells, which represents the outermost layer of the polyp. The principal mass of the tumor is formed by hypertrophic glands; we see tubes, whose walls exhibit numerous shallow and deep involutions, whose end, however, is most abundantly beset with fully formed glandular vesicles. A perfect cylindrical epithelium lines the tubes within, and concentrically stratified tough mucous masses fill the lumen. Beside the mucous glands, a certain quantity of soft connective tissue rich in cells figures, which fibrously condenses only in the pedicle and the radiating threads proceeding thence. The pedicle principally contains the afferent and efferent bloodvessels. Nerves have not as yet been demonstrated in it. It would accordingly be manifest, that the mucoid polypi owe their production to a circumscribed hypertrophy of the mucous membrane, pre-eminently concentrated upon the glands. The favorite seat of the mucoid polypi is the nasal mucous membrane, then that of the uterus. Rarer points of departure are the small and large intestines, the larynx and the trachea, the female urethra, the external auditory passage, as also the cavities of the superior maxillary bone and the frontal sinuses.

§ 360. The *closed glands* of mucous membranes assume a position exceedingly worthy of notice towards chronic catarrhs and to the chronicity of the catarrh. The genuine *hypertrophy of the tonsils* only, which occurs after frequently repeated acute fluxions of the pharyngeal mucous membrane, is quite analogous to the simple hypertrophic processes which we have considered in the foregoing. This depends upon a process of growth uniformly affecting all the histological constituents of the follicle, the reticulum, the vessels, the lymph passages, and the cells. The single follicle attains three to five times its normal volume. The form and size of the entire tonsil changes in accordance with this. It forms a globular, often directly a pediculated tumor, which can arch forward so far into the pharynx that the respiratory process is interfered with thereby. The surface is smooth, except the depressions which correspond to the orifices of those small crypts about which the follicles are grouped. These orifices are otherwise roundish and open; here they are distorted and closed by the swelling.

§ 361. Analogous conditions are not known of the remaining follicular glands of the intestine. Instead, we find in certain individuals peculiarly disposed thereto, the important phenomenon, that in consequence of inflammatory organic affections in general, especially, however, in consequence of catarrhal affections of mucous membranes, the

nearest concerned lymphatic glands experience an enlargement, which distinguishes itself from the formerly considered acute swellings by the gradual growth and persistency, from genuine hypertrophy by the disproportional increase of cellular constituents, and the disorganization of the glands conditioned thereby, from both, however, by the enormous volume which the gland may attain. We mean the scrofulous or caseous degeneration described in § 203 *et seq.*, which, when it affects the mesenteric glands alone, produces the array of symptoms of the so-called tabes mesenterica. This of course also occurs at the solitary and the Peyerian follicles of the intestine, yet they are so intimately connected with the *tuberculous* degeneration of the mucous membrane, and are so regularly combined with it, that it would be unsuitable to separate them. (See below, Tuberculosis of Mucous Membranes.)

2. *Croupous Inflammation* (*Inflam. Pseudo-membranacea.*)

§ 362. Croupous inflammation of the mucous membrane is to be distinguished from the catarrhal by but one essential characteristic. The hyperæmia and swelling may be more intense, of a higher degree, but only the product of the inflamed mucous membrane exhibits a qualitative deviation. This has the macroscopic quality of a coagulated albuminate, and, according to the principal advocates of spontaneous coagulation, is called fibrin or fibrinous exudation. It is a whitish-yellow, compact, elastic substance, which by forcible extension does not draw out into threads, but breaks suddenly, and thereby forms transverse lacerations. Upon the addition of acetic acid, it clears up, and swells up like fibrin; therefore behaves in this connection just the reverse of mucus, which becomes opaque by acetic acid, and coagulates in fibrils. The morphological portion of the phenomenon also awakens the idea involuntarily, as though a body had penetrated to the surface of the mucous membrane, and had immediately coagulated in contact with the atmospheric air; thus, the questionable substance forms in quite characteristic manner a membranous covering of the mucous membrane (pseudo-membrane), which is applied to the surface of the mucous membrane as perfectly as the plaster of Paris to a surface to be moulded. The applied surface of the pseudo-membrane renders an impression of every elevation, every depression of the mucous surface; the pseudo-membrane represents a tube, when the process takes in the whole circumference of the mucous membrane canal; a solid cylinder, when at the same time the lumen of the canal is very narrow; a roundish plate, when the process is circumscribed. In thickness the pseudo-membrane varies from a frost-like trace, up to a rind of a line in height. Not infrequently one observes upon it a spotting of red, which is to be referred to slight extravasations occurring simultaneously with the exudation.

§ 363. All the other properties of the pseudo-membrane, particularly the histological quality of the seeming fibrin, as also the firmness with which the membrane is attached to the mucous membrane, vary with the *locality* of its formation, and find their elucidation in the normal structural relations. Of all the mucous membranes of the body, none is so very prone to croupous inflammation as the mucous membrane of the larynx. In the next place, the mucous membranes of the trachea and pharynx are disposed to it in about equal measure, so that croup of the larynx is now complicated with that of the trachea, then with that of the pharynx; accordingly we can distinguish a laryngo-tracheal and a pharyngo-laryngeal croup. In the current clinical language the former is called "croup" par excellence, the latter falsely "diphtheritis," pharyngeal croup. The physician has every reason for separating these two forms. The clinical pictures which they present, the dangers with which they threaten the life of the patient, above all the treatment, are distinct in points so essential, that spite of the anatomical identity which I cannot avoid proving, I would decidedly oppose a fusion of the two diseases in the clinical department.

§ 364. Croup of the pharynx, the so-called *diphtheritis*, will, first of all, engage our attention. The process here is constantly a circumscribed one. At various points, especially at the isthmus of the fauces, the soft palate, and the uvula, at the surface of the tonsils, the arches of the palate, and the folds of mucous membrane between the base of the tongue and the epiglottis, we observe milk-white, sharply-defined spots upon an intensely hyperæmic ground. The white spot soon elevates itself at the utmost one-half line above the level of the mucous membrane; the pseudo-membrane is complete. If we attempt to remove it with a blunt instrument, we are generally not successful in the earlier period of its existence; rough force causes wounding and bleeding. Afterward it spontaneously separates, since it is loosened by a moderate production of pus, first at the edges, and then raised from its base. The circumscribed catarrhal condition which then still remains for a time, and which is falsely called an ulcer, heals, if left to itself, without loss of substance or scar. Rarely is a secondary enlargement of the pseudo-membrane perceived, never a reproduction at the same spot. In that case it would be that the loosening had ensued before the spontaneous maturation.

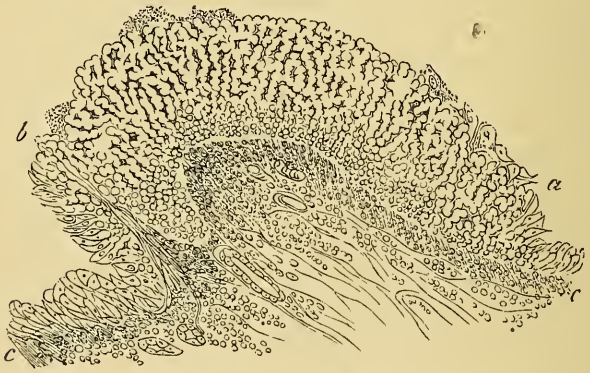
§ 365. These important and striking peculiarities are explained in a satisfactory manner by the microscopical analysis. This, in the first place, brings to light the surprising fact that the pseudo-membranes do not consist of fibrin. If we lay small bits of such in a weak ammoniacal solution of carmine, then wash them and tease them out, we can easily convince ourselves that they are cells, and indeed nothing but cells, which occasion the macroscopic appearance of coagulated fibrin by a peculiar degeneration of their protoplasm and a just as peculiar inter-

connection with one another. Were it not for the carmine-colored points pointing out the nuclei, we would certainly err as to the cellular nature of these irregularly angular, shining lumps, firmly attached to one another. As it is, however, we must accommodate ourselves to the opinion of a cellular metamorphosis, concerning whose position in general pathology we can for the time being only entertain conjectures. According to external appearances, the term used by Weber for the amyloid infiltration—vitreous tumefaction—would be justifiable. That the cells contain more solid substance than normal cells appears certain. If this "more" of substance were fibrin, we might speak of a fibrinous degeneration; as, however, we do not know this, the term "fibrinous degeneration" would only refer to the macroscopic effect, but would be thereby prejudicial, so that I would rather avoid it.

We now make a vertical section, in order to determine concerning the structure and origin of the pseudo-membrane. The section (Fig. 122) embraces the outermost point of a pseudo-membrane and the mucous membrane lying under it.*

Here we convince ourselves at the first glance that the whole pseudo-membrane is actually composed of the elements just described. Origin-

Fig. 122.



Section of a croupous layer of the isthmus faucium, with the fold of mucous membrane lying beneath *a—b*. Croupous membrane. *c*. Normal mucous membrane. 1–300.

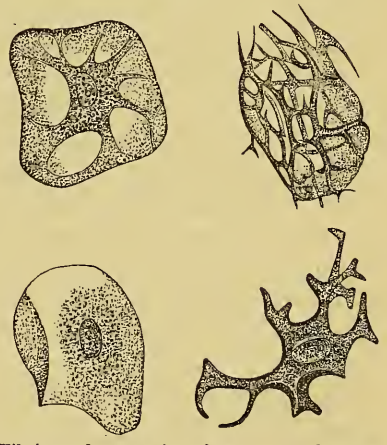
ally of a globular form, they have come into contact with one another at various points, and thus fused together into a coarse network, formed

* As the sections must be exceptionally fine and perfectly vertical, in order to get no deceptive picture, we will here, in few words, mention an excellent method for making such sections. The preparation, from which it is desired to take the sections, is to be laid in a mixture of glycerin and gum arabic, which must be clear and capable of being drawn out into threads. After the preparation has been perfectly saturated with this fluid, it is taken out and thrown into alcohol. The gum now becomes hardish, the glycerin is drawn out, and we have an excellent material for making sections of the desired thinness. If we throw these into a watery fluid, perhaps at once into a carmine solution, the gum is dissolved out, and the microscopic preparation alone remains behind.

in a certain measure only of connecting pieces, not of trabeculæ. So much the more elegant naturally is the system of crescentic branched clefts which penetrates the pseudo-membrane and represents the place of the meshes. By a certain mode of representation, these clefts appear dark, and could therefore easily be regarded as solid; an error which the carmine coloring alone makes impossible. Moreover, the cells of the pseudo-membrane are of various sizes; the further towards the exterior, so much the larger are they, and, at the outmost periphery of the membrane exceed probably twice the volume of a lymph-corpuscle; towards the interior they become smaller. They are smallest immediately at the surface of the mucous membrane. Here the degeneration also is less distinct; the difference from the normal cells which yet lie in the parenchyma of the mucous membrane a disappearing one. The boundary between the mucous and the false membrane is naturally very much obliterated by this gradual transition of the cells of both sides, although it never becomes quite indiscernible. It, however, is undoubtedly evident that the pseudo-membrane is produced by a secretion of young elements at the surface of the irritated mucous membrane, and by their gradual induration, sclerosis, vitreous tumefaction, or by whatever other name we wish to call the degeneration.

The pseudo-membrane consequently exists exactly at the place where the epithelium should be, the degeneration in question in the place of the normal development of the epithelial elements. Where, we ask, remains the original epithelial covering existing here? Is it simply cast off, or does it also take part in the formation of the pseudo-membrane? E. Wagner has treated this question in a later, very estimable investigation, and has made a participation of the epithelium in the process generally undoubted. He describes a very remarkable metamorphosis of the pavement cells (Fig. 123), by virtue of which the protoplasm shrivels up at certain places, and in a certain extent retracts to certain branched lines, which then appear homogeneous and strongly refractive like the ordinary protoplasm. The nucleus disappears; there remains therefore of the whole cell, only a delicate network like the horns of a deer. I believe I also saw this metamorphosis at the edges of the pseudo-membrane, at least in its first stages, but I cannot admit for it a far-reaching

Fig. 123.



Fibrinous degeneration of pavement cells, after E. Wagner.

significance for the formation of the pseudo-membrane; the thin epithelial stratum does not present enough substance for allowing the production of a pseudo-membrane exclusively in this way. Yet, I will gladly leave it to the future to establish more accurately the range of Wagner's discovery.

§ 366. The intimate connection, in which in croup of the pharynx, the secreted product stands with the secreting mucous membrane, is the cause of that firm adherence in the beginning of the process. In the return to the normal, the faulty cellular metamorphosis ceases, the cells secreted by the mucous membrane remain unchanged, and with a small amount of simultaneously exuded serum form a thin layer of purulent fluid, which *eo ipso* involves the loosening of the pseudo-membrane.

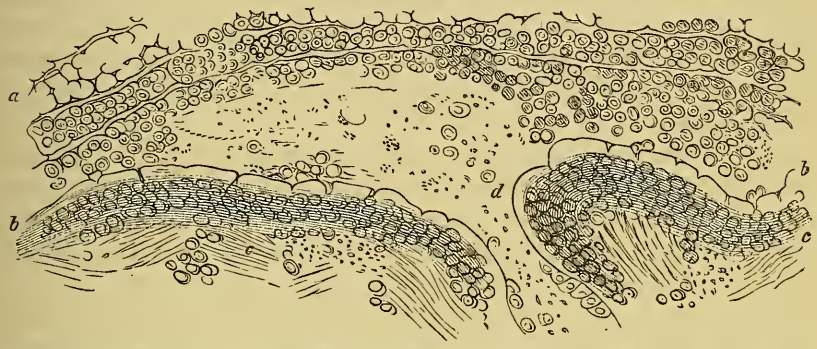
What makes the disturbance a very dangerous one, spite of this superficial character of pharyngeal croup, is upon the one side the simultaneous general affection, upon the other the danger of its extension to the larynx, where then often a very considerable angina laryngea by the swelling of the submucous connective tissue is added to the angina pharyngea.

§ 367. Croup of the *larynx and trachea* shows us a gradual sequence of simple catarrh and pseudo-membranous exudation. The catarrhal stage is already able to bring about the known array of symptoms in the utmost intensity, nay, death itself. Upon the laryngeal mucous membrane, in the condition of the utmost inflammatory irritation and corresponding swelling, there is secreted a tough, abundantly cellular mucus, movable with difficulty; this forms a thick, coherent, yellowish layer, and interferes with the lumen of the laryngeal entrance, in itself so narrow, so considerably, that we need scarcely proceed to the opinion of a reflex spasm of the glottis, in order to find death by suffocation intelligible. Upon this experience a number of physicians have gone so far as to deny generally the fibrinous exudation. We cannot agree with these physicians. The formation of the pseudo-membrane stands in the closest connection with the catarrhal condition, and presents the anatomical climax of the process. One frequently enough finds both side by side, in such manner that a catarrhal layer is here and there broken through by fibrinous plates. Acetic acid upon the instant distinguishes the muco-purulent from the fibrinous portions, so that there can no doubt exist here.

The histological investigation of the pseudo-membrane yields as its first result the fact, that here also cellular elements predominantly participate in the composition. These are far from being so imperceptible as the cells of the pharyngeal pseudo-membrane; they rather for the greater part have the character of ordinary germinal tissue cells. Upon cross sections (Fig. 124), however, we are convinced, that these germinal tissue cells are not the only constituents of the pseudo-membrane. The

pseudo-membrane is of a peculiarly stratified structure, since upon a layer of cells at tolerably equal distances there always follows a layer of fibrin, and this sequence is repeated from one to ten times, according to the thickness of the membrane. Whether I am correct in directly calling those second layers fibrin, must of course remain a question. I do it upon the first impression which its configuration makes, and with the reservation, that therewith I always have in mind only a fluid albu-

Fig. 124.



Croup of the trachea. *a*. The undermost layer of pseudo-membrane. *b*. The basement membrane. *c*. The subepithelial germinal tissue. *d*. Excretory duct of a mucous gland, from which a clear mucus is evacuated and lifts off the pseudo-membrane. 1–1000.

minate, but indurated by the transudation into the air. The substance is lustrous, homogeneous; that it is composed of cells like the pseudo-membrane of the pharynx, I at least could not prove; it forms a thin layer, with processes upwards and downwards, which penetrate into the interstices of the contiguous cells, and by anastomoses form an elegant trelliswork, whose openings have nearly the size of cells (*a*). Under such circumstances, I think the idea presents itself, that a fluid is poured out from the mucous surface, which beside numerous cells has contained in solution that fibrinoid substance, and in the coagulation of the latter the cells were fixed in their present position, while the network was produced by the continuation of the coagulation to the anastomosing interspaces between the round cells. The difficulty of explaining the how, and the where, of the origin of those cells, is dependent upon this. The epithelium has long since become traceless; it may be raised off immediately in the beginning of the process of the development of the pseudo-membrane in a similar manner as in the pharynx; the possibility of a fibrinous degeneration is indicated by Wagner (see above); we could then probably regard the uppermost story of the network as the branched, rigid bodies of the cylindrical cells: this, however, would lead to a want of harmony of the conception, which recommends itself but little. And yet the mucous membrane of the trachea deprived of its epithelium, with its homogeneous boundary layer, reminds but too

much of the open hand of Charles VII,* as that this gap in our manner of representation should not embarrass us. The highest magnifying power only, is of avail here. With one of Hartnack's immersion lenses I have seen that the homogeneous boundary layer is in fact not homogeneous, but perforated by numerous fine openings. Through these pores the cells pass without, of which a certain store is regularly laid up between the homogeneous boundary layer and the elastic layers. The openings indeed are small, but is there in general an opening through which the body of a young formative cell is not able to slip? Whoever knows the amœboid locomotions of cells from his own observation, will answer this question in the negative, and agree with me when I regard the homogeneous boundary layer as no obstacle to the migration of cells.

§ 368. The presence of the homogeneous boundary layer, however, is the cause of another important peculiarity for the croupous membranes of the trachea, namely this, that they from the beginning adhere much less firmly to the mucous surface than do the pseudo-membranes of the pharynx. Not only that the boundary between mucous membrane and false membrane, between the thing secreting and that secreted, is here constantly clearly and distinctly maintained, the smoothness of the surface also offers but few points of support to a lasting connection between the two. To this comes the activity of the mucous glands, which pour out their secretion, which is very often prevented from flowing off freely by the superimposed pseudo-membrane between the mucous and the pseudo-membrane, and thereby raise off the latter (Fig. 124). The joint result is the facile separability of tracheal pseudo-membranes, upon which is based our entire known, nevertheless very impotent therapeusis. Frequently enough the act of loosening itself becomes the cause of death, if the entirely or partially loosened membrane rolls up and completely closes the bronchial lumen.

Beside the loosening, however, the softening of the pseudo-membrane also comes into question in tracheal croup. A gelatinous intumescence of the network, as also a fatty granular disintegration of the inclosed cells, play therein the principal rôle. Fungous vegetations have been seen by several authors in the softening pulp, and they at the same time attribute to the melting down a more putrid character. The macroscopic impression justifies the term of an actual melting down, since the membrane becomes fluid not only around the edges, but also thin places and holes arise in the continuity, which flow together. I saw the thing

[* The allusion here is to the words spoken by Charles VII of France in Schiller's Maid of Orleans, Act I, Scene 3d:

KARL (*verzweiflungsvoll*). Kann ich Armeen aus der Erde stampfen?
Wächst mir ein Kornfeld in der flachen hand?

CHARLES (*desperately*). Can I summon armies from the earth?
Or grow a cornfield in my open palm?

—TRANSLATOR.]

but once, and only yet remember, that the fluid of softening gave with acetic acid a precipitate of mucin, which has caused me to speak of a mucoid softening of the pseudo-membrane.

§ 369. After that we have thus learned to know the croupous process, as it presents itself at the pharynx upon the one hand and at the trachea upon the other, it yet remains to say a few words of the larynx. A croupous process, confined to the larynx and exclusively running its course in it, belongs to the more infrequent occurrences; notwithstanding croup of the larynx is more frequent than any other, because it almost regularly associates itself to the croup of the air-passages, and at least may associate itself to that of the pharynx. The pathological anatomy of laryngeal croup is influenced by the circumstance that the mucous membrane of the larynx in its structure agrees partly with the tracheal and partly with the pharyngeal mucous membrane. The upper and under surface of the epiglottis and the true vocal cords bear a stratified pavement epithelium, which is divided from the connective tissue by no homogeneous boundary layer. On that account pseudo-membranes adhere more firmly at these points than at all the other parts of the interior of the larynx. How often do we find, post mortem, that the pseudo-membrane of the trachea, in continuity with that of the laryngeal funnel, is loosened up to the rima glottidis. Here, however, the membrane adheres, and we get the conviction that it would probably yet have lasted for some time ere a spontaneous separation had occurred. And herewith just the true vocal cords are visited by the inflammation by predilection, while, for example, the ventriculus Morgagni is almost never found to be affected. In general, it appears to me to be of great importance in an etiological relation, that we expressly emphasize the predilection of the process for the most prominent parts; the recesses of the mucous membrane mostly remain intact. It is as though one had lightly passed over the gullet with an escharotic, or as though an irritating gas had been detained for a short time in the primary passages.

3. *The Diphtheritic Inflammation.*

§ 370. After having separated diphtheritis of the throat from the diphtheritic inflammation, a comparatively contracted domain remains for this form of inflammation. We have already gone more minutely into the nature of the process in the consideration of the diphtheritic pock. The question therewith is about an infiltration of the subepithelial connective tissue, relatively to the entire mucosa, with newly-formed cells; an infiltration which is so dense that the vessels are compressed by it, the circulation and nutrition are abolished. As a certain grade of cellular infiltration of the subepithelial connective tissue occurs in every catarrh, as also in the croupous inflammation, the diph-

theritis only appears as a quantitative increase, an excess of this process of new formation. Genuine diphtheritis has no claim to be regarded as a specific process in the same measure as croup. That which macroscopically characterizes it, and has become the occasion of placing it as a membranous inflammation by the side of the pseudo-membranous inflammation, is the formation of a whitish-gray, often discolored by reddish and green (blood-coloring matter) tints, compact, felted membrane, which is elevated perhaps to the height of one-half line above the level of the mucous membrane, but penetrates just as deep into the substance of the mucous membrane, and is most intimately connected with the latter. This membrane is nothing that is superimposed, nothing secreted, but the mucosa itself, as far as it has been partly tumefied, partly rendered anæmic even by the excessive infiltration with cells. This condition has not improperly been compared with a mortification by a chemical agent, with a corrosion, and the diphtheritic membrane been designated as diphtheritic scab; in fact, the diphtheritic membrane is a caput mortuum; it can undergo no other changes than those of putrefaction, of decomposition; and the question only is, how it is loosened and removed from the intimate organic connection in which it stands with the mucous membrane. A sharply defined boundary line separates, as we can convince ourselves with the naked eye, the living from the dead; but numerous connective-tissue fibres, bloodvessels, nerves, and elastic fibres, pass over from the living into the dead; they must all have separated ere the loosening can proceed. The means which are placed at the command of the organism are inflammation and suppuration. We call this inflammation "reactive," and unite with it the idea as though this were an answer to the irritation which the diphtheritic scab exerts upon the surrounding mucous membrane; yet a portion of the hyperæmia also may be explained according to static principles as collateral fluxion. The pus collects between the scab and the healthy parts, and always, accordingly as the fibrous bridges mentioned melt down and tear, the separation begins now at the edges, then at the centre. After it is completed, an ulcer remains behind which is disposed to rapid cicatrization; not infrequently, however, the process repeats itself again at the same place; we have a new scab, and with it anew the necessity of a purulent separation, after whose termination a very considerable loss of substance remains. The cicatrices finally resulting distinguish themselves by their capacity of vigorous retraction, so that the danger of subsequent contraction of mucous membrane canals, especially of the large intestine after dysentery, threatens so much the more, the more diffused the ulceration was.

§ 371. Touching the occurrence of diphtheritis, it is, above all, necessary to state that it attacks such mucous membranes as are in a condition of the severest catarrhal inflammation, at the same time, however, stand in persistent contact at their surface with putrefying bodies under-

going decomposition. In dysentery, which in the beginning is nothing but a catarrh of the large intestine with excessive spasmodic contractions of the muscular coat, diphtheritis in the first place makes its appearance upon the summits of the folds of mucous membrane above the longitudinal bands and the sigmoid folds; beside this, however, by preference at such places, where, from the natural curvatures of the intestinal tube, the most difficulty is opposed to the propulsion of the fecal masses at three successive points of the sigmoid flexure, at the cæcum, and the two hypochondriac flexures. Does not the circumstance that just at these places the longest and most intimate contact of the inflamed mucous membrane with putrid matters takes place, co-operate in the localization of diphtheritis? In like manner diphtheritis associates itself with the catarrhs of retention of the urinary passages. Whether the cause of the retention be founded in a stricture of the urethra, in a hypertrophy of the prostate, in paralysis of the detrusor, &c., the stagnant urine decomposes; the decomposed urine first of all produces a catarrh, then diphtheritis of the mucous membrane. The contact with putrefying matters takes part also in those cases of diphtheritis where not a catarrh, but a wound, forms the ground upon which it appears. I have in mind here, in the first place the diphtheritis of the womb and the vagina immediately after childbirth, where by the expulsion of the decidua the parenchyma of the uterus is exposed like an immense wounded surface. I think of diphtheritis in the second stage of cholera Asiatica, where, by the severe catarrh of the first stage, the mucous membrane is stripped of all epithelium, and exposed in this "flayed" condition to the immediate action of the intestinal contents. I think finally—although this has nothing to do with the tract of mucous membrane—of the diphtheritis of wounds, which is termed hospital gangrene.

Upon the other hand, it is not to be denied that the putrid element may also exist in the organism; that there is a condition of the juices of the individual which disposes to diphtheritic inflammations, or, expressed more precisely, disposes to this, that any other existing inflammation assumes the diphtheritic character. Many diphtheritic inflammations of the throat and of the œsophagus in the last stage of profound nutritive disturbances, may find their explanation in this.

Finally, let us make mention also of the repeatedly advanced assurance of some investigators (Letzerich), according to which the diphtheritic inflammation is called forth by the insinuation of a fungus upon ulcers and mucous membranes. Although I am a friend to this view, still I do not regard it as yet, as such a certain acquisition of science, that I could at this place devote to it a more intimate consideration.

B. Hemorrhage.

§ 372. It is yet questionable whether the right will be conceded to me from all sides, of treating the things which I purpose considering in this chapter, under the superscription of "hemorrhage." Attention was already called formerly (§ 335 and § 240) to this, in how far the vascular arrangements of the stomach and intestine brought with them a certain disposition of the gastric and intestinal mucous membrane to hyperæmia and hemorrhage. We there found in the more active contractions of the muscular structure, which may even occur in slight catarrhs, but especially characterize dysenteric catarrh, a motive for the exit of the blood, either into the parenchyma of the mucous membrane, or at its surface. Now there are at the gastric and intestinal mucous membranes a number of *losses of substance*, which most probably are all to be traced back to a hemorrhage which has occurred, a hemorrhagic infarction of the mucous membrane. This is commonly received for the *hemorrhagic erosions*. We understand thereby certain deficiencies of the mucous surface, of the size of a pin's head, round and sharply defined, which are commonly present in large number, and by preference occupy the summits of the folds in the pyloric region. The very frequently simultaneous finding of just as large infiltrated places yet hemorrhagic, beside the erosions, causes in these cases every doubt as to their origin to disappear. Immediately preceding vomiting may also commonly be demonstrated as the cause of the hemorrhage, so that we may in fine represent the affair to ourselves in the following manner: the act of vomiting leads, by the temporary stagnation of the blood's efflux, to small hemorrhages from the superficial venous trunks of the gastric mucous membrane; therefore, at the summits of the folds, because here in the extremest parts of the extent of the stagnating current, the blood-pressure must be at its highest. The extravasated blood-corpuscles infiltrate a circumscribed section of the mucous membrane in such measure, that the blood capillaries are compressed, and nutrition ceases with the circulation. The hemorrhagic infarction becomes a caput mortuum, its organic connection with the healthy mucous membrane is destroyed, and the actual separation yet only a question of time. If, however, we reflect that the gastric juice dissolves such dead portions with facility, as we have them in the hemorrhagic infarcted mucous membrane, we will find it conceivable that already but few hours after the hemorrhage, instead of the infarction, we will meet with those clean, sharply defined losses of substance, that Cruveilhier called érosion hæmorrhagique.

§ 373. I, with many others, hold to the same course of development for the simple (chronic, round, also perforating) *gastric ulcer*. On December 4th, 1865, a man came to the surgical clinic at Bonn, with a strangulated inguinal hernia. He had been violently vomiting since 5

o'clock in the morning. Fruitless efforts at replacement were made, and at 7 o'clock in the evening the operation for strangulated hernia was performed. He did comparatively well; at 5 o'clock* in the evening, an enema was followed by an abundant stool of dark brown color; at 6, another of a bloody black color. In the night, from 6 to 7, nausea and efforts at vomiting; at 7 in the morning, vomiting of bilious, afterward bloody-striped matters, which was very frequently repeated in the course of the day, and continued with short interruptions up to death, which ensued at 9 A.M. In the post mortem, which was made one hour after death, there were found in the stomach, beside several smaller hemorrhagic infarctions, two round depots of the same size, situated symmetrically to the median line of the lesser curvature, of which one was a complete ulcus simplex; the other presented the condition of a correspondingly large hemorrhagic infarction of the gastric mucous membrane.

Instead of prolix hypotheses concerning the possible or probable origin of the round gastric ulcer, which would exceed the limits of this book, I place here a simple statement of the disease, and what was found at the post mortem, since, upon the one hand, I will thereby verify the view expressed by me, upon the other, however, I will point out how feebly it is generally managed with these reasonings, as even what is found in a single post-mortem section is yet for the time of so great importance to this question.

§ 374. The simple ulcer, therefore, takes its departure from a hemorrhagic infarction. It extends through the entire thickness of the mucous membrane. In the preparation spoken of I could everywhere demonstrate, upon fine sections, the bodies of the tubular glands inundated with blood-corpuscles, as it were imbedded in the coagulum. If the infarction has been dissolved and removed (digested) by the aid of the gastric juice, there remains behind a correspondingly large loss of substance; the ulcus simplex is established. From this time out it may enlarge, it may attain the dreaded developmental climax of a perforating ulcer; upon the other hand it may also become smaller and cicatrize, but I repeat that in its essential peculiarities it is already present immediately after the complete removal of the infarction.

The round form of the deficiency belongs prominently to these essential peculiarities. Taken strictly I should say, the round base of the deficiency; for upon the whole, the deficiency has the form of a very flat cone, whose base is situated at the surface of the mucous membrane, whose apex is excentrically situated in a deeper layer of the gastric wall. If we ask concerning the cause of this conical or funnel-shape formation, the answer again points us to the hemorrhagic infarction as the point of departure of the disturbance. This keeps,

[* The following day?]

like all hemorrhagic infarctions (of the lung, kidney, &c.), within the limits of a larger or smaller vascular territory; the vascular territories of the stomach, however, have the form of flat, obliquely truncated cones, which at the upper half are directed with their points upwards, at the lower half, downwards. The latter circumstance explains, that the deepest point of the funnel-shaped crater is not situated below the centre of the deficiency of the mucous membrane, but respectively nearer the upper and the lower edge.

A second not less characteristic token of the ulcus simplex is the extraordinarily sharp outline and the want of raised edges for the ulcer. The deficiency of the mucous membrane looks like a hole that has been made by a punch. The submucosa is exposed, as white and clean as though it had been carefully prepared, and if the ulcer also extends through it, this also occurs with a second likewise round, sharply cut hole, at whose base now the muscular coat appears with its transverse bundles as though prepared. It appears, that upon the one hand, the formative reaction at the base and edges of the ulcers is only exceedingly small, upon the other, that the peptic destruction and dissolution of the plastic infiltration follows so immediately, that we never get a sight of the plastic infiltration. The great chronicity of the process, which often extends over the lapse of tens of years, speaks especially favorable for the former opinion; for the latter, the circumstance, that we only meet with the ulcus simplex in the stomach and in the upper portion of the duodenum, *i. e.*, only where the intestinal contents react acid, and the solution of albuminates most rapidly proceeds.

§ 375. Concerning the future fate of the ulcer, its possible cicatrization has already been mentioned. The smaller and the more recent the loss of substance is, so much the sooner does it come to the formation of the so-called radiated cicatrix, *i. e.*, certain small, white, flat scars, which probably replace a tenfold greater deficiency of the gastric mucous membrane, and hence necessarily draw up the adjacent mucous membrane in their formation and lay it into radiating folds. Larger ulcers also may cicatrize, yet this rarely occurs, and when it does occur, under the circumstances, it leads to so considerable a stenosis of the centre of the stomach, that the patient is thereby subjected to a new series of sufferings.

Upon the other hand, the gradual enlargement of the primary loss of substance, in a threefold manner threatens the life of the patient; namely, in that the ulcer slowly but inevitably advances outwards, it may,

1. In this route meet with a larger bloodvessel, and by opening it cause a fatal gastric hemorrhage. This most frequently occurs in those ulcers which have their seat just at the posterior wall of the stomach, where the splenic artery runs transversely from right to left; but it also happens that the vascular trunk of the primarily destroyed

vascular territory is opened by ulceration, and a hemorrhage is thereby produced from a branch of the coronary or gastro-epiploic arteries.

2. It may perforate into the cavity of the peritoneum. This regularly occurs by a round, tolerably wide opening, which can scarcely arise otherwise than by a necrosis of the base of the ulcer, and the necrosed piece being thrown off. The perforation most frequently occurs in the first place in duodenal ulcers, and then in ulcers of the anterior gastric wall, because in the movements and displacements of the stomach, this is pushed to and fro in pretty considerable journeys upon the opposing peritoneal layer, which is unfavorable to a preceding inflammatory adhesion, and frustrates it. That such an adhesion is in general possible, we see in the ulcers of the posterior wall and the pyloric region, which almost regularly before perforation, have entered into an intimate connection with the contiguous organs, the liver, the pancreas, the spleen, &c. By this the extremity is avoided, the danger of a rapidly fatal peritonitis averted, and a result attained which we as physicians would strive after, if we could. But we must not conceal from ourselves, that by this bridging over of the peritoneal cavity, a new field is opened to the destructive activity. The ulcer may now,

3. Penetrate into an adjacent organ, and destroy it layer by layer. In this manner are most frequently attacked the spleen and the left lobe of the liver, which, since the destruction advances into their soft parenchymas more easily than in the gastric walls and the connective tissue bridges, are very soon converted into immense recesses, communicating with the cavity of the stomach by a narrower opening. More rarely, the ulcer attacks the head of the pancreas; adhesion to the colon is most rare, whereby afterward a communication arises between the stomach and the colon, and we have the clinical representation of lientery. I once saw an adhesion and communication of the pylorus with the gall-bladder, with consecutive formation of gall-stones, and the evacuation of the stones through the abnormal opening in the stomach, and from hence evacuated by vomiting.

c. Specific Inflammation.

1. *Typhus.*

§ 376. The typhous process, in the by far most frequent form of its appearance, ileotyphus (typhus abdominalis), is combined with certain changes of the intestinal mucous membrane, which undoubtedly have their anatomical peculiarities, although, as in gumma syphiliticum, lepra, and in tubercle, they depend less upon histological than upon macroscopic and submacroscopic circumstances. Only in the third decade of our century was the attention of physicians turned to these changes. They were described at that time as "inflammation of the patches of Peyer." Heusinger then called attention to the resemblance to medullary carcinoma; Rokitansky compared the appearance and the consist-

ency of the changed Peyer's patches to the white brain-substance of young children, and introduced the still customary term of the acme, as "medullary infiltration."

Extensive differences of opinion yet prevail for the time, upon the relation of the intestinal and other anatomical changes (the enlarged spleen) to the constitutional affection. The Vienna school regards the intestinal changes as a casting out of materies peccans from the blood; at present, only one doubt can exist, whether the intestinal changes are related to the general affection as an exanthem, or whether they are to be ascribed to the local action of the typhus poison, since they develop just upon those organs, which according to late investigations (typhus from drinking-water), are probably the passages by which the poison is taken up.

§ 377. Several stages have been distinguished in the course of ileo-typhus; namely, the catarrhal stage, the stage of medullary infiltration, the stage of decomposition, and the stage of ulceration. We will retain these, but premise the remark, that the catarrh of the entire tract, which opens the process, may continue up to the last stage, without essentially decreasing in intensity. Accordingly, the division into stages is completely conformable only to the special condition of the lymphatic follicles, upon which of course the interest of anatomists was already concentrated at an early period. During the catarrhal stage, which is certainly very rarely to be seen anatomically, the collective patches of Peyer and the solitary follicles of the small and large intestine are in the state of swelling described in § 350. The grayish white pearl, surrounded by a dense vascular ring, meanwhile remains the highest condition that is attained in this direction; from this point the swelling in the most, especially in most of the solitary glands, completely retrogrades; in some, however, particularly in the follicles of Peyer's patches, the character of the swelling changes, without having proceeded to a suppuration and evulsion of the follicle. The follicle goes over into the condition of medullary infiltration.

That which especially characterizes this medullary infiltration is, upon the one hand, a further increase of the volume of the follicle up to six times its normal size; upon the other, the extension of the process into the connective tissue adjacent to the follicle. The follicles of Peyer's patches, together with the interposed connective tissue, fuse into an apparently homogeneous, soft, pale-reddish mass, very similar certainly to the white substance of the fœtal brain; the whole forms a long oval tumefaction, about two lines high, being bed-like parallel to the surface, which is sharply defined all around, rising with abrupt edges from the mucous membrane. The solitary follicle by the medullary infiltration becomes a medullary boil of two to four lines in diameter; just here the participation of the mucosa stands out in the most striking manner,

as the boil is evidently formed only for the lesser part by the follicle itself, in by far the greater part by the covering mucous membrane.

§ 378. And how does the microscope explain the medullary infiltration? Can it demonstrate a typical histological process, which, wherever connective tissue or lymphatic elements exist, possesses enough to produce the typhous mass independent up to a certain degree of the preformed structure? Can we speak of a typhous new formation as of a carcinomatous, sarcomatous, syphilitic, &c.? Just upon this point I can bear witness that I have endeavored, according to my powers, by aid of the later methods of investigation, to penetrate into the anatomical nature of the typhus. Yet the result has answered the expectations in but very limited measure. Other authors have stated increase of the nuclei and cellular new formation as the only thing that could be proven. I will at least call attention to several peculiarities, which for lack of other "peculiarities," have always appeared to me to be worthy of mention. First of all, to the enormous dilatation of the capillaries and transition vessels in the medullary infiltrated parts. The otherwise doubly contoured walls disappear to a sharply defined line, which divides the parenchyma from the blood; the blood-current at times appears directly to stagnate, while in the slower coagulation of the blood the colorless blood-corpuscles have collected into small heaps, and at intervals quite alone fill up a capillary vessel. Nevertheless, ecchymoses are very rarely formed, probably because the counter-pressure of the proliferated parenchyma is too great.

In reference to the new formation itself, I have already in the General Part (§ 112) mentioned the circumstance, that not only, as in the catarrhal stage, is the question about a numerical increase of the elements, but next to this, (which also becomes excessive,) about an enlargement of the newly formed element, about the development of a typhus-cell characteristic of the process. We may designate the goal of this development of the individual cell as the typhus-cell, a structure which distinguishes itself from the simple lymph-corpuscle by the greater amount of protoplasm. The protoplasm of the lymph-corpuscles in the amount of space occupied, is scarcely equal to the contained nucleus, while here the protoplasm occupies at least just as much, on the average, however, somewhat more space than the nucleus. The typhus-cell represents the lowest degree, in a certain measure the first onset of an epithelial development; it appears, however, that the persistence and solidity of the epithelial development are wanting to this tumefaction of the protoplasm, as the typhus-cell is maintained for but a short time at this acme, in order then to fall into the most rapid necrobiotic processes.

Finally, touching the peculiarly reddish-white, homogeneous coloring, this is explained by the circumstance that the exuberantly filled capillary net, with its dark red color, here shines through a universally

homogeneous border substance; the dark red shows through this everywhere uniformly toned down into the so-called flesh color.

§ 379. The medullary infiltration is the acme of the typhous changes. From this time the process is backwards, and indeed, in various ways. By far the most of the infiltrated glandular patches slowly return to the normal state by means of colliquative relaxation. The typhus-cells disintegrate into a fatty detritus, and in this form are resorbed like the chyle. Thereafter the tumefaction in the first place disappears from the follicles themselves; the patches of Peyer present a net-like appearance (surface réticulée), in that the places for the follicles sink back everywhere deeply below the level, and thus simulate the meshes of a net, which in other respects is formed by the yet infiltrated interposed mucous membrane. If this has also been freed from its infiltrate, the question is only about a gradual replacement of what was lost, which appears to set in without delay.

§ 380. Meanwhile, the colliquative relaxation is not the only return; a second, less benignant, is presented to us in the so-called sloughing of the typhous new formation. If, in the catarrhal stage, we could establish a participation of almost all the lymphatic apparatus of the intestinal walls, and in the medullary infiltration a very considerable reduction of the process was already observable, in the stage of sloughing an iterated, and indeed, the most considerable reduction of the extension of the disease sets in. Only small sections of individual Peyer's patches, places of the size of a lentil up to three-fourths, nay, even to five-fourths of an inch long, and here and there a solitary gland, instead of the reddish-white, translucent, assume a yellowish-white opaque color, are sharply defined from the surroundings, and then go over into the cheesy necrosis. If this has happened, the healing can only be accomplished by casting off the necrotic parts and by forming ulcers. An increased hyperæmia at the borders of the slough leads to the formation of pus and its loosening, though it is wont for some time to float about attached at the base or to the edges of the ulcer, and by contact and saturation with biliary coloring matter, to assume a yellow, green, or brown color. Finally, it passes away in shreds and leaves behind an ulcer, which, being exactly of the size of the sequestrum, commonly shows the last connective tissue stratum of the submucosa as a base. In severe cases the ulcer penetrates yet deeper, and the casting out of the sequestrum becomes identical with the perforating opening into the abdominal cavity. In that case, from the beginning the infiltration had not only been continued through the entire submucosa, but also into the connective tissue interstices of the muscular coat up to the subserosa and the serosa.

The healing of the typhous ulcers stands in immediate connection with the separating inflammation. If the slough is loosened, a small quantity of germinal tissue is produced at the floor of the ulcer; the

primarily very steep edges of the ulcers sink down in consequence of colliquative relaxation, cover from the sides a portion of the floor, and are soon fastened to it by cicatricial tissue; then that which yet remains uncovered, afterwards forms a smooth, shining surface, pigmented at the edges, upon which villi, glands, or other attributes of the mucous membrane are never again found. By transmitted light these places appear thin and transparent, which is to be ascribed to the want of mucous membrane.

In reference to the not infrequent intestinal hemorrhages in abdominal typhus, it is to be observed that the insignificant and not hazardous ones, which frequently occur, ensue from the very hyperæmic edges of the ulcers by exhalation; the severe ones, on the contrary, from larger vascular branches, which previously conveyed the blood to the necrosed tissues, and which now have been torn through by a somewhat premature loosening of the sequestrum, perhaps by the passing by of balls of excrement.

§ 381. So far the disease proper of the mucous membrane. With it is combined, without exception, an affection of those mesenteric glands which receive the lymph from the medullary infiltrated portions of intestine. As the ileum is constantly wont to be most intensely affected at the ileo-cæcal valve and a foot above it, we have to expect also in this region the most peculiar changes of the lymph-glands. In a histological relation, they are a true copy of the primary diseased condition. To a moderate degree of catarrhal tumefaction follows a colossal medullary intumescence, which is not far behind the scrofulous in circumference. The anatomical boundary between cortical and medullary substance becomes impossible to the naked eye. The microscope shows that the follicles and their prolongations into the medulla (lymph-alveoli and lymph-trabeculæ) are the principal seats of the changes, while the lymph-sinus, and especially the connective tissue, only present a moderate infiltration with typhus-cells. Here, that is to say, in the lymph-alveoli, of which, as is known, fifteen to twenty are to be counted upon a longitudinal section of a medium-sized lymph-gland, we in the first place meet with that enormous ectasy of the capillary net, which appears to me to be generally characteristic of the medullary condition. Beside the ectasy, there is not at all infrequently a striking "occlusion" of very many capillary loops, but also of larger vascular trunks, by a dark granular mass, concerning whose nature I have as yet not been able to come to any satisfactory conclusion. Furthermore, the condition of the adenoid trabecular system is exceedingly surprising. Its collective trabeculæ are thickened three or fourfold, the nuclear places peculiarly tumefied, the nuclei vesicular. Evidently the old net of anastomosing cells has again become alive. The shrivelled cell-bodies are thickened by intussusception; the nucleus is ready again to take up its old rôle as cytoblast. At many places also the continuity of the

net is already interrupted, and we see spherical rounded cell-heaps, which loosely fill out these gaps. The kind of cell-formation is pre-eminently that of simple division. By the side of this, however, the endogenous production also very frequently occurs. The edges of the lymph-trabeculæ, therefore the border of the lymph-current, are often so thickly beset with mother-cells, that more mother-cells may be counted than ordinary lymph-corpuscles. The ultimate goal of the development, however, is here also the typhus-cell as numerously developed as possible. If the climax has been attained, these structures fill every space which offers beside the bloodvessels in the interior of the lymph-gland, among others the lymph-passage itself. It is absolutely impossible, even with the best injection-fluid, to fill up the lymph passage of the medullary gland, and by the injection we can recognize how far the acme of the swelling has advanced in a gland. In this connection the proposition prevails, that here, as in other progressive changes of lymph-glands (scrofulosis, cancer, &c.), the peripheral portion nearest the focus of disease, from which the infectious lymph comes, begins to swell first of all, and that from here the process gradually advances over the whole parenchyma. Decomposition then also proceeds in this sequence. This is almost always a colliquative relaxation, with complete fatty degeneration of the collective typhus-cells. As, however, as we saw, all the lymph and connective tissue corpuscles, *i. e.*, almost all the normal cells of the gland have gone over into the "typhus-mass," we comprehend how almost nothing now remains but the capsule and the bloodvessels. The highest degree of withered collapse is attained, at the same time the temporary hyperæmia has led, especially in the capsule, to distinguishable extravasations, with subsequent formation of pigment, so that a slaty gray coloring also figures as a characteristic sign of typhus-glands that have been swollen.

It must be regarded as a very rare result, when here and there a partial cheesy necrosis takes place in the typhous mesenteric glands. Virchow has repeatedly called attention to this possibility. The caseous slough is then separated by a purulent inflammation; we have a small abscess, and the question now is, what yet occurs. If the abscess bursts through into the abdominal cavity, peritonitis at least threatens. Upon the other hand, the pus may inspissate, afterward calcify. The calcified node is surrounded as a foreign body by a connective tissue induration, and the process is thereby concluded.

§ 382. All other tumefactions coinciding with the typhus processes, new formations, &c., point as the elementary process to the same series of progressive and retrogressive conditions as those hitherto described. We possess the least histological detail in relation to the enlarged spleen. It is not yet decided, in the various stages of the disease, how large the share of the hyperæmia and how large that of the new formation is. A genuine medullary infiltration is here and there observed

upon the Malpighian corpuscles. The more rarely occurring typhus-depots in the various serous membranes, in the liver and kidneys, are quite analogous to the metamorphosis of the intestinal mucous membrane. Upon the changes of the muscles in typhus (Zenker) we will report more minutely at another place.

2. *Tuberculosis.*

§ 383. If one betake himself to the study of tuberculosis of the mucous membrane, one must distinctly distinguish two things, tuberculosis of the mucous membranes, and the diseases of mucous membranes of tuberculous persons. In but few cases is the origin and decay of tubercles the only, somewhat more frequently the main affection; but ordinarily the tubercle formation proper, beside the non-tuberculous changes, plays a directly subordinate rôle, perhaps as the exciting or continuing cause, as the citadel of specificness and incurableness of the process.

§ 384. What tuberculosis may do in itself, what disturbances are to be specially ascribed to it, one best sees in the *tuberculosis* of the urino-genital mucous membrane. The tuberculous ulcer of the urinary bladder is a sharply-circumscribed, roundish loss of substance of the mucous membrane, with dirty yellow, lardaceously infiltrated edge and floor. More accurately examined, this lardaceous infiltration exhibits itself as a layer of "genuine tubercles;" partly gray, partly cheesy miliary nodules lie densely crowded together, bound, and form upon the one side the ulcerated surface; upon the other they advance with the youngest and smallest nodules, placed foremost for some distance, into the healthy parenchyma of the mucous membrane. In fact, here, in the place of the plastic inflammatory infiltration, the formation of miliary tubercles has occurred; in the place of purulent destruction, the softening and dissolution of the tubercles which have become cheesy. As a rule, beside the older, fully formed ulcers, we also find the beginnings of the process in single gray or cheesy miliary nodules, which are sprinkled into the most superficial layer of the mucous connective tissue, alongside of others, which, united into small groups, already exhibit in their centre a slight defect of softening. If the new formation and softening of the tubercles uniformly progresses from hence towards all sides, in the next place there will, of necessity, result a circular deficiency—the tuberculous lenticular ulcer; by the confluence, however, of several lenticular ulcers, larger, often very irregularly-shaped, secondary ulcers are produced. These gradually extend over a constantly larger section of the mucous surface, until it finally happens that we have more diseased than healthy surface, and the relatively intact parts only form narrow borders, which separate the adjacent ulcers from each other.

§ 385. What has been said here first of all of tuberculosis of the urinary bladder, obtains likewise of the other sections of the urino-genital mucous membrane, particularly of the mucous membrane of the ureters. In the latter, however, the catarrhal element already meets us as a very essential complication of the anatomical picture. The tuberculous ureter is in the first place only catarrhal; the swollen mucous membrane yields a thick, tough, purulent secretion, and both swelling and secretion may already call forth a very considerable disturbance in the efflux of the urine, therefore, the clinically most important symptom of tuberculosis of the ureters, ere yet a single tubercle exists. Tuberculosis of the uterus is secondarily complicated with often a very considerable hyperplasia of connective tissue, partly in the submucosa, partly in the muscular structure, hence an actual enlargement of the organ, with which progressive loss of substance at its inner surface is wont to be combined. Still more peculiar is the complication of tuberculous intestinal ulcers with a papillary and polypous hypertrophy of the unimplicated portion of mucous membrane. This may become so considerable, that the dark-red hyperæmic bodies of the polypi up to the size of a pea quite densely cover the surface, and we must first seek the proper ulcerated surface between their bases. Meanwhile this is but a rare complication of intestinal tuberculosis. Much more frequently, and much more difficult to separate from that which actually is tuberculous, just here, is the combination with that scrofulous hyperplasia of the lymph-follicles which we have already learned to know in the mode of its appearance upon the lymph-glands, above (§ 203 *et seq.*).

§ 386. The same localities of the intestine at which the typhous changes take place, are also the principal seats of tuberculosis, namely, the neighborhood of the ileo-cæcal valve and the lymphatic glands there, Peyer's patches, and solitary follicles; only the process is not confined after the manner of typhus to the lymphatic glands and their nearest environs, but only has these for the point of departure, afterwards to follow a peculiar law of extension. And just these primary affections of the closed follicles are of non-tuberculous nature. The gray intumescence, which enlarges the individual follicle to perhaps three times its normal volume, depends upon the same partial new formation of lymph-corpuscles in the lymph-passages and the reticular parenchyma of the follicle, which we have learned to know as the cause of scrofulous bubo; the cheesy metamorphosis, which occurs hereupon, is certainly the same retrogressive process, to which the genuine tubercles also are subject, and consequently from this point a distinction is no longer possible. It is, however, characteristic, that the diseasing of the appertaining mesenteric glands also presents entirely the scrofulous character, and is very well to be distinguished from the quite different anatomical condition of an actually tuberculous lymph-gland.

The cheesy follicles soften from without inwards, and when all the

cheesy material is destroyed, in the relatively healthy tissue we have a sharply circumscribed half spherical loss of substance, the so-called clean ulcer. At Peyer's patches, because of the great proximity of the adjacent follicles, it may even now have proceeded to a confluence of several ulcers of this kind into those larger losses of substance, which because of being bounded on all their outer sides by convex segments of a circle, have been designated as racemose.

§ 387. If we make a most minute vertical section through the edge and floor of one of these ulcers, one perceives everywhere a tolerably broad zone of cellular infiltrated connective tissue. But neither the cells nor the manner of their deposition present anything whatever specifically tuberculous. It also appears that the gradual enlargement of the loss of substance essentially follows, by the advance, step by step, of this infiltration into the neighborhood, and the subsequent resolution of the infiltrate at the surface of the ulcer. The specific tuberculous element accordingly steps completely into the background in the intestinal tuberculosis. We would, however, very much err, if we believed that it was entirely wanting. By more accurate examination we can establish, 1, upon all vessels not capillaries, which are in the neighborhood of the ulcer, and indeed, especially upon the arteries, the presence of a certain amount of miliary nodules in the adventitia; 2, the eventual irruptions beyond the intestinal walls in the subserous and serous connective tissue, upon which we can so often perceive the seat of the changes of the mucous membrane from without, are constantly genuine tubercles. By the experiences given above (§ 115), derived from a minute investigation of the subject, I have convinced myself, that here also they are the lymph-vessels which undergo tuberculous degeneration, that consequently the vascular sheaths only form so strikingly the seats of the tuberculous irruptions, because they at the same time contain the efferent lymph-vessels of the intestine.

The development of the miliary nodules upon the vascular, particularly the lymph-vessel ramifications, is, however, of peculiar interest, because by them the direction is determined in which the ulcer of the intestinal mucous membrane enlarges; namely, this, in contrast to the constantly longitudinal configuration of the typhous ulcers, not exceeding the limits of the patches of Peyer, is decidedly transverse. The tuberculous ulcer of the intestine tends decidedly to the form of a girdle; it, indeed, arises at Peyer's patches, constantly has here also its greatest width, but then pushes beyond the lateral bounds of this, until, at a place on the side opposite to the Peyer's patch of the affected section of intestine, the points furthest advanced, come in contact and flow together. If with this growth of the ulcer we compare the distribution of the bloodvessels upon the intestine, a certain conformity is immediately presented. The arteries and veins enter between the mesenteric duplicature to the intestinal tube at the side situated opposite to the patches

of Peyer, and from here radiate in short trees, whose trunks and main branches run obliquely across the intestinal tube, and whose more minute ramifications from both sides come together where Peyer's patches are situated, at the outer side of the canal. In conformity to this the vascular territories of the intestinal wall are transverse, not longitudinal subdivisions, and a diseased condition which keeps within the bounds of a vascular territory, must *eo ipso* take a transverse direction of development. By finding miliary nodules upon the collective branches of the afferent vessels it is, moreover, clear, that tuberculosis is such a diseased condition, and we comprehend why, in its progress, it maintains a transverse and not a longitudinal direction.

§ 388. Concerning the further consecutive conditions of tuberculous intestinal ulcers, I will only announce, that here hemorrhages and perforation of the intestinal wall are produced in the same manner as in typhus. The tuberculous infiltration of the vascular walls upon the one hand, the serosa upon the other, and the necrobiotic loosening of this infiltrate, even of necessity leads to an opening, at one point of the blood tract, at another of the peritoneal sac. In both cases, however, the failure of those natural healing arrangements is required, which are ordinarily wont to prevent extreme accidents, in the one, the seasonable coagulation of the blood in the endangered vessel, in the other, the seasonable adhesion of the serosa with another part of the peritoneal surface. I have seen in one case, where five tuberculous ulcers of the ileum had perforated, but not into the abdominal cavity, but into other sections of the intestinal tube, which had previously entered into connection from without with the ulcerating places. Naturally at the same time all peristaltic movement was checked here, and the intestinal contents circulated contrary to rule through numerous false passages in the abdominal cavity, as the openings of communication were in part greater than the intestinal lumen itself.

§ 389. If we now pass to tuberculosis of the *laryngeal* and *bronchial mucous membrane*, we enter upon the sphere where the question, how much of it is actually tuberculous? is by far the most difficult to answer. Virchow does not hesitate to admit the actual production of the so-called tuberculous ulcers of the larynx from miliary tubercles, and for their origin and extension in surface and depth lays down the same mode which, in § 384, we learned to know upon tuberculous ulcers of the urino-genital tract. Other authors, of whom I will name Rühle, entirely deny the occurrence and participation of the miliary irruption; and the explanation of Virchow, that the miliary tubercle can so rarely be demonstrated upon the tuberculous ulcers, only because just here it is of a peculiarly perishable nature, at least admits the fact that it can rarely be demonstrated.

If we now seek at the hand of a careful histological analysis, especially with the aid of vertical sections through the affected parts of the

laryngeal and tracheal mucous membrane, in the first place, to separate that which is decidedly non-tuberculous, we must from the very beginning declare as non-tuberculous every affection of the closed follicles. At the larynx proper, it is true, closed follicles do not occur, but certainly immediately above the epiglottis, at the base of the tongue, isthmus of the fauces, and at the upper part of the pharynx; and the tuberculous ulceration is very commonly complicated at the larynx proper, with ulcers, which have their origin in a scrofulous inflammation, hyperplasia, and disintegration of these pharyngeal follicles. Furthermore, the ulcerations proceeding from the outlets of the mucous glands of the larynx and trachea are non-tuberculous. At another place (§ 356) I have more fully stated how, in long-persistent catarrhal conditions of mucous membranes, the mucous glands are wont to be ectatically hyperplastic. Here a second form of the participation of these organs follows upon the chronic catarrhal changes of the mucous membrane, which, to be sure, I have as yet only found at this one place, and in this one case. Hence, for the present, I must regard it as a peculiarity of the laryngo-tracheal mucous membrane, and specially as a very important constituent of that anatomical entity, which we concisely designate as laryngeal phthisis.

If we bend open a trachea, whose mucous membrane is in a condition of chronic catarrh, and wipe away the mucus from the surface, we perceive very well with the naked eye the numerous outlets of the mucous glands. They are very densely placed in the interstices between the rings of cartilage, and are also peculiarly wide here, while upon the elevations over the cartilaginous rings they are less numerous and narrow, in some places also they are entirely wanting. If now from below we exert a slight pressure upon the trachea, at the spot pressed upon, out of the openings mentioned small quantities of tough mucus will stand out, which are sharply defined all around, and look like gray translucent pearls. If now one of these pearls, upon accurate examination, exhibit at its periphery a narrow yellowish-white border, we have to do with the beginning of the ulceration now in question. For this yellow border is pus, pus which was produced by the subepithelial connective tissue of the glandular excretory duct concerned, and was poured out into its lumen. By the emptying of the accumulated glandular contents this drop of pus was first of all pressed out, in order then to be uniformly distributed at the periphery of the drop of mucus following after.

The formation of pus in the glandular excretory ducts may exist for a time as a purulent catarrhal secretion, but it certainly very soon goes over into a formation of pus with loss of substance,—an ulceration. We get a round, low, funnel-shaped ulcer, with a narrow, but intensely yellow edge, by which it is sharply defined from the surrounding hyperæmic mucous membrane. In the centre of the loss of substance, either

the dilated excretory duct, or the gland itself, or after suppuration of the glandular body, a correspondingly large, roundish excavation forms at the same time the deepest point of the floor of the ulcer, so that the catarrhal ulceration of glandular excretory ducts in fact possesses peculiarities enough to distinguish it from allied conditions. Only when in the continued course the ulcer extends as well in surface as in depth, do its original characters disappear. By the confluence of adjacent ulcers, for example, arise "racemose" contours, the same which have generally been regarded as characteristic of the "tuberculous" ulcer, nay, the cluster form is peculiarly beautiful here, and yet more distinctly stamped than in the tuberculous ulcers of the intestine. The advance of the floor of the ulcer in depth is especially favored by the suppuration of the bodies of the mucous glands. A purulent inflammation of the encapsuling and the interstitial connective tissue of the gland, leads to the decay and dissolution of the acini, the whole gland melts away, and if we consider that the mucous glands of the air-passages do not lie in the mucosa, but in the submucosa, we comprehend that just these ulcers most rapidly bring about deeply penetrating destructions. In fact we very soon find the floor of the ulcer reaching the neighborhood of the cartilaginous rings or the laryngeal cartilage, and thereby a new field is opened to the destruction.

The cartilage of the larynx and trachea, from its non-vascularity and its manifestly sluggish nutrition, is more disposed to necrosis than to a gradual dissolution layer by layer. Hence, if the inflammatory irritation attacks the perichondrium, it not at all infrequently happens that ere the cartilage itself has undergone any considerable change in its form, color, and consistency, a purulent perichondritis has islolated the whole organ, sequestered it, and placed it ready for being cast out as soon as the communication of the abscess with the floor of the ulcer is wide enough to allow of its passing through (arytenoid cartilage). To be sure, as a rule, this catastrophe is preceded by a stage of the ulceration proper, in which the cartilage is only laid bare at one side, and forms by this the base of the ulcer, while otherwise the perichondrium is yet everywhere firmly connected with the surface of the cartilage. Upon vertical sections we can then very well perceive the progress of the destruction, in that the outermost cartilage-cells have been transformed by division into groups of pus-corpuscles, while at the same time the cartilage-cavities have increased in circumference at the expense of the basis-substance to such an extent, that immediately before the opening externally they are in contact by their periphery. Hence the floor of the ulcer, so far as it lies in the cartilage, is entirely tapestried with widened and pus-filled cartilage-capsules. Meanwhile, these changes, though very considerable, are confined to a comparatively small space. Already the third or fourth row of the contiguous cartilage-cells is quite unscathed; at most we may here and there perceive

the beginning division of the nucleus. At the trachea, in the course of this ulceration, it may go so far that the majority of the cartilage-rings are laid bare at their inner surface, whereupon one after the other, in the next place, is raised at the ends, in order gradually to be entirely loosened and cast out by an impulse of coughing.

§ 390. Consequently, when we see that the most important and the severest destructions of the larynx and the trachea are produced alone by catarrhal inflammation and ulceration, we reasonably ask ourselves what then remains there for tuberculosis to do? Are there in general tubercles in "phthisis laryngea," and what part do they take? It is manifest that, according to my experience, I must hesitate to simply transfer the mode of origin and growth of "tuberculous ulcers" in the tuberculosis of the urino-genital mucous membrane to the laryngeal mucous membrane. I must much rather maintain that the real destruction is not accomplished by the decay of the tuberculous infiltrate, but by means of an inflammatory new formation. Notwithstanding this, I believe I may regard myself as convinced that miliary tubercles may certainly here also come to development, since, in the first place, I appeal to the authority of Virchow, who has indisputably observed tuberculous ulcers at the larynx; upon the other hand, upon certain occurrences upon the cross-sections of ulcers described above, which I can provisionally interpret only as irruptions of miliary tubercles; thus, especially upon the ulcers of the larynx and epiglottis we very commonly find at some distance from the surface in the midst of yet intact connective tissue, roundish depots of cells of the size perhaps of a glandular acinus, cell-depots, which take the carmine coloring far more greedily at the edges than at the centre, which points to a globular grouping, and reminds very much of the behavior of miliary tubercle. These tubercles certainly lie so individualized and beside the inflammatory infiltration of the real surface of ulceration, are such insignificant new formation, that I would only regard them as a pledge of the connection of this process with constitutional tuberculosis. At the most, we might ascribe to them the valuation of a permanent inflammatory irritation, and to trace back to this the obstinacy and the tendency to relapse, which is peculiar to these catarrhal inflammatory conditions.

On the occurrence of genuine miliary tubercles upon the smaller bronchi, in the proximity of the so-called tuberculous cavities, we will treat under the Respiratory Organs.

D. Tumors.

1. *Papilloma.*

§ 391. The papillomas of the mucous membrane are decidedly to be distinguished from the tuberous and polypous elevations of the mucous

surface conditioned by hypertrophy and ectasy of the glands. We meet with the papilloma in the following various forms and at the following various points.

a. Upon the mucous membrane of the oral cavity, the vagina, the inner edge of the anus, in short, at those half mucous membranes, which form the transition from the outer skin, the papillary forms of the outer skin are again found in but little modified structure. The ordinary wart is represented by roundish, flatly attached, berry-like bodies on the gums or the inner surface of the cheeks, which are very similar to condylomata, and distinguish themselves from them only by the greater compactness of the epithelial covering. Pointed and broad condylomata occur in so much purer form, as the quality of the indigenous epithelium is originally more similar to the epithelium of these tumors. Meanwhile, the pointed condylomata keep as rigidly as possible to the borders of the external skin, while, to be sure, broad condylomata are here and there also found in the oral cavity or the vagina itself.

b. Upon the mucous membrane of the gall-bladder, the urinary bladder, and the external orifice of the uterus, at places, therefore, where a cylindrical epithelium or a transition epithelium normally exists, the papillomas are also covered with cylindrical epithelium.

The papilloma of the urinary bladder, also called villous cancer, better, villous tumor of the urinary bladder, has its seat constantly in the trigonum between the outlets of the two ureters. There arises here a roundish, very soft tumor upon a broad base, an inch high above the level of the mucous membrane. This is clothed by so thick a layer of cylindrical epithelium that the very wide vessels shine through with a rosy color, and the whole appears externally not unlike a medullary cancer. In itself, however, this tumor has nothing whatever to do with carcinoma; rather, even a superficial examination proves, that the tumor may be broken up into richly branched villous trees, and in general consists of nothing but such villi. It is conformable to this when we hear of successful extirpations of a papilloma of the urinary bladder without a relapse. The individual villus is, upon the one hand, characterized by an enormously wide and thin-walled bloodvessel, which rises into its centre and towards the apex curves with a varicose dilatation; upon the other hand, by the already mentioned three to four-fold stratum of cylindrical cells, which are placed so immediately upon the bloodvessels spoken of, that we cannot properly speak of a real connective tissue body of the villus.

At the external orifice of the uterus the papillomas are richer in connective tissue, less rich in vessels and epithelium. A simple cylindrical epithelium covers the tolerably plumply formed terminal club of the dendritic vegetation, and in no case could an ectasy be demonstrated

upon the vessels. The explanation concerning papilloma cysticum given in § 70, moreover, refers just to these papillomas.

At the gall-bladder in man there occur only extraordinarily small and insignificant forms of papilloma; on the contrary, Virchow observed and described the gall-bladder of a cow, upon whose thickened wall "so large an amount of partly villous, partly cylindrical, solid outgrowths were seated, that the mucous surface seemed to have quite vanished at a certain zone."

§ 392. The relation of the mucous membrane papilloma to the epithelial carcinoma of the mucous membrane is interesting and important. Namely, there not only demonstrably occurs a transition of papilloma into epithelioma, or of the secondary combination of an epithelioma with papillary proliferation at the edge and floor of the ulcer, but it is also frequently asserted, that the mucous membrane over a cancer developing in the submucosa is disposed to papillary proliferation. For my own part I have never observed the like, and hence can state nothing as to the more intimate connection of both these phenomena. According to Virchow's perception, the papilloma formation is, in the first place, a simple hyperplasia, caused by the irritation of the contiguous carcinomatous depot; afterwards the possibility enters of a transformation into a genuine villous cancer, if the carcinoma advances by the continuous infiltration from below into the connective tissue of the papillæ; the stomach and urinary bladder are the main seats of this genuine villous cancer, which meanwhile may be identical with our cylindrical epithelioma.

2. *Carcinoma.*

§ 393. The mucous membranes as epithelial-clad outer surfaces of the organism, are everywhere disposed to the production of epithelial carcinomas, to the production of glandular carcinomas, naturally only in so far as they contain open-mouthed glands. The striking dissimilarities in the average distribution of carcinoma over the mucous tract are especially to be traced to the latter circumstance. Furthermore the transition-place of the individual sections of the mucous tract appear to be selected with predilection on the part of epithelial carcinoma, probably because especially at such places, as a rule, there is superadded some mechanical injury, although physiologically occasioned.

§ 394. If we begin our consideration with the antechambers of the mucous membrane system, which are situated in the head, we meet, apart from the cancers of the lips, eyelids, and alæ of the nose belonging to the outer skin, with a genuine soft glandular cancer of the mucous membrane in the *nasal cavity*. This develops in older individuals upon the ground of a hyperæmic condition of the collective structural parts of the mucous membrane which has already existed for some time; in children it arises without any preliminary stage. The car-

cinoma has a predilection for advancing into the antrum highmorianum, swells out the superior maxilla, and appears as one of the various so-called carcinomas of the superior maxilla. The decline of the patient by cachexy is so rapid, that we now begin to desist from all operative attempts; the tumor consists entirely of incompletely developed glandular tubules, which are produced by an excessive proliferation of the epithelium of the mucous glands.

§ 395. In the *oral cavity* the tongue especially presents a favorite object for the carcinomatous destruction. As a rule, the question is about a squamous epithelioma, which, however, corresponding to the greater delicacy of the normal pavement epithelium of the tongue, distinguishes itself from the harder squamous epitheliomas of the outer skin by its softness and a rapidly occurring tendency to break down. The abundance of bloodvessels, loose connective tissue, and above all of wide lymph-passages in the tongue, make its parenchyma an exceedingly favorable soil for infiltrative new formations. Hence the local destruction comes decidedly into the foreground of the entire representation of the disease. The first nodule is apt to be seated at one of the edges of the tongue. We say, the irritation of a sharp-edged, because decayed, tooth may contribute its part to the development of the cancer. The first nodule is generally extirpated by a V-shaped cut, but the relapse follows already very soon after the extirpation, and so after each new extirpation in always a shorter time, until the whole tongue is destroyed. We have metastases indeed as well in the adjacent lymph-glands as in the lungs, but these secondary cancers constantly remain of very subordinate significance.

The so-called soft carcinoma of the tonsils is a soft lymphadenoid sarcoma, which readily passes from the tonsils to the palatine arches and the isthmus.

§ 396. At the entrance into the *respiratory tract* we meet with a tolerably soft squamous epithelioma, which characterizes itself from the squamous epithelioma of the tongue by its tendency to papillary proliferations. The new formation finds in the substratum of the laryngeal mucous membrane a soil, than which one more unfavorable to the progress of an infiltrative new formation could scarcely be imagined. Upon a quite tense fibrous submucosa follows a layer of tendon-like tissue; under this and throughout the entire submucosa and mucosa are distributed rich nets of elastic fibres. What wonder, if the new formation takes more of an outer direction, and for years produces long papillary proliferations ere it penetrates into the deeper parts of the neck.

§ 397. At the *œsophagus* first one hard squamous epithelioma after another forms a girdle tumor, afterwards a girdle tumor with infiltrated edges and base; the tumor enlarges, it may finally happen that the mucous membrane is deficient all around for the distance of two to three inches, while the base of the tumor has attacked the adjacent air-

passages from without and has destroyed them. The opening of the air-passages through the base of the ulcer is a very critical catastrophe. The point of this abnormal communication of the œsophagus and the air-passage is, as a rule, not in the trachea, but in the posterior wall of the left bronchus. As is known, the left bronchus crosses the œsophagus in its middle third, and just here the œsophageal cancer is wont to take its position. It is correctly conjectured, that a mechanical force co-operates in this localization, and as such the circumstance is accused, that every large morsel gliding down the œsophagus, presses the anterior wall of this against the posterior wall of the rigid bronchus. Naturally the perforation of the air-passages is only one of the numerous dangers which the œsophageal cancroid occasions to its bearer. The girdle tumor may destroy by stenosis; the transition to the mediastinum favors, during the inspiratory decrease of pressure in the cavity of the chest, the entrance of air from the œsophagus into the loose cellular tissue, and may become the cause of a genuine emphysema of the whole subcutaneous cellular tissue; the floor of the ulcer may become a regular ulcerative cavity, in which the food sticks and decomposes, &c.

Alongside of carcinoma of the middle third, carcinoma of the cardia and other points of the œsophagus are in point of frequency very much in the background; on the other hand, I was twice in a situation to observe one quite flat and very many softer cancer-forms which had extended more diffusely over entire sections of the œsophagus.

§ 398. The *stomach* is characterized as the peculiarly frequent site for carcinomas, since here in equal frequency are found a soft, a hard, and a gelatinous glandular cancer, as well as a cylindrical epithelioma. The collective glandular carcinomas arise in the mucosa proper, and then pass over from here to the submucosa. I say this expressly, because we formerly made an essential difference between "submucous" and "mucous" cancers of the stomach. It is correct, that, as a rule, the transition spoken of ensues at a very early period, and that the cancerous proliferation proceeds much more rapidly in the wide and numerous nets of lymph-vessels of the submucosa than in the mucosa. Hence the cancer not at all infrequently imposes as a level infiltration of the gastric walls, over which the, for the greater part unchanged, or merely atrophic, mucous membrane passes and is movable upon it, while it is completely adherent to it at but one point. This one point is the point of departure, and the oldest part of the entire degeneration. In most of the cases which are investigated, it is beset with an ulcer, which has destroyed the place of the first origin of the carcinoma, and therewith the possibility of passing a valid judgment upon the participation of the glands of the mucous membrane in the first origin of the cancer. So much the more valuable, therefore, are the statements of Waldeyer (Virchow, Archiv, vol. 41) who in spite of these difficulties succeeded

in establishing the mucous and peptic glands as the developmental foci of the new formation.

A condition more commonly found in *soft carcinoma* of the stomach, therefore, is that of an ulcerating surface of several square inches in extent, surrounded by a bulwark-like thickened, because already carcinomatously infiltrated, edge of mucous membrane. The tumor, as very frequently occurs, arises at the lesser curvature, and from here has passed partly to the anterior, partly to the posterior gastric walls. The ulcerated surface itself is covered with shreds of tissue, which float when water is poured upon it. They are the remains of the cancer-stroma, which withstand the destruction somewhat longer than the cancer-cells. They are now loosened piecemeal, especially under the action of the gastric juice, and thereby give occasion to those pathognomonic hemorrhages, in which the blood is poured out in small portions, immediately coagulates, and assumes a brownish-black color, so that numberless particles of this coagulated blood give the contents of the stomach, that is, what is vomited, the appearance of coffee-grounds, chocolate, &c. If we observe a cross section through the wall of the ulcer, we perceive, how at the border towards the healthy parts, the glandular layer of the mucous membrane is raised up by the tumor, how it is suddenly depressed over the summit of the tumefaction, in that the glands are uniformly pressed together from both their ends, and the contiguous ones separated. At last, only an interrupted chain of atrophic glandular remains points out the place of the veritable mucosa; between it and the muscular coat lies the whole thickness of the cancerous degeneration, which may amount to from four to six lines. Upon the other side, the transition to ulceration is brought about by the fatty degeneration of the cancer-cells. Even the unaided eye recognizes the yellow points and streaks of the retrograde cancer, and sees these everywhere surrounding the floor and the edges of the ulcer. The disintegration itself may here be accelerated by the action of the gastric juice upon the necrobiotic tissues, at least this is wont to be more protracted in the quite analogous diseases of the uterus, the urinary bladder, &c., and also not to make such rapid progress.

It is otherwise with *scirrhus ventriculi*. This much slower growing carcinoma mostly succeeds, by starting from the lesser curvature, where also it most readily arises, in surrounding the entire periphery of the stomach. The submucosa and the mucosa are transformed into a white, compact induration, of from two to three lines thick, which, when the circle is completed, for its part bestows upon the central part of the stomach the form of a rigid tube, between one and two inches in diameter, at which the fundus hangs like a loose bag. Microscopic investigations just here shows a very decided analogy to the epithelial arrangement with glandular epithelium. Not that the cells and cell-

nests are peculiarly large and numerous; on the contrary, the connective tissue stroma decidedly predominates. But the form of the cell-nests is relatively regular; namely, they are lengthy stretched tubuli, circular upon a cross section, in which the small, but among themselves of equal size, epithelial cells are arranged almost radiating, although a central lumen is wanting.

The *gelatinous cancer* of the stomach also characterizes itself by its predominant tendency to destruction, in contrast to ulceration, and constantly attains the condition of a girdle tumor before open ulceration. In this manner it may bring about very considerable stenoses. The ulcer is a slower disintegration advancing from within outwards, without hemorrhage or any great secretion. Were it not for the possibility of the carcinoma extending to the peritoneum, the gelatinous cancer, as well as scirrhus, would be characterized from the other carcinomas, by a certain absence of danger of the primary changes.

In reference to the texture, the horizontal sections of Köster have become of importance, in so far as they undoubtedly place the growth of the infiltration in the lymph-passages of the gastric walls. The same author is disposed to transfer his acquisitions obtained upon the cylindroma (§ 173) concerning the participation of the endothelium in the processes of new formation, also to the gelatinous cancer of the stomach. That I cannot well raise any fundamental objections against this, my ideas of hard, glandular carcinoma, laid down in § 159, may prove. I would regard this condition as an original epithelial infection of the lymph-endothelia proceeding from the glands. Still I beg that regard may be had to the reserved position which I assumed in the case of colloid cancer.

§ 399. Of greater clinical importance, and of just as great anatomical interest, is the *extension of the three gastric cancers mentioned, to the contiguous organs.* After the submucosa follows, in the first place, the muscular coat. In the muscular coat the carcinomatous infiltration traces out the narrow lines of the interstitial connective tissue. The muscular bundles undergo therewith—probably in consequence of the persistent irritative condition in which they exist—a hyperplastic thickening. At least this is the rule in gelatinous cancer and in scirrhus ventriculi. Upon a vertical section through the gastric walls, even with the unaided eye we can trace the gradual increase of thickness of the muscular bundles from the healthy towards the diseased parts. If to this we reckon the amount of substance which the carcinomatous degeneration of the interstitial connective tissue adds, we comprehend how the muscular coat may be thickened from three to five times its normal volume.

If the muscular coat is destroyed, the cancer reaches the visceral peritoneum. The first nodules then arise in the subserous connective tissue. We often distinctly see how primarily, in their arrangement,

they are placed in rows dependent upon the run of the muscular bundles, *i. e.*, along the connective tissue septa corresponding to these. The adjacent ones, however, soon flow together, and we get flat, irregular nodes, which present to us the peculiarities of the carcinoma concerned, in the purest possible form.

The signal for a general degeneration of the entire sac is almost always given with this appearance at the peritoneum. Probably by the mutual displacements of the viscera, portions of these cancerous nodules are loosened and are pushed to and fro over the smooth surfaces, until they remain sticking in a fold, a recess, or such like, and give occasion here for the development of new cancer-nodules. The whole impression—to use Virchow's language—is, as though seed had been sown, which had fallen here and there and had germinated. In this connection the soft carcinoma and scirrhus behave quite alike. Only the gelatinous cancer now also assumes a distinct position, since it pursues the prodigious task of converting the whole peritoneum into gelatinous carcinoma, entirely by continuous infiltration, without leaping from place to place. The thickness which the single peritoneal layer attains after complete infiltration is the very considerable one of from two to three lines; the omentum, as a duplicature of the peritoneum, is transformed into a board-like plate of the thickness of a thumb, likewise the mesentery, the ligaments. It is manifest that under these circumstances the most considerable disturbances in the peristalsis are unavoidable. To all this, however, inflammatory processes are yet associated, an abundant outpouring of sero-fibrinous exudation, smaller hemorrhages, adhesions. The same are also found with soft cancers and with scirrhus. Yet scirrhus, beside this, characterizes itself by an exceedingly remarkable peculiarity, which, without doubt, depends upon more minute histological processes, but the principal point of which has remained up to the present completely unapproachable: I mean the contraction of the connective tissue in the surroundings of the scirrhus nodes. Even the narrowing of the stomach occurring simultaneously with the thickening, of which we spoke above, is to be placed to the account of this retraction. Here, however, there exists no prospect at all of ascertaining anything more special concerning the process. The relations are much more observable at the peritoneum. Especially may we expect to obtain disclosures in the transparent structure of the omentum. In fact the omentum shrinks together into a hard cord penetrated by cancer-nodes, which omentum, if the ascites permit, is already to be felt through the abdominal coverings in the region of the transverse colon. If, however, we spread it out and seek to ascertain the cause of the shrinking, we get the impression, if we make use of a low magnifying power, as though we had grasped at one place a flatly spread-out cloth, and had gathered it together; the folds radiate from all sides upon this point; instead of the part gathered together, how-

ever, the smooth, white scirrhus node appears as the central point of these radiating folds. For myself I am now indeed convinced that actually a certain consumption of pre-existing connective tissue takes place here, and that the scirrhus node represents this quantity of consumed connective tissue; I am not, however, in a position to give an explanation concerning the "how" of this consumption.

This degeneration of the peritoneal sac naturally also leads to a rigidity and shortening of the mesentery, consequently to the most considerable disturbances of the peristalsis; as a rule, however, to this is added a very intimate adhesion of the abdominal organs to each other, so that, for example, the small intestine is wont to be converted into a single globular ball, within which the intestinal lumen has a perfectly labyrinthine course, that presents almost insurmountable obstacles to its anatomical pursuit.

§ 400. In the place of the various squamous epithelial cancers, which we have learned to know from the lips down to the cardia, the *cylindrical epithelioma* begins at the cardia. This chooses its seat in the stomach, by far most frequently in the pyloric region; it is often seated exactly upon the fold of mucous membrane which divides the stomach and the duodenum. Here it successively forms a flat tuberous elevation, a fungus seated upon a broad base, and, finally, a polyp, often globular, above the size of a pigeon egg, which is attached by a relatively short pedicle. In the latter form the tumor is particularly adapted to actually stop up the lumen of the duodenum, and in this manner, *i. e.*, by mechanical interruption to the taking up of nutriment and to digestion, to produce conditions of acute marasmus, which become fatal, if a seasonable softening and dissolution of the tumor do not occur. Thereupon there remains a smooth loss of substance, in whose edges we can follow the formation of the tumor further. It here presents itself in that close relation to adenoma of the intestinal tract, which I have more specially described in § 171.

§ 401. In the lower sections of the digestive tract there yet follows a soft glandular cancer of the *colon*, which readily forms girdling ulcers with strongly contracted, because induratively thickened, bases, and thereby gives occasion to stenoses of the intestine and their consequences. Just there is found a flat adenoma; one similar occurs at the rectum. (Klebs, Leyden.) The squamous epithelioma of the rectum, immediately above the anus, in the form of cauliflower tumor, is wont to attain a considerable circumference, ere from the mucous glands it penetrates destructively into the deeper parts (§ 166, note 2).

§ 402. Of the urino-genital tract—if we reckon the cancroid of the penis to the outer skin—the *uterus* is undoubtedly the part most threatened with carcinomas. Fully one-half of all cases of the so frequent uterine cancers are epitheliomas. These either proceed from the mucous membrane of the cervical canal, or from the vaginal por-

tion, in such manner, that in both cases the boundary between the vaginal portion and that of the cervical canal is not overstepped for some time. The cancroids of the vaginal portion very commonly arise as soft papillomas or cauliflower growths; the transition ensues, like as in the papillomas of the outer skin, by the descent of the epithelial border into the subepithelial connective tissue. The destructions which the epithelial carcinoma of the uterus cause are, under the circumstances, quite enormous. The muscular structure presents the longest resistance. If this is destroyed, the loose connective tissue between the organs of the true pelvis forms a very much more fertile domain for the luxuriant enlargement of the tumor. A cavity of several inches in diameter, whose interior is the place of the most offensive, putrefactive products of decomposition, is bounded above by the yet undestroyed remains of the body of the uterus, anteriorly by the posterior wall of the bladder, and behind by the anterior wall of the rectum, while below, the vagina, likewise destroyed at its upper part, forms the way outwards. At a later period, perforations follow in the floor of the ulcer; the opening into the bladder produces a vesico-vaginal fistula, the opening into the rectum a recto-vaginal fistula, the opening into the peritoneal sac produces peritonitis. The latter very often forms the close of the painful condition of the sufferer.

§ 403. The glandular cancers of the womb have their seat in the body proper of the uterus. They condition a frequently very considerable, more uniform increase of volume of the latter; the cavity of the true pelvis is filled up, the rectum and the bladder pressed upon and displaced. If we open the organ, the cavity is seen distorted by the cushion-like, convexly projecting walls, the wall in its entire thickness (up to three inches) uniformly medullary white; the difference between mucous membrane and muscular structure has disappeared, since the proliferated glandular tubuli have penetrated through the entire thickness of the latter.

§ 404. Of the *urinary bladder*, the villous cancers, which occur at the trigonum vesicæ, are especially worthy of mention. (See § 392.) Furthermore, there is now and then found a squamous epithelioma in the calyces and the pelvis of the kidneys. It is wont here, at a tolerably early period, to pass over to the apices of the adjacent papillæ, and to advance into the renal parenchyma by a milk-white zone of infiltration from two to three lines thick, a genuine phthisis renum cancrosa.

VI. ANOMALIES OF THE LUNGS.

§ 405. In all treatises which are concerned with the respiratory organs, we distinguish between the *air-passages* on the one hand, and the *parenchyma* proper upon the other. This distinction is thoroughly natural, not only with regard to the function of the parts, but also because the smallest bronchi do not pass over gradually into the infundibula, but by a very distinctly marked break. Pathological histology, also, has no cause to set this aside. Hence, if we, in the following section, intend treating of the pathological histology of the lung, we understand thereby only the changes of the respiratory parenchyma; the changes of the bronchial mucous membrane were already, by implication, treated of in the preceding section, and if, nevertheless, we will frequently enough be in a situation to mention certain alterations of the bronchi, which stand in causal connection with alterations of the parenchyma, we will deal partly with known quantities, partly we will have several gaps to fill up, which had to be left open there in the interest of the representation.

§ 406. Meanwhile before we subject the pathological changes of the parenchyma of the lung to a more searching analysis, we must touch upon a question of the normal histology of the lung; the positive or negative answering of which is of the utmost importance to us, but which, notwithstanding many investigations only lately directed to it, must yet always be regarded as open: Has the inner surface of the alveoli an epithelium or has it none?

As the function of the lungs depends entirely upon the most intimate possible contact of the blood contained in the capillaries with the air, from a physiological standpoint an epithelial covering appears rather as an obstacle of the function, and this reflection must necessarily exert a great influence upon our judgment, the instant the anatomical proof cannot be exhibited with satisfactory certainty. Upon the other hand, the history of the development of the lung, which is thoroughly analogous to the development of all other open-mouthed glands, and begins by an epithelial proliferation from the intestinal glandular layer, speaks most decidedly for the acceptation of an epithelial covering, and the latest investigations of Colberg (Germ. Archiv

of Clin. Med., ii, p. 453) prove with complete evidence, that the human lung yet retains its epithelium even after birth. Colberg could demonstrate this, upon the lung of a child almost one year old, as a continuous covering of cells clothing also the vessels; these cells appeared spindle-formed upon a cross section and were easily lifted from their connection with the substratum. In explanation of their almost regular absence from the normal lungs of adults, he announces that, in order to get sufficiently thin sections, every infundibulum or a part of the alveoli forming such, must be cut twice, consequently the epithelial covering likewise twice cut, would remain as a very minute segment at the inner surface of the alveolus, which, in removing the section from the razor and in spreading it upon the glass, &c., might easily be lost. Meanwhile, fortunately, there is no necessity for us to cast the severe reproach upon the incompleteness of our science, that it directly withholds from us an actually existing structural constituent of the lung. An epithelium can be demonstrated upon every lung; an epithelium, it is true, which at the first glance appears to be anything else than a continuous cell-stratum, which, however, still represents the necessary final product of that metamorphosis, whose first links we have learned to know in the embryonal foundation, and in the epithelial formation of the infant lung described by Colberg. The epithelial lining of the alveoli of an embryo of four months consists of distinctly distinguishable cells, with large vesicular nuclei, which are at least just as long as broad, and in their palisade-like arrangements, side by side, form an uninterrupted band between the free surface upon the one hand, and the capillaries upon the other. In embryos of six months, the epithelium of the alveoli may already be called a single-layered pavement epithelium. The cells are yet distinguishable as distinct elements, but very much broader than high. Then in the continued lowering of the cell-body there ensues a fusion of them at the periphery. Upon the lungs of the mature child it is no longer possible to demonstrate cell-boundaries by the nitrate of silver method. On the other hand, a band supplied with flat nuclei and spindle-formed swellings yet lifts itself, after the first year of life, from the cross-section of the alveoli. We can no longer see this upon the lungs of older individuals; on the contrary, we find as well in the juices scraped off from a cut surface of the lung, as in the sections of the alveoli, certain exceedingly delicate, veil-like and wrinkled shreds, that may remain hid for a long time from even a skilled observer, because one does not at all think of taking the apparently disconnected fine contours, which are commonly scattered over the greater part of a field of view, as the boundary lines and the summits of the folds of a membrane. One rather thinks of small inequalities of the object or cover glass, and yet, when we have once discovered the connection, we will find it again everywhere and recognize it for what it really is. In

these finest membranes, which I have depicted in Fig. 125, one also discovers, by carmine coloring, the remains of nuclei, namely, small crescentic, strongly refractive bodies, which are arranged in regular interspaces. These nuclei form one side of an oval ring, whose other side is only designated by a dotted line; the ring in its contours corresponds to the former vesicular nucleus, whose proper substance is shrivelled up to this inconsiderable crescentic remainder. Notwithstanding this, these cells are not to be regarded as effete. Rather we will see that the nuclei just described, in irritant conditions, again increase in body; we will see how they surround themselves with protoplasm, divide, &c. In short, the inner surface of the infundibula and alveoli is lined with a most delicate membrane, which proves to be the last product of the flattening and fusing of the epithelium of the lungs, already beginning in the earliest phases of life. In looking at the surface, the membrane withdraws from observation; at the most, one observes, after coloring with carmine, the crescentic remainders of nuclei where they lie in the interspaces of the capillary loops; in profile, on the contrary, we recognize the epithelial membrane as a sharp, simple contour, which, without being interrupted by a single capillary loop, passes over to another, and likewise covers the edge portions of the alveoli, which come into view between them. The membrane adheres pretty closely to the substratum; especially does it not necessarily loosen, when its nuclei again become active and loosen themselves as cells from the alveolar wall; rather, the simple serous transudation in œdema pulmonum initiates a partial loosening; at least in the scraped-off fluid of œdematous lungs, I met the membrane described peculiarly frequent.

Fig. 125.

The normal epithelium of adult lung. The most delicate homogeneous membranes with rudimentary nuclei. 1-500.

§ 407. In returning, after this short digression, to our theme, we straightway find ourselves face to face with a new difficulty, namely, the laying down of a classification of lung diseases both conformable to nature and practically useful. Here also it is necessary to use somewhat more prolixity.

Morbid phenomena are the ordinary vital expressions of the organism under the influence of any extraordinary, generally injurious or dangerous condition, which we call the cause of the disease. A sure knowledge of the causes would permit us to treat pathology as a branch of exact physiology, and to observe the course of a morbid process in the same manner, to control and to vary it, as the progress of a muscular contraction or the digestion of fat; the highest aim of our medical investigation would be attainable before our eyes. But, unfortunately, we are yet very far distant from any such certain knowledge. We must

provisionally satisfy ourselves with several fragments of this etiological series, and because of large gaps which these also yet present, we will often enough be in the position of quite renouncing the natural system and of admitting the technicalities, inflammation, hypertrophy, new formation, &c., as categories of diseases. We can, least of all, blame the anatomist for this. Meanwhile, neither must we prevent the latter from placing himself upon that most general of bases, and I have found that the anatomical anomalies of the lung are above all suited for being treated in an etiological series. Only in this way can we in any measure become masters of the great multiplicity of inflammations, hyperæmias, hemorrhages, pigmentations, &c., while by laying down these conditions as categories of disease we are continually necessitated to separate what is naturally allied, and *vice versâ*, to treat things side by side which are not at all related.

1. Diseases of the Lungs, with Inflammation and Catarrh of the Bronchi.

a. *Emphysema.*

§ 408. If we spread out upon a dark background the sputum of an individual affected with catarrh of the larger bronchial branches (tracheo-bronchitis), we very commonly observe therein globular, white, or grayish accumulations, of the size of a pin's head, which, upon closer observation, again break up into a number of smaller globules or half globules, and consist of a tough mucus, with inclosed cellular elements. These balls are derived from the larger and at the same time ectatic mucous glands; they are casts of the inner spaces of individual acini, which must of necessity form from the tough secretion, if this, as frequently happens here, is retained for a longer time at the place of its formation. These balls have erroneously been considered as secretions, that is, casts of the alveoli of the lung, and the view was deduced therefrom, that also the ordinary and slightest bronchial catarrhs extended up to the parenchyma of the lung. This, however, is not so. Even the bronchi of the calibre of a crow's quill are wont to be perfectly free in these catarrhs; the parenchyma of the lung, however, itself suffers only by the irregularities of the distribution of air, which must necessarily be produced by the tumefaction of the mucous membrane, the presence of the secretion, and the forced movements of respiration, especially coughing and hawking. Even this affection, the so-called emphysema pulmonum, is only developed after a longer continuance of the catarrh, although then so frequently and regularly, that we cannot well doubt of an intimate causal connection between the two, although the detail

of the etiology cannot yet be stated with the wished-for precision.* A few indications in this connection must suffice for our purposes.

§ 409. The expression emphysema really denotes the filling up, the inflation of the interstitial connective tissue of any organ with air, as œdema denotes the filling up of just the same with a serous fluid. Now, although a genuine emphysema also occurs at the lung, we are yet wont to make an exception of the lung, and to immediately designate as emphysema a condition in which the pre-existing air-spaces, the infundibula and alveoli are dilated beyond the normal measure, are ectatic. This ectasy, which sooner or later is followed by an atrophy of the ectatic parenchyma, is apparently produced by the influence of a centrifugal force, whether it be a pressure from within or a traction from without. That this traction qualitatively can be no other than the ordinary traction of inspiration, this pressure no other than the ordinary pressure of expiration, is manifest. The question only is, in how far by the existence of a bronchial catarrh the one or the other is increased and may be rendered capable of such extreme effects. He who in this connection carefully observes the mechanism of the respiratory process, will have to say to himself, that an increase of one or the other, exceeding the physiological boundaries, can constantly be but a partial one, since, 1, the effort of inspiration, which acts upon a section of the lung, can only then exceed the normal bounds when other sections of the same lung are prevented from the normal dilatation, and in consequence thereof, the relatively healthy remainder is forced to a vicarious filling up of space; and, 2, the pressure of expiration can only in so far exert an ectatic action as there exists in the thorax a yielding place, towards which a divergence, a kind of hernial protrusion, may be imagined. This place is the upper thoracic aperture, with its large vascular trunks, subject to great variations of calibre, and its other soft and movable contents. A uniform emphysema extended over the entire lung, therefore, could not at all be explained by an increased expiratory pressure, and by an increased inspiratory pressure, only by making the very plausible supposition that in the originating bronchitis at one time this, at another, that, bronchial trunk is occluded by secretion, and thus now this, now that, section of lung is the point of attack of an abnormal dilatation. Therewith the predominant affection of the anterior *borders of the lung*, lying nearest to the thoracic aperture and the large vessels, would indicate to us that the increased expiratory pressure, especially in coughing, also contributes its share to the production of the emphysema.

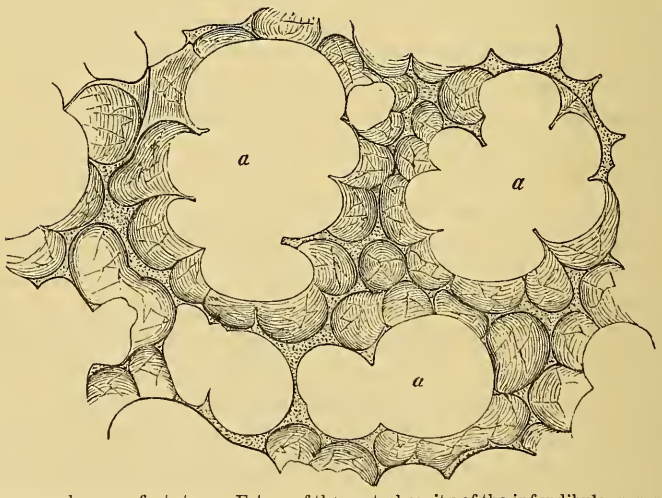
§ 410. That the abnormal conditions of tension of the alveolar parenchyma are followed by an atrophy of the same is easily conceivable,

* Compare Biermer, in Virchow's Handbook of Special Pathology and Therapeusis, vol. v, div. 1; 5, fascicle.

from the known experiences concerning the action of pressure and traction upon the tissues, consequently the second cause of the anatomical changes, the atrophy, could also be derived quite unconstrainedly from the same causal forces. Yet precaution is necessary here. We ask, could not also the atrophy be conversely the primary, and the emphysema the consequence, of lowered capacity of resistance of the lung? The answer, in fact, does not absolutely contradict this. We know of an atrophy of the lung, without catarrh, as a constituent of the senile involution of the body, and must confess that the aspect which a cross-section of these lungs gives, reminds very much of emphysema, and may also be anatomically considered from the same points of view. In other respects, however, we will do well to regard the disturbance of nutrition as a secondary result, wherein we, in picturing it to ourselves, either simply acquiesce in an atrophy from pressure or traction ; or in the blood-displacing action of the expiratory pressure (which, indeed, is subject to no doubt in relation to the vascular trunks of the thoracic aperture, and can also extend to the vessels of the lung itself, and bring about a deficient filling of these), which, as we will see, plays a prominent rôle in atrophy.

§ 411. The emphysematous ectasy of the lung-parenchyma regularly begins with a dilatation of that central cavity, the infundibulum, into which the laterally attached alveoli open. (Compare Fig. 126 with the

Fig. 126.



Pulmonary emphysema, first stage. Ectasy of the central cavity of the infundibula, *a*, *a*, *a*. 1–100.

explanation.) This cavity, under normal circumstances, exceeds the alveoli on an average by one-third of its diameter, so that upon every cross-section of a dried lung, with a strong lens, or at most, by magnifying it fifty diameters, we can determine by the larger rings placed

at regular distances, the number of infundibula cut through. A double row of small rings is interposed between each of these, which is very simply explained by this, that each infundibulum possesses its peculiar wreath of alveoli, consequently from the centre of one to the next in order, two alveolar wreaths must be measured through. In the first degree of emphysema, this organization becomes peculiarly distinct, since those central spaces, which are related to the alveoli as the impluvium of an ancient house to its apartments, gradually becomes wider and wider. In a degree of emphysema yet moderate, as I have depicted it in Fig. 126, even with the naked eye we can recognize the large openings recurring at regular distances.

The increased demand for space, which this first change makes necessary, is covered for the greater part by a persistent increase of volume of the emphysematous portion of lung. Hence, these lungs appear larger than the normal; the anterior borders of both lungs push forward against the sternum, and touch each other, since they simultaneously crowd the heart from the anterior thoracic wall backwards. The sharp edge, which we otherwise find here, is more and more effaced, and gives place to a roundish roll, which forms the transition from the inner to the outer surface.

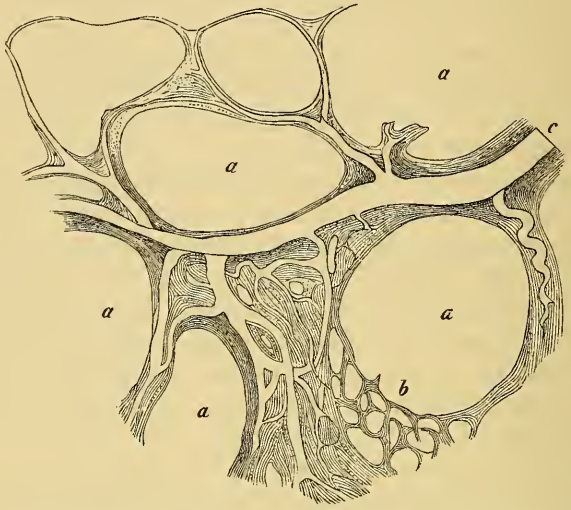
Meanwhile, this external increase of volume is never to be accepted as a hypertrophy. On the contrary, at an early period, atrophy, in the form of a depression of the alveolar partition walls, associates itself to the dilatation of the central infundibular space. The infundibulum is converted into a larger, but still conical, air-sac, whose inner surface yet exhibits the former alveolar subdivision by a partition into fields by projecting ridges. This condition may be compared to what is normally found in the lung of the frog. In man, it denotes an already very far gone atrophy, and the destruction of a large part of the respiratory surface.

By the way, I have never, in this first stage of emphysema, observed a preceding perforation of the thinnest place of the alveolar partition walls, which certainly would be the case if the atrophy were primary, but constantly the depression described, which without doubt points to a mechanical force, which endeavors to convert the space formed of numerous divisions into a conical vesicle. Compare the far-reaching analogy to the production of cysts of retention, § 70.

§ 412. The second study of emphysema may properly be described as a continued simplifying process of the structure of the lung, in which the pressure exerted by two adjacent air-spaces upon one another is the most active force. Where two infundibula come into contact, there occurs a rarefaction of the partition wall; at a central thin place, an opening arises, the opening enlarges; of two separate infundibula one cavity is produced, which only exhibits as the remains of the destroyed

arrangement a ring-shaped ridge, which designates the communicating opening which had continued to enlarge. (Fig. 127, *a*.) Thus, whole groups of infundibula fuse together, the new cavities all tend to the globular form, and there arise, especially at the borders of the lung,

Fig. 127.



Pulmonary emphysema, later stage. The cavities *a*, *a*, have been produced by the complete atrophy of the alveolar partitions, each of an infundibulum, partly also by the fusion of contiguous infundibula. *b*. Remains of septa which are characterized by their abounding in smooth muscular fibres. (Compare Fig. 128.) *c*. Branches of pulmonary artery. 1–50.

those simple, thin-walled vesicles of the size of a pea to a walnut, which we concisely call emphysema-vesicles.

In the still higher grades of emphysema, especially in the senile form, the atrophy of the lung-parenchyma also becomes striking in this, that upon opening the thoracic cavity, the lungs collapse far beyond the normal measure; if we take hold of them and attempt to cut into them, they collapse yet more, since the remainder of the air is easily expelled from them. If we pour water over the cut surface, the lung-parenchyma, again swelled up, thereby affords a picture of the destruction. The wide cavity which the pleura pulmonalis incloses is only yet permeated by a few trabeculæ, which correspond to the principal ramifications of the bronchi and vessels, as well as several larger interlobular septa. All the more minute detail has been swept away. Here and there it yet hangs like a torn veil upon the trabeculæ, spans over the angles, and fills out the corners. All appears black from the immensely accumulated pigment, as just those constituents have remained, which contain the most pigment, especially the vascular sheaths and the bronchi.

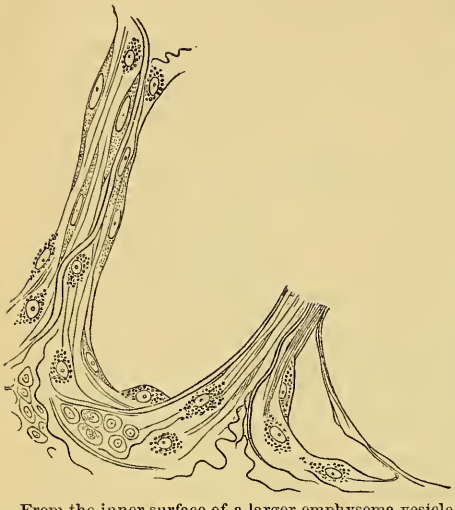
§ 413. After having thus followed the emphysematous destruction

from its microscopic beginnings to its last consequences, it is in the next place incumbent upon us to consider the peculiar textural disturbances which accompany, that is, condition, the disorganization. The various tissues which composed the alveolar parenchyma, by no means behave therein similarly. The elastic tissue, and what exists of the basis-substance of the connective tissue, only really falls into a simple atrophy, a uniform diminution and disappearance. The retrogressive metamorphosis of the vessels is already more complicated. In the first place, the quantity of blood passing through here in a given time evidently diminishes, and I even allowed myself to point out, that probably in this displacement of blood, the connecting medium was to be sought between the mechanical cause of the emphysema and the disturbance of nutrition. The vessel gradually and uniformly contracts to a smaller calibre; the flow of blood may then, at times, finally definitively cease; the walls of the vessel are smoothly applied to each other, and there remains but a narrow string-like stripe, which is recognized as the *obliterated vessel* by this, that by transmitted light it appears lighter in the midst of a dark, often pigmented parenchyma, and by similar stripes unites into the known anastomotic net. We find the same at the borders of all partition walls of an emphysematous lung, which are affected with atrophy and depression. The smaller veins and arteries follow, with inconsiderable variations of the anatomical picture (contraction of the walls instead of falling together), the capillaries, of which what has hitherto been said obtains; the vascular tree dies at its apex, then the larger branches also wither. The main branches of the arteria pulmonalis maintain themselves the longest. The flow of blood through the capillaries is almost entirely suspended; instead several relatively wide anastomoses between the pulmonary artery on the one hand and the pulmonary and bronchial veins upon the other are opened, so that, at least in some measure, the possibility of the efflux of the blood is provided for. These anastomoses, when examined in well-injected lungs, form peculiarly long-extended, vascular loops, without branches, and hence, of uniform thickness throughout their entire course, which stand in the most striking contrast with a very much larger number of very tortuous and ectatic arteries, for whose contents a similar supplementary efflux has not been provided, and which, therefore, furnish us with a visible expression of the considerable increase of the pressure in the pulmonary artery. (Fig. 127, *c*.) At a former place (§ 235), this increase of the pressure was mentioned as a cause of the hypertrophy of the right ventricle.

§ 414. The changes which the *epithelium* experiences, are the only ones upon which hitherto any especial attention has been bestowed, since it was believed that, by their aid, we could prove that the atrophy was primary; thus, there constantly occurs a very considerable accumulation of fat-globules about the nuclear remains of the former epi-

thelial cells, so that the fatty degenerated elements are, in fact, better to be seen than the normal. (Fig. 128.) These granular heaps lie at regular distances, and can very easily be demonstrated in all stages of emphysema. Of course we must leave undecided, whether a portion of these does not belong to the connective tissue, or even to the obliterated vessels. For all these cells evidently undergo simultaneous destruction, and we know of all, that they can just as well fall into the fatty metamorphosis as the epithelia. In addition, the nuclei of the vessels lie at least so superficial, that it really would not be quite easy to adduce the strict proof of the epithelial nature of these granular cells.

Fig. 128.



From the inner surface of a larger emphysema vesicle. Fatty remains of the lung-tissue, containing elastic fibres, smooth muscular fibres, and covered with fatty degenerated epithelia. 1–500. Compare 127. *b*,

§ 415. The only tissue which does not unconditionally join this general atrophy, is the tissue of the smooth muscular fibre. That there are scattered bundles of smooth muscular fibre in the normal lung, and indeed, in the alveolar walls, has been lately again confirmed by Colberg. But I cannot agree with the worthy expert, that these are wanting just in emphysema. On the contrary I have found exactly the thickest bundles in the trabecular work of extremely emphysematous, already rarefied parts of lung (Fig. 128), and consider myself justified, from having found this, when I even affirm a certain hypertrophy of these bundles, inasmuch as one would scarcely meet with such in normal lungs. Of course, it is not intended to say, thereby, that all muscular bundles must be hypertrophic. It is very possible, although I have not observed it, that decomposition and destruction of the smooth muscular fibres occurs at other places, and hypertrophy and excess of formation only in certain directions, which are probably maintained just on that account in the remaining parenchyma.

b. *Catarrhal-Pneumonia—Broncho-pneumonia.*

§ 416. The lung, because of its lobular, if you will, acinous structure, has just as often been reckoned with the glands with open excretory ducts, as because of the continuous transition of the respiratory mucous membrane upon the walls of the alveoli, it has been declared to a certain extent a strongly distended mucous membrane. Each of these

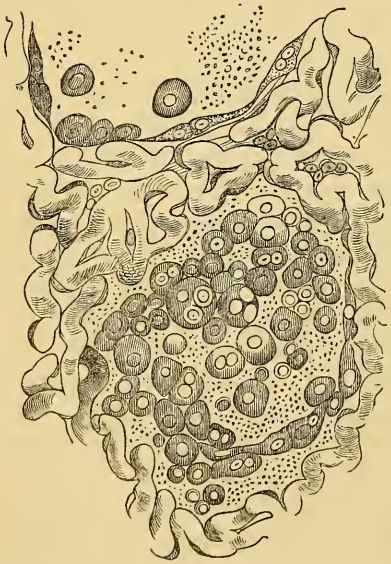
two views may be defended and combated upon good grounds, a proof that the question in itself is one of those "awkward" questions which nature will not answer. I would certainly also not have touched upon it here, if the pathological changes of the lung did not require a certain, even though but a superficial enunciation of the same; thus, with reference to these it undoubtedly commends itself to emphasize the mucous-membranous character of the alveolar walls; for in fact just the most important and the most frequently occurring morbid processes of the parenchyma of the lung become very much more comprehensible and capable of interpretation, by making a parallel with the corresponding conditions of the mucous membrane tract, than they would be without this. Before all others, I here have in view inflammations of the lung, pneumonias; for, just as upon mucous membranes we distinguish a catarrhal and a croupous form of inflammation, and therewith consider the alveolar walls as a mucous surface, upon which in the one case a cellular secretion analogous to epithelial catarrh takes place, in the other a fibrinous exudation. The conformity as to histological detail leaves herein less to be wished for than the clinical conformity; for whilst the catarrhal inflammation of the mucous membrane is a far slighter affection than the croupous, it is just the reverse in the corresponding conditions of the parenchyma of the lung. The croupous inflammation is the ordinary acute pneumonia, of which we know that in the great majority of cases it allows of a favorable prognosis, while catarrhal pneumonia, in its acute as in its chronic manifestation, forms one of the most dangerous of affections, and among others the anatomical foundation of phthisis pulmonum.

§ 417. *The acute form.* If, first of all, we continue with acute catarrhal pneumonia, the proof is not difficult, that youth presents a peculiar predisposition to this affection. In children under five years old, there generally occurs no other than the catarrhal form of inflammation of the lung, and the cause of this peculiar behavior appears to me to depend entirely upon the greater irritability of the epithelial elements, which still adhere to the infant lung from its development. The epithelial cells are far larger, richer in protoplasm, and less firmly connected with the alveolar surface than is afterward the case. To this is to be added, that mostly a catarrhal irritation of the bronchial mucous membrane precedes the actual inflammation of the lung, so that, considered from this side, the latter appears as a transferral of the catarrh from the smallest bronchi to the alveolar parenchyma, which had been already prepared for some time before. Several events are possible here. In the first place, there is the acute bronchitis which accompanies measles, characterized by this, that commonly in the stage of desquamation it passes over from the nasal mucous membrane and from the trachea to the smaller bronchi (capillary bronchitis), and then calls forth inflammation of single larger sections of the lung, perhaps half

a lobe; furthermore, there is the inflammation of the lower and hinder portions of the lung in croupous laryngitis, which is essentially produced under the influence of that unequal distribution of blood and air and bronchial secretion which is characteristic of this form of dyspnœa; thus, while the air, by preference, accumulates in the upper lobules and along the anterior borders of both lungs, and produces here acute forms of emphysema and bronchiectasy, the secretion and blood, partly giving way to the pressure of air, partly following the law of gravity, sink downward and backward; we have atelectasy, œdema, and finally catarrhal inflammation (comp. § 425, *et seq.*). That series of cases is also to be mentioned, where a simple bronchitis from the commencement extends into the smallest ramifications of the bronchial tree, which is the case most frequently in poor, scrofulous children, and in those reduced by disease. By the side of these, of course, we frequently enough have acute pneumonias of the catarrhal form *without* bronchitis.

§ 418. Congestion of blood, and the exudation of an abundant quantity of serum of the blood, everywhere precede the histological changes. The latter have first commenced when the cut surface, beside a certain increased consistence, presents a lighter color, passing into a reddish-white, together with the absolute exclusion of air and greater dryness. The whole affected portion of the lung is wont to exhibit this condition at the height of the disease; if, however, we surprise the latter in being formed, in development, we are convinced that at least for a time it is insular, since, in the first place, the reddish-white infiltrates form around the afferent bronchial trunks, while the interposed parenchyma is indeed œdematous and void of air, but still hyperæmic (marbled lung).

FIG. 129.



Catarrhal pneumonia. One and half of an alveolus. The tortuous capillaries of the septa injected. Filling of the lumina with epithelial cells of the walls which multiply by division. 1–300.

Colberg has lately described the beginning of the histological changes. The epithelial cells of the alveoli swell up and form a thick connected layer of protoplasm, which elevates itself upon cross-sections from the walls of the alveoli as a band with nuclei. The individual cells then branch off, their nuclei divide, an active new formation of cells sets in; there arise large globular cells provided with vesicular nuclei, which cannot be otherwise designated than as epithelial structures, and more

and more fill up the alveoli, since they are diffused in the fluid of the œdema there stagnant. (Fig. 129.) The intensity of this cellular formative process, the quantity of the formed epithelial elements, determine the future course of the inflammation. Without doubt, a complete return to the normal state is possible. Concerning the histological detail of this healing, nothing certain is known from proximate grounds; yet we may accept that in such cases we must have a pre-eminently serous infiltrate less rich in cells, as conversely we may defend the position, that an inflammatory infiltrate so much the less attains to resolution and resorption, and so much the sooner falls into the second way of decomposition; thus, the cheesy metamorphosis, the richer it is in those large, epithelial protoplasma lumps, which the alveoli of the lung secrete in catarrhal pneumonia.

Thus, we have a quite direct transition, capable of being followed through all the stages, from a merely abundant cellular to a purely cellular, and finally to a caseous infiltrate; this transition, at the same time, corresponds to the so common transition of acute catarrhal inflammation into the chronic form, and may be regarded as the essential anatomical foundation of the latter.

§ 419. *The chronic form.* It is a very difficult task for the pathological anatomist to decide, without the aid of clinical data, whether a catarrhal pneumonia, in which the infiltrate has passed over into the condition of the *cheesy metamorphosis*, and which has thereby received the stamp of chronicity, whether this *originated* as acute or chronic. This difficulty depends on the one hand upon this, that the caseous infiltrate may for a very long time exist unchanged in the lung; upon the other hand upon this, that the conditions which precede the actual inflammation, and are accordingly found beside the caseous depot as stages of development and preparation, very frequently present the same anatomical pictures, without yet possessing the same physiological dignity. I here especially mean hyperæmia and œdema, which also introduce the primarily chronic inflammation, which, however, are here by no means phenomena of irritation, but must be regarded as the immediate consequence of the air and blood circulation disturbed by the bronchitis. We will have to discuss this point more minutely; it forms one of the most important and interesting connecting links which exists in the chronic catarrhal pneumonia between the primary bronchitis and the inflammatory processes of the lung; thus, in the etiology of chronic broncho-pneumonia, the "leaping" of the inflammation from the bronchial mucous membrane to the parenchyma (just as the immediately primary origin of the parenchymatous changes), does not play by far as important a rôle as in the acute; it is converted into a more gradual "creeping over" (Hinüberkriechen). Instead, however, we can report a greater series of concomitant and intervening phenomena, which impart to the process now this, now that external stamp,

and bring about the tolerably considerable variations in the anatomical picture of *pulmonary phthisis*. In order to proceed as surely as possible in this difficult sphere, let us keep separate, 1, the changes in the lumen and the walls of the bronchi; 2, the changes of the sections of the parenchyma, to which those bronchi form the access.

§ 420. It is a sufficiently known fact, that in many cases the phthisical destruction of the lung takes its origin in a catarrhal affection of the respiratory mucous membrane, most frequently in a catarrh of those bronchi which ramify in the upper lobes of the lung. This catarrh distinguishes itself from other catarrhs, partly by its obstinacy and the tendency to relapse, partly by the never-failing scrofulous intumescence of the retro-bronchial lymph-glands (Virchow). The secretion is extraordinarily rich in cells, hence tough, concentrated, and is loosened from the walls of the air-passages with difficulty, on which account a disproportionately frequent, although fruitless coughing and hawking take place. In the anatomical examination we find the larger bronchi abundantly provided with this secretion, whilst a *number of smaller bronchi* appear directly and completely filled up with it. If we examine the latter in cross-sections, we find their walls permeated with numberless cellular elements, the boundary between epithelium and connective tissue effaced, and the former replaced by the thick layer of secreted purulent mucus just mentioned. I found this condition upon bronchi of 0.5 to 0.3 millimetres in diameter, and place this in connection with the premature destruction of the basal membrane, so exceeding delicate (if generally present?) in these small bronchi. The basal membrane is a security, exceedingly worthy of notice at the trachea and the larger bronchi, against the deeply penetrating catarrhal processes, as upon the other hand, the abundance of elastic fibrous nets gives a certain counterpoise against the distension of the mucosa by inflammatory infiltrates. Both arrangements disappear more and more, as we advance from the trunk of the respiratory tract towards its branches, and hence it comes that the bronchi, the smaller they are, have so much more the capability of being occluded by swelling, and the secretion, in consequence, of simple catarrhal conditions. To this is to be added, that this occurs almost without exception in such individuals as are either originally endowed with a delicate respiratory organ (inheritance of pulmonary phthisis), or who have been reduced by a febrile or other consuming disease in all their vital energies, consequently, also in their respiratory mechanism. The task which, in the removal of this tough, adhering secretion, is placed upon expiration, proves to be too great for the existing energies; in inspiration, also because of the imminent and easily possible "compensatory distension of adjacent parts of the lung," air no longer enters beside the tough mucus-plug into the parenchyma beyond, the occlusion becomes persistent and finally definitive.

The further effects of the so persistent, more or less complete bronchial occlusion, may be followed in various directions (§ 425); for the present, we will still continue with the primary disease.

§ 421. Provided the muco-purulent secretion actually comes to complete stagnation, it inspissates more and more, the cells die, there arises a yellowish-white, smeary plug, which upon exerting lateral pressure upon the cut surface, is pushed out, and thus designates the place where we must seek the lumen of the bronchus. Afterward, it may possibly come to a separation of chlolesterin and salts of lime in the interior of the plug; this, however, almost only in common with calcareous impregnations of larger pneumonic depots, which, as we will see, form round about the occluded bronchi.*

Under these circumstances, the bronchial wall itself cannot remain indifferent. The stagnant secretion acts as a persistent inflammatory irritant, more or less intense, according to the forming products of decomposition. Consequently, those phenomena of anomalous formative activity in the bronchial wall, of which short mention was made above, increase in intensity and extent, and there develops in the common picture of a "reaction against the superficial irritation," a series of well-marked, pathologico-anatomical conditions.

§ 422. There is, 1, an inflammatory hyperplasia of all the constituents of the bronchial wall, especially, however, a progressive indurating thickening of the peribronchial connective tissue, *peribronchitis chronica* (Virchow). If it is ordinarily difficult to follow the finer ramifications with the knife, we find here that the bronchi, the more we approximate their terminal ramification and breaking up, become relatively thick. Upon a cross-section, which one is much more apt to see in cutting into the organ than a longitudinal cut, the thickened bronchi therefore look strikingly like solid knots; the lumen, namely, almost entirely disappears, partly by the thickening itself, partly by the tough secretion, and thus it happened, that we formerly regarded these things as tubercles, which is so much the more excusable, as upon the one hand, a very intimate connection of conditions of this kind to tuberculosis cannot be denied; upon the other hand, however, by the previously mentioned cross-section of the thickened bronchi, if the section has passed just through a final tuft-formed breaking up of a bronchus and the single branches were uniformly diseased, the appearance of a "nest of miliary tubercles" is certainly presented to the naked eye. Moreover, we find peribronchitis regularly combined with an indurated

* It has been asserted that the so-called lung-stones (calculi pulmonales) are to be regarded entirely as inspissated and calcified bronchial secretion; I must oppose this view, in so far, that I indeed admit the formation of bronchial stones, but on the other hand, assert, that very many calculi pulmonum, especially, however, those which are periodically coughed up in great numbers, and have given phthisis calculosa its name, represent entire lobules of lung, which after calcification are loosened as foreign bodies by suppuration in the interstitial connective tissue (see below).

hyperplasia of the interlobular connective tissue, which may be most simply explained by the immediate continuity in which the interlobular connective tissue stands with the peribronchial at the roots of the lobules of the lung.

§ 423. At a later period, 2, the accumulation of the bronchial secretion may become so considerable, that the lumen of the bronchus dilates for a short distance, the walls, however, are thinned, consequently a condition arises, which would be analogous to the retentions of secretion, and the retention-cysts of other organs. Meanwhile, in this condition it is not to be overlooked, that its etiology may also be complicated, and in most cases probably will be so. The partial obstruction of the bronchial branches by secretion, necessarily has as a consequence an increased pressure of air to the portions of the lung not obstructed, and this again a persistent ectasy of the latter. We are reminded, that just the phenomena of vicarious emphysema are most accessible to a mechanical explanation. In the phthisical lung, of course, it very rarely comes to a vicarious emphysema, instead, however, very commonly, to a *cylindrical ectasy of the collective smaller bronchi*, especially of those which immediately enter into the alveolar parenchyma. In cutting open the bronchial lumen from the root of the lung, we find that the blade of the scissors advances so much the more easily and surely, the more we approach the periphery; we can frequently follow bronchial branches of the width of a crow's quill, close up to the pleural surface. This bronchiectasy, in contrast to the ordinary, catarrhal bronchiectasy, in which the bronchial wall appears hyperplastic in all its constituents, is characterized by a peculiar thinning of the wall. This may go so far, that the wall entirely loses its character as such, and only yet appears as a thin, lustrous lining of a larger cavity. The elastic fibrous nets are dragged asunder therein, the muscular coat, since it divides into broader and narrower bundles, and these move asunder, allows corresponding gaps and clefts to appear; meanwhile, I have not found the mucosa proper thinner than it normally is, so that the attenuation is still more to be placed to the account of the outer layers of the bronchial wall. The poverty of vessels in the ectatic bronchi is very striking. The capillary meshes are very wide; arteries and veins are stretched, and of limited calibre. In addition, the surface is constantly catarrhal; a general bronchial catarrh forms the basis of the whole group of disturbances in question, and I would even allow myself to conjecture, that the greater intrinsic mobility of the inflamed bronchial wall, has a very essential share in the production of the ectasy. The catarrhal secretion is extraordinarily rich in cells and poor in water; it adheres to the bronchial wall, and exhibits a tendency to accumulate in larger quantities. In the face of this fact, however, it is certainly not difficult to comprehend once for all, that in the condition above described, of ectatic

bronchi, filled with secretion, the ectasy is primary, the accumulation of secretion secondary. Herewith, we at the same time, obtain a valuable standpoint for judging of the entire process, since its advance from the parts of lung first attacked to the surrounding parts is somewhat prepared by the mediation of that preceding vicarious ectasy of the bronchial terminations. For the continued course, especially for the changes in the parenchyma of the lung, it is a matter of indifference whether the obstructed bronchus was dilated or not.

§ 424. 3. A third turn, which the processes may at any time take upon the inflamed bronchial mucous membrane, is the *transition into ulceration.* By this we do not understand that simple excoriation, such as we are wont to term catarrhal ulcer in the oral cavity and upon the outer skin, but an actually destructive process, which separates the mucous membrane itself, infiltrated with cells, *layer by layer*, and converts it into secretion. Concerning the nature of this ulcerating process only this is to be remarked, that in individual cases it is correctly designated as tuberculous. I have the preparation of a phthisical lung, upon whose dilated bronchi of the second and third order the tuberculous ulceration is developed in perfectly typical form (§ 384). Moreover, Virchow has repeatedly pointed to scattered miliary nodules upon such bronchi as lead to fully formed cavities. It accordingly appears as though the tuberculosis *could* play a rôle in this bronchial ulceration not to be under-estimated; we are certainly not justified in saying more. Ordinarily there are no miliary nodules to be found. The process of destruction must then be regarded as a simple ulceration. Under the influence, be it chemical or mechanical, of the stagnating secretion, the outermost layer of the infiltrated mucous membrane becomes here and there necrobiotic. There follows a more or less active reaction in the deeper layers, which has the loosening of the necrobiotic layer as a result. We then find a sharply defined shallow loss of substance, frequently only a kind of roughness, from which a whitish-yellow, crumbly coating cannot be washed, but can only be scraped off with some force. If the same process is frequently repeated, the material which the infiltrated bronchial wall presents is soon consumed, the ulceration passes over to the parenchyma of the lung, which has about this time already lost its buoyant constitution, and is transformed into a mass which offers the most favorable chances to the further progress of the destruction. Of this meanwhile hereafter.

§ 425. As we now turn to the *parenchymatous changes*, we must, in the first place, take into consideration, in a well-marked series of phenomena, the effects of the bronchial obstruction upon the parenchyma of the lung lying beyond the obliterated bronchus. It is in our power to produce just this series of phenomena artificially. The experiment of dividing the par vagum on both sides, whereby the deficient closure of the glottis permits the passage of particles of food from the gullet

into the air-passages, whereby extensive occlusions of the bronchi are produced, brings regularly before our eyes its first stages in very pregnant pictures. We here first of all touch upon *atelectasy*, *i. e.*, the condition of non-inflation of the alveoli. A conical, sharply defined section of the parenchyma of the lung, whose extent is proportional to the calibre of the occluded bronchus, receives in inspiration less and less air; finally, the access of air ceases entirely; the inspiratory forces hitherto applied to the inflation of this part of the lung now expend their energies upon the adjacent parenchyma (vicarious bronchiectasy, see the preceding paragraph); the part is perfectly left to itself. Conformably to this the elastic retraction of the parenchyma prevails, and the part, by entirely driving out the air yet contained in it, strives to get its natural size. If it succeed in this, there is no difference between congenital atelectasy, *i. e.*, of the lung which has not yet breathed, and this acquired atelectasy. The part is smaller than previously; if it lie, as is commonly the case, with its base at the surface of the lung, we perceive a correspondingly large depression of the level, and those flat elevations so characteristic of fœtal atelectasy appear, one for each lobule of the lung.* The surface, accordingly, is unevenly tuberous. The color, also, and the amount of blood contained remind, at least in the first stage, of fœtal atelectasy. The wedge under consideration appears dark flesh-colored; it shines through the covering pleura with a bluish tint. But just in the amount of blood contained there soon sets in a very thoroughgoing difference, and one characteristic of the further development of the condition, since in acquired atelectasy, the primarily only apparently greater abundance of blood, by the approximation of the capillaries forms an actual *hyperæmia*.

§ 426. In the fœtal lung no disproportion can properly exist between the length and width of the capillaries upon the one hand, and the spaces in which they are imbedded, upon the other. The vessels could not extend and develop further than the space once given allows. It is entirely different in acquired atelectasy. Here the non-inflation is an anomalous condition, whose recurrence at any time in the extra-uterine metamorphosis of the lung into a respiratory organ—so to say—was not taken into consideration, was not calculated upon. This transformation into the respiratory organ, however, requires the most luxuriant possible development of the vascular apparatus. If, therefore, at a time when this development has become an irrevocable fact, a complete contraction of the elastic parts of the lung sets in, this will bring with it a disproportional injury to the calibre and the length of the vessels. The framework of the elastic fibres becomes a mechanical obstacle, which pushes in between the part of the vascular tract projecting free into the lumen of the infundibulum and the alveoli, therefore

* Lobule of the lung, not to be confounded with the infundibulum, of which as many as twenty go to form a lobule of the lung.

especially the capillaries, and between the interstitial, respectively the interlobular afferent and efferent vessels. The blood-current therefore becomes slower, the blood accumulates in the capillaries, the atelectatic part becomes hyperæmic.

To the hyperæmia there sooner or later associates itself an exudation of serum of the blood into the lumen of the alveoli; the atelectatic part becomes *œdematous*. In the measure that this occurs, the part is again distended; it moves up to the old level, nay, it projects as a flat, elastic tumefaction above it. It is now of doughy consistence; the touching finger leaves behind a persistent impression; at the free surface it is bluish, upon the section dark reddish-brown, moist, smooth, in short, in its outward appearance it resembles the spleen so much, that the term *splenization* appears very suitably chosen. Now it is manifest that the splenization of the parenchyma of the lung does not presuppose for its production perhaps a preceding atelectasy, but only a sufficiently strong hyperæmia with exudation of serum into the alveoli. Every static hyperæmia, especially, however, the hypostatic hyperæmias of the lower lobes of the lung (such as the gradual declension of the heart's power in most death agonies, in disease of the heart, from typhous and other marasmi, brings with it), can lead to conditions of splenization by the interposition of an œdema excluding the air. Consequently our process would from this point be robbed of every characteristic anatomical peculiarity; we would not be able to perceive upon the splenizated part of lung, whether it had formerly been atelectatic, if the "circumscribed occurrence of the atelectasy, confined to a wedge-shaped piece," as well as the circumstance that those hypostatic splenizations are only found in the dependent parts of the lung, did not now guide us. Under the circumstances it would, of course, be impossible to recognize an atelectatic splenizated wedge within a hypostatic splenizated lower lobe of the lung.

§ 427. Splenization quite generally taken, appears to present extraordinarily favorable preliminary conditions for the occurrence of inflammatory changes. It may directly represent the initial hyperæmia of acute inflammation, and be followed by lobular and lobar, but constantly catarrhal infiltrates. Such are the relations in the hypostatic pneumonia of typhous patients and those in marasmi; so in the broncho-pneumonic conditions of phthisis, to be considered immediately.

If inflammation does not supervene, in the case of diffuse splenization of the lower lobes, there occurs either healing or death; in case of atelectatic or lobular splenization, a series of further changes, which are consistently developed by the continued action of the forces once put in motion. From this series we especially render prominent two conditions, "inveterate œdema" and the "slaty induration."

§ 428. "*Inveterate œdema*" distinguishes itself from splenization, above all by the absence of hyperæmia. It appears as though by the

continued increase of the serous exudation, the access of the blood to the splenizated depot is rendered the more difficult the longer it continues, a relation which occurs in all pneumonic infiltrations (compare § 431); the infiltrate, which cannot give way, because it is in an inclosed and not *ad infinitum* distensible space, dislodges the blood, which can give way, *i. e.*, can enter upon other routes than just those leading through the infiltrated depot. The latter, where it is possible, swells up somewhat more, while at the same time it becomes paler, and finally only yet exhibits a few red arterioles in its otherwise quite uniformly pale yellow color. If we cut into it, there flows from the cut surface a clear, very concentrated serum, perfectly free of foam, in which the eye of the observer here and there recognizes yellowish-white, atomic particles. The cut surface also appears covered with yellow atoms, which in the microscopic examination immediately prove to be fatty degenerated cells, the so-called granular globules. The great pallor and the peculiar brawny constitution of this depot contrasts very strikingly with the often very lively red of the surrounding parts, which is yet intensified in the nearest environs by the collateral fluxion, *i. e.*, by the accumulation of the blood not admitted into the depot.

§ 429. We may also regard the *slaty induration*, at least what concerns the parenchyma, as the close of a very protracted atelectatic condition, not as a chronic inflammation. It is true, it is not easy to maintain a strict separation here; for, the slaty induration is regularly found in combination with the peribronchitis chronica, described in § 422, which for its part is almost as regularly combined with an inflammatory hyperplasia of the interstitial, *i. e.*, interlobular connective tissue. The latter, in the form of trabeculæ ever becoming broader, pushes in from all sides between the parenchymatous islands, partly crowds these asunder, partly constringes them, and generally occupies more of the foreground of the anatomical picture. Besides this, however, it is yet important to state, that the alveolar parenchyma itself does not take an active part in this inflammatory process. The small portions which we meet with are perfectly devoid of air and blood; nevertheless, the individual alveolar septa may be yet right well demonstrated; only at a quite late period the actual growing together of the contiguous surfaces, and therewith an obliteration of the lumina, sets in. In attempts at injecting, the vessels of the interlobular connective tissue only fill up, while the former parenchyma takes up none of the injecting fluid. The presence of large amounts of black lung-pigment is the most characteristic sign of the slaty induration. This is found as well in the interstitial connective tissue as in the atelectatic parenchyma. It consists of small black granules, which are mostly united in cells into small heaps, but are also diffusely scattered in the tissue. At single places, mostly roundish or elongated, of the size of a lentil, the deposit is very peculiarly dense, the color an intensely deep black. Hemor-

rhages have at some time occurred here; they are old hemorrhagic depots. The derivation of the black pigment from the coloring matter of the blood is principally to be maintained exactly for this slaty induration. Not only does the limitation of the stronger deposit of pigment upon a portion of the lung, excluded at an early period from the circulation of air, make the contrary opinion, that this black pigment also had been inhaled, untenable, but we also find, just here beside the black pigment, numerous transitions of brown and red pigment-bodies, which are more closely related to the coloring matter of the blood, and represent the earlier stages of the pigment metamorphosis. We will yet observe, that the picture, which a portion of lung affected with peribronchitis, development of interstitial connective tissue, and with slaty induration presents, is so typical, that it for a long time was estimated as the picture of healed tuberculosis; "upon the pleura almost cartilaginous layers of exudation, which permit white bands to radiate into the lobular interstices; in the centre a number of transversely divided bronchi, whose lumina are closed by caseous or even calcified plugs, whose walls are indurated and thickened, and between the two there is a slaty gray, dry, airless, and very tough parenchyma."

§ 430. *Inflammation and cheesy metamorphosis.* In what has hitherto been said we have throughout conducted our consideration up to the point where inflammation of the parenchyma of the lung sets in. We have seen that, upon the one hand, the soil upon which the inflammation appears, as a rule, is already no longer the normal parenchyma of the lung, but in various degrees a hyperæmic, atelectatic, splenizated or œdematous lung-tissue. We have seen, upon the other hand, that the inflammatory changes in the bronchi have already attained a certain height ere they pass over to the surrounding parenchyma. Because of the latter etiological relation, Virchow has introduced the name of broncho-pneumonia for the inflammation in question; from the same author also the terms cheesy, dry pneumonia are derived, which refer to the quality of the infiltrate. The term catarrhal inflammation, to which we yet add the clinical character of chronicity, because of the tardiness of its entire course, represents the histological standpoint.

In the surroundings of the diseased bronchi, the infundibula and the alveoli fill up with cells. These cells are loosened from the walls; they are of an epithelial character, large, globular, or at least obtusely angular, provided with a round, relatively small, but lustrous nucleus. We therefore have to do with the same histological detail as in the acute catarrhal inflammation described in § 418. We must even add that in a recent, *i. e.*, an infiltration not already gone over into the cheesy metamorphosis, we are quite unable to distinguish between acute and chronic, and that even when the clinical course proves the chronicity of the entire process, even when we find the various stages of devel-

opment of the inflammation side by side in the same lung, nevertheless the opinion cannot be reduced *ad absurdum*, that the actual infiltration, according to the analogy of that formerly considered, is a result running a rapid course. The correlative to this we find in the possibility discussed in § 418, that every acute catarrhal pneumonia may pass over with an ever so sharply marked onset into the chronic form, may become cheesy, and lead to pulmonary phthisis.

§ 431. After all this we must entirely renounce the idea of finding in the developing series of changes any characteristic token of the chronic in opposition to the acute inflammation; however, we find such a one in the declining series, and, indeed, in the *cheesy metamorphosis* of the inflammatory infiltrate. The entrance of the cheesy metamorphosis, a fatty degeneration modified by the abstraction of water, of the cellular elementary parts (§ 33), presupposes the meeting of various favorable conditions. Among these figure foremost, the excessive accumulation of cells, and their intimate contact, with the exclusion of all intercellular fluid; besides this a gradual interruption of the circulation of the blood, which brings about the actual disturbance of nutrition. Now, in the catarrhal inflammation, in the *epithelial desquamation* continued beyond a certain time, combined with the difficult or, because of bronchial obstruction, the downright *impossibility of removal* of the desquamated epithelia, we have a sufficient cause for the most injurious accumulation of the latter in the alveolar parenchyma, for the driving out, as well of the intercellular fluid as of the blood, consequently just for the cheesy form of necrobiosis. The fatty-granular cloudiness of the cells which fill the alveoli already betrays itself to the unaided eye as a sharply defined yellowish-white opacity in the centre of the depot, and nothing can be so positively determined, without the use of the microscope, as the progress at the time of these changes. Within their sphere the structure of the lung completely disappears, only the pigment here and there occasions a blackish-gray marbling of the otherwise quite uniform and homogeneous appearing cheesy mass. By this it is not intended to say that now already the collective structural constituents of the lung are actually destroyed, have disappeared; they are certainly all lost to the organism, but the more resistant of them, the elastic fibres and the walls of the larger arteries, are yet maintained for a long time, and again become visible in the probable subsequent softening.

§ 432. If the cheesy metamorphosis has been completed, there is a condition established thereby which in itself has but little tendency to further metamorphoses, and, therefore, guarantees a certain durability of the whole process. From this we derive the justification of claiming just the cheesy metamorphosis as an anatomical token of the chronic course of the inflammation. In order, however, to connect with the older teaching, which in power and in spirit has become so effete to us,

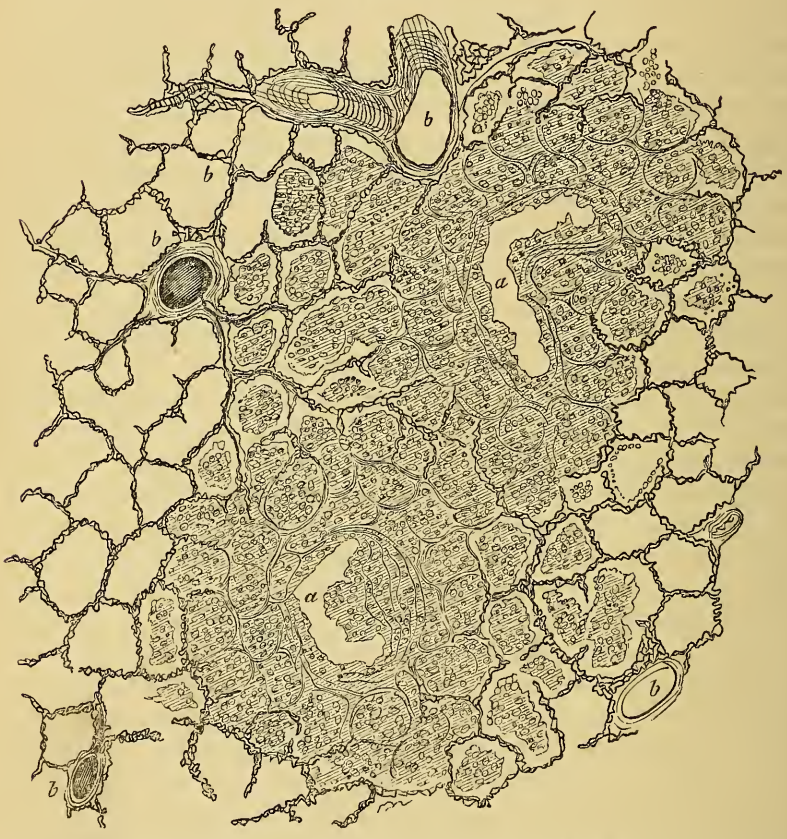
that without a fundamental knowledge of it we can scarcely be intelligible to older experts, we will remark here that the cheesy material in question is exactly the same substance which was formerly termed crude tubercle, and was regarded as the one and only point of departure of phthisis. At the present day we must, indeed, reserve the term "phthisis tuberculosa" for the—otherwise very large—number of those cases in which we succeed in *proving an irruption of miliary nodules* upon the connective tissue and the vessels of the diseased lung; we may, however, always admit that the older authors have placed a fundamental truth at the head of their teaching, when they assert that phthisis pulmonum, at a certain time, makes its further advance from a yellowish-white crumbly substance; nay, we may go further, we may also uphold the distinction of Laennec, between infiltrated and granulated tuberculosis, in so far as we recognize in it the two most principal macroscopic modes of appearance of catarrhal broncho-pneumonia.

§ 433, *a*. The *pseudo-tuberculous broncho-pneumonia*, that pre-eminently frequent occurrence, where the inflammatory infiltration of the alveolar parenchyma first of all strictly confines itself to the circumference of the smaller and the smallest bronchi, corresponds to the tuberculous granulation of Laennec. Here upon the cut surface, grayish translucent, whitish in the centre, nodules, of the size of a poppy to a millet-seed, therefore really exceedingly similar to miliary tubercle, project; they feel compact, seldom stand singly, mostly in groups of five to ten, in such manner indeed, that the centre of the lobuli are principally occupied by these groups, while the periphery remains free. The parenchyma, in which they lie imbedded, is at times of apparently normal constitution, never actually normal, but either hyperæmic or atelectatic, splenizated, or only œdematous, seldom pale and emphysematous. The frequent occurrence of a zone immediately surrounding the nodules, which harbors a grayish-red, clear or slightly clouded, synovia-like, viscous infiltrate, the "infiltration gélatineuse" of Laennec, is characteristic, whether in other respects the parenchyma have this or that constitution. The zone denotes a loosening and puffing up of the tissues immediately preceding the cellular infiltration; it is at one time merely indicated, at another so widely diffused that it forms a common area for a group of nodules, finally again is diffused over an entire lobule, nay, over large wedge-shaped portions of lung. If the latter is the case, it is certainly difficult, nay, almost impossible, to keep separate any longer the gelatinous infiltration and the inveterate œdema of an atelectatic portion; I mean in fact, that both have been frequently mistaken for each other.

§ 434. I have illustrated in Fig. 130 what is yielded by histological investigation of the gray nodules. In this preparation, under a low power, we have before us two broncho-pneumonic depots of the size of a millet seed (pseudo-tubercles). At *a*, *a*, therefore, at the two central

points of the nodules, are found two transversely, that is, obliquely, divided bronchioles; their lumina are obstructed by a cheesy mass, which, however, because of their great friability, has partially fallen out in making the section, the elastic layers of the walls are pressed asunder, and

Fig 130.



Two smallest broncho-pneumonic depots. Tubercle granulation of Laennec. *a, a.* The lumina of two adjacent small bronchi, the caseous secretion partly fallen out; the walls infiltrated with cells and directly going over into the catarrhal infiltration of the surrounding parenchyma. By the course of the elastic fibres we may recognize everywhere how large the number of infiltrated alveoli is. *b, b, b.* Blood-vessels. 1–100 mm.

just like the nearest adjacent alveoli, provided with an earlier cellular, now already caseous infiltrate. The zone of the cheesy metamorphosis extends over two to three rows of alveoli, of which we can satisfy ourselves at the persistently elastic parts of the alveolar frames. Then follows a zone, within which the infiltration is yet upon the increase; under higher powers we would get appearances here as in Fig. 129; still farther outwards then follows relatively normal lung-tissue. A successful injection of the pulmonary artery shows us, moreover, how far from without, the blood-passages were yet pervious to blood. One sees,

that this perviousness nowhere reaches into the cheesy part of the depot, while in the region of the recent inflammation the vessels have everywhere filled. I repeat, that we must regard this phenomenon as a compression of the bloodvessels by the disproportionately increasing infiltrate, consequently the cheesy metamorphosis as a self-made necrobiosis of the latter.

§ 435. The continued advances of the changes may be very well studied even with the naked eye upon the whole cut surface of the diseased organ. The gray nodules enlarge more and more, the central opacity develops into a distinctly cheesy spot; the nodules touch one another and fuse into a larger knot, soon becoming cheesy, upon whose roundishly incurved contours we can yet for a long time recognize the construction out of numerous small nodules; at length the whole lobule is infiltrated, and sooner or later fuses together, with its likewise infiltrated neighbors, into a continuous whole; there arise knots becoming ever larger and larger, whose fate we will consider further below.

§ 436, *b*. The *diffuse* lobular or lobar *inflammation*, Laennec's *tuberculous infiltration*, forms a certain, at least anatomical contrast to the pseudo-tuberculous form. Without the bronchial places being particularly marked, there here presents itself upon a section a uniform infiltration of larger or smaller wedge-shaped sections of lung. The latter have evidently undergone the change simultaneously in all parts; for the inflammatory infiltrate is everywhere in the same stage of metamorphosis; the whole depot is either reddish-gray, gelatinous, or yellowish-white, cheesy, homogeneous. What therefore is attained in the pseudo-tuberculous form more gradually, and from certain points (the bronchi), a larger caseous depot is here produced more after the manner of acute catarrhal inflammation, less by means of a leaping over of the inflammatory condition from the bronchi to the entire parenchyma beyond.

§ 437. *Softening of the caseous knot, formation of a cavity.* How long the caseous knot remains unchanged in the lung depends partly upon the size, partly upon circumstances which have hitherto entirely evaded our investigation. We may say, the larger the circumference of a cheesy knot is, and—probably—also, the more rapidly it had attained this circumference, so much the more imminent is the danger of a central softening and the formation of a cavity. The ordinary caseous depot, produced by the confluence of numerous smaller nodules, mostly attains the size of a hazelnut, ere the first traces of softening set in; on the contrary, rapidly produced caseous infiltrations of single lobuli, or larger connected groups, are wont also to soften comparatively rapidly, so that we find side by side small and large cheesy depots, which collectively have progressed equally far into softening.

§ 438. The softening process itself is an act of simple intumescence by fluid, without any further development of formed constituents. The

dead, shrivelled cells and the molecular detritus, into which they have broken down, loosen, and are suspended in a moderate amount of fluid, which appears in the centre of the knot. It is certainly difficult to understand the necessity of this so constant phenomenon. I accept, that a portion of the solid albuminates, by long digesting at 100° F., goes over into the soluble modification, and these then attract from their surroundings as much water as is necessary to their solution.

§ 439. As observed, it is constantly the centre of the caseous depot, at which the melting down to a flaky, puslike pulp of softening begins. This circumstance introduces the question, in how far probably, the bronchial branches situated just here participate in the formation of cavities. In them we have preformed cavities. But we have also seen, that as a rule, they are obstructed by a plug of secretion of older date. Only when the latter falls into the softening, could we say, that the formation of the cavity proceeds from the bronchi. This, in fact, mostly appears to be the case. If we except the multiple lobular infiltration of rapid course, already cited, in which larger depots of softening occur without any communication with the bronchi (phthisis acuta), we may regard it as an almost constant phenomenon, that the *ulceration of the bronchial walls*, more minutely described in § 424, prepares the actual formation of a cavity, be it, in that before the caseous metamorphosis of the surrounding parenchyma, and before the general rigidity which is brought about by this, it enlarges the lumen of the bronchus at the expense of the walls, or be it, that the caseous metamorphosis in general only arises as a "zone of infiltrated tissue" around the bronchial walls, and thus the destruction of the parenchyma of the lung immediately joins the complete destruction of the bronchial walls. The latter is especially the case in the previously ectatic bronchi, so that in cutting them open we meet with excavated places in the mucous membrane, through which we reach with a probe into the softened centre of a small caseous depot. If the cavity has once attained a certain size, as a rule, the afferent bronchus opens by a small, as though cut off stump into the lumen of the cavity, and nothing positive can be said concerning its participation in the formation of the latter.

§ 440. The most important force of this series, next to softening itself, in every case, is the establishment of a free communication of the larger air-passages with the abnormal cavity; in this connection, however, against opposing statements I must assert, that the trunk of the bronchus leading to the cheesy depot is constantly opened, seldom one passing by it. The appearance of a lateral opening can, however, easily be suggested by this, that the cavity, after complete destruction of the bronchus leading to it, has advanced up to a point where the latter branched off at an angle from a larger bronchus, so that now the opening where the one branched off upon the one hand appears as a hole in

the wall of the principal bronchus, upon the other forms the direct and immediate entrance to the interior of the cavity.

After the first evacuation of the accumulated products of softening, putrefactive transformations are very commonly associated to the processes of softening, putrefactive transformations which are meanwhile constantly confined only to the most superficial layer of the cheesy substance, and therefore are of lesser importance to the life of the patient. Small yellowish fragments, which look like remains of food, bread-crumbs, &c., are continually loosened at the inner surface of the cavity. If we investigate them more accurately, we find a considerable amount of elastic parenchyma, involved among shrivelled cells and fatty, stinking, putrefactive detritus. Their occurrence in the sputa is a certain sign that the affected cavity is still increasing.

§ 441. Let us now place beside the picture of destruction and decay, which has hitherto been unfolded, those processes and changes, which are destined by nature to restrain the devastation. These proceed collectively from the interlobular connective tissue and pleura, and in general, have the character of "a reactive inflammation at the periphery of the lobules," called forth by the extensive disorganizations in their interior; individually, however, they present a variegated multiplicity of phenomena, which is directly proportional to the *macroscopic relations of the phthisical lung* in the later stages.

Each fragment of cheesy infiltrated lung-parenchyma is a caput mortuum; the connection in which it stands with the organism, must in some manner, sooner or later, be completely dissolved; the organism must be closed in from this side. This task is most simply fulfilled, when all around the cheesy infiltrated lobule a separating suppuration of the interlobular connective tissue sets in, in virtue of which all the bridges which lead across and back are broken down. I have once observed this, the *first* anatomical picture of pulmonary phthisis, in a scrofulous child of seven years of age;* a lung-lobule of the size of a walnut had been changed into a cheesy mass, and lay free in a correspondingly large cavity lined with a pyogenic membrane; the bronchus leading to it, together with the vessels, formed a pedicle, to which it was yet provisionally attached. Beside this, a second cheesy mass of the same size in an earlier stage of separation on all sides.

§ 442. In the *second place*, the separating suppuration certainly only develops when the zone of softening of the caseous mass moves nearer to the periphery of the lobule, so that it appears as though the above-mentioned slight putrefactive decompositions at the ulcerative surface, first excited the slumbering formative activity of the connective tissue. Reddish, vascular granulations then spring up here and there upon the walls of the cavity, and where all the cheesy material has been removed,

* The preparation exists in the collection of the Patholog. Anat. Institute at Zurich.

we see that these granulations belong to a pyogenic membrane, which lines the entire cavity. The latter yields a thickly fluid purulent secretion, and is very frequently the seat of small parenchymatous hemorrhages, which may very well be explained by the softness of the granulation-tissue, by the thin walls of the vessels, and the continual change in the distribution of the blood [by the formation of new capillary loops in the granulations.—TRANSLATORS]. The hemorrhages for their part leave behind brown and black pigment, which imparts frequently a very foreign appearance to the pyogenic membrane. This, however, cannot prevent us from attributing to it all the virtues of a new membrane formed by second intention, for there can be no doubt that by its continued metamorphoses into a connective tissue induration, the complete healing of the cavity can be attained, and that, when the individual was so fortunate as to possess only this one cavity, he is healed. It is true, as a rule, there are several cavities, and beside them there yet exist numerous caseous depots, so that the continuance of the trouble has been more than sufficiently provided for. Herewith the adjacent production of several cavities not at all infrequently gives occasion to the formation of a complicated system of cavities, since the dividing partition-walls are consumed except the larger vascular trunks. The whole upper lobe of a lung, or at least, the upper half, in very protracted cases of pulmonary phthisis, is wont to be converted into a single cavity, through which pass the obliterated main branches of the pulmonary artery. A gray, pyogenic membrane lines the cavity, clothes also the vascular trunks mentioned, and is only here and there interrupted by more recent red granulations, or by the last remains of the cheesy parenchyma.

§ 443. *A third*, very rare anatomical picture is afforded by pulmonary phthisis, when the reactive inflammation of the interlobular septa arises at an early period with the character of a hyperplastic connective tissue proliferation. Broad connective tissue indurations then penetrate through the entire organ, and are placed in connection on the one hand with the thickened pleural coverings, upon the other with the peribronchial and perivascular connective tissue sheaths. Each cavity remains separate, and if the alveolar parenchyma has been entirely destroyed, instead, we have a larger number of smaller cavities, each lined with a smooth, pyogenic membrane, and separated from its neighbor by a thick connective tissue induration. The larger bronchi are regularly in a condition of dilatation and hypertrophy, so that I cannot resist the conjecture, that there is present here the certainly rare case, where the catarrhal cheesy inflammation has associated with a bronchiectasia hypertrophica.

§ 444. In the *fourth place*, finally, we must once more go back to phthisis acuta or florida. The rapid decay of the cheesy depot, which we observe here, is the consequence of a *purulent melting down of the*

entire connective tissue situated within the depot; a purulent melting down, which sets in early enough, in order yet before the entrance of actual necrobiosis to convert the greater part of the alveolar parenchyma into a fluid, into pus, and thus to prepare the way for the immediately following softening. Just this form has been designated as purulent-ulcerative, and an actual formation of abscess recognized in the melting down of the cheesy depot. The future course is wont to justify this representation; not at all infrequently the depots of softening, when they moreover lie at the surface of the lung, like other abscesses, break through into the pleural cavity, instead of emptying their contents through the bronchi leading to them. A diffuse pleuritis soon arises with a copious purulent exudation, and moreover, if the bronchus leading to it is in communication with the interior of the cavity, the condition of pyopneumothorax is unavoidable. Again, the rupture into the pleural cavity is also in ordinary lung-cavities a constantly threatening catastrophe, which is only avoided by the preceding inflammatory adhesion of the pleura pulmonalis to the pleura costalis.

§ 445. *Lung-calculi.* We have hitherto only spoken of the softening of the cheesy mass, and have learned to know in it a certainly most frequent and most important metamorphosis. Next to it the possibility of calcification appears only as an interesting curiosity. It only occurs in the small, and the smallest caseous nodules, that by an abundant deposition of the phosphate and carbonate of lime, by an actual petrifaction, therefore, a stop is put to all further metamorphoses, especially softening. Thus arise lung-stones, calculi pulmonales; hard bodies of the size of half a pea and under, whose surface is either smooth or delicately lobulated like a mulberry. There are individuals who are much troubled with bronchial catarrhs, but who from time to time, under somewhat severer febrile phenomena, evacuate a larger number of such lung-stones per sputum. It is manifest that evacuations of this kind can only depend upon a separating suppuration, which the calculi as foreign bodies bring about in the adjacent parts. A second presumption, however, is the simultaneous opening of a correspondingly large bronchial tube, for it can be most positively proven by microscopic investigation, that the lung-stones evacuated in phthisis calculosa are caseous lime-infiltrated lobules of the lung. The elastic tissue, as also the black pigment, is maintained unchanged in the calcification, so that by macerating in muriatic acid the whole areolar framework of some infundibula besides the alveoli can constantly be demonstrated. Bronchial stones (see § 421) are much rarer; they are constantly smooth, globular, or elliptic, and are found in one or more bronchiectatic cavities. Moreover, encapsulated calculi do not at all infrequently occur scattered in the lung, where we may accept, that the irritation exerted by them was indeed able to call forth a chronic hyperplasia of the connective tissue in the immediate surroundings, but not a suppuration.

2. Tuberculosis.

§ 446. As in the present representation of lung diseases we do not depend so much upon a systematic description as upon a consideration of the etiology, we will permit ourselves to speak of the genuine tuberculosis of the lung in immediate connection with that disease, with which it has for so long a time been regarded as an affiliated whole, but with which in fact it has the most intimate points of contact.

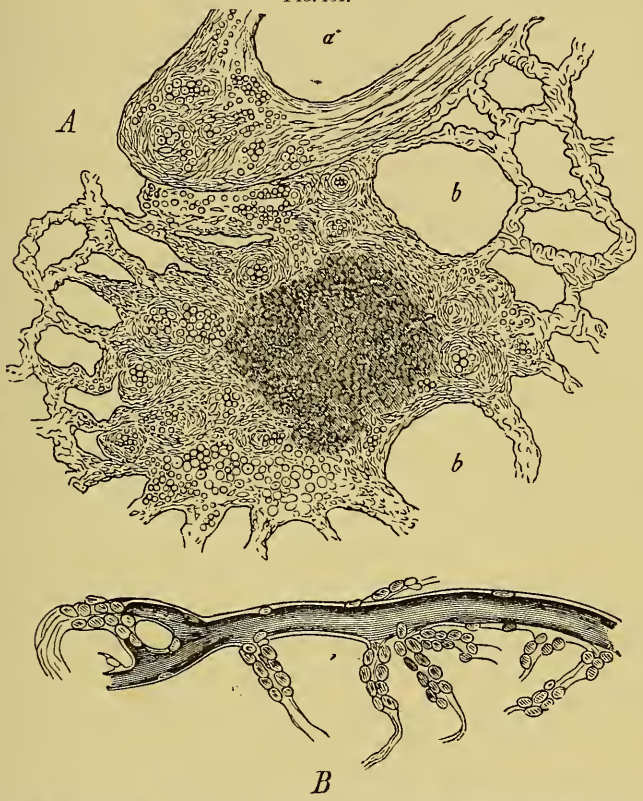
We find the miliary tubercle represented in the lung like as in several other organs in two typical modes of appearance, which we may most suitably designate as disseminated and localized tuberculosis.

§ 447. *Disseminated* tuberculosis is constantly the sign of a constitutional disease, for we find yet other organs beside the lungs permeated or strewn over with miliary tubercles; thus the liver, the serous sacs, the pia mater, the choroid. Just this, probably never-failing coincidence, gives us the guarantee that we also have the right of regarding the miliary nodules of the lung as genuine tubercles, and not perhaps as accidental connective tissue knots, such as, for example, we can produce by injecting small, chemically indifferent particles into the arteries of the lung. It mostly occurs in children from three to seven years, more seldom in adults. The whole lung, including the pleura, is as a rule, permeated tolerably uniformly with the miliary nodules; deviations in the uniformity of the permeation occur less frequently than in this, that in one case the lungs are more abundantly provided, in another less abundantly; namely, the density varies between one and twenty to a square inch of surface, that is, the cut surface. Touching the size of the single nodules, in this respect certainly not inconsiderable variations occur; variations, in the different cases, from the scarcely visible or macroscopically actually indistinguishable point, up to nodules of the size of a large pin's head, even of a hemp-seed. The larger a nodule is, so much the more may we accept, that at the periphery of the real tubercle there exists a circumscribed zone of catarrhally inflamed parenchyma, a circumstance which we will yet have to consider further.

§ 448. The connective tissue of the lungs is the seat of these disseminated tubercles. In individual cases (Deichler) they are exclusively the sheaths of the small arteries and veins within which the miliary nodules have developed, more frequently the interlobular and interinfundibular connective tissue. In reference to structure and texture the nodules are related throughout, like the miliary tubercles of other organs, perhaps like the simultaneously existing tubercles of the omentum, or of the pia mater. Upon larger nodules (Fig. 131), as a rule, we can demonstrate several centres of development, *i. e.*, points in the interior, around which a part of the tubercle-cells is concentrically grouped, while the others form bands which pass along between the nodules. At the periphery of the nodules the swelling of the alveolar

septa, which are inserted here, immediately becomes apparent. It is evident that the process of new formation, provided it is yet progressing, does not advance by an infiltration of the alveolar lumina, but by a tumefaction of the alveolar wall itself. The lumina of the alveoli,

Fig. 131.



Miliary tubercle of the lung. *A*. Part of cross-section of a small vessel in whose walls as well as in the adjacent connective tissue the cellular new formation has developed, which appears to the naked eye as white nodules. *A, b*. Infundibula. 1-100. *B*. A transition vessel from the neighborhood, showing increase of nuclei. After Colberg. 1-300.

if a catarrhal inflammation is not added, are only distorted and filled up by the inward projection of the tubercles. In a tubercle as large as the one here represented, there may always be a number of alveoli obliterated, but this obliteration and the exclusion of air conditioned thereby is something accidental, not the principal thing, as in catarrhal obstruction.

If we investigate the broad junctions of the alveolar septa to the tubercle, so to say the radicles which the growing nodule sends out, we constantly find here a decided participation of the perivascular connective tissue, yes, of the vascular wall itself, in the proliferative process. Fig. 131, *B*, which particularly beautifully shows this relation, I have borrowed from Colberg. Here all the capillaries proceeding from a

larger transition vessel are covered with adhering cell-heaps, which most probably are derivatives of the cells of the vascular walls themselves.* The vessel represented has, moreover, been torn away from its natural connection, which we must likewise imagine in the most luxuriant proliferation.

§ 449. A catarrhal co-affection of the adjacent alveoli we do not perceive in our tubercles (Fig. 131, *A*); still I must point out that this is quite a common accident, and that by it the miliary tubercle frequently attains double the circumference. The combination of disseminated tuberculosis with a diffuse, probably lobar catarrhal pneumonia, likewise occurs and allows the construction, that the tuberculosis has acted here as the predisposing cause.

§ 450. After having given in the preceding a sufficing characteristic of what we may call tubercle in the lung, we may enter upon the answer to the question: what share has tuberculosis in phthisis pulmonum? It has already been mentioned, that from a too comprehensive definition of the word tubercle we for a long time identified phthisis and tuberculosis pulmonum; now, however, we must also not fall into the opposite error, in that we too closely prune the domain of tuberculosis. We must rather most carefully investigate in which of the anatomical conditions of phthisis pulmonalis, announced above in § 433, *et seq.*, a simultaneous development of miliary tubercles is observed. The final result of a large series of investigations directed singly to this point now is this, that only in a relatively small number of cases the miliary tuberculosis is actually entirely wanting. I failed to find it in two cases of rapidily proceeding cheesy infiltration with multiple formation of depots of softening (phthisis florida); I missed it in the few cases of secondary phthisis after measles, which came under my observation, especially in one case, in which all the bronchioles of a certain order, but not the very last, were in ulcerative ectasy with cheesy pneumonia of the nearest surroundings, and consequently presented the delusive picture of a uniformly disseminated miliary tuberculosis. For the remaining forms, in which the complication with tuberculosis could be distinctly demonstrated, I feel myself constrained to state a similar relation of the coexistence of inflammation and tuberculosis, such as we learned to know in the "tuberculous" ulcerations of mucous membranes. The tubercles appear there only exceptionally as actually destroying new formations (urinary passages); we ordinarily observe them in the nearest surroundings, probably also scattered at the base and edges of the ulcers named after them (intestine, larynx), and they thus presented an accident worthy of being inquired into, but not yet well known in its intimate relation to the destructive processes. In opposition to the

* According to the investigations of Cohnheim (Virchow's Ar., 40, p. 1), to which I will return in Croupous Inflammation, the interpretation of these cells as migrated colorless blood-corpuscles, is also admissible.

disseminated miliary tuberculosis, such an occurrence deserves the designation "*localized tuberculosis.*" At the lung, however, we can in general distinguish two forms of localized tuberculosis.

§ 451. The by far most common occurrence is that of less numerous, but well-characterized, miliary nodules, beside the broncho-pneumonia (tubercle-granulation of Laennec), designated in § 433 as pseudo-tuberculous. If we only indefatigably seek, we will meet with the specific new formation, either in the interstitial or parenchymatous connective tissue, upon the vessels, or at the pleura and its inflammatory efflorescences, or finally at the bronchial mucous membrane, probably in all cases, although not decidedly numerous. For this occurrence the view appears of late to make headway, that the tubercles are the result of a local infection through the cheesy material of the inflammatory depot. Although we do not yet know how perhaps this infection may be accomplished, and the way of "embolia" is especially to be entirely rejected, because vessels, upon which tubercles have formed, have by no means been found occluded at those places, and because we may be convinced that every injury of the lumen is exclusively the consequence of a tumefaction, not of a plugging, I say, although we can yet dispute concerning the way of this infection, yet the view in itself appears to me very probable. Therein I rely, upon the one hand, upon the experiments lately contrived by Hoffman, Lebert, and Wyss, by Klebs, Cohnheim, and others, by whom at least something tubercle-like was produced by the inoculation of cheesy detritus; upon the other hand, upon the frequent observation of miliary nodules in the environs of a single caseous depot, be it in the lung, or in a cheesy metamorphosed, mediastinal, or mesenteric gland. Only a short time ago a case came before me, wherein a child, which otherwise presented no tubercle in any part of its body, the pleura pulmonalis dextra, and, mark well, also the opposing place of the pleura costalis, contained miliary nodules in a tolerable amount. Upon the pleura pulmonalis the nodules were placed more closely together towards the lower border of the upper lobe, and finally formed a dense pavement, generally stellated, exactly above a place where, in the upper lobe, an old cheesy depot, broken down at the centre, was met with, while the entire remaining respiratory organ had remained free. How near the conjecture lies here, of a secondary origin of tubercle by infection from the side of the old inflammatory depot, in whose surroundings we so exclusively find the small nodules. If, however, in these cases, we ask concerning the "way" by which the infection of the pleura *costalis* ensued, it will probably scarcely occur to any one to think here of a transportation of coarse-bodied particles by way of the blood tract, but every one will have to concede that the infection was effected by the contact with the already diseased pleura pulmonalis.

§ 452. With less assurance, then, we claim as a localized tuberculosis, a process, which certainly, according to the macroscopic appearance, appears more than any other as a dense grouping of miliary nodules, and which at the same time has certainly nothing to do with catarrhal pneumonia, but in histological relations presents so much of the non-tuberculous, that a certain reserve in reference to giving it a name appears to me for the present to be in place.

Commonly, in the neighborhood of a larger cavity, which occupies the apex of the lung, in a parenchyma otherwise little altered, we meet with an exceedingly great number of equal-sized, and indeed real miliary nodules of very compact, springy, elastic consistence, and grayish, translucent coloring, whitish at the centre. If the section is a favorable one, we probably also observe that the nodules are not quite irregularly scattered, but according to a certain plan, for example, in lines branching tree-like, or arranged radiating around a central point, peculiarly densely beset. The alveolar spaces of the affected region are *not* filled; the septa partly participate in the new formation, are destroyed in it; in general, however, the displacement, anæmia, and devastation of the parenchyma, decidedly predominates over the just-mentioned states of disorganization; even the presence of air can be shown until the deposition of the nodules occupies the entire space. With this last result there is, then, a condition brought about, which indeed is not to be called an infiltration in the more contracted sense, but which appears to condition just as unfavorable relations for nutrition, and therefore to bring about the dissolution and disintegration of the depot. The formation of a cavity herewith constantly proceeds from a larger bronchus, in whose walls the nodules have likewise fixed themselves. It is especially the peribronchial connective tissue in which they form a connected layer, then they also dip down into the submucous tissue, less numerously into the mucous membrane itself; here, however, the destruction begins with the formation of flat lenticular ulcers, which rapidly enlarge in surface and depth.

§ 453. If we make the microscopic analysis of these nodules, the fact strikes us at the first sight that these in their principal mass do not consist of granulation-tissue, but of a very compact, well-joined connective tissue. A hyaline, translucent, evidently very dense, sclerosed basis-substance, is divided by imbedded, stellated, upon a cross-section, spindle-shaped, anastomosing cells, into a certain number of layers, which are concentrically grouped around a circular darker centre. Where the nodules lie closer together, the peripheral layers of this connective tissue pass over from the one to the other; whole groups of nodules (5–10) may be united into a larger whole. It forthwith becomes evident to us that two of the most prominent peculiarities of our nodules, and at the same time those which contribute the most

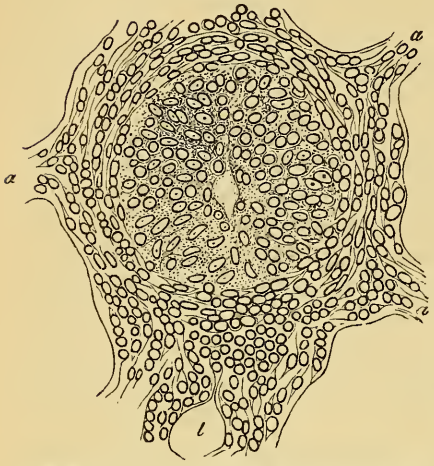
towards regarding them from the very beginning as tubercles, are conditioned by a tissue which in itself has nothing whatever to do with tubercles. Our entire attention is now turned to the centre. It may be that at least here, where the unaided eye perceived a yellowish white opacity, there is to be found a miliary tubercle, which then is inclosed in a connective tissue sac, is encapsulated. The best known authors (among others Rokitansky, Text-book, iii, 87) maintain this view of encysted or encapsulated tubercles already set up by Bayle and Laennec, against which Virchow (Morbid Tumors, ii, 648) believes that he cannot with sufficient impressiveness warn off an imminent delusion. The nodules might be transversely divided bronchi with a thickened adventitia, bronchi, whose mucous membrane degenerated, by a chronic catarrhal or an actually tuberculous process, in which, however, the superficial irritation had led to a reactive inflammation of the deeper layers of connective tissue, to peribronchitis. The almost constant finding of a lumen in the otherwise exceedingly dark and opaque centre of the nodule supports this interpretation. One actually either observes there an angularly distorted gap, or one sees how a homogeneous, translucent substance, which cannot be more minutely characterized, forms a closed ring, which is laid in folds in a similar manner as the intima of a contracted artery. (Fig. 132.) On the other hand it must be observed that at the larger bronchi the nodules themselves furnish the material for the peribronchitic thickening, and that we also do not fail to find in these the central lumina, therefore in the nodules situated in the walls of the bronchi. Furthermore, these nodules also occur at places where bronchi do not pass. They are peculiarly frequent in and upon the connective tissue septa of the lobuli, and just this appearance first called my attention to the fact that they join themselves to the courses of the lymph-vessels with surprising uniformity.* In the pleura, at the connective tissue ensheathings of the primary and secondary lobuli, upon the sheaths of the vessels and bronchi, finally in the submucosa and mucosa of the respiratory mucous membrane itself, the nodules are found, while they are more rare in the parenchyma proper. I succeeded in gaining one step further towards perceiving that in fact the lymph-vessels are those preformed canals from whose walls the miliary nodules are developed. The connection is the following.

§ 454. At a determined point, or better at a short extent of the lymph-capillaries, the inner (epithelial) as well as the outer (connective tissue) layer of the walls experiences a progressive metamorphosis, which gives rise to a considerable thickening of both, principally, how-

* I hereby take up for the second time an hypothesis erected by Virchow, and again abandoned by him. Meanwhile, especially, Klebs has developed the doctrine of the lymph-vessel origin of miliary tubercle.

ever, to a circumscribed knotty distension of the lymph-capillaries. A proliferative multiplication of the epithelial cells leads to the formation of a germinal tissue cushion, which from all sides swells out towards the lumen of the lymph-vessel and closes it, except a small cleft-like remainder. Upon a cross-section (Fig. 132) the cells of this cushion are arranged radiating; each radius appears to correspond to a pre-existing mother element; genuine lymphatic elements alternate therein with larger epithelioid forms, rich in protoplasm, as we are certainly also accustomed to find them in miliary tubercle. From this radiating central layer, or centre, a circularly arranged border layer is pretty sharply defined. This is of the same thickness as the other, but does not consist of cells alone, but beside the cells contains a quantity at least equally as great of homogeneous basis-substance. The lamellar arrangement of the latter, combined with a corresponding arrangement in rows of the cellular elements, produces the concentric arrangement mentioned; here also the small rows of two to seven cells may represent the derivatives of a pre-existing connective tissue cell, yet it is conceivable that we cannot judge with certainty here, as perhaps upon proliferating cartilaginous tissue.

Fig. 132.



Cross-section of a lymph-vessel in tuberculous lymphangitis. *l*. Lumen of a vessel as yet but little degenerated. *a*. Alveolar septa, which proceed from the degenerated lobular septum.

In order to see the changes described well, we must make use of the thinnest sections (according to method given in note to § 365), and where it is possible, investigate where the nodules are yet individually disseminated in the connective tissue septa. Here we best succeed in seeing the connection of the lumen with a still less changed trunk of a lymph-vessel; here we also are most likely to get a view of the earliest period of development. The condition, such as I have described it above, thus, is of but short duration. Very soon a peculiar sclerosis of the central substance sets in, which begins at one, or simultaneously at several places, and soon so very much obscures the centre of the nodule, that the distinction of individual cells becomes quite impossible. From this time, it is true, the connective tissue cortical substance comes out so much the more distinct in its texture and structure; concerning these, however, we have never been in doubt. The gray opacity at the centre of the nodule gives the decision. But how shall we,

after having now actually ascertained its nature, name the process? We are only justified to the title of lymphangitis nodosa. Were we to say "tuberculosa," we would have to pursue the following reasoning: the miliary tubercle arises in the connective tissue; where, however, the connective tissue has a free surface that is covered with an endothelium, it arises by preference through a proliferation of this endothelium. The miliary tubercle of the omentum (§ 283, Fig. 108) furnishes us the best proof for this. Now, however, the epithelia of the lymph-vessels, like those of serous membranes, are to be reckoned with the endothelia, and, moreover, as the cell forms simulate the tubercle-cells, we can see in lymphangitis nodosa only a modification of the ordinary tubercle formation conditioned by the locality.

3. Pleurogenous Pneumonia.

§ 455. In the numerous combinations of pneumonic and pleuritic conditions, it is not always easy to establish which of the two is primary, which secondary. For the most part, it is true, we will deal with the secondary excitement of pleuritic processes through preceding inflammatory processes in the contiguous lung-parenchyma. Thus we will learn to know the pyæmic pleuritis as a consequence of embolic pneumonia; thus the cheesy pneumonia and tuberculosis, almost without exception, call forth acute and chronic pleuritic processes; thus croupous pneumonia obtained its old name of pleuropneumonia, because almost always, when the disease had attained its acme in yellow hepatization, a delicate pleuritic exudation sets in upon the surface of the affected lobe, and the characteristic friction is heard at the walls of the chest. The reverse case is far more rare. In speaking of inflammations of serous membranes, I did not at the time mention the unimportant circumstance, that very commonly in pleuritic processes we find the outermost row of infundibula, which lies immediately under the inflamed pleura, filled with a fibrinous exudation. This infiltration afterwards again dissolves, and just as little occasions a considerable complication of the course, as does the supervention of pleuritis in croupous pneumonia. In fact, in the so-called pneumonia dissecans we also know an example, it is true, on a large scale, of pleuritic processes continued to the lung. The pneumonia dissecans occurs but exceedingly seldom in the human being, while it is more frequent among neat-cattle, and furnishes the pathologico-anatomical foundation of the lung fever.

§ 456. Pneumonia dissecans is a purulent inflammation, let us say a suppuration of the connective tissue septa, which connect the larger lobular subdivisions of the lung. The dissolution of the latter into pus necessarily leads herein to a breaking down of the lobules of the lung into smaller subdivisions, and hence is derived the very appropriate name.

As a rule, we may convince ourselves even by the unassisted eye, that here the lymph-vessels, which in those connective tissue septa pass from the pleural surface down to the root of the lung, are answerable for the conveyance of the inflammatory irritant. If we have cleansed the surface of the lung from the often great accumulation of purulently disintegrating pleural exudation, we perceive the net of lymph-vessels filled with and encapsuled by pus, as they surround the secondary lobules as yellowish-white varicose cords, and descend upon the lateral surfaces of the larger lobules already separated from each other. The division of the lung into lobules may be a more or less complete one; as a rule, however, the fatal issue occurs so early, that it ends with a partial separation, or even only with an indication of separation. We often find only a brawny infiltration of the septa, here and there supplied with purulent stripes; the septa being thickened to many times their normal breadth.

4. Diseases from Inhalation of Dust.

§ 457. Only in the course of the last ten years has it been proven as an incontrovertible fact, that molecular bodies, which are suspended in the respired air, may penetrate from the bronchi and alveoli into the lung-parenchyma, to either persistently remain here, or to be conveyed onward with the lymph-current to the lymph-glands of the root of the lung, and then be deposited there. A relation of this kind, it is true, had been conjectured already for a long time; above all, English physicians had interpreted in this sense the black lung of their workers in coal (the coal-miner's lung); against this there was opposition raised in Germany, and this opposition, conducted by Hasse and Virchow, has at least had this good result, that at present, beside the inhalation of carbon, we also admit the autochthonous origin of the lung pigment from transformed coloring matter of the blood, and indeed in extensive limits, and thereby certainly come nearer to the truth, than if, in an unjustifiable partiality, we should only recognize the one way as possible. I was at that time myself present in the Pathological Institute of Berlin, and actively participated in the histological investigation of that black lung, which in the year 1860 was furnished to the dissecting-table from Traube's clinic, and upon which the microscopic forms of inhaled charcoal-dust could be demonstrated with all certainty. Since then the question has been more to determine the range of a fact in itself established, a task, in whose solution Zenker has participated in a prominent manner. At present we distinguish the following forms of *pneumonokoniosis* (diseases from the inhalation of dust).

§ 458. 1. Inhalation of coal-dust, *anthracosis*. It appears that actually a large part of the black pigment, which in increasing age accumulates in ever larger quantity in our respiratory organs, is inhaled coal-

dust. This is commonly derived from the incomplete combustion of wood, turf, coal, illuminating materials, and other combustible substances, and was suspended in the atmosphere as *soot* or *smoke*, until it reached the respiratory passages by inspiration, and remained attached here to the moist walls. The fate of the exceedingly small granules is various according to the place at which they remain attached. As far as the bronchial mucous membrane is covered by ciliated epithelium, the pigment cannot penetrate into its parenchyma. It settles here upon the mucous covering, and in part gradually by the ciliary motion, in part suddenly by coughing, is pushed with the mucus towards the glottis, and forwarded towards the exterior. If we widely open the throat of a frog and strew its upper covering, which is clad with ciliated epithelium, with coal-dust, we see with the naked eye how the black granules move towards the front; just so the transportation may ensue upon the mucous membrane of the human respiratory tract, and when the bacchanalian student, upon the morning after a jovial evening, finds his sputum "blackish-gray," he may confidently recognize in this black substance a portion of the previous evening's inhaled lamp-soot, which during the night was conveyed into the trachea by the ciliary movement, and placed ready for expectoration. If we examine such a sputum microscopically, we find the small black granules for the greater part inclosed in round cells. The membraneless cells of the sputum, also called mucus-corpuscles, have utilized the time (in analogy with the colorless blood-corpuscles), to take up into themselves a portion of the solid particles which existed in the mucus surrounding them.

Those coal particles which reached the alveolar parenchyma, behave quite otherwise. There can be just as little question here of a mucus secretion as of ciliary movement. The particles of coal, therefore, remain quiescent for the time being, in order afterward to *penetrate* into the soft tissues. If we ask, how is the latter possible? where are the impelling forces? I would answer in the first place by pointing to the difficulty, nay, the impossibility of removing the particles of coal once adhering to the alveolar wall. Furthermore, the great hardness and angularity by which the solid coal is characterized, probably as well in the minutest atoms as in larger fragments, makes these atoms peculiarly fitted to penetrate the soft tissues of the body, if but the slightest impulse is given them from any side whatever. Hence, so soon as the atoms of coal have entered upon the lung-parenchyma proper, they will in general follow the current of the extra-vascular fluid, and with this will finally tend towards the system of lymph-vessels. Upon this route, however, they here and there meet cellular elements, which have the capacity to persistently fix small solid bodies in their protoplasm. The stellate connective tissue corpuscles come foremost into consideration here; in the next place also the migrating cells of amœboid nature existing in the connective tissue of the lung, which carry along with

them the black coloring matter taken up, wherever they meet it. That which remains, which is not retained in cells upon the route to the lymph-vessels, then flows towards the root of the lung, and reaches the lymph-glands of the mediastinum. Here an insurmountable obstacle first opposes their continued advance, since all the numberless lymph-corpuscles which are here stored up, are ready to feed upon the black granules, and to take up as many of them as can possibly find place in their protoplasm.

§ 459. The preceding is, it is true, but a theoretic representation upon the probable way, which the particles of coal having reached the lung-parenchyma may enter upon, a representation, however, which in fact most intimately agrees with the condition found of the anatomical distribution of the pigment in the lung. In the first place, if we observe the lung of an older individual from its outside, and with the naked eye, we see the boundaries of the contiguous lobuli marked by black lines and spots; by magnifying with a lens at these lines we can see more minute ramifications penetrating into the interior of the lobule, and follow them up to the infundibular septa. Upon cross-sections, the accumulation of pigment in the connective tissue, which surrounds the bronchi and the vascular trunks, is the most striking. This in general corresponds to the arrangement of the lymph-vessel system, whose radicles lie in the infundibular septa, while the larger branches meet together in the lobular septa into a network, for whose drainage partly the pleural, partly the peribronchial and perivascular lymph-passages are employed. They are, therefore, the borders of this lymph-current, in which we find the chief places for the deposit of this lung-pigment. In the microscopic investigation, wherever the pigmentation is less dense and dark, we can establish the predominant participation of the stellate connective tissue cells in the pigmentary absorption, while the surroundings of the larger lymph-tracts, as a rule, are covered with a perfectly dense cloud of black granules, making every structure indiscernible.

§ 460. As the pigmentation of the lung advances, the pigmentation also of the lymph-glands at the root of the lung develops more and more. Here, also, we can make the observation, that in the first place the borders themselves of the lymph-current take up the black coloring matter; thus, there is a stage of pigmentation of the lymph-glands, in which first of all only the capsule, the lymph-sinus, which surrounds the terminal alveoli, and the medullary substance are colored. The structure of the lymph-gland, under these circumstances, becomes most elegantly perceptible even to the unaided eye; if we investigate more minutely, we find the black granules partly in the delicate cellular net, which is expanded in the lymph-sinus, partly in a variously broad zone of lymph-corpuscles, which are the nearest contiguous to the lymph-sinus. Afterwards, it is true, the pigment penetrates into all parts of the lymph-gland, every indication of a structure is effaced, and disappears in a

uniform deep black coloring, which is connected with a moderate increase of volume of the organ. In § 461 we will speak of a yet further metamorphosis.

§ 461. From the hitherto considered, I might say, physiological anthracosis, it is but a short step to the anthracosis of the coal carriers and miners. The coal here does not only penetrate into the air-passages in the form of minutest atoms, but also less minute, and finally quite coarse particles, discernible even by the naked eye. In the parenchymatous juice of the above-mentioned lung of Traube, I found a carbonized so-called dotted cell of fir-wood, upon which I counted seven porous canals, side by side. The particle of coal had half the length of the alveolar diameter. Such large "atoms," now, it is true, do not penetrate into the parenchyma of the lung, but are soonor or later again thrown out with the sputum. Constantly, however, the penetrating particles are also considerably larger than in ordinary melanosis, and we can very distinctly see and admire upon them the sharp edges and pointed angles, which make them fit for penetrating. The charcoal splinters especially distinguish themselves by thorn-like prominences, and furthermore in thin layers by a remarkable ruby-red translucent color. All parts of the lung-parenchyma are uniformly deluged by this pigment. Upon every connective tissue septum, alveolar and infundibular as well as lobular, beside a depot of larger particles of coal at the centre, we find a less dense accumulation round about at the edges. (Fig. 133.) Whatever cells there are, round as well as spindle-

Fig. 133.

Anthracosis. Coal-dust inhaled into the alveolar septa of the lung. 1–300.

formed and stellate, are overburdened with minute black granules; here and there we also see larger particles of coal lying in the parenchyma of a small round cell, which we especially meet with in the sputum.

It is manifest that the intrusion at least of mechanically irritating bodies in such measure, cannot remain without the most detrimental

influence upon the respiratory organs. Hence, we find among their consequences at one time bronchial catarrh with muco-purulent sputum, in addition to this emphysema, more rarely parenchymatous changes of an inflammatory kind, which merit a more exact investigation. According to older statements (Thomson, 1826) we have a partial consolidation of the lung-tissue and the formation of small cavities, which are filled with an inky fluid, therefore, in general probably lobular catarrhal pneumonias with indications of eventuating in phthisis.

In the anthracosis also of coal miners, the bronchial lymph-glands decidedly participate, and are wont to partake pretty vigorously in the inflammatory reactions of the parenchyma. In the common physiological anthracosis I twice saw a consecutive suppuration of the glands and opening of the main bronchi; in the anthracosis of coal miners this is said to occur more frequently; that which we can almost always observe is a gradual thickening and condensation of the connective tissue of the melanotic lymph-gland, which slowly but surely produces the obsolescence of the organ. Not only does the capsule thicken, the delicate trabeculæ especially sclerose, which stretch across the lymph-sinus and form the connective tissue framework of the lymph-alveoli and tubules. The lymph-corpuscles disintegrate; finally, there only remains yet an abundant fibrillar connective tissue, which by its arrangement in concentric circles, indicates the former globular structure of the alveoli.

§ 462. 3. Inhalation of iron-dust, *siderosis*. First observed by Zenker in factory hands, who manipulate much with oxide of iron,—English red,—therefore, in mirror polishers, dyers, workers of gold leaf, &c. The inhaled dust is here an extraordinarily fine, light brownish-red powder. Hence, to use Zenker's language, for the description of the microscopic and macroscopic relations of the "iron lung" (Eisenlunge), we need only exchange the word "black" for "red" in the description of the coal-lung, in the representation (Fig. 133); instead of the coal atoms there existing, we need only insert red, and of course on an average smaller, especially very uniform particles, in order to suggest completely a true conception of the condition of the iron-lung.

The consecutive changes consist partly in a catarrhal affection of the bronchial mucous membrane, partly in certain multiple lobular affections, which were designated by Zenker as indurating interstitial pneumonias. A hyperplasia of the interstitial connective tissue, "whilst exempting the walls of individual vessels, brings about a consumption of the elastic tissue, at the same time, in a way not yet certainly fixed, leads to the obliteration of the alveolar spaces, and places in the place of the spongy lung-tissue, a solid induration." Thus we find the whole lung more or less thickly permeated by roundish, compact, grayish, transparent nodules of the size of a pin's head to a pea, which evidently present the beginnings of a simultaneously existing formation of cavities. This con-

dition has for me too great a resemblance to the form of localized tuberculosis of the lung, described in § 452, that I should not think of a more than accidental coincidence, yet I will by no means hereby influence the independent judgment of my readers.

Concerning the inhalation of other kinds of dust, particularly silicious dust, there is up to the present but little extant; Kussmaul and Schmidt found in the ashes of the lung of a stonecutter three times as much silicic acid as in other individuals.

5. Croupous Pneumonia.

§ 463. One of the most frequent and, therefore, best known in its symptoms, its course and issues, of lung diseases, the croupous pneumonia, is at the same time less approachable in an etiological relation than all the others, and even when, based upon some unequivocal observations, we have proclaimed the taking cold as the common cause, there has yet by this no insight been obtained into the process of taking cold. For what has the partial refrigeration of the outer skin to do with the inflammation of an interior organ?

The term croupous pneumonia, which is now generally customary and has taken the place of the older appellation, for example, peripneumonia, arises from an intimate resemblance to croup of the larynx and trachea. In both there is deposited upon the surface a firm, fibrinous exudation; in the latter, upon the surface of the mucous membrane; in the former at the surface of the aveoli and infundibula. The interposed sections of the respiratory tract, namely, the smaller and larger bronchial tubes, may participate as well in laryngeal as in parenchymatous croup. The fibrinous exudation commonly forms here solid, *i. e.*, because of the narrowness of the tubes, no longer hollow cylinders, which, in conformity to the bronchial ramifications, divide forked likewise, and, as a rule, upon being thrown out, yet present a coagulum branched tree-like. It is manifest that this bronchitis crouposa is only of high clinical interest in laryngeal croup, while in parenchymatous croup it does not much matter whether the bronchi, leading to the parenchyma incapable of respiration in any event, convey air or not. The bronchial ramifications are very rarely the exclusive seat of croupous exudations; a young man in the environs of Zurich, for several years in succession, had a febrile affection with the most extreme dyspnœa, which was wont to disappear with the evacuation of numerous bronchial coagula. The coagulum, which was given to me for examination, was derived from a medium-sized bronchus. The starting-point of the extension of the process at each time naturally began here (compare Biermer in Virchow's Handbook of Special Pathology and Therapeutics, div. 1, p. 714). But let us return to our subject.

§ 464. The oldest teaching conceived pneumonia as a parenchyma-

tous swelling. This, based upon the coarsest perception of changes that had taken place, was done without a suspicion that it had its seat much less in the parenchyma than in the hollow spaces of the latter. Laelius de Fonte compared the inflamed lung, principally because of its consistence, probably, also, because of its color, to the liver, and called its condition hepatization. He thus became the founder of our present nomenclature. We distinguish yet more specially between a red and a yellow hepatization, and add to these two principal stages of inflammation yet an initiatory stage (engorgement, Anschoppung, engouement), and a terminal stage (purulent infiltration and resolution).

Croupous pneumonia presents us the best opportunity, the most beautiful and the most exact example, of proving how a histological process, whose individual members of necessity develop the one from the other, upon the one hand directly explains the macroscopic changes of an organ, upon the other elucidates the alterations of its function and the physical symptoms. We will attempt to prove this step by step, whilst we let the corresponding phenomena follow the "histological detail" of each stage, in the sphere which is of secondary importance to us.

§ 465. First stage, engorgement. All the vessels of a larger section of a lung (mostly an entire lobe), are exuberantly filled with blood. If we harden small pieces, tied and cut off, in Müller's fluid, then in alcohol, and make thin sections, we are surprised at the considerable dilatation and coiling which the capillaries have experienced. They arch forward far into the lumen of the alveoli, and visibly diminish it. The commencing exudation of a viscid fluid rich in albumen introduces the coming exudation and extravasation. Here and there, especially in the connective tissue septa and under the pleura, it has already come to small punctated extravasations of blood.

For the naked eye the portion of lung distinguishes itself by its red color, for the sense of touch, the loss of elasticity is especially striking, also the compactness, density, and weight, beside the scanty amount of air. The air present may be churned to and fro, because the viscid fluid mentioned prevents it from escaping. The inspiration and expiration also have to contend with this viscid fluid, as the crackling sound shows; for function, however, this portion of the lung is now already as good as lost, and as the patient is not yet accustomed to the vicarious function of the healthy remainder of his respiratory organ, the dyspnœa, and what of subjective symptoms are joined to this, are wont even now to be developed in the highest degree.

§ 466. Second stage. Red hepatization. It comes to the exit of constituents of the blood from the exuberantly filled capillaries. Red blood-corpuscles, colorless blood-corpuscles, and liquor sanguinis appear free upon the inner surface of the infundibula and alveoli, and are here combined, by the fibrin coagulating between them, into a solid body, filling the lumen, the pneumonic exudation. Since Harvey's great dis-

covery of the continuity of the vascular walls throughout the whole body, pathologists have constantly been at some pains to find a suitable explanation for certain phenomena in the province of hemorrhage and exudation, which do not so well accord with this principle. The pneumonic exudation pre-eminently belongs to these. A recently hepatized piece of lung is injected from the pulmonary artery with a blue glutinous mass, then hardened, and thin sections are made. Upon these sections (Fig. 134) we find the alveolar walls exactly constituted as though we had injected a perfectly healthy lung (*a*), the same number

FIG. 134.

Recent croupous pneumonia. *a*. Alveolar septa with injected capillary vessels. *b*. The exudation. 1-300.

of intervascular and vascular nuclei, that most external layer of scattered, rudimentary nuclei, which we regard as the remains of the epithelium, all unchanged. And yet within the lumen there is a finely filamented coagulum (*b*), which incloses numerous colored and colorless cells. The cells must therefore proceed directly from the vessels, they must have passed through, migrated through their walls, although we cannot discover the slightest abnormal opening upon the walls. We, in conformity with Virchow, having been at pains to trace back everywhere the plastic exudation of the humoral pathology to a local proliferation of the connective tissue, must in face of this picture be convinced, that our teaching is in want of a very essential limitation and modification. Cohnheim* also has already obtained a sure foundation for the new doctrine, by the more exact study of the inflammatory processes upon the exposed mesentery of the frog. We know, that there, in the measure that the circulation of the blood becomes slower in the dilated veins and capillaries, the colorless cells adhere to the walls of

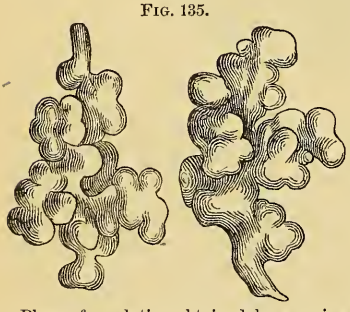
* Loc. cit.

the vessels, and thereupon migrate externally through minute preformed stigmata. This then may also be the process which lies at the foundation of the pneumonic exudation.

The composition of the infiltrate is subjected to very considerable variations. It is true the red blood-corpuscles are never wanting, yet in the one case they constitute but a small fragment of the cells present, while in another they amount to more than double the colorless, in individual more rare cases, however, are so massively accumulated, that we with reason ask, whether this must not rather be termed an extravasation than an exudation.

This "hemorrhagic character" of the exudation gives the impress to the whole second stage of pneumonia. We are reminded of this by the "prune-juice colored" sputa of the patients, by the term "red" hepatization. In fact we must ascribe the decidedly red, liver-like color of the infiltrated portion of lung more to the extravasated blood than to that contained in the vessels, as the quantity of the latter stands in pretty accurate inverse proportion to the quantity of the exudation, consequently is already less than in the stage of engorgement, for example. The greater weight and compactness of the hepatized lung, the complete exclusion of air depend upon this, that now also the last remains of the infundibular and alveolar lumen is filled by a solid mass. If we scrape the cut surface with the edge of the knife, and observe this in reflected light, we see the small exudation plugs projecting above the level in the forms of roundish tuberosities, and indeed may also feel them by touching. We call this the pneumonic granulation. (Fig. 135.) In this dense, actually liver-like parenchyma, the inspiratory sound, as it arises from the rushing of the air into the trachea and the larger bronchi, without its tone being essentially changed, is transmitted to the ear of the physician, which is applied externally at the thorax. We hear the bronchial respiration at most mixed with some large vesicular crackling sound, but no longer drowned and changed by vesicular respiration or the fine crackling sound. The percussion-sound has become perfectly dull; we may determine the extent of the inflammatory depot within half a centimetre.

Fig. 135.



Plugs of exudation obtained by scraping the granular cut surface of a hepatized lung. They are specially fitted for studying the forms of the infundibular spaces of which they are casts. Compare § 411. 1-30.

§ 467. Third stage, yellow hepatization. After the red hepatization, as we saw, has been acomplished without any assistance of the proper lung-tissue, the subsequent entrance of *parenchymatous* textural changes forms the proper central point of the stage now following. That which we in vain seek for in Fig. 134, namely, a luxuriant cell-formation in the

province of the pre-existing connective tissue and epithelium of the alveolar parenchyma, we find abundantly represented in Fig. 136. In all the vascular interstices are found heaps of young cells; the whole inner surface is covered with a compound layer of epithelial elements, which are abundantly mixed with lymph-corpuscles. We have here, in fact, the indication of a genuine catarrhal inflammation, and will have to return to this point more specially. In the first place, now, the parenchymatous infiltration causes a further increase of volume, a still greater weight, elasticity, and density of the inflamed portion of lung; the pneumonic granulation is less decided than formerly, because of the swelling of the septa. The most striking, however, is the change of color, which passes over from dark reddish-brown into a reddish-yellow, and finally, whitish-yellow. As the principal cause of this, the circumstance is undoubtedly to be regarded, that by the newly added infiltrate, the bloodvessels are placed under an external pressure, which interferes with the influx and the passage of blood. Furthermore, it is owing to the locality of the infiltrate, close around and between the blood-vessels, that the color of the blood yet present, makes itself less obvious; finally, in the third place, we have to bring into account the already commencing decoloration of the extravasated red blood-corpuscles, which specially effects the paling of the infiltrate, and the prevalence of the whitish purulent tint determined by the colorless blood-corpuscles.

Moreover, we would seriously err, did we assume that the yellow hepatized lung already during life presented the same high grade of anæmia which it presents after death; for I have constantly succeeded in injecting completely, and without very considerable pressure, the yellow hepatized lung, although, on taking it out, it contained no longer any blood. This is as much as to say, the soft, elastic pressure, under which the lung-capillaries are placed on the part of the exudation, is indeed overcome by the force of the living heart, but if the heart becomes feeble, and finally, ceases to beat entirely, this pressure suffices to press the blood out of the capillaries, and in the general equalization after death, to place it, perhaps, in the heart, or in the large veins of the body.

§ 468. Fourth stage, purulent infiltration, resolution. As the stage of yellow hepatization is introduced by a change of the parenchyma, so the final stage of pneumonia is introduced by a metamorphosis of the exudation; namely, while the parenchyma for a time yet continues in its purulent catarrhal cell-production, the connections in which the exudation had hitherto stood with the surface of the alveoli, are everywhere broken up; the fine fibrinous filaments, which we can yet see pass to and fro, in Fig. 134, melt down with the remaining fibrin to a soft, amorphous gelatine, which incloses the colorless, and the remains of the colored, blood-corpuscles, and unites them into a lump, lying loose in the lumen of the alveolus. (Fig. 136.) That this jelly also takes up numer-

ous elements derived from the walls, is probable to me, because we very commonly meet with large amounts of black granular pigment in it, which perfectly agrees with the known lung-pigment. This pigment (see Fig. 133) formerly rested in the interstices and cells of the connective tissue of the lungs, and can only have reached the surface by the black cells being floated out or migrating.

Fig. 136.

Croupous pneumonia in a later stage of development. Melting down of the exudation. Catarrhal desquamation of the alveolar walls. 1–300.

Touching the chemical part of the metamorphosis of fibrin, I have already, formerly (§ 39), expressed myself for a transformation of the fibrin into mucus. This was done in respect to the changed behavior of the exudation towards acetic acid. Acetic acid, which during the red hepatization only serves to clear up the exudation, and to dissolve the fibrinous filaments, now effects a distinct precipitation of mucin. Still, it is well to bear in mind herewith, that this mucin, which we find in the later stages of inflammation of the lung, may also arise from another source, that, for example, it may owe its origin to a mucoid metamorphosis of cellular elements, while upon the other hand the fibrin may have been converted into a soluble modification, which need not necessarily be mucus.

Thus, therefore, the rigid masses, which fill up the alveolar parenchyma, are gradually dissolved into a slippery, slimy substance, which becomes continually more thinly fluid in the course of time. If we now scrape over the grayish-white still anæmic cut surface with the scalpel, we no longer observe a trace of granulation, while an abundant quantity of purulent fluid runs down the knife-blade. Pieces of the organ cut off can scarcely be held in the hand because of their great slipperiness.

The very last stage may be regarded as a preparation for the removal of the pneumonic exudation; thus, the removal is accomplished in only the smallest part, by the way of fatty degeneration, and the resorption of the detritus; the principal mass of the exudation is expectorated, is cast out per sputum. For this, however, the relations are, in themselves, as unfavorable as possible. The infundibula only communicate with the afferent bronchus by a comparatively small open-

ing. Upon the fibrinous casts, Fig. 135, the pedicle, *a*, represents the lumen of the opening through which the entire voluminous fruit, which hangs from this stem, is to be evacuated. This can evidently only be possible when it has completely lost its original rigidity, when it has been converted into a semi-fluid condition. Then a vigorous effort at expiration may suffice to pass the plug through the narrow opening, and thus relieve the infundibulum of its abnormal contents. As a rule, a complete liquefaction of the exudation into "purulent mucus" precedes the evacuation, as we meet with the casts of the infundibula, but sparsely upon the whole, in the sputum coctum of pneumonic patients.

§ 469. As the evacuation progresses, the anæmia ceases; nay, the blood is wont now to return with relatively greater force, so that, when everything is again accessible to the air, rather a darker color of the part that was diseased results. This is derived from a certain relaxation, especially of the contractile and elastic parts, in consequence of the long-continued disturbance of nutrition in so high a degree. This relaxation may be so considerable, already in the stage of resolution, that the parenchyma, upon slight pressure under the pleura, breaks in. The gap thus produced then rapidly fills with pus, and looks like a subpleural abscess. The want of elasticity, moreover, remains behind for a long time after the healing, and only gradually yields to better relations for nutrition, a circumstance which the attending physician should constantly bear in mind.

§ 470. In what has preceded we have pictured the typical course of inflammation of the lung, as it attacks either, but one lobe, or, as is yet more frequently the case, as it is wont to attack several lobes in succession, or even simultaneously. In passing, we merely indicated the points at which the byways branched off from the main road, and we will now return to follow up these byways. These are the *varieties and abnormal issues* of lung inflammation.

§ 471. *a.* Issue into gangrene. There are principally two causes, which predispose the transition of an inflammatory infiltrated section of lung into gangrene. The one, we find, in the existence of some bronchiectatic cavities with putrid secretion within the pneumonic lobe. We may here in the most cases regard the ill-disposed bronchiectasy itself as the cause of inflammation, and we may conceive, that also the putrid character of the future metamorphoses of the infiltrate may be directly transferred from the putrid contents of the bronchiectasy.

The relations are different in those cases of gangrene of the lung in which the putrid element—so to say—develops autochthonously. The question here generally, as my own investigations have taught me, is about a peculiarly decided prominence of the *hemorrhagic element* in the stage of exudation. At another place we will learn to know the circumscribed gangrene of the lung as the typical issue of hemorrhagic infarction of the lung. In the latter the air-spaces are actually filled

with coagulated blood, the circulation entirely ceases, and, as it is known that no body under favorable conditions putrefies so easily as coagulated blood, we may comprehend how, in the hemorrhagic infarction of the lung, the gangrene *must* occur of necessity. There are, however, pneumonic exudations, which are so rich in red blood-corpuscles and fibrin, that the difference from hemorrhagic infarction is very slight, and an unpracticed observer might actually fall into doubt. Then it must, therefore, not surprise us if similar causes produce similar effects, and gangrene also sets in here.

In reference to the appearances of gangrene the prominent participation of vegetable parasites in the processes of decomposition has lately been announced. According to Leyden and Jaffe the yellowish-white pulpy plugs, of the size of a millet-seed to a bean, with smooth surface and a decidedly unpleasant odor, occurring in the sputum in gangrene of the lung, consist, beside an amount of minute fat-globules, fat-crystals, pigment-granules, and elastic fibres, of an immense amount of small granules and short staff-like bodies, which, upon the addition of some fluid, undergo a lively oscillatory movement. According to the views of the authors mentioned we have to do here with the roving spores of a fungus, and, indeed, with derivatives of the leptothrix buccalis originating in the mouth. They believe that the germs of this fungus constantly pass in large amounts into the air-passages, and reach the lungs, but only come to multiplication and higher development when in a putrefactive depot, in a stagnant, putrefactive fluid (bronchiectasy), they find a soil suited to this. According to the latest investigations of Joh. Lüders we need not at all recur to the migration from the air-passages; the germs are everywhere present in the form of quiescent vibriones, and ready to proceed to further developments, when the medium in which they exist begins to putrefy. For the blood the presence of quiescent vibriones has been quite specially demonstrated, and it has been shown that the quiescent vibriones change into movable ones as soon as the blood dies.

In other respects the phenomena of gangrene are made up of the processes in the putrefaction of the blood, the protoplasma cells, the glue-yielding substances, and of the elastic tissue as we described it in §§ 11 and 19. In the diffuse gangrene of the lung the parenchyma to a greater extent has been converted into a grayish-green, exceedingly discolored, and disagreeably smelling pulp, within which the more resistant structures, especially the vascular walls with the elastic fibrous bundles attached to them, are maintained, yet recognizable for a long time while all remaining formed parts are destroyed. Here and there, by the partial expectoration of the gangrenous ichor, cavities are formed with torn shreddy walls. At the periphery of the gangrenous depot, we find a more gradual transition into recently hepatized lung-tissue; pneumonic infiltrates of more recent date, and evidently first called

forth by the existence of the depot of gangrene. Only in very limited extension of the gangrenous changes, and especially when the gangrene first set in at a later stage, when already a vigorous reaction of the lung-tissue had begun, is the healing of conditions of this kind to be thought of; the healing ensues with the ordinary means. We will have to mention it on the occasion of circumscribed gangrene.

§ 472. *b.* Issue into phthisis. In considering the yellow hepatization we pointed to the decided catarrhal condition upon which the alveolar wall enters, since it answers the inflammatory irritant by a productive behavior of its cellular elements. The epithelium behaves therein in entirely the same manner as in catarrhal pneumonia. It yields larger, roundish, or roundish-angular cells, richer in protoplasm, which are associated to the remaining contents of the alveoli. Meanwhile in general this homologous epithelial formation is but just indicated, and subsides upon the production of pus-corpuscles, combined with a strong serous saturation of the whole. There are, however, cases where the croupous exudation, to a certain extent, only figures as an introduction to a genuine catarrhal pneumonia; where the fibrinous exudation present is thereafter inclosed in a dry secretion rich in cells of the alveolar walls, and with it falls into the necrobiosis. In vain then does the physician await the resolution of the pneumonic depot, and must afterward convince himself that he has been dealing with a cheesy pneumonia of certainly acute origin. The future course, then, does not distinguish itself from the ordinary appearances of phthisis broncho-pneumonica.

§ 473. *c.* Issue into the *formation of abscess.* This issue is also brought about by the behavior, not of the exudation, but of the parenchyma. It is threatened when the cell-production in the alveolar walls does not keep to the ordinary bounds; when it becomes excessive, and leads to the solution and liquefaction of the support and form-giving interstitial connective tissue. There are, then, in the first place formed small cavities filled with pus and the shreds of lung-structure. These may flow together by the melting down of the parts lying between, and thus give occasion to the formation of larger abscesses, and finally of one quite large, perhaps of an abscess occupying a half or a whole lobe. But the reactive inflammation at the periphery of the depot may also, at any time, produce a vigorous germinal tissue membrane, one inhibiting further progress, which is consequently in relation with the abscess as a granulation surface, continuing yet for a time in forming pus, and finally contracting more and more, and thereby diminishing the abscess-cavity itself.

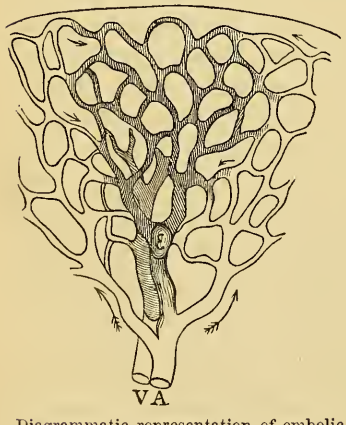
6. Embolic Pneumonia.

§ 474. The kind of conditions which are produced at the lung-parenchyma by the intrusion of coarser particles into the lesser circulation, depends, indeed, as experiment tells us, in every case upon the size of these particles, and yet more upon their chemico-physical constitution;

in human pathology, however, the question is constantly, as far as is now known, about but one condition. Somewhere in the body there is established a process of inflammation and suppuration; the wound of an operation, the fracture of a bone, parturition, &c., have given occasion to this. The veins which run within this depot are filled with thrombi. The thrombosis reaches into the larger venous trunks of the body; here the coagulum breaks up and softens, the fragments arrive into the pulmonary artery through the right heart, and wedge themselves into a branch corresponding to their size (see § 194 *et seq.*, 196 *et seq.*). Now these emboli are of a strongly irritant constitution. Less chemical substances, which may probably form in the decomposition at other times of albuminates, than certain ferments—probably the vibriones constantly present in large amount—impress upon the whole process the stamp of a septic inflammation. While, by the injection of indifferent bodies, as for example, globules of wax, into the pulmonary artery, we always only attain a kind of indurating inflammation; in the case under consideration, suppuration is an unavoidable, necrosis a common, phenomenon. Because of this regular "issue into suppuration" upon the one side, because of the secondary production upon the other, the term embolic pneumonia as "metastatic abscess" has then also come into use.

§ 475. If we have the opportunity, which is not infrequently the case, of studying also the first beginnings of this inflammation, beside the more advanced stages, the deep red coloring, the swelling and the induration of a sharply circumscribed, wedge-formed section of the lung-parenchyma, especially strike us. The occlusion of the afferent artery (Fig. 137, A) has produced a hyperæmia, in the first place static, of the region of its distribution, so enormous that the tensely filled capillaries are here and there torn, and beside the other transudation, a great quantity of red blood-corpuscles has passed out into the alveolar lumina. This *transudation of blood*—as I should like to call the process so as to distinguish it from inflammatory exudation upon the one hand, and from extravasation upon the other—is only the prelude to the actual inflammation, and as the next consequence of the vascular occlusion together with this forms the irritation, towards which the inflammation behaves as a reaction of the organ-

Fig. 137.



Diagrammatic representation of embolic hyperæmia of the lung. A. Small artery occluded at *E* by an embolus. V. Small vein filled even into its trunk by a blood coagulum. The shaded part of the capillary net is the static hyperæmic territory of distribution of the artery, which thereafter becomes the seat of a hemorrhagic exudation. The arrows indicate the collateral routes from which the abnormal congestion is produced. C. O. Weber has given a similar diagram.

ism, or at least as something supervening, something secondary. The more blood actually reaches the surface in this first irritation, the more an actual *stasis* develops from the slower current in the capillaries, so much the more decided will be the gangrenous impulse in the subsequent process; for stasis is death, and, as already mentioned, the stagnating blood, when it is in a moist space, and not excluded from the atmospheric air, is extraordinarily disposed to putrefactive decompositions. For inflammation and new formation, however, there is required the continued renewal of the blood, just as much as in normal nutrition; inflammation and new formation will, therefore, under the circumstances, not at all set in, in certain more central regions of the depot in general, by which then, the always to be marked multiplicity of the anatomical picture in the later stages is explained.

§ 476. *The inflammation*, in itself, presents us the typical picture of a purulent infiltration, with subsequent formation of abscess. The place at which the pus-cells form, is undoubtedly to be sought in the connective tissue of the alveolar and infundibular septa. From here the pus-corpuscles penetrate, migrating to the free surface, and from that side fill up the spaces intended for the air more and more. If this is accomplished, a tolerably rigid hepatization presents itself, upon whose cut surface the unaided eye perceives, upon a whitish-gray ground, very elegant red lines and circles. The gray ground is the purulent infiltrate, the red lines are the alveolar septa, whose bloodvessels are yet pervious to this point, and are filled with blood. In the expressed exudation, the microscope shows, beside the ordinary pus-corpuscles, here mostly englobed and adhering, numerous larger cells, which I imagine in a more intimate relation to the alveolar epithelia, in the first place, because they are very similar to the cells of catarrhal pneumonia, and again, because they not at all infrequently exhibit endogenous cell-formation.

The formation of abscess follows in the footstep of the infiltration. By the complete dissolution of the hitherto sustaining and supporting parenchyma, the entire rigid hepatization melts down into a yellow, creamy pus, in which but few fragments of the alveolar framework, especially elastic fibres and arterial walls, float. The affected part of the parenchyma is thereby actually cast out, destroyed; an abscess cavity has taken its place.

§ 477. Let us now consider the conditions of various kinds which are produced, upon the one hand from the combination of hemorrhagic hyperæmia, and of purulent inflammation upon the other. Here we have, 1, the case, where, by a larger embolus, a larger arterial branch, perhaps supplying the fifth part of a lobe, is occluded. The collateral congestion of the region thus supplied is a very complete one, but the danger of stagnation is also very imminent, hence a condition is devel-

oped, which comes as near as possible to the hemorrhagic infarction. The inflammation remains limited to the bounds of the depot; here we find a zone of a line in breadth, either purulently infiltrated or already liquefied; we get the impression of a circumscribed necrosis and a sequestering suppuration accomplishing the casting out of the necrotic parts. The diametric contrast to this is, 2, the case, where a very friable embolus is shattered into numerous fragments at the various points of division which it has to pass, each of which fragments occludes only a relatively small vessel. We then find in the affected lobe of lung a large number of depots of the size of a hemp-seed up to a cherry, hepatized through and through, or undergoing a purulent fusion. The stagnation of blood here did not proceed to stasis, but only so far as perhaps an inflammatory hyperæmia would also have gone, so that the whole process could present itself as a circumscribed purulent inflammation without actual necrosis. Between these two extremes, however, there yet lie very manifold combinations; thus, for example, we not infrequently find small thoroughly hemorrhagic depots, which are surrounded by narrow inflammatory areas; at another time the extension of the inflammation stands in no relation whatever to the diminutiveness of the occluded vessel, the hepatization—it is true, then, not always a purulent, but just as often a croupous infiltration—extends over a half or a whole lobe, &c.

§ 478. The superficial, subpleural position of most metastatic abscesses is characteristic, and as yet not well explained. We rarely find them in the middle of the organ towards the root of the lung. Hence, also, the never-failing participation of the pleura in the inflammatory process. An originally adhesive inflammation, with abundant serous transudation, which very soon passes over into the purulent form (§ 276), is the condition ordinarily found. The infection ensues by means of the diffusion of putrid fluid from the abscess or gangrenous depot into the pleural cavity. The continuity of the pleura commonly remains undisturbed herewith, nay, the striking appearance is not infrequently seen, that just the spot of the pleura under which the abscess lies, shows no ostensible change, while all around, everything is covered by a yellowish-white, tough layer of exudation. We may indeed assume that here it could not come to an exudation, because the pleural vessels had from the beginning become impervious through the pressure of the lobular infiltrate; afterward, however, the entrance of gangrene excluded the possibility of inflammation. At times a perforation of the pleura ensues either above the centre of the depot or at the edge; the macerated, softened, and half-liquefied connective tissue fibres separate and allow the pus, the ichor and air access to the pleural cavity. It is manifest that the danger of the condition is immeasurably increased by this catastrophe. If to this time the pleuritis may have run its course in moderate intensity, after the perforation it will immediately

assume the most malignant character, so that in fact all hope of the possibility of healing is to be given up.

7. Diseases of the Lung in consequence of Anomalies of the Heart.

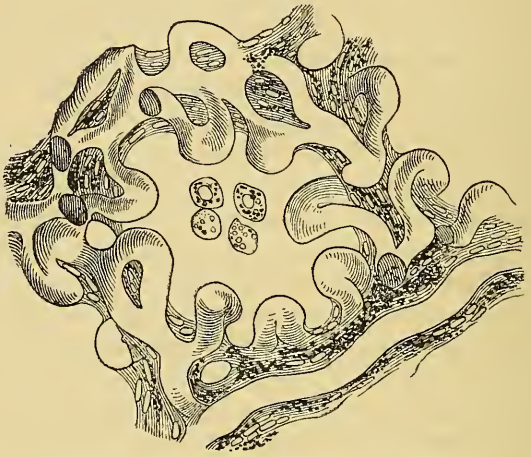
§ 479. In the close relation in which the heart and lung, heart-function and lung-function stand to each other, we cannot be surprised when, in diseases of the heart, the lungs among all the organs of the body are the soonest drawn into sympathy. They are especially the obstacles of circulation in the left heart (insufficiency and stenosis of the mitral valve and of the aortic valves), which almost without exception have, as a consequence, an "exaltation of the blood-pressure in the lesser circulation" (§ 255), and in connection with this a series of anomalies of the respiratory apparatus.

§ 480. 1. *Bronchial catarrh.* The larger bronchi have, indeed, their peculiar vessels derived from the greater circulation (the bronchial arteries and veins), which in themselves would be indifferent to an exaltation of blood-pressure in the lesser circulation; according to the investigations of Rossignol, however, there occur tolerably wide anastomoses between these and the proper pulmonary vessels, and thus is explained, why in most individuals who suffer from insufficiency and stenosis of the mitral valve, in a persistent static hyperæmia of the bronchial mucous membrane, a strong disposition to catarrhal inflammation is given; why exceedingly obstinate and easily relapsing bronchial catarrhs belong to the ordinary symptoms of that affection.

§ 481. 2. The *brown induration* of the lung. This was formerly generally conceived as a peculiar form of chronic inflammation. Rokitansky thinks he recognizes in it a hypertrophy of the connective tissue of the lung, combined with a diffuse, brownish pigmentation, giving the lung an icterous tint. And in fact such an interpretation must not surprise us; for, the lungs, upon taking them out of the thoracic cavity, appear very heavy, turgid, elastic, and compact, but not infiltrated, not even œdematous, but everywhere moderately air-containing; therewith speckled brownish-yellow, and what is the most important, in the microscopic examination of a recent segment, a quite decided thickening of the alveolar and infundibular septa prevails, which we without doubt must regard as the proximate cause of the whole anomaly. The interpretation of this thickening as inflammatory induration was premature. Although a certain increase of the interstitial connective tissue cannot and shall not be denied, yet we must not lay the main stress upon this, but upon the condition of the capillaries. These are *elongated* and *dilated* in a high degree. If we inject a brown indurated lung with a transparent glue (Buhl), or if we place pieces of lung, naturally well injected, previously tied and cut off, into hydrochloric

acid, and then in alcohol (Colberg), in the one as in the other case, upon moderately thin sections, we can prove the interesting fact, that the known capillary tendrils, which run over the septa of the alveoli, arch forward far more into the lumen of the alveoli than under normal circumstances, are therewith considerably dilated, and often appear actually varicose at the points of bending. (Fig. 138.) The dilatation amounts to from 0.01–0.02 mm. of average diameter, while the variations of diameters in normal capillaries are constantly found to be between 0.003–0.007 mm. Through the greater prominence on all sides of

Fig. 138.



Brown induration. An alveolus of the lung with ectatic capillary vessels and deposition of pigment, partly in the connective tissue of the septa, partly in the catarrhal cells which are in the lumen. 1–400.

the capillary loops, the lumen of the alveolus is naturally diminished essentially; hence the scanty amount of air in these lungs. For explaining the older view, however, it must be observed that, when the blood is emptied out of the capillary loops, as is always the case in recently taken sections, we can no longer distinguish the capillary vessel as such, from the remaining constituents of the walls, and the whole imposes on us as a simple thickening of the alveolar septa. Even the larger interlobular vessels, especially the branches of the pulmonary artery, are considerably dilated; yet just here beside the vascular ectasy, a not inconsiderable hyperplasia of the interlobular connective tissue also obtains, a phenomenon which we also find in the liver and the kidneys of persons with diseased heart, as well as wherever long-continued passive hyperæmias have prevailed.

In consequence of continued hyperæmia of the lung-parenchyma, it here and there comes to minute lacerations of the capillary and transition vessels. The extravasated blood, accordingly as it becomes free upon the surface of the alveoli or remains in the parenchyma, will have a different fate. In the former case it is cast out with the sputum, and

imparts to this a light yellow color; in the latter case, it gives the impulse to the oft-mentioned yellowish-brown pigmentation of the lung, which beside the intrinsic increase of volume, forms the most prominent macroscopic characteristic. If we examine more accurately, beside the diffuse imbibition, as well under the pleura as especially upon the cut surface, we observe brown and yellow points beside recent red depots of extravasation. The brown and yellow points are derived from deposits of granular pigment, which evidently have remained behind at such places where extravasations had previously taken place. The pigment in part is free, in part inclosed in cells, like as in the coal- and iron-lung. (Fig. 138.) It deserves to be mentioned herewith, that the pigment-granules are also especially found in such cells which lie free in the lumen of the alveoli, and have by authors been declared as cast-off epithelial cells. That this "pigment of the epithelial cells" should first have arisen in the alveoli is very improbable, because the formation of solid pigment-bodies out of dissolved coloring matter of the blood, requires at least several weeks, consequently a much longer time than those so-called epithelial cells are in general maintained in the alveoli. The pigment-granules, therefore, can only have migrated out of the connective tissue parenchyma, and as they would scarcely enter of their own accord the direction towards the free surface, we come to the idea quite naturally, that they were carried along by the cells in which they are inclosed, consequently, that these cells themselves are migratory cells which have passed to the surface, and not actual epithelial cells. Their diminutiveness also speaks for this, in opposition to those elements which fill the alveoli in catarrhal pneumonia. The real epithelia of the alveoli, as far as my observations reach, are quite unchanged; we must be especially very reserved with the assumption of a desquamative alveolar catarrh, as the lung epithelia of adults are to reckoned with the less irritable elements of the body.

§ 482. 3. *The hemorrhagic infarction* and the *circumscribed gangrene* of the lung. By this we understand the complete filling up of the air-spaces of a circumscribed part of the lung with extravasated blood. If we remember what was imparted above on the occasion of the hemorrhagic and gangrenous pneumonia, as well as on the occasion of the embolic lung processes, we will of our own accord perceive the great anatomical similarity, which the hemorrhagic infarction must have, and in fact also has, especially with the first stage of embolic pneumonia. We can actually say, the hemorrhagic infarction may be an embolic process, for we cannot avoid diagnosticating the anatomical condition of the infarction, when in consequence of an embolism of larger branches of the pulmonary artery we find the hemorrhagic transudation (see § 474) advanced to actual hemorrhage. Cases of this kind also occur in individuals with diseased hearts; namely, when, in consequence of stagnation in the trabecular work of the right auricle or ven-

tricle, coagula have formed in the shape of the so-called heart polyps (§ 258), which, being loosened, serve as emboli. Meanwhile, these embolic infarctions may be distinguished from those produced by the laceration of a larger vessel, by the transition in them from the infarcted parenchyma to the normal surroundings being a very gradual one, and carried through all the phases of hemorrhagic-hyperæmic and simple-hyperæmic infarctions, while in the non-embolic infarction, the injured part elevates itself immediately from the surrounding healthy tissue as a firm, everywhere uniformly dense, dark blood-red wedge. This kind of "blood wedges," as was said, does not arise by embolism, but by the rupture of a larger vessel, and is found, par excellence, in individuals with diseased hearts. The increase of the pressure in the lesser circulation must be regarded as the predisposing cause in their production. In this connection the infarction presents itself as a quantitative excess of those capillary hemorrhages which we have learned to know in the brown induration. As more proximate causes, especially determining the locality of the vascular laceration, we may most probably regard, in all cases, the "fatty usure of the medium and smaller branches of the pulmonary artery." In order to prove this, a very subtle examination of the ramifications of the pulmonary artery is certainly indispensable, as in the main trunks we meet with no possible trace of a process so threatening to the stability of the smaller vessels (compare § 220). Finally, as an occasional cause, probably in all cases a temporary fluxion of the lung is to be supposed, in consequence of which the diminished resistance of the vessels comes into collision with the increased demand made upon them.

§ 483. If the laceration has been accomplished, the blood, with all the force of the abnormal blood-pressure prevailing in the lesser circulation, forces a way into the nearest bronchus. Here upon the one hand it is respired, and thus fills the lobule of the lung concerned, completely up to its terminal vesicles; upon the other hand it flows forwards into the widening bronchus, and since in this route it passes by where new bronchial lumina are continually given off, it is also drawn into these during respiration. At length coagulation setting in, makes an end to this dangerous play. According to the size of the bursted vessel, up to this point,—up to the occurrence of coagulation,—more or less blood will have time to leave the vessel, therefore, also a larger or smaller wedge-shaped section of the lung-parenchyma will be infarcted. We may also imagine the cessation of the hemorrhage conditioned by this, that the blood poured out, by tightly filling and distending the elastic parenchyma, itself produces the counter-pressure which closes the opening and prevents further extravasation. This tense repletion is certainly characteristic, and we must make it quite specially answerable for the further course of the lung-infarction, since it not only has the most beneficial effect in compressing the bleeding vessel, but also the most

injurious, by generally compressing every vessel within the infarction, thereby directly putting a stop to the circulation and producing the death, the gangrene of the part.

§ 484. Over against the diffuse gangrene, considered above in § 471, we therefore at this place bring forward a *circumscribed gangrene of the lung* as a regular issue of hemorrhagic infarction. The firm, dark blood-red mass, elevated bed-like above the level of the surface, or, the cut surface, necroses all at once in all its parts. The red color gives place to one dirty green, the coagulated blood putrefies and becomes fluid; with it are dissolved also the soft constituents of the parenchyma; only the elastic fibres and the thicker, more compact accumulations of connective tissue around the vessels and the bronchi resist solution and form a shreddy tinder, which, being attached at the points of entrance of the vessels and bronchi, float in the gangrenous ichor. The masses are of an exceedingly repulsive odor, which makes itself perceptible to the patient at the moment when the occluding blood-clot of the bronchus leading to the gangrenous depot is also softened, and its contents begin to be expectorated. In the sputum we find elastic fibres in further confirmation of the diagnosis.

Touching the further development of the condition, this is essentially dependent upon the behavior of the neighborhood of the gangrenous depot. It is manifest that in the latter an exceedingly intense inflammatory irritant is given. Hence, a croupous inflammation of the lobules of the lung, bounding the gangrenous depot, forms a very common and mostly also a fatal complication of circumscribed gangrene; likewise gangrenous depots, which lie close to the pleural surface, without exception, call forth pleurisies with disintegrating ichorous purulent exudations. Beside these larger extensions of the disease we however have also to report of a more limited inflammatory process, which is consummated in the immediate neighborhood of the gangrenous depot, and which, when it is developed at the proper time, has as results a salutary influence, and the not at all infrequent healing of the gangrenous depot; I mean the bounding inflammation and suppuration which takes place everywhere at the borders of the gangrenous depot, and shuts this off from the healthy surroundings. Thanks to the peculiar manner of production of the infarction, more minutely described above, this most strictly remains within the bounds of the lobules. Hence, whatever form and size it may have, it will still be surrounded at its periphery, in the first place, by a layer of interstitial connective tissue, and this, as is known, is far better suited than the lung-parenchyma itself for suppurating in a short time, so that no connection any longer exists between the infarction upon the one hand and the healthy parenchyma upon the other. The complete healing is accomplished after the melting down and evacuation of the infarction, by the

formation of a granulation-membrane and the cicatricial diminution of the cavity.

8. Tumors of the Lung.

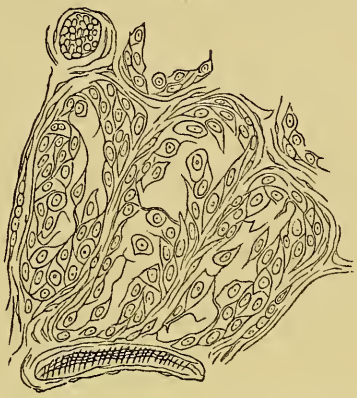
§ 485. The lung is extraordinarily little disposed to primary formation of tumor. Here and there we are surprised in making examinations by finding a small enchondroma of "hyaline-cartilaginous" constitution and gland-like tuberous contours, at most of the size of a walnut, and generally situated subpleural. In such cases, however, we should be well on our guard, whether there is not present, perhaps, a primary enchondroma at another place, or that one had been extirpated, for the lung is a preferred organ for the rare metastases of enchondromas.

The same obtains of carcinoma of the lung. Primary carcinomas occur very rarely, and only in the form of a circumscribed medullary infiltration, while secondary nodes are found somewhat more frequently. The epithelial carcinoma only occurs secondarily, and constantly forms a small nodule of the size of a millet-seed to a pea.

§ 486. Now touching the histological part of the formation of tumor, herein the stroma of the lung exclusively comes into consideration. Nevertheless although in the first microscopic investigations it have the appearance as though we were dealing, beside the *swelling* of the alveolar *septa* everywhere, also with a *filling up* of the alveolar *lumina*, yet we must not overlook the fact that the latter is necessarily conditioned by the former. Like the miliary tubercle, which we upon sufficient grounds have previously taken up, § 446, all tumors, at a certain phase of their production, protrude into the alveolar lumina; they also fill these, but are on that account yet by no means to be compared to an inflammatory exudation, as indeed occurs in the former conceptions of Rokitansky. O. Weber has the merit of having lately called attention to this histologically most important point. Unfortunately, however, I can only recognize the representation given by him of the production of epithelial cancer in its general significance for new formations in general, as the principal case made use of by him, the entire preparations of which yet exist in Bonn, was indeed originally an epithelial carcinoma of the tongue, but in its relapses a simple carcinoma. The description, also, of epithelial cancer of the lung, given by Virchow and Dupuy, suits at least in a histological relation to ordinary cancer. Now either there actually prevails here a certain monotony of histological processes, or the variety has not yet been sufficiently exhibited. I, for my own part, for the carcinomatous degeneration, only know the one picture, delineated by the authors mentioned; the alveolar meshwork of the lung produces numerous nests and rows of cancer-cells, which fill up the lumen laterally. (Fig. 139.) Furthermore, I would like to call attention to the great frequency of a complicating inflammation of the

immediately contiguous parenchyma, an inflammation which has points of comparison with the catarrhal inflammation and leads to filling the alveoli with a dry infiltrate, rich in cells. There is the utmost difficulty in separating from each other, in individual cases, these two processes.

Fig. 139.



Cancer of the lung. Filling up of the alveoli. Degeneration of the septa. 1–300.

And yet often only by such a division can we attain to a correct judgment of the actual size of the cancer nodes. As we see, the histology of cancer of the lung is yet in its first beginnings, for which the relative rarity of suitable material for investigation must bear the principal blame.

VII. ANOMALIES OF THE LIVER.

§ 487. If at one glance we overlook the various morbid forms of the liver, the observation involuntarily impresses itself that the most of them have a determined structural constituent of the organ, either the liver-cells, the interacinous connective tissue, or the vessels, as the point of departure. Hence, it is very convenient to classify the diseases of the liver according to these, their histological starting-points; this should quite specially recommend itself for a text-book of pathological histology. And, nevertheless, I prefer just in the liver, instead of any classification, to allow a loose arrangement side by side, because I regard every anatomical subdivision of diseases, although it appear ever so inviting, as a mistake which gives occasion to errors in the clinical sphere. In the liver, under the rubric diseases of the liver-cells, would appear side by side, the fatty liver, the amyloid liver, and the liver with inflamed parenchyma, conditions, which in fact, have nothing at all in common with each other. On the other hand, the parenchymatous inflammation would be separated from the other forms of inflammation which proceed from the connective tissue, consequently that would be torn apart, which, according to nature, belongs together. Hence, of that subdivision I will only borrow so much, that I will begin with several disturbances proceeding from the liver-cells, because they at the same time are the more simple and more appreciable; afterward, however, I will let the pictures of the diseases follow more according to the clinical relevancy.

1. Fatty Infiltration of the Liver-Cells. Fatty Liver.

§ 488. We have discussed in the General Part (see § 61 *et seq.*) the points of view, under which, besides other fatty infiltrations, the fatty infiltration of the liver-cells is to be considered. We find this just as well in excessive absorption of fat into the blood, as in incomplete combustion of fat, most frequently, where both causes come together, in well-nourished individuals, who take little exercise, in nurslings shortly after taking nutriment, in persons with diseased lungs, especially with tuberculosis, in persons with diseased hearts, beside the peculiar structural changes which are produced by the venous stagnation in drunk-

ards, beside the development of interstitial connective tissue (cirrhosis). The liver serves in all these cases as the storehouse for a portion of the serum-fat absorbed in the intestinal canal, but not yet oxidized, because of the surplus of this article. That the fat from the blood reaches the liver-cells is expressed with surprising probability in the fact, that the fatty infiltration constantly takes its beginning in the region of distribution of the principal afferent vessel, the portal vein.* In slighter

* In the course of the representation we will several times have to return to these territories of distribution of the various afferent and efferent vessels, and hence, I will make use of the first opportunity presenting itself, to impart some words of guidance on this important point.

According to my judgment the structure of the liver may best be clearly and comprehensively demonstrated, if we start from the hepatic vein. Since the minutest ramifications of the hepatic vein, the venulæ intralobulares, occupy exactly the centre, the axis of the structural unities of the organ, the liver acini, they to a certain extent take the place, which in other glands, appertains to the excretory duct. The hepatic vein with its smaller and most minute branches forms the central framework, to which all the other structural constituents are related as an outer investment. The complete and uniform filling-out, or rather the permeation of the space between the larger branches, is accomplished by an arrangement, unique of its kind, that these larger branches, beside the gradual tapering which we perceive in the branches of every tree, experience also a sudden diminution in calibre. If we observe the inner surface of an excised hepatic vein, we can everywhere discover numberless small openings, which either belong to actual small central veins, or still venous branches, whose lumen stands in no proportion whatever to the lumen of the main vein.

The venula centralis, as before said, lies in the axis of the elongated ovoid liver acinus; from all sides the capillary vessels open radiating into its lumen, generally like as we observe in the bristles of certain round brushes, which are used for cleansing bottles. The capillary net in this direction forms parallelogramic meshes, in which the liver-cells are imbedded. The sum of these, as the filling-out mass of a network, presents also on its part a network, the so-called liver-cell net, concerning whose intrinsic organization the latest time only has diffused a happy light. (Ludwig, Hering.) We now know, that this wonderful moulding of the secerning parenchyma into the gaps of a vascular net, that abandonment of an independent structural unity, as we have it in the terminal vesicles of an acinous gland, or in the terminal sac of a tubular gland, still presents but an apparent deviation from the universal law. Although, a single liver-cell is touched on two sides by capillary vessels, it yet has—considered as dice—four surfaces for contact with its neighbors, and at these surfaces of contact the minutest biliary ducts are disposed of as exceedingly minute, but still injectible round intercellular ducts, in such manner, that they present a most minute network, which everywhere avoids the vascular network, and everywhere remains separated from it by the entire thickness of a cell. Upon sections we commonly see a double row of cells between two adjacent capillaries, in whose centre a bile-duct can be followed up for some distance. The trabeculæ of the liver-cell net—*considered in this manner*—appear directly as the tubuli of another gland, in which a central canal, serving for conducting the secretion, is separated on all sides by a cellular layer from the membrana propria and the bloodvessels. The junction of the bile-capillaries into larger biliary ducts ensues at the periphery of the acini, where we will find the latter united with the branches of the vena portæ and hepatic artery.

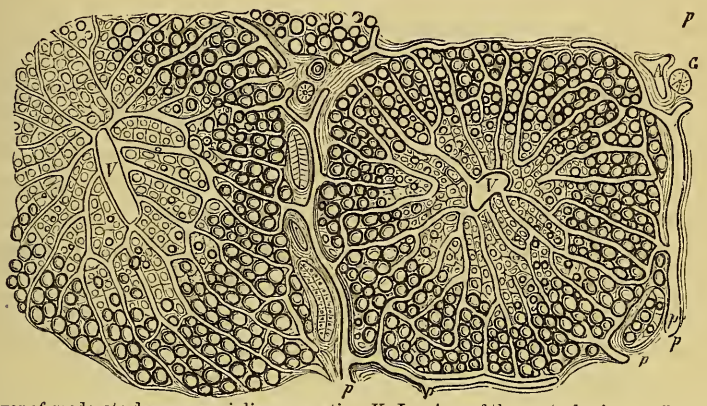
Since we now return to the hepatic vein, whose finest branches are invested all around by the proper liver-parenchyma just delineated, we must state, that by its eight to ten main branches the liver is subdivided into as many lobes, which of course are not prominent upon a quite normal human liver, but indeed, in certain morbid

degrees of fatty liver, hence we only see the outermost edge portions of the acini infiltrated and get the impression, as though the acinous subdivision was rendered somewhat more distinct by yellowish lines, which correspond to the fatty infiltration. The histological detail is typical in its course. In this connection I may content myself by pointing to the discussions and illustrations at § 61 of the General Part. The illustration here adjoining, represents to us a somewhat higher grade of the fatty infiltration (Fig. 140), as we not infrequently meet with it in tuberculous individuals and those with heart disease. The portal zone of the acini is completely impregnated, in the intermediate region the first beginnings are observable, while the centre has yet remained free. The unaided eye now takes notice of that peculiar marking of the cut surface, which has been compared to the cut surface of a nutmeg. There, the cross-sections of the elegantly folded, light-yellowish cotyledons contrast with the dark surroundings; here, they are the yellowish-white portal zones of the acini, which are in contrast with the darker central zone. We find the comparison particularly apt, when we turn our attention not to the single acinus, but to the ramification of a smaller portal canal, which, because its branches are on all sides framed in by the fatty zone, appears not unlike a leaf-formed figure, perhaps, an oak leaf, if you will, a folded cotyledon of the nutmeg. The term nutmeg-liver, moreover, denotes only a light periphery, beside a rela-

changes, and especially beautifully in the congenital lobulation of the organ. The interspaces between the lobes are filled by the so-called *portal canals*. The trunk of this second tree entering into the structure of the organ lies, as is known, at the under surface (porta) and is formed by the united trunks of the hepatic artery, vena portæ and hepatic duct. An abundant amount of loose connective tissue, which is in uninterrupted connection with the subserous connective tissue of the peritoneum (capsule of Glisson), forms the common bed for all three, and this relation is maintained in all the further ramifications. If we observe a microscopic section, we can never be in doubt long, whether a vascular branch, which we hit upon, is a venula centralis, or an afferent vessel. The venulæ centrales are constantly isolated and separated from the adjacent vessels by a broad bridge of liver-substance. The arteriolæ hepaticæ and venulæ interlobulares are either joined into parties of three, as in the porta of the liver, with a correspondingly small biliary duct, and we then have yet a portal canal of a higher order, or we find them distributed in the interspaces at the periphery of the acini, but we can prove their belonging together by the last remains of the common connective tissue capsule, which thread- or membrane-like passes from one vessel to another; namely, the portal vessels separate from each other, first at the periphery of the acini, in such manner, indeed, that the branches of the venæ portæ run where three or more acini meet, and from this point send out their final branches between each two of them. (Fig. 140, *p*.) The arteries penetrate halfway into the interior of the acini, and here first break up into the capillary net. Consequently, we may divide the acinus into three concentric zones; the nearest surroundings of the hepatic vein forms the centre, the distribution of the portal vein the periphery, and the distribution of the hepatic artery an intermediate zone of the acinus. The question herewith, is naturally not about limited territories of a current; on the contrary, the community of the capillary net makes a stricter division directly impossible; yet for judging a series of disturbances, it is of importance to know the intimate relation of these three zones to the vascular connections.

tively dark centre of the acini, wherein it yet remains doubtful whether the periphery is abnormally light, or the centre abnormally dark. A nutmeg-liver of the latter kind is especially observed in persons with

Fig. 140.



Fatty liver of moderate degree, semi-diagrammatic. *V.* Lumina of the central veins. *p.* Interlobular branches of the vena portæ. *A.* Arterial branches. *G.* Biliary ducts.

heart disease, where an ectasy of the venulæ centrales, to be described farther below, gives occasion beside the formation of pigment to a deepening of the central tint. If the fatty liver exists at the same time, the contrast will naturally come out so much the more glaring.

§ 489. If the fatty infiltration advance yet further, so that finally all the liver-cells without exception contain fat-globules, the bounds of the acini are effaced, and one can easily mistake between the border and the centre. The color of the organ is then a quite uniform yellowish-white or brownish-yellow, the consistence is soft, doughy, the finger leaves a lasting impression behind, the circumference and the absolute weight have risen to double the normal, while the specific gravity has decreased; all sharper outlines are effaced, the anterior border especially is rounded off and has come down into the umbilical region. (Fig. 150, vi.) All these characteristics of the fatty liver are readily explained by the quality and the quantity of the infiltrate, likewise the excessive anæmia, which we never fail to find. Still, in the latter connection, we must not believe that the anæmia, which we find post mortem, was already in as high a degree during life. The question here is about a pressure and a counterpressure. Without doubt an abnormal pressure, which for the vessels of the liver has the value of an external pressure, grows out of the tense filling up of the liver-cells. This pressure is, however, elastic, and is overcome up to a certain point by the counterpressure of the blood, of which we may convince ourselves by an injection of the portal vein, which constantly succeeds without any special exertion of force. Only when the propelling force of the blood ceases entirely, this elastic pres-

sure of the fat-cells comes fully into play, and presses the blood yet present out of the parenchyma back into the vascular trunks.

2. Amyloid Infiltration of the Liver-Cells. Lardaceous Liver.

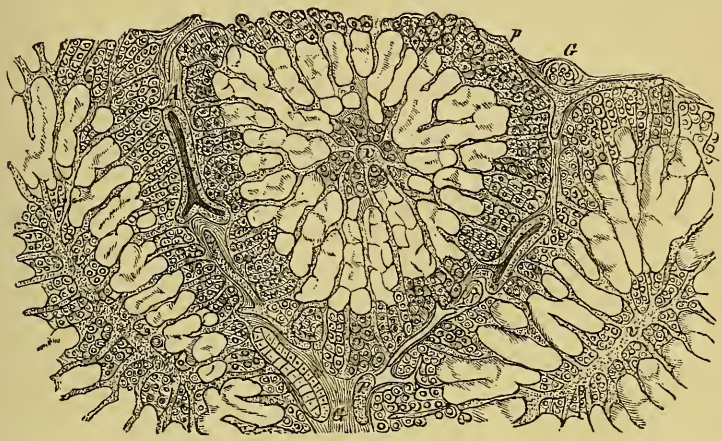
§ 489. The amyloid infiltration of the liver-cells, in very many points, presents the greatest analogy to the fatty infiltration. If we cared only about an approximate representation of the histological processes, we could, almost without more ado, substitute the lardaceous for the fatty. It is true in thus proceeding we must look away from the close relationship in which the genuine fat bacon stands to fat. The substance taken up into the liver-cells is an albuminate, which reminds of the non-nitrogenous, organic substances, especially starch, only by its peculiar behavior towards iodine, by the mahogany red color which it takes on when treated with this reagent. This resemblance meanwhile has been more than sufficiently taken into account, when we retain the name amyloid. In other respects I point to the General Part, § 46, where, beside the question as to the origin and the chemical position of the amyloid substance, the histological detail also of the liver-cell infiltration was discussed. We there saw how the individual element became larger by the intussuscèption of the amyloid substance, how it loses its sharp contours, how its contents become uniform, homogeneously dull, the nucleus vanishes, and how, finally, a vitreous clod or lump proceeds from it.

§ 490. If we now follow the course of the changes at the acinus we cannot fail to find the first deposit of the amyloid substance in the territory which I designated above (see note) as the region of the outlet of the hepatic artery. In the annexed illustration (Fig. 141), which presents a moderate degree of liver-amyloid, one clearly sees how the vitreous intumescence of the liver-cell net has for the present left the periphery of the acinus entirely free, begins perhaps half-way from the periphery towards the centre, and from here reaches to various distances into the region of the venula centralis. In this fact is expressed a certain analogy with the amyloid degeneration of other organs, where the infiltration begins at the small arteries themselves, and is continued from here to the capillaries. The small arteries are wont also to be coaffected in the amyloid degeneration of the liver, but instead of advancing to the capillary walls it advances to the liver-cells, which nearest surround the arterial capillaries.

In the further course of the disease, in the next place, the region of the hepatic veins is completely filled, then the infiltration is first continued to the cells of the region of the portal vein. If this is also complete, each single hepatic cell, consequently also the entire organ, contains from one to two times more solid albuminous substances than normal; each single liver-cell, consequently also the whole organ, is one to two

times larger and heavier than normal; each single liver-cell, consequently also the whole organ, is of a pale gray color, translucent, of wax-like consistence. The sharper edges, which the normal liver has,

Fig. 141.



Amyloid liver. *A*. Interlobular artery with amyloid walls. *G, G*. Biliary ducts. *p, p*. Portal vessels. *V, V*. Interlobular veins. The liver-cells in the central zones of the acini are infiltrated with amyloid substance. 1–300.

have here also, as in the fatty liver, given place to more rounded, swollen contours; the delineation in the diagram (Fig. 150, vii) gives an idea of the colossal enlargement.

The small amount of blood contained in the organ also deserves mention here. This naturally depends in exact proportion upon the increased demand of space which is put forth on the part of the liver-cells. Hence the greater the infiltration becomes, so much less blood moves in a given time through the organ, so much the more also from this side—and quite apart from the direct injury of the liver-cells—will also the function of the liver suffer. There is only a very scanty and thinly fluid bile secreted, which, it is true, may suffice in the otherwise very enfeebled nutrition of the individual. Moreover, the perviousness of the capillaries is maintained to the last. Lardaceous livers of every degree can be completely injected, and we even have the opportunity of establishing the seat of the affection in the liver-cells.

§ 491. Beside the diffuse lardaceous infiltration of the liver there is also yet a deposition into depots, which as yet I have met with but once, and, indeed, in a case of red atrophy (see below). In a liver otherwise presenting the amyloid infiltration only by traces, but actually divided into lobes by the atrophy by congestion mentioned, there were found, at several places in the lobes, solid knots of the size of a walnut, each containing a soft spot at its centre. More exact investigation showed amyloid infiltration of high degree with central suppuration. The suppuration was evidently secondary, for in the scanty pus coming

from the connective tissue of the portal canals were floating the isolated acini, lardaceously infiltrated, and, because of the great chemical indifference of the infiltrate, but little changed.

Combinations of amyloid- and fatty-infiltration are not rare; mostly however so constituted, that the fatty-infiltration appears as an occasional accident.

3. Hypertrophic Conditions.

§ 492. As genuine hypertrophy of the liver we can properly only designate such conditions in which a distinctly demonstrable increase of volume, of a uniform enlargement, or increase of all the textures going into the structure of the organ has been produced. Hence, we recognize and conclude upon hypertrophy of the liver from a decided and striking enlargement of the acini, which in so far forms a certain contrast with a completely normal constitution, as in by far the most cases of similar enlargement we can demonstrate an infiltrate or new formation as the cause of it. It has been believed that we could specially distinguish between a hypertrophy and a hyperplasia of the liver, in the sense that the former was produced by an increase of the size, the latter by an increase of the number of the liver-cells. I must declare the utility of such a distinction as problematical, because we too frequently perceive considerable differences of size, and processes of division in quite healthy livers. The only point of support for our judgment is presented to us by the fact, that a new formation of acini is not observed under any circumstances, that consequently every hypertrophy must in the first place present itself as an enlargement of the acini. The appreciation of the size, however, is facilitated by this, that at least hypertrophic conditions of *high degree* constantly only occur in circumscribed sections of the organ; the question is mostly about vicarious hypertrophies, about a replacement of that which is lost at other points by atrophy, so that not infrequently beside the normal acini we see such acini as are too small, and such as are too large. Here belong the compensatory hypertrophies of single liver-lobules in cicatricial formation, atrophy by pressure, devastation in other regions, which are even not infrequently observed. The judgment may be more difficult in that general hypertrophy, but of lesser degree, which is observed partly in consequence of leukæmia, of diabetes mellitus, partly from long residence in hot climates. Here it, above all, depends upon not mistaking genuine and false hypertrophy. This is most imminent in the leukæmic swelling, which in most cases depends upon an infiltration with colorless blood-cells; in diabetes mellitus also I advise precaution. As a rule we can there prove a different relation of the three vascular distributions in the acinus. The region of the portal vein shows us the liver-cell net in a condition more swollen by imbibition than enlarged, the nuclei upon the addition of iodine color wine-red, which

probably indicates glycogenous substance; the contours of the cells shade into one another, which *probably* is to be referred to an increase of volume of the latter. The arterial region, the intermediate region, is infiltrated with fat, the centre on the other hand almost normal; the condition of the liver-cells at the periphery is here exibited only by indications.

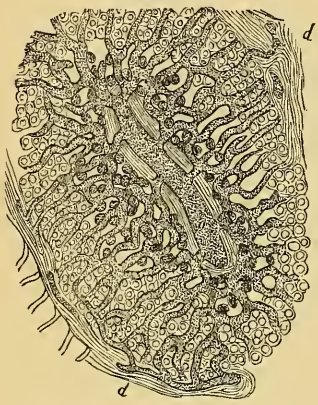
4. Atrophic Conditions.

§ 493. *Simple Atrophy.* In starved individuals, in stricture of the œsophagus, in the refusal of nutriment by persons with mental disease, in marasmus of all kinds, we find the liver strikingly small, brown, the capsule loose or wrinkled, and as the cause of this *general decrease of volume* a diminution of all the liver-cells to a third of their normal extent, which is connected with a development of yellow and brown pigment granules in the protoplasm. We here evidently have the opposite conditions to those which lie at the foundation of the production of hypertrophy; we observe, however, that defective nutrition, the deficient functional irritation makes itself felt in an exclusive atrophy of the liver-cells, while the other portions of the structure yet remain normal. Now, however, as these remaining structural parts exclusively consist of connective tissue and vessels, the relative preponderance of this "fibrous part" causes a tough, leather-like consistence of the organ, which becomes especially perceptible in cutting it, and which might easily give occasion to the erroneous conjecture of a cirrhosis.

§ 494. *Red Atrophy.* A second form of general atrophy develops in connection with those heart and lung affections which are accompanied by a stagnation of blood in the venous system of the body. The hepatic veins, which open into the vena cava scarcely an inch below the opening of the vena cava itself into the right auricle, must indeed be foremost exposed to the effects of the abnormal pressure. A persistent venous hyperæmia of high degree, therefore, forms the proper foundation of all the anatomical changes. At least one-half of the space contained in the liver is intended for the blood. Hence it is not surprising, if even a moderate degree of hyperæmia brings about a very considerable increase of volume of the whole organ. Hence, were the capillaries also to be distended to only double their normal calibre, which, as is known, is already the case in moderate hyperæmias, an increased demand for space would already arise therefrom, which amounts to about one-half of the normal volume of the liver. The greater part of this increased demand is covered by a corresponding increase of volume of the whole organ; the remainder is gradually obtained at the expense of the parenchyma which is inclosed between the vessels. The parenchyma becomes atrophic, and because ectatic bloodvessels take the place of the vanishing liver-cells, Virchow has very suitably termed this the red atrophy.

§ 495. As is to be expected, the disappearance does not develop uniformly in all parts, but it begins in each acinus at the side from which the abnormal pressure comes, in the region of the vena centralis. What above all strikes us in a microscopic preparation, which by injection and suitable hardening has been made fit for investigation by sections (Fig. 142), is the dilatation of the lumen of the central vein. The vein, however, is not only dilated, but also in every case somewhat, often very considerably thickened. At various places we see the communication with the surrounding capillary system provided for by larger branches of transition vessels, which either break through the walls in a straight line or in a short spiral. Beyond the walls the spaces intended for the liver-cells are empty for a considerable distance. Only scattered, very small elements, moreover filled with yellowish-brown or black pigment granules, show the place of the former liver-cell net. These, however, rarely lie immediately at the bloodvessels; they are rather separated from them by a light interspace, which, with Biesiadecki, I recognize as the lumina of lymph-vessels, or perivascular lymph-spaces. As we therefore see, the liver-cells have been destroyed by the blood and lymph stagnation as though by an external pressure, and this condition extends variously far from within outwards. In the direction of the trunks of the main veins as a rule, the destruction has gone the farthest. It may be that we find, upon the surface of the liver when taken out, three to five furrows, which extend from the posterior border anteriorly, here become shallow and at the same time break up into a number of smaller furrows, as the course of a stream near its head divides into many smaller side streams. Whatever this depression below the level of the surface of the liver amounts to, so many liver-cells have been lost here. Thousands of acini are present here, in which there is not a single cell left; they are partly obliterated, partly yet may be completely injected. Beside these we find half-destroyed, and finally acini, which are yet relatively intact. How very carefully, though, we must here guard against a mistaking for those inflammations, which by the development of connective tissue in the portal canals and the cicatricial contraction of the connective tissue, condition a quite similar inequality of the surface of the liver, namely lobulation and granulation. (See Cirrhosis.) We must so much the more guard against this, as combinations of red atrophy with the development of connective tissue in the portal canals do not infrequently occur. How

Fig. 142.



Red atrophy. *a*. The lumen of the vena centralis of an hepatic acinus. *d*. Interlobular connective tissue, increased. The remainder see in text. 1-200.

this combination is to be explained we will not venture once for all. to decide. We may conceive that the abundance of nutritive material in the hyperæmic liver causes a predisposition to neoplasia; we may, however, also imagine a primary cirrhosis, which is afterward complicated with atrophy by stagnation.

§ 496. The complication of red atrophy with the fatty liver has already been mentioned at § 488. Tense fatty infiltration of the border zones of the acini, depression and deep red or brown coloring of the centre—we comprehend, how this combination above all others must bring about the term nutmeg-liver. We will call it the pigmented nutmeg-liver.

§ 497. The *yellow atrophy.* (Acute yellow softening.) With the occurrence of a clinical picture of disease in every way characteristic, the so-called icterus gravis, corresponds a likewise characteristic anatomical metamorphosis of the liver, which, according to the two most prominent signs, is wont to be called yellow atrophy. According to the statements of various authors, the liver dwindles in a manner perceptible even externally within three or four days, nay, in yet a shorter time, from its normal size to an extraordinarily small volume. At the post mortem we find it intensely yellow-colored, very anæmic, of smooth surface, and upon a cross section, so homogeneous, that we cannot distinguish the individual acini by the naked eye. The latter observation, nevertheless, is only correct with certain limitations. Frerichs and R. Demme have several times found remains of less changed liver-parenchyma within the homogeneous substance; they described larger and smaller groups of acini, which especially at their borders had so far maintained themselves, that individual liver-cells and bloodvessels could yet be discovered. Where the liver-substance appears homogeneous, the latter is possible in only a very incomplete manner. A granular mass, most richly mixed with fat-drops and globules, here and there probably also with pigment-granules or blood-corpuscles, beside vessels and connective tissue in a manner macerated, finally crystals of leucin and tyrosin, this is all that the microscopic investigation of the parenchyma brings to light. The term softening (biliary colliquation, according to Henoch, v. Dusch), chosen by several authors, refers also to the finding of these things; from general appearances, this is to be rejected, as the liver is rather hard or leather-like.

§ 498. The process lying at the foundation of the yellow atrophy of the liver is yet enveloped in obscurity. It is undoubted, that the question is about a dissolution of the liver-parenchyma, especially of the liver-cells. We are almost unanimous upon this, that this dissolution ensues by *fatty degeneration.* Here, however, the differences already begin. Several later investigators (Ph. Munk, Leyden, and others), wish to consider this fatty degeneration from the point of view of the fatty degeneration in poisoning by phosphorus; Munk even permits

the possibility to peep out, that all cases of acute yellow atrophy are to be traced back to phosphorus. In the liver trouble, after taking phosphorus, however, the main stress is laid upon the occurrence of fat-globules in the liver-cells, though here, also, a preceding parenchymatous swelling may not have been wanting. According to a second view (Frerichs, Demme), this latter forms the essential nature of yellow atrophy of the liver. The yellow atrophy of the liver is the issue of an acute inflammation of the parenchyma. This by preference resides in the borders of the acinus, and can be demonstrated upon the remains of the structure mentioned above. The swelling of the border causes, at the same time, an obstruction of the smallest bile-ducts coming from the acinus, consequently a stagnation of bile in the interior of the acini, resorption into the blood, and icterus. One sees this view will at the same time explain the wonderful fact, that the larger bile-passages are constantly found empty, or filled with a colorless mucus, and jaundice is nevertheless produced. A third view (Henoch, v. Dusch) straightway makes the retention of bile in the liver the central point of the phenomena. The liver-cells are said, according to this, to dissolve in the retained bile; the yellow atrophy is a biliary colliquation of the liver. Nevertheless, liver-cells may be preserved for days in bile without dissolving. Probably we may save ourselves the pains generally of explaining the icterus gravis as an icterus of resorption. Everything rather indicates that here we have to do with an acute, infectious disease, in which numerous colored blood-corpusles are dissolved, or at least washed out, and the coloring matter of the blood having become free, goes over into biliary coloring matter without the aid of the liver. This alteration of the blood forms the one principal impulse of the disease; it furthermore expresses itself in considerable extravasations of blood, partly parenchymatous (skin, mesentery), partly superficial (intestine, nose). Whether the severe accidents are produced on the part of the central nervous apparatus directly by the poison, or whether they are a result of the blood adulteration, observations are yet wanting to decide. Frerichs was of the opinion, that the leucin and tyrosin, arising from the disintegration of the liver-cells and reaching the blood, brought about the nervous symptoms; yet the experiments referred to have shown, that considerable amounts of these bodies may be introduced into the circulation without producing coma, delirium, convulsions, &c. This, also, is not yet decided, whether the liver destruction is a direct or indirect effect of the poison. We may choose whether we will suppose the disintegration of the liver-cells, as in the poisoning by phosphorus, under the immediate influence of the poison, or whether we will assume that the blood undergoing abnormal processes of transformation has given the impulse to the disintegration. I am inclined to the first view, and place generally all the phenomena

directly upon the chemical peculiarities of the poison yet to be discovered.

According to a series of good observations (Waldeyer, Klebs), it may be regarded as certain, that the yellow atrophy of the liver-parenchyma may also take a more protracted course, and therein pass into a condition, which is designated by Klebs as red atrophy. In such livers we find, between larger and smaller portions of yellow atrophied parenchyma, still more deeply depressed, pale reddish colored parts, whose microscopic investigation exhibits a wavy, loose connective tissue, which contains in narrow, cleft-like spaces, fat-globules and granules of biliary coloring matter, furthermore, however, in regularly branching lines and apparently blind-ending tubes, cells of the character of the epithelia of the biliary ducts. Waldeyer perceives in the latter a reparatory epithelial proliferation, proceeding from the biliary ducts, which is intended for replacing the lost tubes of liver-cells, while Klebs declines this explanation and would regard them only as modified old tubes of liver-cells.

§ 499. *Circumscribed atrophies* of the liver-parenchyma, which go along with a gradual diminution and resorption of the liver-cells, and with an obliteration of the remaining framework of bloodvessels, are observed everywhere at such places where the liver is exposed to mechanical injuries.

To this place belongs pre-eminently the atrophy of the liver from lacing. By the compression of the lower circumference of the chest in lacing, the organ is, in the first place, laterally compressed ; a number of shallow folds are formed, which run from the posterior part of the right lobe to the free edge. At the same time the anterior thoracic wall is pressed against the surface of the liver. The acini situated here atrophy and are replaced by an indurated connective tissue, which upon superficial examination presents itself as a thickening of the capsule penetrating into the liver-parenchyma. The capsule, however, may also actually be somewhat thickened. Thus arises a furrow ever becoming deeper, which cuts off the anterior parts as well of the right as of the left lobe, and finally, may go so far, that the border and the lobes are only connected with each other by a thick ligamentous bridge. The part separated by the constriction is rounded club-shaped, because the col lective vessels, which are intended to carry off from it the blood and bile, are compressed in their continuity, and in consequence undergo a corresponding ectasy. We can observe even with the naked eye the swollen and varicose veins, and alongside of them the biliary ducts, which are already no longer filled with bile, but with the secretion of their walls, a clear mucus. At the right lobe of the liver, the abnormal mobility of the free border may under circumstances lead to a very considerable flexion upwards, and to being pinched under the ribs. As the gall-bladder is attached to it, by the distortion of the ductus cysticus and

choledochus, the closure of the latter, and icterus may be occasioned. (Virchow.)

§ 500. In a similar manner, as in the atrophy from lacing, there is produced by the pressure of exudations, which have been inclosed between the liver and the diaphragm, also by pleuritic and pericardial exudations, a partial atrophy of the liver. The same also by pressure of abdominal tumors. I lately had the opportunity of observing a very remarkable case in point. The case was a rachitic woman in the puerperal state. The gravid uterus had pressed forwards the anterior portion of the liver in such fashion against the curvature of the ribs, that beside an older furrow from lacing, numerous atrophic places of more recent date were present. These were sunken, reddish-brown and contrasted very strongly with the adjacent healthy parenchyma; this occurred in curved lines, which presented their concavity outwards; consequently the places were stellate; they differed in size from the diameter of one millimetre up to a circumference of several square inches. The microscopic examination showed an almost entire absence of liver-cells, while the vascular framework was yet complete and could be well injected. Without doubt, we had here a subacute atrophy, as the uterus only has during a short time, so considerable an extent that it can injure the liver. The fact, however, is worthy of notice, that in such cases the liver-cells suffer first of all, while the bloodvessels for the time remain intact. I might believe, that here even a restitutio in integrum were possible. For this it would be necessary that the empty spaces between the bloodvessels would be filled anew with liver-cells, which might be accomplished, either on the part of the few remaining glandular elements, or on the part of the connective tissue.

5. Inflammation.

§ 501. *Parenchymatous inflammation.* When we find a liver, which is moderately enlarged in all its dimensions, therewith yellowish-gray, anæmic and of a peculiar, inelastic, doughy tightness, smooth upon the surface, strikingly dry upon cut surfaces, perhaps, like smoked meat, we have cause to refer all these peculiarities to an alteration of the liver-cells, which has been designated by Virchow as the cloudy swelling, and has been recognized as the essential foundation of the parenchymatous inflammation. We understand, thereby, an enlargement of the cell, produced by the appearance of numerous dark (albuminous) granules in the protoplasm. As the normal liver-cells also contain numerous granules in their protoplasm, it is, as may be conceived, very difficult to determine upon a single element the point where this repletion with granules begins to become pathological. In very well-marked cases, of course, the amount of granules is so large, that merely because of the dark points we are no longer able to perceive the *nuclei* of the

liver-cells; but these cases are rare. The increase of volume also estimated by a single cell, is an inadmissible criterion. We advance much further by the examination of thin sections. Here, above all, the considerable enlargement of the acini and a certain isolated prominence of them strikes the eye. I believe to have found the cause for the latter in a strong serous saturation of the interacinous connective tissue. The liver-cell net is tolerably thickened, but more striking is a certain disturbance of its structural relations. In place of the regular and careful arrangement side by side of the single elements there has entered a very much looser combination, a disorder difficult to describe; above all the cells are separated frequently by small interspaces; many however, have actually left the rows, so that we can no longer correctly speak of trabeculæ of the liver-cell net. The œdema of the portal canal, perhaps, also extends into the interior of the acini; perhaps the greater rounding of the cells also does its part towards loosening the connection. What further struck me, and which is of great importance for interpreting the purulent inflammation, to be considered in the next place, was that the connective tissue cells of the portal canals as well as the nuclei of the bloodvessels are in a condition of formative irritation. The capillary vessels are often covered with long rows or irregular heaps of nuclei; we also perceive just such heaps of nuclei in the portal canals, above all, however, in the centre of the substance of the individual acini. The latter are so large, that I cannot avoid of thinking directly of miliary abscesses.

§ 502. The diffuse parenchymatous inflammation in its mildest forms occurs, so to say, symptomatically in very many infectious diseases; we occasionally find it in typhus, in the acute exanthems, especially variola, in chemical, septic, and animal poisoning, puerperal fever, &c. There cannot well be a doubt, that a return to the normal condition here everywhere lies within the bounds of possibility. For, notwithstanding that now already for tens of years the attention of investigators has been directed to this point, they have not yet succeeded in furnishing a stringent proof for this, that the acute parenchymatous inflammation is also capable of another issue. It is true, we saw above, that several authors regard the acute yellow atrophy as such an issue, and I myself would incline to the view, that the idiopathic hepatic abscess is the result of a diffuse parenchymatous inflammation, yet, here as there, sufficient proof is wanting.

§ 503. *Purulent inflammation. Hepatic abscess.* We distinguish between idiopathic and deuteropathic or metastatic hepatic abscesses. The deuteropathic are of an embolic or thrombotic kind. They develop when an inflammatory and suppurative process already exists at some other point of the organism, especially, of course, in the region of the radicles of the portal vein, and has led to the coagulation of the blood in the vessels. The thrombi may then grow out of the region of

the radicles of the portal vein directly into the trunk and branches of the portal vein (pylephlebitis in the more contracted sense); mostly, however, here, as wherever the primary focus of disease is not situated in the region of the portal vein, embolism is the mediator of the secondary hepatic affection. It was one of the first results of pathological anatomy to establish the not uncommon occurrence of hepatic abscesses after injuries to the head. In these and similar cases we must carefully see whether, perhaps, a simultaneously injured rib has not wounded the liver, or whether a succussion has not taken place in the interior. If we deduct these accidents, there remains a sum of purely metastatic processes, which may be arranged in three series: 1. Hepatic abscesses after primary disease in the region of the portal vein; 2. Hepatic abscesses after primary disease in the region of the lesser or greater circulation, the latter along with embolic processes in the lung. In this case we have ground for assuming that coagula of the pulmonary veins have passed through the left heart into the hepatic artery; 3. Hepatic abscesses after primary disease in the region of the greater circulation without abscesses of the lung. For this series we must, upon the one hand, accuse the viability of the pulmonary capillaries and the anastomoses between the pulmonary artery and vein for smaller emboli; upon the other hand, the incompleteness of the investigation. Upon closer examination, beside the most grave wounds, suppurations, &c., we probably find yet a less extensive affection, but combined with thrombosis, in such regions from which the portal vein may receive an embolus (at the neck of the bladder, in the region of the hemorrhoidal veins, &c.).

§ 504. The anatomical process in the hepatic inflammation forming abscess in its coarser outlines is, indeed, constantly the same, typically recurring; the histological detail, however, the dovetailing of the individual members of the process, adjusts itself in some measure according to the manner of production, as will be seen further below. Under the coarser outlines I understand the occurrence of suppuration in the portal canals, the growth of the abscesses, the formation of pyogenic membranes, &c. That the suppuration takes its beginning throughout in the portal canals, we may refer to the greater accumulation of connective tissue at this place. This was supposed to happen hitherto in the sense that we regarded the connective tissue actually as the place of formation of the pus-corpuscles. By the investigations of Cohnheim, however (see above, § 89), this view has lost its support; formerly it appeared surprising to every conscientious histologist, probably, that in the known picture of the proliferation of connective tissue (Fig. 106), we had comparatively seldom obtained a view of the actual *division of cells*, and had based the theory *only upon the presence of smaller and larger cellular chains at the same place*, where we had the right to expect a simple connective tissue corpuscle; in the next place the discovery of v. Recklinghausen on the "migrating connective tissue cor-

puscles" made a modification of our views necessary. The young cells, which in local irritations fill the connective tissue interstices, ought and must for the greater part be regarded as having "migrated" in. But there still remain provisionally connective tissue cells, and their place of formation was the surrounding connective tissue. Even to-day yet we must not look upon the connective tissue as quite unfruitful, because an experiment of v. Recklinghausen proves that even excised pieces of the cornea, under proper conditions, are capable of a moderate cell-production. It is true, however, this source of derivation of the young cells is placed very much in the background, since we know that the colorless blood-corpuscles in propria persona migrate from the vessels and bring about all kinds of plastic infiltrations. These considerations now recur wherever the question is about suppuration and heterologous new formation in general. We must modify our views accordingly, and although we hereafter continue to speak of the *cellular infiltration of the connective tissue*, we must not forget that we use the word infiltration more than hitherto in its proper significance, as an impregnation with the constituents of the blood. The circumstance that now as ever the connective tissue forms a mantle about the vascular system, which pushes in between the blood and the parenchyma, and thereby more than the parenchyma gives room for an infiltrative repletion, will now explain to us how the connective tissue is so exactly the chosen seat of pathological new formation.

If now, after this digression, we return to our theme, the hepatic abscess, here also the regular occurrence of suppuration in the portal canals may be explained by the presence, more than in the interior of the acinus, of spaces capable of dilatation. To this is, of course, to be added that, at least in the thrombotic and embolic abscesses, the noxious influences of the portal canals pass to the liver. Here, however, the differences above mentioned, of the histological processes, already begin.

§ 505. If we are dealing with a *thrombosis* of the vena portæ we can demonstrate the breaking-down blood-clots in several branches of the vessel to about the point where the smaller interlobular veins take their origin. The walls of the vessel are here throughout in the condition which I have delineated above (§ 212) as acute phlebitis. The capsule of Glisson also is changed for long distances, and we not at all infrequently find a larger abscess already around the trunk of the portal vascular tree. Upon the interlobular veins we can no longer distinguish between lumen and wall. The walls are so completely impregnated with colorless cells, that with the contents of the vessel, which also consist entirely and altogether of colorless cells, they form a whole.* These elongated cylindrical, probably also ramified bodies,

* Compare herewith the lately published work of Buhl, on the Origin of the Cells in the Vascular Lumen, cited farther below, § 530.

which we may very well compare to the core of a furuncle, surrounded by pus, lie in a cavity, which has established itself between the vessel and its connective tissue sheath. The connective tissue sheath itself is infiltrated with colorless cells to such an extent, that it forms a cushion perhaps one quarter line thick, and appearing intensely white to the naked eye. This cushion pushes in everywhere between the portal vessels and the liver-parenchyma, and as the former can be observed far along their ramifications in favorable sections, the thrombotic abscess at a certain stage of its development presents the appearance of a branch full of leaves. Each leaflet has perhaps the dimensions of a normal acinus of the liver, but must on no account be mistaken for such; it is composed of a degenerated interlobular vessel as the leaf-stalk and the connective tissue sheath of both sides cut through as the leaf expansion. The latter must at the same time be regarded as the foundation of a pyogenic membrane. Its cells are not furnished perhaps by the interlobular vessels, but by the surrounding parenchyma. Hence, it is also in the most intimate organic connection with the latter, and it may be demonstrated by injecting, that only its inner surface turned to the portal vessel continually breaks down purulent or secretes pus, while the parenchymatous half is formed of vascularized germinal tissue. In this manner the parenchyma is protected against purulent destruction. I have never found here a transferral of the pus to the acinus, just as little a thrombosis of the hepatic vein; instead, it suffers so much the more from the mechanical effects which the enormous swelling of the interlobular spaces brings with it. If we make sections which hit transversely several adjacent portal canals, we may convince ourselves how the interposed acini are altered by the pressure, first, in their structure, and finally, destroyed in their textural constituents. The trabeculæ of the liver-cell net, which are originally placed radiating like the bloodvessels towards the vena centralis, are pushed together just in this direction. The globular surface of the enlarged portal canal gives the measure for this arrangement of the cell-rows. The latter surround the portal canal as concentric rings, which are stratified upon each other so much the more numerous the thicker the portal canal is. Soon it becomes difficult to find the place of the central vein, and as this place occupies exactly the central point of the old structure, the old structure itself is herewith to be regarded as broken up. At a later period the existence of the cells themselves is threatened; namely, the more they are grouped in the mentioned concentric rings, and the more the pressure acting from within outwards continually endeavors to stretch and burst these rings, so much the more also is the originally cubic form of the cell lost; it becomes narrower, spindle-formed, ribbon-like, finally so attenuated, that we can only appreciate it as a fibre. I have never been able to prove that they participate in the new formation by division and endogenous development. Here and there we see

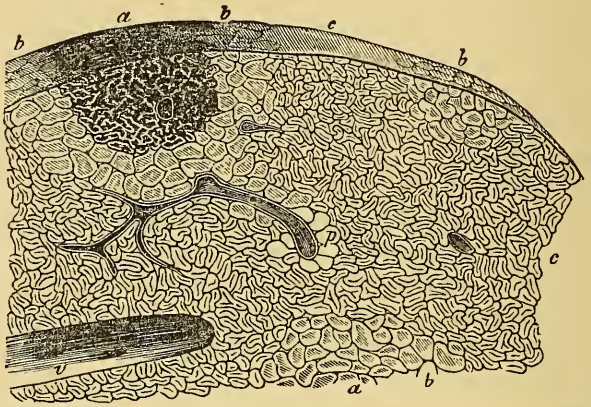
probably a liver-cell with many nuclei; but what does one cell amount to? The most evidently perish atrophic, and when the period of the complete destruction of the acinus has arrived, the germinal tissue cushions of the adjacent portal canals come into contact, they flow together and form a new whole. This whole has again about the size and shape of an acinus; it is therewith not the same anatomical unity which we above designated as acinus-like, but it has actually gradually taken the place of an acinus; but nevertheless, on that account, it is not a "suppurated acinus," although the appearance of this white lobule, now floating perfectly free in pus and touching perfectly the outlines of the abscess cavity, may invite such an interpretation. It is the greatest mystification which pathological histology here exhibits to the naked eye, since it awakens the involuntary idea, that in hepatic abscess the question was simply about a maceration of the acini in the pus of the portal canals, while in the supposed acini only fragments of pyogenic membrane are presented, the liver parenchyma, however, having long since perished.

In the continued enlargement of the abscess, one pseudo-lobule after another melts down, while at the periphery new ones continually form and are isolated. Only where there are main branches of the hepatic vein, these for a longer time form a point of support for a larger number of adhering pyogenic lobules, which contributes not a little to give the abscess cavity a ragged, irregular appearance.

§ 506. The *embolic* abscess distinguishes itself only in its first stages of development from the thrombotic; namely, it begins by a circumscribed hyperæmia of the region of the liver, in which the occluded vessel, be it the artery or the vena portæ, is distributed. This hyperæmia is enormous, the capillaries are distended to the utmost, it regularly comes to a complete stasis. We have here the analogous condition, as in embolism of the lung, yet at the liver it does not come to hemorrhage, as is common there. The liver in general, spite of its great vascularity, perhaps also, because of it, is less disposed to parenchymatous hemorrhages than any other organ. If the laceration of a vessel is to be produced, there must exist a difference between the blood pressure within and the parenchymatous pressure without; in the liver, however, every pressure or excessive pressure prevailing in the vessels is immediately imparted to the liver-cell net; where then shall the blood be poured out? Hence we only see hepatic hemorrhages produced, when by wounds or disintegration abnormal cavities have arisen, into which the blood may pour, not otherwise. That enormous stasis, however, which we designated as the beginning of embolic abscesses, may be regarded as the *equivalent of a hemorrhage*, a hemorrhagic infarction; for it is shown, that here there is just as little prospect of a re-establishment of the circulation as in the hemorrhagic infiltrations of other organs, the entire portion of liver affected perishes

and thus forms a caput mortuum, to which the subsequent inflammatory and suppurative processes are related as secondary, reactive or sequestering. As we observe in the annexed representation (Fig. 143),

Fig. 143.



Embolic abscess of liver, after Frerichs.* *a*. Zone of stagnation of the blood. *b*. Zone of parenchymatous inflammation. *c*. Normal parenchyma. *v*. Hepatic vein.

the zone of the stagnation of blood is sharply defined on all sides by the bounds of the liver-lobule. Just so the sequestering inflammation and suppuration, with reference to its development as to space, in the first place at least, extends to the bounds of the acini. In a circle of two to three lines the acini are swollen and colored whitish-gray (Fig. 142, *b*). The most are in the condition of the above-described parenchymatous inflammation; œdema and cloudy swelling of the liver-cells especially characterize the border-zone towards the healthy parts. The relation is different in those hepatic acini which lie nearest to the depot of blood. These are permeated by numberless pus-corpuscles, and are manifestly encountering a complete melting down. We find the pus-corpuscles between the rows of liver-cells, this side of the membrane of the capillary vessels. According to the manner of representing this hitherto, we would have thought of a new formation of these on the part of the nuclei of the bloodvessels, and I cannot exactly reconcile myself to the latest interpretation for this case (see above); the colorless cells thus lie, as we can see in teased-out preparations, in small alternating heaps upon the vessels, an arrangement which involuntarily reminds of the alternate position of the capillary nuclei. I am not in a position to prove an active participation of the liver-cells in the formation of pus, but it appeared to me, as though in the disintegration the protoplasm vanished and the nuclei became free.

* Frerichs has not comprehended the condition represented by him as "embolic" depots, as Klebs correctly remarks. Meanwhile his representation agrees so perfectly with embolic depots, which I have had the opportunity of examining, that I believe I can spare myself the trouble of taking up this subject anew.

Thus far the first stage of embolic inflammation of the liver, so far also the disagreement with the thrombotic form. From this time a thrombosis of the vena portæ, as far as its branches fall within the sphere of the abscess, is associated to the inflammation, and the suppuration concentrates in the manner formerly described, around the portal canals. Abscesses, which exceed the size of a cubic inch, no longer exhibit any anatomical differences among each other, provided, of course, that they are yet progressing, enlarging.

§ 507. I advanced the view above, that the *idiopathic*, hepatic abscesses represent one mode of issue of acute parenchymatous hepatitis. I did this, based upon the one hand upon the occurrence of isolated cellular infiltrations in the parenchymatous hepatitis; upon the other, upon this, that the parenchymatous hepatitis appears in embolic abscesses as the initiatory stage. That we can give so few exact statements upon this point, depends upon this, that idiopathic abscesses of the liver do not occur very frequently in Europe, but in India and the African coasts. The disease has an acute course, attended by fever, jaundice, and swelling of the liver. In post mortems, we often find colossal depots of pus in the thickest parts of the liver, especially in the posterior part of the right lobe.

§ 508. The *traumatic* liver abscesses have lately been repeatedly made the subject of histological investigation. Upon the third or fourth day, after irritating the liver by red-hot needles, &c., Köster finds in the interlobular connective tissue around the divided vessels, closely crowded colorless blood-corpuscles; the rows of liver-cells separate from each other and likewise take between them colorless blood-corpuscles. Holm also assumes an active participation of the liver-cells in the suppuration. Upon the whole, the traumatic suppuration of the liver appears to develop according to the pattern of the thrombotic.

§ 509. The further course of the hepatic abscess is the same for all cases. The question arises, will the suppuration by the continued melting down of the parenchyma attain the surface of the organ at some point, or yet before this catastrophe will the pyogenic layer have obtained a sufficient thickness and capacity of resistance against the chemical actions of the decomposing pus, that it may pass over to the formation of an encapsuling layer of compact connective tissue? In the latter, the favorable case, the new formation of pus gradually ceases, that present inspissates, and is finally resorbed, excepting small cheesy or calcified remains. The connective tissue capsule contracts into a radiating cicatrix, which can naturally only incompletely cover the considerable deficiency. In cases of progressive enlargement the abscess then reaches the capsule of the liver; an inflammatory adhesion of the latter with the opposing portion of the peritoneum is probably able to avert perforation into the peritoneal cavity, yet for this it must have a considerable firmness; it has not infrequently been seen that

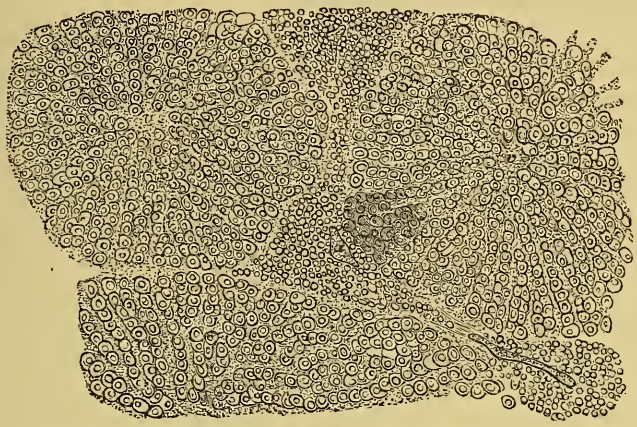
the pus ruptured a too weak adhesion, and thus forced its way into the abdomen. Otherwise the adhesion transfers the pus, step by step, to other organs. Most frequently the diaphragm is broken through, the danger of a perforating pleuritis follows; if this also has been overcome, a purulent inflammation of the lung threatens; finally, it comes to perforation into a bronchial branch, and with this the evacuation of the hepatic pus through the air-passages. If adhesion of the liver to the anterior abdominal wall ensues, the pus never pushes forward in a straight line into the abdominal coverings. It rather evades the bellies of the muscles, and is evacuated at distant points, perhaps near the ensiform cartilage, or in the last intercostal space. Perforations into the stomach, the colon, duodenum, the biliary passages, are very rare.

§ 510. *Indurating inflammation.* *Active* hyperæmias of the liver, persisting for a long time, or frequently recurring, form the foundation of the indurating inflammation. As is known, after each meal, by the increase of volume of the organ, the known feeling of pressure and fulness in the right hypochondrium, we can establish the participation, moreover, also proven by vivisections, of our livers in the digestive hyperæmia of the collective abdominal organs. Injurious ingesta, condiments, above all the abundant use of *alcohol*, increase this hyperæmia above the normal medium, and cause, that this ever less completely declines, and finally becomes habitual. Intermittent fever also leads to an active hyperæmia of the liver, which is characterized by the very considerable tumefaction, or, as we say, engorgement of the organ (fever cake).* In both cases it is of the utmost importance to the physician to bring back the liver to its normal bounds, as long as the condition of a simple active hyperæmia is present without further complications. Otherwise, both infallibly lead to a persistent, absolutely irreparable organic change, which generally makes itself known as a hyperplasia of the interlobular connective tissue. Well may also in this new formation, just as in suppuration, the migration of colorless blood-corpuscles from the vessels, particularly from the interlobular branches of the vena portæ, play a rôle. For a long time we contented ourselves in demonstrating the accumulation of young cells in the immediate neighborhood of the vessels mentioned, as the starting-point of indurating inflammation. In a preparation given me by Billroth, we see at those places at which more than two liver-lobules come together, which therefore, according to position, correspond to the portal branches of the smaller size, entire depots of germinal tissue, which, accordingly as the section has hit the portal canal transversely, obliquely, or longitudinally, either present themselves in circular or elliptical, probably also as branched figures. (Fig. 144.) Such an early stage of the hyperplasia of the interstitial connective tissue is certainly rarely observed. We mostly find in the course of the portal canals a pre-eminently

[* With us enlargement of spleen is ague-cake.]

fibrous connective tissue, poor in cells, which in its textural relations is allied to the cicatricial tissue. Actual germinal tissue is either no longer found at all, or can only be demonstrated yet as a narrow zone,

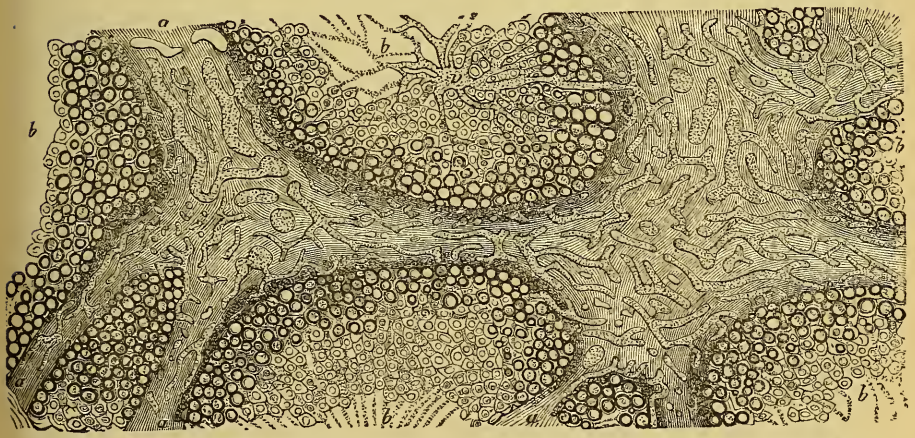
Fig. 144.



Indurating inflammation of the liver, first stage. *a.* Lumina of interlobular vessels, in whose environs there is a small-celled infiltration. *v.* Lumina of intralobular vessels. 1–300.

which pushes in between the cicatricial tissue (*a*) upon the one side, and the adjacent parenchyma (*b*) upon the other. (Fig. 145.) But

Fig. 145.



Indurating inflammation of liver, second stage. *a, a.* Broad stripes of a fibrous connective tissue, which is very rich in vessels without walls, and is bounded towards *b* by an interrupted layer of young connective tissue. *b.* Groups of acini of the liver infiltrated with fat externally. 1–200.

just this latter very common condition allows us an insight into the way and the manner in which the connective tissue hyperplasia advances, I might say, into the gradations (Stadiologie) of the process. The primary infiltrate of the portal canals (Fig. 144) is transformed into cicatricial tissue. This transformation has first ensued at the centre of the depot, in the nearest surroundings of the portal vessels,

and has thereupon gradually advanced outwards. During this, and yet ere all the germinal tissue present has become cicatricial tissue, the cellular infiltration has also increased, and forms a seam of germinal tissue, which everywhere pushes in between the cicatrix on the one side, and the parenchyma on the other.

§ 511. It is manifest that this new formation must injure the secerning parenchyma of the liver in a great degree. They are principally two forces, which show themselves active in this sense. In the first place, the proliferation of the young connective tissue into the substance of the adjacent acini, a process that we may observe wherever the several times mentioned zone of infiltration yet has a certain power. The liver-cells vanish in the measure that the young connective tissue elements make room for themselves between their rows, and for their part advance along the capillary vessels. Step by step in this manner, single acini or whole groups of acini, which lie between each two or three adjacent portal canals, are destroyed. If the period has then arrived when they cease to exist, the germinal tissue layers pressing forward from all sides touch and fuse, as waves come together above a drowning man, and at this place there is nothing left of the whole texture of the liver but connective tissue and vessels.

A second, upon a large scale, probably still more effectual means of destruction of the secerning substance of the organ, lies in the vigorous traction which the connective tissue exerts in its transformation into cicatricial tissue. The "cicatricial retraction" (§ 93) prevails just here in an eminent manner. From the minutest ramifications of the portal canals, its action becoming ever more vigorous, passes to the main branches, and finally to the trunk. A decrease of volume of the whole organ, a shrinking of the liver in all its dimensions, is the unavoidable consequence But if we ask, what portion of the liver particularly becomes smaller in this shrinking? first of all, the cellular parenchyma of the acini presents itself, because this is least fitted to offer resistance to mechanical force. The last processes of the portal canals are laid like so many loops around corresponding portions of the liver-parenchyma; from their common trunk, however, the traction is exerted, which continually tends to diminish the loops, and finally to close them. The proliferation of the connective tissue into the acinus, which I described above, appears to us from this standpoint as the means by which the interlobular traction actually extinguishes the acinous parenchyma; perhaps the opinion might even be defended, that this cellular infiltration advances under the influence of the interlobular pressure, so that the atrophy of the secerning parenchyma might be considered as the result of a single process connected in its various members.

§ 512. Thus much of the detail of the histological processes, which constantly recur in the same manner in the various forms of indurating

inflammation of the liver. Of these we can in general distinguish three, the indurated, the granulated, and the lobulated liver. The production of the one or other form is determined by the circumstance, that the connective tissue development takes place, in the one case, in the minutest ramifications of the portal canals, in the other, in their medium or in the main branches.

Induration of the liver. A uniform decrease of volume of the organ in all its diameters, combined with a considerable condensation, with a board-like rigidity and dryness of the substance, with diminution of the acini, and the surrounding of each single one by a whitish stripe of connective tissue—this is the ensemble of changes, which we particularly designate as induration of the liver. Herein the connective tissue hyperplasia is as uniformly as possible distributed throughout the whole interlobular tissue; as was already observed, each single acinus is separated from its neighbor by a normal connective tissue septum, each individual one is exposed for itself to the atrophying pressure of the cicatricial tissue, and this is the reason why we do not observe here, as in the cirrhosed liver, a greater prominence of the relatively normal parenchyma above the level of the natural and the cut surface, why the indurated liver appears but little granulated.

The induration of the liver is most frequently observed after long continuance of intermittent fever. It is at times associated here with a second series of anatomical changes, which I spoke of on a former occasion, namely, with the melanæmic pigment formation and deposition in the liver. (See § 184.) The indurated liver is then of a slate color, and we can demonstrate that numerous black scales of pigment lie outside and around the portal vein as well as the capillaries. These scales of pigment are either the remains of extravasations of a former stage of development, or they penetrated as such through the walls of the vessels. At all events, they must not and cannot be mistaken for atrophying liver-cells, as they, everywhere in the acini, maintain their place between the pervious capillaries and the perfectly intact rows of liver-cells, and hence do not at all appear as something "infiltrated, penetrated."

§ 513. *Granulation of the liver, cirrhosis.* If the connective tissue hyperplasia has its seat only in the larger and medium ramifications of the portal canals, correspondingly larger portions of the secerning parenchyma will be bound in and strangulated. The whole mechanical force of the indurating inflammation is then concentrated in certain directions; all the acini which lie in these directions are entirely destroyed, the adjacent ones, more or less, completely, while the interposed ones remain indeed relatively intact, but are placed continually under a so considerable external pressure, that wherever space permits, they bulge out cushion-like. The entire free surface of the cirrhosed liver is therefore covered with half-spherical elevations, which, accord-

ing to the size of the strangulated portions of liver, are of the circumference of half a millet-seed up to half a hazelnut and over (see Lobulation of the Liver). Upon every recent cut surface of the organ also, this "granulation" exhibits itself, although less distinctly. The granules, therefore, are not, as Laennec erroneously assumed,* the pathological part, but the connective tissue between the granules is abnormal; the granules themselves represent what yet remains of the normal liver-parenchyma.

When we call the parenchyma of the liver normal, this is certainly not always to be taken in the strict sense of the word. Very commonly the liver-cells are collectively infiltrated with fat; where they touch upon the cicatricial tissue, we very frequently see a very intense pigment-infiltration, which may probably be regarded as the accompaniment of the destruction progressing here. Above all, however, a very considerable disturbance of the structure strikes us, namely, an extensive displacement and distortion of the rows of liver-cells, which makes it impossible for us to distinguish the bounds of the acini, and perhaps, to count how many of them are contained in each granule.

The hyperplastic connective tissue also deserves to be yet somewhat more minutely considered. The above cited analogy with cicatricial tissue might, perhaps, cause the conjecture, that we were here dealing with a substance as poor in vessels as possible. This, however, is not so; the white cicatricial connective tissue is rather penetrated so richly with bloodvessels, that upon well-injected preparations we might be in doubt whether the lumina of the bloodvessels or the connective tissue takes up the greater part of the space. Proper membranes are not to be discovered in these bloodvessels; the uppermost layer of the connective tissue, covered by a single layer of epithelium, takes their place,—a circumstance which imparts to the whole structure a certain resemblance to the cavernous tissue. The whole phenomenon is undoubtedly connected with the great vascularity of the normal liver. Only under the condition, that at least the greatest portion of the blood continually flowing to the liver, also finds routes to pass the liver, can extensive cicatricial processes obtain in this organ. Much will, of course, herein depend upon the pressure of the affluent blood, and as this is very much greater in the hepatic artery than in the portal vein and its branches, the peculiar phenomenon is hereby explained, that those blood-spaces in the cicatricial tissue, according to the proof of injections, are not supplied by the portal vein, but from the hepatic artery. We very commonly find the medium-sized branches of the portal vein obliterated. In one instance, spite of the greatest possible exertion of pressure, it was not possible for me from the portal vein to fill more than the trunk and the three or four main branches. These were at

* Laennec identified the granules with cheesy tubercles.

the same time strongly distended, and more exact investigations showed, that in this case the blood of the portal vein in general did not flow through the liver, but through a number of very much dilated anastomoses of the mesenteric veins with the spermatic veins, and entered directly into the vena cava inferior. In other cases the blood of the portal vein went directly into the parenchymatous granules, and then from here into the vascular system of the cicatrix, while the latter was filled directly from the artery.

After all this, two things appear to me of importance for the distribution of blood in the cirrhosed liver, 1, that the ramifications of the portal vein are compressed and obliterated by the cicatricial formation, while 2, an ever larger region of distribution is provided for the ramifications of the hepatic artery. The injury to the branches of the portal vein is the cause of the manifold phenomena of stagnation in the intestine and spleen, the ascites, &c., and conditions the development of collateral anastomoses between the portal vein and the inferior vena cava. The enlargement of the arterial ramifications allows a partial transfer of the office of the portal vein to this vessel; the bile is therefore principally secreted from arterial blood.

Touching the biliary ducts, these appear to be generally kept open. We seldom see here and there a dark yellow, brown, or even green parenchymatous granule, in which the efferent biliary duct had been compressed by the cicatrix, and consequently an accumulation of bile must occur. Hence, the tolerably frequent occurrence of jaundice in cirrhosis of the liver may only be referred to a closure by swelling of the outlet of the ductus choledochus with simultaneous catarrh of the duodenum.

§ 514. *Lobulation of the liver*, as a rule, is a companion of granulation of the liver. Having proceeded from the same causes and produced by the same process, it only reminds us, that the most considerable deformities must naturally come to pass, when the trunk of the system of portal canals itself and its main branches are indurated. Then the division (Gliederung) of the organ, so to say, concealed in the normal liver, appears more or less distinctly as a number of lobules, which, as we saw, is conditioned by the grouping of the parenchyma around the larger and medium venous branches. The granules either form secondary elevations of the lobulated liver, or we find a gradual transition from the smallest granules through ever larger to the portions of parenchyma of the lobulated liver of the size of a walnut.*

* The pathological lobulation of the liver must of course not be mistaken for the congenitally lobulated condition of the organ, which is immediately distinguished from it by the want of all connective tissue vegetation. A second possible mistake is with the syphilitic new formation, which is the more excusable, because in it an indurating inflammation and an induration actually comes to pass. (See § 521.)

6. Tumors.

§ 515. *Cavernous Tumor.* The choice and the sequence, in which the various objects of investigation of pathological histology have been taken in hand, have not always been directed according to the needs of the physician. Otherwise, it would be a striking phenomenon that several exceedingly important questions upon the origin and growth of cancers in the liver yet await elucidation, while a form of tumor very unimportant in a clinical relation, the cavernous tumor, already very early found its elaborators among the strongest minds of our science. Upon those occasionally occurring, sharply defined gaps of the substance of the liver, of the size of a pea to a walnut, filled with erectile tissue, and hence, also, in a half-filled condition appearing dark bluish-red, we have not only ample histological information, but also a view put forth by Virchow, upon their origin and growth, which is, probably, more than a mere hypothesis.

§ 516. A trabecular work of connective tissue, whose interspaces stand open for the blood to flow through, forms the proper substance of the tumor. If we subject a single connective tissue trabecula to microscopic investigation, we distinguish upon it a covering of unilayered pavement epithelium, under this a striped basis-substance with moderately numerous spindle-formed cells, which have been declared by several authors as smooth muscular fibres. Elastic fibres, arranged in nets, partly surrounding, partly penetrating, give the whole a certain similarity to the alveolar septa of the lung. The average size, also, of the meshes which they inclose, agrees with those of the pulmonary alveoli. In other respects we can only establish so much concerning the structure, that the septa are grouped radiating around one or more centrally situated points, which are only characterized by a somewhat larger accumulation of connective substance, but according to their nature and significance are only intelligible from the mode of development of the tumor.

If we pass with the microscope along the periphery of the tumor, we are very soon convinced that this is everywhere separated from the adjacent parenchyma of the liver by a moderately broad layer of connective tissue; here and there we see how this connective tissue sends in a three-cornered process into the interspace between two acini. These processes also contain vascular lumina, but less numerous and separated by broader bridges of connective tissue. But we evidently have here, if anywhere, before our eyes the mode of development of the tumor: an interlobular hyperplasia of the connective tissue, which is followed by a cavernous metamorphosis (§ 130). The tumor, therefore, connects, upon the one hand, with the interstitial hepatitis formerly described; upon the other, with the fibroid formation. The cirrhosed connective tissue also was characterized by vascularity; we point to

the possibility that this quality might depend upon a local predisposition, namely, the enormous vascularity of the liver, and may also lay claim to this local predisposition in the present case. It furnishes us here, instead of a simple, a telangiectatic, if you will, a cavernous fibroid.

§ 517. With this insight into the development, the necessity at the same time disappears for tracing the blood-spaces of our tumor back to the pre-existing arteries, veins, or capillaries, in the sense that they are produced by an ectasy of them. The parenchyma of the liver with all its vessels is destroyed very slowly and without any preceding distortion, but very completely, by the pressure of the development of the tumor by lobules advancing in the smallest portal canals. With the capillary circulation, however, the lumina of the affected hepatic veins also shrink, the venous walls collapse, and finally form those dense accumulations of connective substance, from which the septa of the completed tumor appear to proceed radiated, because the development of the tumor proceeded from all sides convergent towards them, *i. e.*, the points where the veins lie.

Thus it is then also explained, when it was demonstrated by Virchow's injections, that the spaces of the tumor could be injected from the portal vein and from the artery, but not from the hepatic vein. For in the portal canals there are only branches of the portal vein or of the artery, and a tumor which grows in the portal canals will naturally derive its bloodvessels from these, and not from the veins situated beyond the liver-parenchyma.

§ 518. There is little to be said of the secondary metamorphoses of the cavernous tumor. I once saw a partial obliteration of the blood-spaces, which, without doubt, came from a coagulation. The centre of the tumor, of perhaps the size of a hazelnut, was occupied by a compact white knot of the size of a pea, while all around there existed a zone of a line's breadth of open cavernous tissue. A vertical section, however, showed that the system of septa was continued through this knot, and that there evidently had been a secondary filling with young connective tissue masses.

§ 519. *Cysts.* If we leave out of consideration the echinococcus vesicles and accidental cysts (softened cancer-nodules, abscesses, &c.), there only remains a small group of hepatic cysts, which are collectively to be regarded as cysts of retention of the biliary passages. These are every now and then met with single and of considerable size; it is much more rare to find multiple cysts which vary in size, from being scarcely visible, up to the appreciable circumference of a pigeon's egg. Like several other authors (Rokitansky, Foerster), I also found this formation of multiple cysts of the liver, beside cystoid degeneration of higher degree of both kidneys; namely, the liver in its anterior part was very rich in cysts, the free border of the left lobe was entirely occupied by medium-sized vesicles, while more towards the interior and posteriorly

the vesicles were more individualized, but so much the larger. Here also the best opportunity offered of following the development of the cysts.

Now in these studies the great uniformity of the origin of the cysts, with what Naunyn has lately described as cystosarcoma hepatis, immediately struck me. In the midst of certain white connective tissue nodules, of the size of a large millet-seed, which are imbedded in the more minute portal canals, one observes, even with the naked eye, a dot-like opening, which, upon more accurate examination, proves to be the dilated lumen of an interlobular biliary duct. This dilatation, of which the epithelium formed of low cylindrical cells is continuously extended to the epithelium of the efferent biliary duct, has in the smallest tumors a simple ellipsoid form, in the larger it bulges out in various directions, nay, not rarely beset with numerous tubular structures, which project into the adjacent parenchyma. Naunyn wished to deduce from this an enlargement of the tumor by epithelial shoots, and to class the latter on that account with the adenomas (see below). But they resemble the adenomas only according to the older conception of Billroth, in which the term adenoma is used for such tumors of the mamma, in which a progressive superficial increase of the excretory ducts is brought about by a sarcomatous degeneration of the *subepithelial connective tissue*. We cannot, therefore, think of anything cancerous, as is also shown by the future development. (Compare § 626, Adenoma.)

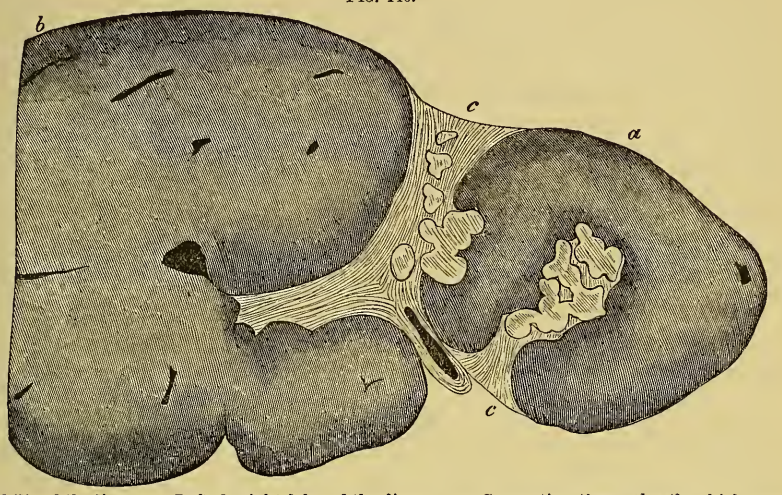
In fact, upon the liver mentioned above, I could demonstrate all transitions, from the just described beginnings of tumors to simple globular cysts. The transition takes place by the depression, probably also the perforation of those folds, which push in between the single diverticuli at the walls of the central cavity, and thereby give the whole an appearance of compartments. If these folds have disappeared, the cavity fills more and more with a thinly fluid secretion, clear as water; we have from this time before us only simple cysts of retention, with smooth walls.

§ 520. *Syphilis.* In reference to the general forms of the syphilitic new formations, I point to the general part of the text-book. The syphilis of the liver belongs to those profound disturbances of the later periods of the disease, which are well designated as tertiary. The anatomical changes are composed of two impulses combined with each other in various ways; of an indurating connective tissue hyperplasia on the one hand, of the formation of gummata on the other.

§ 521. The by far most common case is, that beside analogous processes in other provinces of the organism (at the cranial bones, at the pharynx and larynx, &c.), in the parenchyma of the liver, one or more depots of compact white connective tissue are formed, which radiate in various directions into the surrounding parenchyma, and by the retrac-

tion acting vigorously in these directions, have, as a consequence, a corresponding retraction and lobulation of the surface. (Fig. 146.) As a rule, these conditions are most marked along the insertion of the suspensory ligament of the liver; here we occasionally observe three or more radiating cicatrices, or, the liver in its entire thickness is replaced

FIG. 146.



Syphilis of the liver. *a*. Left, *b*, right lobe of the liver. *c, c*. Connective tissue sheath which penetrates the organ in the direction from the porta to the lig. suspensor., and contains gummata.

by a single colossal induration. It is probable that the traction, although mild, which the ligament exerts upon the organ in gliding to and fro at the diaphragm, may be regarded as the predisposing cause for this localization; that it is not inevitable, the modes of appearance of hepatic syphilis, to be spoken of further below, will show.

Not always, but still very frequently, gumma nodules, of various age and size, are found in and beside the cicatricial tissue, more rarely by themselves in an otherwise intact parenchyma. Yellowish-white, cheesy, very juiceless nodules, of the size of a cherry-stone, are more frequent than the younger, still soft formations, upon which the histological characters of the specific syphilitic texture may be studied. We there find fatty degenerated, but still remaining in the condition of granular cells, partly round, partly spindle-formed and stellate elements, the round ones in the centre, the stellate and spindle-formed ones at the periphery of the spherical nodule. The basis-substance is swollen by imbibition, soft, and gives with acetic acid a precipitate of mucin. The cheesy nodules evidently owe their existence only to a further metamorphosis of these proper gummata, and must on no account be regarded as inspissated pus, cancerous nodules having undergone the cheesy metamorphosis, or the like. They may only in rare cases be subject to a still further change, perhaps a softening and resorption,

and hence will constantly be to us a welcome sign, that the radiating connective tissue cicatrices, which might have originated in another manner, are of syphilitic origin.

§ 522. Far more rare than the localization in single large depots, is the localization of syphilis in numerous (thirty to sixty) smaller depots distributed throughout the entire parenchyma. Let us imagine gumma nodules, far below the size of a millet-seed, united in groups of five to ten into a small, roundish tumor, united by compact connective tissue with cartilaginous transparent basis-substance and beautifully developed spindle-formed cells; the connective tissue forms an area, which extends with radiating processes more or less far into the environs, and gives the whole place a gray translucent appearance. The central part of each single nodule consists of round cells, even of polynucleated giant cells, which encounter a fatty disintegration, and a kind of concentric stratification can often be demonstrated, as we find it upon the cross-sections of the degenerated vessels. The question, which vessels, is, of course, not easy to answer, as the portal canals are the standing situations of the gummata spoken of, and just here arteries, veins, biliary ducts, and lymph-vessels run side by side. Upon single nodules, which lay close under the capsule, I believe I have convinced myself that we are dealing with lymph-vessels; still, further investigations are necessary.

§ 523. A third form of hepatic syphilis is the hereditary cirrhosis, which is observed in new-born children that come from a syphilitic mother. Whether the enigmatical cases of well-marked, and indeed, very pregnantly developed cirrhoses of the liver, which we occasionally find in children of ten to fifteen years, and which, as I found, characterized by a complete obliteration of the branches of the portal vein, are a further development of that hereditary form, may be difficult to decide. To this points the exceedingly complete compensatory arrangements, which just here regulate the circulation of the portal vein, and are only explained by this, that the liver already, during its development, had encountered the disturbance.

§ 524. *Leukæmic swelling.* In considering leukæmia (§ 177 *et seq.*), I have stated the general outlines of all leukæmic infiltrations. The liver is one of its favorite seats, and at the same time the organ where it may be best followed histologically.

Since we know that the walls of smaller vessels permit the passage, under circumstances, of colorless blood-cells, we will have, above all others, to regard the leukæmic "new formation of lymph-adenoid tissue" as an infiltration conditioned by the migration of colorless blood-corpuscles. The increased number of them in the blood brings this interpretation too close for us to avoid it. To this, however, is added, that what is found histologically speaks thoroughly for a migratory theory. Because of the great conformity which the outer form

of leukæmic depots at the kidneys, have with depots of blood at the same place, I had long entertained the thought whether it were possible and in what manner the leukæmic depots could be traced back to original extravasations. The only thing, however, that I could adduce in support of this view, was the slight density of the vessels within those regions, which in injections regularly led to larger extravasations. Now in the liver we see how the leukæmic infiltration everywhere most intimately connects itself with the course of the vessels. Upon every cross-cut of a material, furthermore well prepared, injected, and hardened, we see how the colorless cells form rows, which accompany the capillary vessels through the entire acinus. In spots, the cells are so densely crowded that they appear like an epithelial stratum, which is seated externally upon the capillary walls. We find the same particularly in the border parts of the acini, while the centre is less provided for. It may especially be esteemed as established, that this infiltration—like, *mutatis mutandis*, the fatty infiltration—penetrates the acinus from without inwards. The liver-cells remain passive therein. Crowded off from the vessels, the source of their life and functional capacity, they perish atrophic, and we can often perceive, even with the naked eye, a brown speckling of the liver-substance, which is to be traced back to heaps of pigment granules, the last remains of liver-cells. This becomes so much the more prominent, as the color, which the liver-acinus acquires in the leukæmic infiltration, is a very pure milky-white. We can commonly see all stages of the changes side by side in one and the same liver, as the borders of the acini become by no means indistinct with the advancing infiltration, but on the contrary become constantly more sharply defined. Beside the normal acini of the liver, we then see there, those whose border zone has experienced a slight swelling and whitish coloring; others again, which are enlarged throughout by perhaps one-third, and at the same time are colored uniformly brownish-gray; finally, acini of monstrous circumference and milk-white color, therewith peculiarly dry, and projecting cushion-like above the level of the cut surface. The various degrees of the infiltration are commonly distributed in such manner, that the portion of the organ most pressed (under the edges of the ribs, for example), are less changed, the portions more remote from this point are changed in a higher degree, yet many deviations occur. A rarer form of leukæmic affection of the liver is presented in certain circumscribed grayish-white nodules, which are in a certain measure similar to the miliary tubercles, but are to be distinguished from them especially by the slighter consistency. The nodules have their seat in the portal canals, and are for the most part found beside the previously described infiltration.

The circumference and weight of the leukæmic liver may become very considerable, and in this connection become equal to the carcin-

omatous degeneration. (Fig. 150, *VIII.*) Leukæmic livers have been observed of fourteen pounds weight.

§ 525. *Tubercle.* In the general tuberculosis of the serous membranes, the lung, the heart, &c., which we most frequently observe in children, there are probably also miliary nodules found more or less abundantly distributed in the liver. They arise here at the smallest branches of the hepatic artery, and hence are not exclusively found in the interlobular spaces, but here and there, also, in the middle of the acini, where they have occupied room by crowding away the parenchyma. According to Schüppel (Archiv der Heilkunde, Bd. ix, Hft. vi), the cellular elements of the tubercles of the liver do not develop beside, but in the bloodvessels. In this case I would be disposed to let them proceed from a proliferation of the endothelium, because I could establish this mode of origin upon the lymph-vessels and the serous membranes. (See § 115.) Against this Schüppel himself declares the tubercle-cells as derivatives of the white corpuscles, and will entirely disregard a proliferation of the endothelia, which is very well known to him from his studies upon carcinoma.

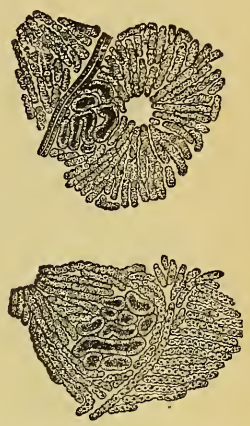
Even should the tubercles of the liver attain a considerable circumference, which here and there occurs, they are still but a local affection of very subordinate significance. We then often find a cheesy necrosis of the central part, which is followed by the imbibition of bile, since whatever is dead takes up obtruded pigment, which is rejected by the living.

§ 526. *Adenoma.* Genuine epithelial cancer of the liver is a very rare occurrence; it is constantly metastatic, and arises in the smallest nodules. On the other hand, adenoma is, indeed, likewise a rare, but always a primary affection of the organ, and appears to a certain extent to represent the ordinary epithelial cancer. After Rokitansky had already formerly called attention to the occurrence of a tumor-like deposit of liver-tissue of new formation, this interesting species of hepatic tumors has lately been more frequently met with. If we, according to Hoffman's precedent, separate the cases of excessive formation of genuine hepatic substance in small globular portions, that can only have a teratological interest, there remains as adenoma hepatis a form of tumor, which is distinguished by exceedingly pregnant histological and macroscopic characters. The latter, however, are so easily explained by their history of origin and growth, that I cannot refuse to treat of both simultaneously.

If we follow, which was hitherto possible only in one case of multiple adenoma formation, the nodules to their smallest beginnings, no longer visible to the naked eye, we discover these in certain places of the individual acini of the liver, characterized by form and color (Fig. 147). If in the investigation we made use of carmine imbibition, the

morbid parenchyma is marked by a strikingly deep coloring; and hence it becomes doubly easy to see, that here in place of the anastomosing trabeculæ of the liver-cell net, have entered oval cell-cylinders, which manifoldly curve round each other, and in this manner fill up a globular space, which at the same time occupies perhaps the sixth part of an acinus of the liver, without crowding the adjacent cell-rows, *i. e.*, replaces it, has taken its place. This first change is brought about by this, that within the region alluded to, the trabeculæ of the liver-cell net separated from each other at the points of connection, and each for itself, assumed the form of a cellular cylinder; as we, moreover, only find it in the production of open- mouthed glands and in epithelial cancer. With this transformation is combined a moderate increase of the liver-cells, the effect of which meanwhile is equalized for the time by the simultaneous diminution of the elements.

Fig. 147.

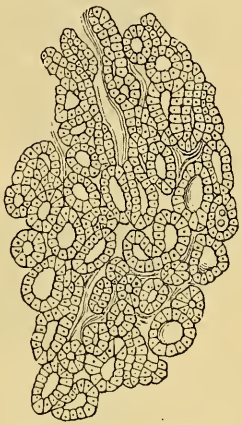


Adenoma of the liver. Smallest nodule produced by the partial metamorphosis of an acinus.

§ 527. The further growth of the nodule so begun, ensues upon the one hand, by the excentric extension of the trouble; upon the other, by the *formation of shoots on the part of the existing cellular cylinders.* When the tumor has attained the size of a small pin's head, the latter is the exclusive mode of growth. The tumor already at this time receives a connective tissue envelope, which excludes it toward the surrounding hepatic tissue. The latter is entirely crowded out and stifled, so far as it does not participate by nodules of its own. The former, however, grows from the point alluded to by its own means. The peculiar intention, which is expressed in the whole foundation, advances to a delusive imitation of a tubular gland, perhaps the kidney. Figs. 148 and 149, which both represent sections taken from a nodule of perhaps the size of a hemp-seed, show us central lumina of various width, in most of the existing pseudo-glandular tubules, which are filled with a yellowish gelatinous substance, or with a thin fluid, clear as water. Meanwhile, it must be stated, that the acme of development is nevertheless not frequently attained, and that, as a rule, it stops with the solid cell-cylinders. In Fig. 149, a part of the connective tissue capsule is at the same time visible, which limits the nodule externally. In nodules which have attained the size of a cherry and over, this connective tissue capsule turns to the nodule a perfectly smooth surface clad with serous epithelium; there actually exists therefore a serous space at the periphery of the nodule, which is bridged over at but few points by the afferent and efferent vessels. Experiments by injection have taught me, that the vascular tracts of the nodules,

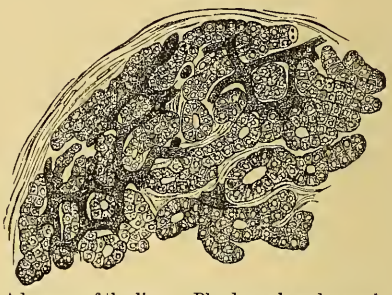
although they originally form a fraction of the acinous capillary net, and consequently are accessible to each of the three species of vessels of the liver, are afterwards always exclusively supplied by the hepatic

Fig. 148.



Adenoma of the liver. Tubular structure of the tumor. 1-300.

Fig. 149.



Adenoma of the liver. Bloodvessels and capsule of the nodule. 1-300.

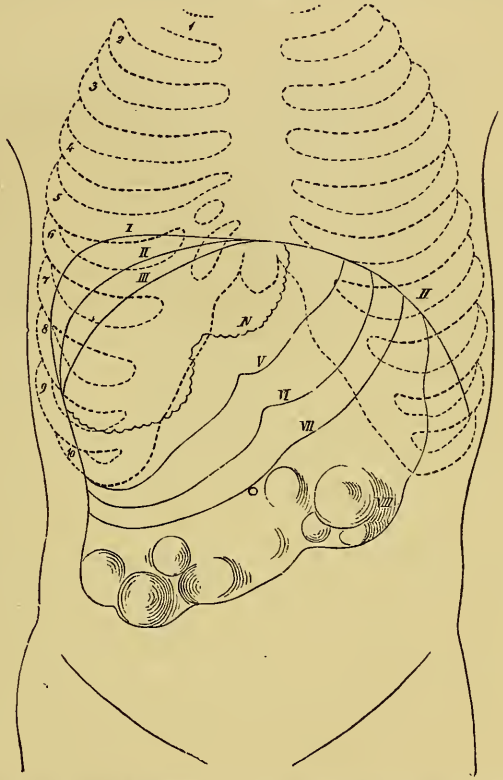
artery. In the larger specimens of adenoma nodules, the injection could only be forced in from the artery. We will again find something similar in the genuine cancers.

After all this, the fully developed adenoma nodule is a globular tumor, invested in a connective tissue membrane; its consistence is swellingly soft, elastic; its color, a light liver-brown, somewhat darker upon single nodules. The tumor occurs singly and multiple; in the latter case, the nodules attain the considerable size of two inches in diameter. Only by the mutual pressure of growth, does the original spherical form of the nodule go over into all kinds of crushed and distorted forms. At a later period a softening mostly occurs of single nodules, the cells undergo fatty degeneration, the serous surface of the sac produces also a certain quantity of pus, so that finally complete abscess cavities arise, that may also burst, and then become fatal by peritonitis. The circumference and the weight of the adenomatous liver depend upon the number and size of the nodules; both may be very considerable, as in hepatic cancer (Fig. 150, *VIII*).

§ 528. *Carcinoma.* Carcinoma of the liver is exceedingly various in its external appearance. We have there, in the first place, milk-white, tolerably compact nodules protruding at the surface of the organ, as well as upon every cut surface, from the size of a millet-seed to a fist, imbedded in moderate numbers in the dark brownish-red, atrophic liver parenchyma (carcinoma simplex). Then there is a liver even monstrously developed (Fig. 150, *VIII*), which, as the cut surface tells us,

is composed almost only of soft cancer nodules, of all sizes and phases of development (carcinoma medullare). There is a moderately enlarged liver, which, beside some superficially situated nodules of the

FIG. 150.



The volume of the liver in various diseases. 1-10. Ribs. *I.* Position of the diaphragm in the highest degree of tumefaction of the liver (carcinoma). *II, II.* Normal position of the diaphragm. *II, III.* Relative dulness. *III.* Position of the diaphragm at the anterior wall of chest, at the same time the line of dulness of the normal liver. *IV.* Edge of liver in cirrhosis. *V.* In the normal liver. *VI.* Fatty liver. *VII.* Amyloid liver. *VIII.* Cancer, leukæmia, adenoma. All of proportional size.

size of a fist, provided with a central depression, a cancer-navel, exhibits numberless smaller and most minute nodules (cancer disseminée of the French). Furthermore, the rare form of a true diffuse infiltration, in which the acini retain their form, but become thicker and broader, as also they assume a more grayish-white, ultimately quite white color. The radiating cancer, characterized by the arrangement of the cancer-mass in lines, which extend radiating from the centre of the nodule towards all points, mostly a pigmented medullary cancer. Finally, the gelatinous cancer, which is rarely observed, and only in single nodes as a secondary affection.

§ 529. It is certainly very important to become masters of this great variety by going back to the source, namely, the histological develop-

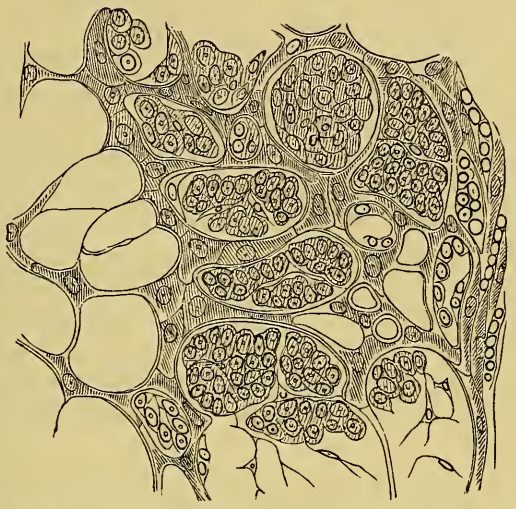
ment of the various cancers, in order, by its aid, first of all, to understand its structure, and in connection therewith the macroscopic peculiarities. This path has, indeed, been already frequently trodden, but has hitherto only led to a true forest of individualized phenomena, which will yet afford many an investigator opportunity for further deeds.

Let us, in the next place, connect it with the fact that more than three-fourths of all hepatic cancers are metastatic, and of the metastatic again two-thirds are metastases after primary disease in the region of the portal vein, one-third metastases after primary disease in other parts of the body, with and without preceding affection of the lung. The predominant occurrence of metastatic cancer might possibly be traced back to a wandering in of cancerous emboli into the portal vein, or the hepatic artery. For this speak, 1, a great list of the published observations of various authors upon cancerous thrombosis of the vena portæ. According to Virchow, there is a quite independent (*i. e.*, not imparted by carcinomas of the neighborhood) carcinoma formation in the lumen of the vena portæ. A thrombus, which fills up the vessel from several of its ramifications into the trunk, without breaking through any place of its walls, consists quite of cancer-mass. This appearance can probably be only so interpreted that here, in connection with one or more cancerous emboli, first a thrombosis of the portal vein had taken place, and then a carcinomatous transformation of the thrombus. For this rarity, of course, the far more common case must not be mistaken, where a hepatic carcinoma passes over to the portal vein, destroys the walls, and from here grows further into the lumen. On the other hand, an observation of Naunyn somewhat more correctly belongs here, where, after primary cancer of the kidney, with cancerous thrombosis of the adjoining veins of the mesocolon, numerous spots of the liver, of the size of a millet-seed, exhibited everywhere the transverse or longitudinal cut of a cancerously thrombosed branch of the portal vein, surrounded by one of the smallest cancer tumors. One might entertain the meaning that we have here the immediate view of the cancerous embolus and its pernicious influence upon the surroundings. Nevertheless, I believe I must warn against a too extended application of this explanation, as such conditions are by no means so frequent as the observer mentioned appears to accept. We can generally only confirm the fact that in very many cases, where the cancer occurs with numerous isolated nodules, these nodules have their seat in the portal canals. This, however, obtains for almost all tumors, and may be connected with other relations.

§ 530. A very interesting observation, which transfers the cancerous thrombosis of the larger vessels and the questions connected with it to the capillaries of the parenchyma, is presented to us in the development and growth of the pigmented radiating cancer. The peculiar structure

of this tumor is derived from this, that here the capillaries are occluded by the black cancer-cells up to the hepatic veins, and in consequence of this, the known whorl-formation makes its appearance, by which that side of the vascular apparatus characterizes itself in black stellate structures of all possible dimensions. Fig. 151 brings to view the border por-

Fig. 151.



Carcinoma hepatis. The production and structure of pigmented radiary cancer. The liver-cell net forms the first foundation of the stroma, while the cancer-cells are deposited in the lumen of the vessels. 1–400.

tion of a cancer-nodule; we distinguish stroma and cell-nests; the stroma, however, in its main trabeculæ, shows liver-cells, which are partly very much distorted, stretched in length, here and there also richly pigmented black and brown, but which yet in part are characterized by the known peculiarities, in part by their immediate connection with the contiguous parts of the liver-cell net, as genuine liver-cells. The more delicate trabeculæ of the stroma are spindle-formed and stellate cells, which of course have nothing whatever to do with the liver-cells. The presence of liver-cells in the main trabeculæ only shows us, that they are *not* the liver-cells, which furnish here the cancer-cells (in contrast to common cancer); it, however, at the same time serves us for drawing a conclusion as to the place where the cancer-cells are deposited. This is no other than the lumen of the bloodvessels. We may recognize the double contour of the capillary membrane as it completely surrounds the smaller cell-nests, the larger, at least partly; there can be no doubt, therefore, that the cancer-cells actually are placed where the blood-corpuscles formerly circulated. The question now is, how they come there, how they originated? Up to within a short time, I did not venture to give a positive answer to this. In my own mind, it is true, I cherished the view, that the *cells of the vessels are the producers*

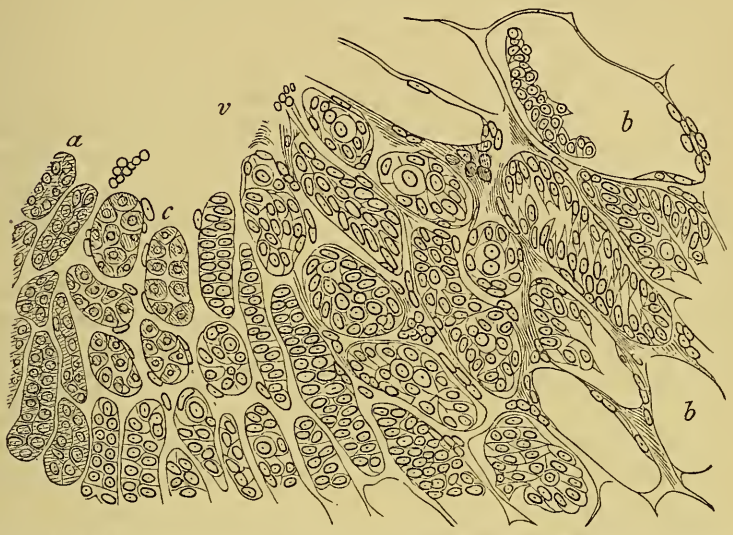
of the cancerous elements; the pictures, which elucidate to us this process—nuclear division and double nuclei in cells, which clinging closely to the walls of the vessels project crescentically into the lumen, cells which are attached to the walls of the vessel like a proliferating epithelium—these pictures, I say, we can find at the borders of the cancer-nodules in abundance; the adjoining illustration also shows it at several places. But I still hesitated, until recently the beautiful investigations of Thiersch and Buhl have made the fruitfulness of the vascular epithelia plausible in the highest degree. Thiersch concedes a prominent significance to the epithelia of the vessels in the organization of thrombi; Buhl proves, that the formation of pus in the branches of the vena portæ in phlebitis thrombotica (see § 505), depends upon a proliferation of the epithelia of the vessels. After these two observations I no longer hesitate to trace back the origin and accumulation of the cancer-cells in the lumina of the vessels, in the radiating pigment-cancer, to a proliferation of the epithelia of the vessels, and I am rejoiced to be able to report, that the beautiful studies of Schüppel and his scholars, upon the histogenesis of hepatic cancer (Fetzer, Inaugural Dissert., 1868), have completely justified this statement. Fetzer is disposed to claim intravascular origin and growth for the majority of all secondary hepatic cancers.

§ 531. The observation quoted above forms at the same time the transition to a second series of studies, which concerns more the growth of the cancer-nodules. The most comprehensive and simple relations are presented in this connection by the *diffuse hepatic cancer*, that remarkable degeneration of the acini of the liver, in which they, without sacrificing their form and limits in general, are yet gradually converted into cancer-mass. Fig. 152 presents the most instructive part of a half-degenerated acinus, and I believe, that we may here be convinced without difficulty, that they are the liver-cells themselves which become cancer-cells by multiple division and transformation, while the capillary net gives the first foundation of the cancer stroma. At *v*, is the centre of the acinus, the venous lumen here very much dilated, from which, in the manner known, the capillaries radiate. At *a*, the liver-cells are normal; at *c*, quite the same separation and loosening of the more rounded and enlarged cells, which I have alleged in § 501 as characteristic of parenchymatous inflammation. Then follow intermediate forms, until at *b* very wide meshes of the cancer stroma, here complete, are filled with the numberless derivatives of the liver-cells.

This transforming process must of course be regarded as valid in the first place only for the diffuse hepatic cancer, but there can be no doubt that the nodular hepatic cancers *may* at least grow in the same manner. If we examine, to begin at once with the most unfavorable case, the border of a large and compact carcinoma nodule towards the contiguous liver parenchyma, we will find, that by the pressure of the

growing nodule, all the adjacent acini are pressed out of their structure and converted into flat discs, which lie parallel to the spherical surface of the cancer. The liver-cells encircle the cancer by five or more con-

Fig. 152.



Carcinoma hepatis. The production and structure of diffuse medullary cancer. The vascular network forms the first foundation of the stroma, while the liver-cells are converted into cancer-cells. *a*. Normal liver-cells. *c*. Parenchymatous inflammation. *b*. Nests of cancer-cells. *v*. Vena centralis. 1-400.

centric rows. This picture certainly makes the impression, as though the liver-cells must rather be impeding, than conducive to the further enlargement of the nodule, and we are but confirmed in this opinion when we see, that just these nodules present the most admirable examples of the growth of the tumors by leaps. Beyond this girdle of liver-cells and nearest to the outer connection with the principal nodule, there is established a new nodule, which growing independently towards all sides, finally reaches the principal nodule, and fuses together with it into a whole. We often see the whole periphery of the principal nodule beset with additional nodules of this kind, and by its outwardly bulged out contours we may conclude that these are not the first "adjacent depots" which it has annexed. From all this, however, only so much can be concluded, that the liver-cells by the pressure of the carcinoma, perish atrophic, ere yet they are able to prove their vital force by participating in the metamorphosis. Herewith, however, let the possibility, that those small nodules formed their cancer-cells from liver-cells, remain entirely untouched.

A quite different and, for the view alluded to, much more favorable picture is presented by the investigation of the softer multiple carcinoma, which, indeed, we by far most frequently see. For this Frerichs especially has adduced the proliferation of the cancer mass from the

portal canals into the contiguous acini. The numerous injections undertaken by this investigator, at the same time, left no doubt in his mind, that this growth ensues, so to say, under the auspices of the hepatic artery, as the cancer nodules could be filled only from this constantly very much dilated vascular trunk, while the branches of the portal vein were compressed and took up no injection material. His Fig. IV (Plate VII, Atlas, second fasciculus) is a very instructive picture, where we see the adjacent acini of a cancer nodule directly fusing into the new formation. This figure, of whose truthfulness we cannot have the slightest doubt, gives thoroughly the impression of a transubstantiation of the liver-parenchyma, of the liver-cells themselves, and speaks a more intelligible language than all the reasonings based upon deficient observation.

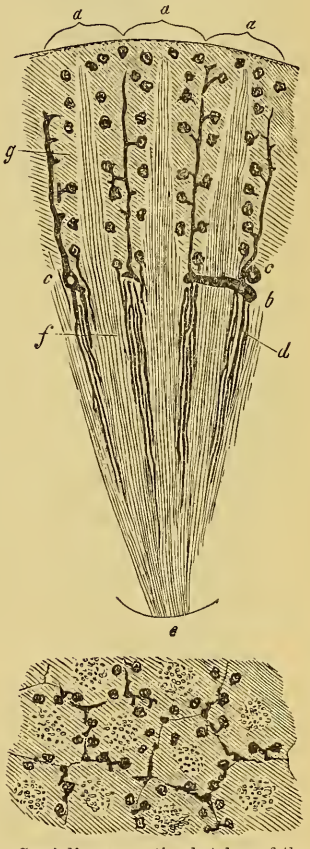
That which, finally, in our judgment, speaks likewise for the direct metamorphosis of the liver-cells, is the great vascularity which characterizes all the softer hepatic cancers. The stroma of the smaller nodules is everywhere formed entirely of wide and thin walled capillary vessels. Afterward there is added a peculiar growth of the stroma by spindle-cells and connective tissue (see § 155), the trabeculæ of the stroma become somewhat thicker, but the main framework always contains in each of its trabeculæ a bloodvessel of larger calibre, which I hold for the derivative of an original hepatic capillary.

§ 532. Herewith, I believe that I have everywhere conducted the reader to the point where the thread of investigation is cut. It is not yet possible to give a conclusive judgment upon the origin and growth of hepatic cancers. It is different with the decomposition of carcinoma, which, in by far the most cases, is introduced by a fatty degeneration of the first produced, hence, oldest and most centrally situated cells of each nodule. We can estimate the extent of this change of a brownish-yellow or yellowish-white decoloration, already by the naked eye, and convince ourselves, that just these places are especially soft, pulpy, and liquefying. The fatty detritus is capable of resorption. But it is only resorbed, when the nodule lies superficially, in which case the side situated towards the peritoneum can sink in, which is not the case in nodules more deeply situated, which have upon all sides equally thick and rigid tumor-walls. Hence, here we have the formation of actual cancerous abscesses, while upon the superficial nodules we observe the phenomenon of a depression or formation of a navel. As cancer-navel we designate the dish-like depression which forms at the collapsed centre of a cancer-nodule. If we make a vertical section here, we touch upon the so-called cancer-cicatrix, that is, the sum of what yet remains of the structure of the carcinoma after the loss of the cancer-cells, the stroma, the obliterated, and the few yet preserved bloodvessels, all united into a solid cicatricial tissue, which radiates everywhere from the periphery into the stroma of the yet florid tumor-mass.

VIII. ANOMALIES OF THE KIDNEYS.

§ 533. It is here and there correctly stated as an aim of pathologico-histological studies, that up to a certain degree we may learn to judge of the changes that have taken place by the unassisted eye. Upon no organ can we go so far in this connection, as upon the kidneys. To this end, we must divide the substance of the kidney into certain anatomical regions, within which the disturbances partly begin, partly produce groups of anatomical changes of characteristic appearance. In the first place we have the principal division of the kidney into medulla and cortex; these are characterized by the course of the main branches of the renal artery and vein upon the one side; upon the other, by the exclusive finding of convoluted urinary tubuli and Malpighian corpuscles in the cortical substance. Further on, however, we distinguish upon the *cortex*, 1. The region of the Malpighian corpuscles, and the convoluted portions of the tubuli uriniferi. (Fig. 153, *g*.) This embraces four-fifths of the entire cortex. As the *capsules* of the Malpighian corpuscles are at the same time the beginnings of the urinary tubules, the convoluted portions of the urinary tubules, at the same time the termination of them, therefore, the substance in question represents the most important part of the secretory parenchyma. Furthermore, it contains the collective arterial and venous trunks of the cortex, the collective rete mirabile with corresponding vasa afferentia and efferentia, and the venous half of the capillary system; 2. The region of the straight tubuli uriniferi. I should rather say, the regions, for in

Fig. 153.



Semi-diagrammatic sketches of the structure of the kidney in cross and horizontal sections through the cortical substance. *a*, *a*, *a*. The bases of renal lobuli which appear as polygonal figures upon the horizontal section. *b*. A main branch of the renal artery, which divides the medulla and cortex, and sends up the arteriolæ ascendentes with the Malpighian corpuscles into the cortical substance. *c*. Lumina of renal veins which receive the interfascicular vessels; the latter appear as stellate figures upon the horizontal section. *d*. Vasa recta. *e*. Surface of the renal papilla. *f*. A fasciculus of straight urinary tubuli, which radiate into the connective substance as pyramids of Ferrein.

Fig. 154.

Diagrammatic sketch of the course and subdivisions of a single urinary tubulus. *a*. Vas afferens. *v*. Vas efferens of a Malpighian coil (*g*.) *b*. Convoluted end of the urinary tubulus, with the Malpighian capsule. *c*. Transition of the convoluted urinary tubulus into the descending branch of the loop-formed. *d*. Loop. *e*. Outlet of the ascending branch of the loop-formed urinary tubulus into the system of excretory tubules (*f*, f^1, f^2, f^3). c^2, c^3, c^4. Places where other ascending urinary tubuli empty.

truth, this region is divided into just as many subdivisions as the kidney has lobules. Every renal lobulus (Fig. 153, *a*, *a*), consists in its medullary portion only of straight urinary tubules, and indeed, upon the one hand, of the comparatively wide discharging tubules, (Fig. 154, *f*), emptying at the papilla (Fig. 153, *e*), upon the other of the very narrow *looped-formed* sections of the urinary tubules, which by one radicle come from a convoluted tubule, and empty by the other obliquely from below into a discharging tubule. (Fig. 154, *c*, *d*, *e*.) The thickness of the bundle upon every cross-section depends upon the number of these loops. The loops of the most peripherally situated Malpighian corpuscles just reach into the medullary substance, while the most central glomeruli, therefore, situated at the boundary of medulla and cortex, send down their loops until close above the papillæ; the intermediate ones, however, corresponding to their situation, form loops at all possible distances between the papillæ and the medullary boundary. Thus it comes, that close to the limit of the cortex in the medullary parts of the lobule, the ascending and descending limbs of the collective curved urinary tubuli are united in *one cross-section*, while towards the papilla the loops coming from the peripheral capsules, towards the periphery, those coming from the central capsules disappear more and more. Conformably, the bundle of straight urinary tubules of each renal lobule tapers from the medullary limit towards both sides. In the cortical substance it is continued as the so-called pyramid of Ferrein. Now these pyramids of Ferrein are identical with the extent of the straight urinary tubules in the cortical substance. The small-meshed capillary net, which is woven around these tubuli uriniferi, is at the same time the arterial

half of the collective capillary system of the kidney; namely, the vasa efferentia, after leaving the glomerulus Malpighianus, penetrate directly into the centre of the pyramids of Ferrein, and here first break up into capillaries, so that the blood in each renal lobule flows from within outwards, notwithstanding the afferent vessels, the arteriolæ ascendentes (Fig. 153, *b*), are situated at the periphery. Upon the *medullary substance* we distinguish,

3. The region of the straight urinary tubules, *i. e.*, the medullary portion of the renal lobule. (See under 2, and compare Fig. 153, *f.*)

4. The region of the vasa recta. From the medullary limit small bundles of veins and arteries push in between the bundles of straight urinary tubules, each belonging to a lobule. (Fig. 153, *d.*) As these vessels are likewise characterized by their straight course, in an empty condition they are difficult to distinguish from the adjacent tubuli uriniferi. The limits of the lobuli, under the circumstances, are indistinct to the naked eye. In reality, however, the vasa recta are almost always filled, and thus furnish us an exceedingly valuable macroscopic criterion for distinguishing the adjacent lobuli. They come, as far as they are arterial, by far the greater part from the glomeruli, situated most towards the medulla, and are very much elongated vasa efferentia; for the smaller part they arise directly from the main branches of the renal artery, which run between the medulla and cortex. The veins unite near the medullary limit to short trunks, which open directly into the main branches of the renal vein. The vasa recta are surrounded by a moderate quantity of loose connective tissue, the last processes of the connective tissue sheath, which invests the principal vessels at their entrance at the hilus of the kidney.

Further consideration will now teach in how far these regional subdivisions of the kidney will come to our aid as the most essential guide in the "*microscopy with the unaided eye.*"

1. Inflammation in General.

§ 534. The pathological anatomy of renal inflammation is, in truth, the most cherished, and withal the least finished chapter of our entire teaching; thus, far from being able to delineate an anatomical picture of disease, divided into stages, under the name of renal inflammation, according to my judgment, we must regard as premature even the attempts of Rayer, Förster, and others, to draw stricter bounds between a simple, an albuminous, parenchymatous, interstitial, and a croupous nephritis. This incompleteness and uncertainty in pathologico-anatomical spheres is also reflected, especially in the fluctuating state of clinical diagnosis, where the exceedingly elastic idea of morbus Brightii (certainly not merely from doing honor to John Bright) yet enjoys an undiminished consequence. In the face of this, the position

of pathological histologist may be called a comparatively easy one. We are at liberty to consider by themselves the changes which are observed upon the individual structural constituents, the urinary tubules, the connective tissue and the bloodvessels, and thus at least present the elements of the anatomical changes in unmixed purity, while it is only secondarily our office, by the combination of these elements, to group the principal anatomical pictures of the total disease.

a. *Changes in the Tubuli Uriniferi.*

§ 535. *Desquamative catarrh.* If we exert a lateral pressure upon the papillæ of a not quite recent kidney, taken from the corpse, there regularly flows out of the urinary tubules, there opening, a little whitish, cloudy urine; the whitish cloudiness is derived from the admixture of epithelial cells, which, by their partial apposition into tubules, prove to be the cast off epithelial linings of the tubuli uriniferi. As this appearance is constant, it must appear venturesome to wish to recognize the existence of a desquamative catarrh of the urinary tubules, from their increased appearance at any time; from their being more readily loosened post mortem we cannot once draw the conclusion that during life, also, the epithelium of the urinary tubules adhered more loosely to the membrana propria; on the contrary, we are called upon by this to be suspicious of the finding of urinary tubules free of epithelium under all circumstances. In such urinary tubules of the renal papillæ, apparently free of epithelium, upon cross-sections, I have not at all infrequently found fractional parts of the garland of epithelial cells, which, in the preparation, had remained isolated, probably only by chance, but gave so much the more eloquent testimony that the absent portion of the garland had fallen out just as the epithelial lining of the perfectly naked tubules.

Accordingly it might almost appear as if I were inclined to deny in general the existence of a desquamative catarrh of the urinary tubules. This, however, is by no means so. I refer to but one much used, and yet quite useless, criterion of its existence. The course of *desquamative catarrh* of the urinary tubules is on this wise, that in the first place there occurs a granular cloudiness and a casting off of the existing epithelial lining, hereupon, however, a more abundant production of young cells on the part of the connective tissue in the surroundings of the urinary tubules, to a more rapid exchange of the epithelial cells, and to the separation of numerous, but always single, older and younger cell-forms. Certainly the question recurs here of the place of formation of the epithelia, and the presence of the membrana propria between the connective tissue and epithelium, is very well calculated to call forth doubts and scruples as to the possibility of a restoration of the epithelium on the part of the connective tissue. Meanwhile, by the recent

discovery of Cohnheim (§ 89), the belief in the absolute homogeneity of the capillaries has received a heavy blow, which will, without doubt, be continued to all homogeneous membranes. I described above (§ 367) the migration of young connective tissue cells through the basement-membrane of the tracheal mucous membrane in croup of the latter. I, moreover, cited the investigations of Iwanoff on the migration of corneal elements through the anterior layer of the cornea into the epithelium in certain forms of pannus; the tubules of Bellini also already, years ago, were investigated by Axel Key for this possibility, and, indeed, not without positive results. In other respects, I refer to the adjoining figures. Fig. 155 presents transverse and oblique sections of catarrhal urinary

Fig. 155.

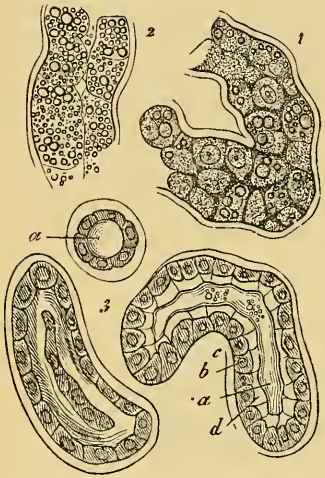
Transverse and oblique sections of catarrhal urinary tubuli. 1–500.

tubules. The central one of the three is entirely deprived of its normal epithelial lining, and in its stead exhibits young cell-forms without firm connection. The two others show more or less loosened epithelial linings, as also younger cells upon and beneath the epithelium. The cellular infiltration of the connective tissue is also indicated. I have hitherto only observed these changes in the system of tubules opening at the papilla, which we can distinguish within the medullary substance from the loop-formed urinary tubules by their considerably larger calibre; in the cortex by their lighter epithelium, and likewise by their calibre, although but little larger, from the convoluted urinary tubules.

§ 536. *Cloudy swelling.* One of the most important affections of the urinary tubules is the *cloudy swelling* of the epithelial cells. It is characterized by the more abundant appearance of minute dark granules in the protoplasm, and an evident increase of volume of the single elements conditioned thereby. The greater space which is here required, is covered, upon the one hand by a considerable increase of thickness of the whole urinary tubule, upon the other by the cells swelling towards the interior, and completely filling up also the lumen of the urinary tubule. They then divide in the existing room at the expense of their outer form. The one part, with their conical points, push towards the interior; the others become more globular, and form bellied projections at the external contour of the affected urinary tubules. (Fig. 156, 1.) The nuclei, indeed, become indistinct under the dense cloud of minute granules which clouds the protoplasm, but even in cases of very high degree of cloudy swelling, I have always yet

been able to make them distinct by carmine imbibition and acetic acid. Herewith it would appear to me as though more frequently than we ordinarily accept, there occurred a nuclear and cellular division, still I will not allow myself a definitive judgment, because all histological criteria are so extraordinarily uncertain, just in the cloudy swelling of the epithelia; for this is exclusively observed at the convoluted portions of the urinary tubuli, and we know that just here a finely granular clouding of the epithelial cells is found, even under normal circumstances, in such manner, that these cells have a more cubic or cylindrical form; the cloudy swelling would consequently appear only as a quantitative, and therefore very difficult to be estimated excess, if the perverse arrangement of the existing epithelia and the closure of the lumen by swelling did not present further points of support. It is similar with the nuclear and cellular division, which may also be observed in the normal kidney. We must undoubtedly lay the most weight upon the total effect of the changed tubuli upon sections; their decided dilatation, the varicosity of the outer contour, finally a certain not inconsiderable swelling and increase of thickness of the tunica propria (which, according to my experience, is never wanting), insure the microscopic recognition of the morbid condition better than the observation of a single epithelial cell.

Fig. 156.



1. Cloudy swelling and commencing fatty degeneration of the epithelia of the convoluted urinary tubuli. 2. Advanced fatty degeneration. 3. Formation of fibrinous cylinders. *a.* Cross-cut of a urinary tubulus, with a gelatinous cylinder filling the lumen. *b.* Epithelium. *c.* Tunica propria. *d.* Renewed production of colloid at the surface of the epithelial cells, which elevates the older. 1–500.

What kind of chemical changes take place in the cloudy swelling at the protoplasm has not yet been ascertained. There probably is an impregnation with an albuminoid body, as the cloudiness, as we saw above, can be made to disappear by the addition of acetic acid. In a general pathological relation we must regard the cloudy swelling as the consequence of an irritation, which has attacked the cell from the blood. The question is mostly about poisonings and infections, poisoning by phosphorus, variola, and other acute exanthems, typhus, puerperal, and septic fevers, in all of which the poison is taken up at another place, but is conveyed to the kidneys, as to other organs, by the blood.

§ 537. *Fatty degeneration.* The future changes of the "cloudy swelled" epithelial cells are various. Slighter degrees of the affection appear to be no obstacle to the return of the cells to the normal state. If we imagine the granular masses as nutritive material, which remains

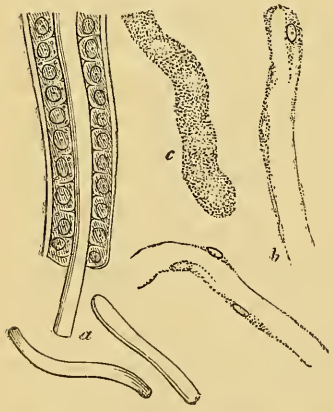
in the cell in consequence of disturbance of the exchange of material in the cell and separates in a solid form, we may represent to ourselves the return to the normal as a resolution and consumption of the solid mass. Direct observations upon this point are quite wanting from apparent grounds. Upon the other hand, *fatty degeneration* threatens the swollen epithelia. Then beside the minute albuminous molecules, darker and larger granules arise, which by their microchemical reactions (solubility in alcohol and ether) prove to be fat-globules. I have often wondered at the very various sizes of these fat-globules. Some are atomically small, others of such an extent that one might almost think of fatty infiltration (Fig. 156, 2), if the formation of granular corpuscles and the final disintegration to a fatty detritus did not pronounce too distinctly the destructive tendency of the process. The fatty metamorphosis, as long as the cells are yet to be distinguished as particular structures, is connected with a further distension of the tubulus, which is of course but temporary, and in the next place passes over into the opposite condition of collapse; thus, one imagines that the fatty detritus is partly evacuated with the urine pressing from behind, part resorbed, and that then the urinary tubules naturally remain empty and flaccid. The known finding of fatty globules and granular corpuscles in the urine speaks for the possibility of the evacuation of the fatty detritus. The latter still adhere here and there externally to the fibrinous cylinders (see below), evacuated at the same time, and thus make known their derivation from the urinary tubuli. Meanwhile the greater part of the fatty mass is undoubtedly removed by resorption. Beer found the stroma of the kidney, especially the stellate gaps for the connective tissue cells, flooded with fat-globules. The pictures which he gives us of this correspond too nearly with the known appearance of the intestinal villi during the absorption of fat, that there should remain a doubt of any weight. The complete deprivation of the urinary tubuli of epithelium appears to me to be less fully made out. The complete disappearance of the urinary tubuli in the destruction of the connective tissue of the organ, therefore, in the later stages of shrinking of the kidneys, can properly only be adduced for this. A kidney, however, whose cortical substance consisted exclusively, or even only in part of collapsed urinary tubuli, and without epithelium, I have never seen. Hence it may be probable that the loss in cells, which the fatty metamorphosis, occurring after the acute cloudy swelling at the epithelial lining of the convoluted urinary tubules, causes, is provisionally covered by a corresponding after-growth and replacement, and that in this way a complete equalization of the disturbance lies in the bounds of possibility. Clinical experience also agrees with this.

It is certainly somewhat different, when the epithelium of a urinary tubule, strangulated by the interstitial connective tissue development, or cut off from nutrition, whose complete destruction is only yet a ques-

tion of time, undergoes fatty degeneration. We meet with conditions of this kind with extraordinary frequency in such kidneys, upon which the nephritis, having become chronic, has half completed its work of destruction. (See § 562.) Here, however, the fatty degeneration is by no means a consequence of former cloudy swelling, but entirely the proof that the affected urinary tubuli are no longer sufficiently provided with nutritive material, and that in consequence of this the epithelial cells, rich in protoplasm and hence much in need of nutriment, fall into necrobiosis. The histological detail is, of course, also in this fatty degeneration the same as in the acute form; yet all the cells do not die at once; we rather find side by side the most various changes of the process, as also the etiology of the trouble it brings with it.

§ 538. *Fibrinous cylinders.* One of the most important signs for the existence of an affection of the kidneys, falling under the province of hyperæmia and inflammation, the physician finds in the presence of the so-called fibrinous cylinders in the sediment of urine. We call fibrinous cylinders certain hyaline, colorless, in fact cylindrical bodies, which according to their form agree so completely with the dimensions of the lumina of the urinary tubuli, that it scarcely needs the proof, at the very spot, to declare them as "casts of the straight urinary tubuli." (Fig. 157.) We attain one step further to the conception, that these casts may have arisen in the same manner as the casts of narrow bronchial lumina in croupous pneumonia, and in that this idea was followed up, we finally came to the assertion of a croupous nephritis with fibrinous secretion of the surface. To this came the exceedingly plausible explanation of Traube, according to which the growing height of the blood-pressure in the cones of the renal medulla was said to lead to a filtration of ever thicker constituents of the blood, first albumen, afterward fibrin, at length blood-corpuscles; an explanation which, from the great popularity of the investigator mentioned in this sphere, could not fail to be established in the imaginations of the medical public. Against this, we can to-day also only make this one objection, that the so-called fibrinous cylinders have not yet been recognized by chemists as actual fibrin. This objection, however, leaves untouched the main point of Traube's conception, namely, that the albuminuria arises, increases, and falls with the hyperæmia of the renal medullary substance.

Fig. 157.



Fibrinous cylinders. *a.* Within a urinary tubulus. *b, c.* From the urine, more or less richly covered with molecules of fat. 1–500.

It is questionable whether the fibrinous cylinders generally could

arise without an active participation of the urinary tubuli. For some time I defended the view, that the epithelial cells of the straight urinary tubuli prepared in their protoplasm a colloid substance, which they allow to pass out into the lumen of the tubuli uriniferi. Fig. 156, 3, appeared to me to be only explained in the sense, that after the consolidation of a first fibrinous cylinder *a*, which occupies the central lumen of a urinary tubule, a renewed production of colloid substance *d* has taken place on the part of the contiguous epithelial cells *b*. Still I must concede to Klebs, that here also the interpretation of a simple, perhaps post-mortem, or caused by the preparation, swelling out from the protoplasm of the epithelial cells, is not to be excluded. The matter is consequently by no means ready to be pronounced upon, and as it has lately been proven (Heynsius), that the blood-corpuscles contain fibrin, the possibility is also to be considered, that the fibrinous cylinders are a product, washed out of extravasated blood-corpuscles. We will provisionally maintain, that a fluid albuminate poured out into the lumen of the urinary tubules becomes rigid, and thereby forms the fibrinous cylinder. If there are cast-off cells in this lumen of the urinary tubule, as is the case in catarrhal conditions, these are fixed in the centre of the cylinder. The outer contours of the cylinder are then more sharply defined, and the onward movement, the evacuation of the structure, begins. This is accomplished by the pressure of the urine from behind, and meets with no difficulties, because of the extraordinarily soft, and in every direction pliable, slippery, smooth constitution of the fibrinous cylinder, notwithstanding the numerous curves of the route that at least some of them have to pass over. (Fig. 154.) The passage from the ascending limb of the loop-formed canals into the straight tubuli, takes place with peculiar ease because of the greater width of the latter. The majority of the fibrinous cylinders are formed in the looped canals; the ordinary thickness of those which are found in the sediment of urine correspond to their lumen, much rarer to the greater calibre of the straight tubules. In the convoluted portions of the urinary tubuli fibrinous cylinders are probably only exceptionally formed, and those which we meet with upon sections of the cortical substance do not lie in the convoluted tubes, but in the spaces of Schweigger, or in the excretory ducts, which, indeed, according to Henle's investigations, are uniformly distributed through the entire cortical substance and as an independent system of canals, and may accordingly also be met with between the convoluted urinary tubuli.

§ 539. *Amyloid infiltration.* I am convinced that fibrinous cylinders, which remain sticking at places of the urinary tubuli difficult to be passed, especially at the curves of the "looped-formed ones," undergo the vitreous tumefaction in the course of time, and assume the microchemical reactions of amyloid substance, become brownish-red upon

the addition of iodine. Only in this manner can I explain to myself, when in kidneys, which are indeed exceedingly altered in their other structural constituents, but are yet not exactly amyloid infiltrated, at the mentioned curves, cylinders of amyloid substance are found, which occlude the urinary tubules for a greater distance. These cylinders cannot be regarded as metamorphosed epithelia (see below), for the epithelium lies well preserved between them and the membrana propria of the urinary tubules. The amyloid infiltration of the epithelia is in general only found in the extremest cases of general renal amyloid, so that for these amyloid cylinders standing quite alone we must fall back upon the local production of the amyloid substance from "coagulated albuminates which have remained lying," more minutely discussed in § 50.

Now, touching that general renal amyloid (comp. § 564), the urinary tubules are wont to be affected only in the second place. The principal depot is then found in the membranes clear as glass, which swell up considerably, in sections by transmitted light become clearly transparent, and present the well-known iodine reaction. The epithelial cells offer a much longer resistance. If they also finally enter upon the metamorphosis, they swell out, their contours become indistinct, those contiguous fuse together, and since the central lumen entirely vanishes, there arises a cylinder of amyloid substance, which still exhibits its composition by cells, by its bulging outlines (Key). The amyloid infiltration of the urinary tubuli beside that of the blood-vessels, especially of the vasa recta, is found par excellence at the renal papillæ, extends, however, from here, radiating, probably even into the pyramids of Ferrein. I have not yet observed it upon the convoluted urinary tubuli, but I by no means doubt of the possibility of its occurring there. One will always have difficulty here in distinguishing the diseased tubuli from the simultaneously diseased vessels.

§ 540. The *cystoid degeneration* of the urinary tubuli depends either upon an obstruction, or upon an obliteration of their lumen, and arises according to the general type of retention cysts, yet the latter undergoes just here several very essential modifications.

A very common obstruction to the efflux of the urine is presented by the amyloid cylinders in the curved urinary canals, mentioned in the preceding paragraph. Beside these we not at all infrequently find smaller and larger cysts, up to the size of a pea, which are dispersed through the medullary substance of the kidney; now there are but few of them, now they are so densely sown that they touch each other, perhaps form elegant rows, like strings of pearls, &c. (Fig. 160, *f.*)

The second fourth of the medullary substance, reckoned from the apex, is undoubtedly the favorite seat of this kind of renal cysts. From here towards the cortical substance they gradually lose themselves; at the papillæ they are just as little found as in the immediate neighbor-

hood of the medullary limits or of the pyramids of Ferrein. Touching the details of their development, in the first stage of the ectasy, a gelatinous softening of the obstructing material itself appears to play an important rôle. Up to the size of a pin's head, perhaps, the cysts by no means contain a clear or urinous fluid, but a substance which readily solidifies in alcohol, chromic acid, &c., and then exhibits a concentric arrangement upon cross-sections which impregnates with carmine, and retains this color quite peculiarly; in short, a half solid, gelatinous albuminate. Upon single cysts of the calibre just mentioned, there can be demonstrated neither epithelium nor tunica propria; and the transition into the surroundings is so indistinct that for these cases it is impossible to banish thoughts of a centrifugal process of softening. For this latter certainly tolerably narrow limits are drawn; a sharply limiting seam of connective tissue forms, upon still larger specimens of these cysts, the boundary towards the surroundings; at the same time the contents become structureless, clear as water, and thinly fluid. Meanwhile these more profound changes must not prevent us from upholding the acceptation already founded by Beckmann and received by Virchow, according to which the smaller multiple cysts of the medullary substance, which we find in interstitial nephritis, are cysts of retention.

§ 541. Cysts by constriction are found in the cortical substance of such kidneys, in which an inflammatory hyperplasia of the connective tissue has particularly attacked the environs of the larger renal vessels at the medullary limits. These cysts are either single, or they even occur so numerous, that the whole cortical substance is occupied by them, and but few remains yet exist of relatively intact parenchyma. In the latter case (cystoid degeneration) we have the best opportunity yet of following the development of the cysts in all their stages. Virchow has but recently correctly warned against the assumption that the cysts arose each from a urinary tubule. The foundation of cysts is rather formed by a roundish circumscribed spot of perhaps the size of a hempseed, in the region of the convoluted urinary tubules, within which all the tubuli are considerably dilated; the walls, however, have fused together, so that the whole even now makes the impression of a cyst subdivided by narrow septa. Afterward the partition walls atrophy at the thinnest places, the ectatic urinary tubuli open into one another, and finally run together into a single larger cyst. The remains of the partition walls fall back like a torn spider's web against the walls, and may yet be demonstrated here even upon larger cysts. The contents of the cysts is originally a urinous fluid; even in larger specimens, by evaporating with many times its volume of alcohol, extracting the remainder with absolute alcohol and some ether, and treating the extract with nitric acid, I found urea in tolerably large amount, which appears to me worthy of notice in contrast to the—upon the whole—negative

results of Beckmann. There is also not infrequently blood found in the cysts, whereby they get a brownish or ochrous yellow color, finally albumen, which may be coagulated by boiling.

§ 542. The *congenital renal cysts* have a quite similar manner of production as those acquired by interstitial nephritis. A child is born, but either dies during parturition, or after having several times vainly attempted to breathe. As the cause of death there is found a cystoid degeneration of both kidneys, by virtue of which these two organs have grown into tumors of two inches long and one and a half thick. The diaphragm is pressed upward, the lower half of the chest, dilated funnel-shaped, is occupied by the liver, so that no space exists for the movements of the lungs. If we here trace up the origin of the cysts, the Malpighian corpuscles constantly prove to be the points of departure. Beside quite normal corpuscles, we find such in which the wall has drawn back from the vascular coil, so that between the two there gapes a more or less broad crescentic interspace. The larger the latter becomes, so much the more the Malpighian corpuscle becomes a projection at the wall, which, however, may yet be found as such in cysts of the size of a pea. The urinary tubuli may also degenerate in their continuity, but it is constantly but one urinary tubule; the cysts here never arise or grow by the confluence of several. The partition walls rather appear, the larger the cysts become, to become so much the thicker. The partition walls, moreover, are very rich in lymph spaces, which may be excellently filled from the perivascular connective tissue of the hilus. The vascular system is exceedingly deficiently developed, the renal artery at its origin from the aorta has so narrow a lumen that we can just enter it with a pin; the vein is proportionally wider.

As a proper cause of this congenital cystoid degeneration, Virchow has announced an intercalation of a mass of connective tissue between the renal calyces and the renal papillæ—a statement to which I also accede, without allowing myself a certain judgment as to the significance of this connective tissue. If it is true that the urinary tubules and the renal calyces grow towards each other in the development of the organ in these cases, as it appears, they have not attained the connection.

b. *Changes of the Connective Tissue.*

§ 543. Before we study the changes proceeding from the connective tissue of the kidneys, it is necessary in a few words to point out the nature and the distribution of this substance in the normal condition. If we tease out a bit of recent kidney upon an object-glass as minutely as possible, and place the preparation under the microscope, one would almost doubt whether there was here any connective tissue in general. Nothing but urinary tubuli and bloodvessels present themselves, appa-

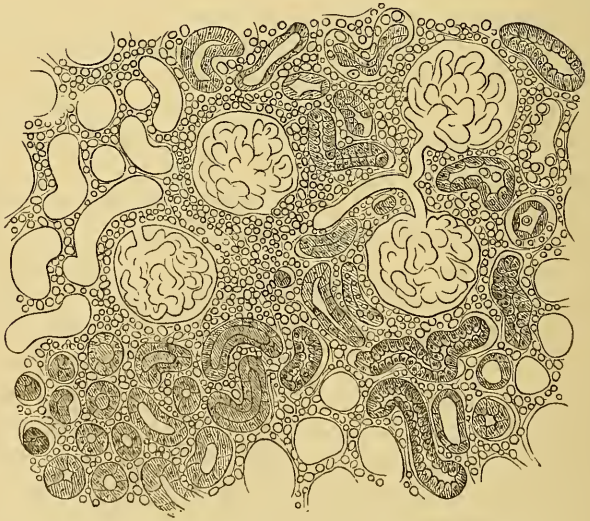
rently completely naked, to the eye. It requires already a very attentive review of the individual urinary tubules to discover adhering upon them, here and there, the smallest heaps and shreds of a coagulum-like, often finely granular substance, which, in fact, is to be interpreted as connective substance. On the other hand, sections from the various regions of the organ, which have lain some time in carmine solution, and then in acetic acid, are much more useful for the investigation. Upon them we can most certainly be convinced that everywhere, as well in the medullary as in the cortical substance, the urinary tubuli upon the one hand, the bloodvessels upon the other, are glued and held together by an organized cement, which is nothing else than the sought-for connective substance. A basal substance, which clears with acetic acid, contains in corresponding spindle-formed and stellate gaps the known cells of connective tissue. We mostly find a cellular element upon each of the small three-cornered spaces, which, upon cross-sections, remain between the round contours of the mentioned tubuli. This is the relation, especially in the region of the convoluted tubuli; towards the medullary papillæ with the increasing breadth of the three-cornered interstices, the cells also become somewhat more numerous, the apex of the papilla is formed by a very compact connective tissue layer, which in consequence of the numerous perforations on the part of the urinary tubuli, appears cribriform. Larger accumulations of connective tissue, even with fibrillar indications in the basal substance, then occur, as already observed above, in the surroundings of the larger vessels and of the vasa recta.

§ 544. A formative irritation of the connective tissue of the kidneys is present more or less expressed, primary or secondary, diffuse or circumscribed, in all inflammatory conditions of the organ. Since we reserve the better part of this variety for the elaboration of the representations of "inflamed kidneys" to be given below, it is only necessary for us here to follow the histological process. This may be accomplished in various directions. Beer distinguishes between a simple and a cellular hyperplasia, and understands by the former a gradual swelling of the interstitial tissue, whereby but the one modification becomes perceptible in its condition, that the cellular elements easily enlarge; their number remains the same. As concerns the intercellular substance, it appears to be increased in a measure corresponding to the enlargement of the connective tissue bodies; the further changes are of a subordinate kind; it especially appears that the intercellular substance, the more abundantly it accumulates, so much the more assumes the "fibrillar" character. In general, this entire series may be regarded as hyperplasia of the connective tissue in the more contracted sense, as a uniform increase of all the textural parts present in the connective tissue. It does not occur as well in the actually inflammatory conditions, as it develops in consequence of persistent venous hyperæmia;

still mistakes may be very readily made here, since the active hyperæmias of the kidneys, which are wont to introduce inflammatory conditions, likewise go along with a tumefaction of the basis-substance of the connective tissue cells, and with a strong serous saturation, consequently a swelling by imbibition of the basis-substance.

§ 545. More important for the doctrine of nephritis is the process designated by Beer as cellular hyperplasia; it is the recent inflammatory or plastic infiltration of the connective tissue so often described by us, the accumulation of young membraneless cells with the character of colorless blood-corpuscles, the formative cells, &c., wherever space is found for their accumulation. Whence these cells come, it is difficult to say. Not because we are in want of a plausible idea as to their derivation; on the contrary, we have but too many of them. We must leave it undecided, in how far the existing cells are migrated colorless blood-corpuscles, or newly-formed derivatives of the connective tissue cells of the kidney. In the histological investigation we find upon transverse sections the connective tissue septa, between the adjacent urinary tubuli, often thickened to three times their normal extent, widened. The young cells lie in elegant rows where they are less dense, in continuous masses where they are most densely crowded. A double or triple ring of such cells is wont to engirdle the Malpighian corpuscles, which is of very considerable significance, especially for the following stage of the degeneration. (Fig. 158.)

Fig. 158.



Cellular hyperplasia of the interstitial connective tissue. 1–300.

§ 546. Only in quite definitive cases (see below), does the cell new formation exceed those limits which are drawn between germinal tissue

and pus. The pus collects without exception in abscesses, whose form and size are determined by the cause of the suppuration. There commonly follows upon the germinal tissue condition of the interstitial connective tissue, as we have hitherto observed it, a reduction of volume, which we cannot avoid placing by the side of cicatricial *shrinking*. Yet, important objections may be admitted here; namely, what actually does occur, and can be everywhere readily demonstrated, is not a change in the quality of the connective tissue, but a withering and destruction of the other structural constituents of the kidney imbedded in the connective tissue, the urinary tubuli, the bloodvessels, the Malpighian corpuscles. Upon all these structures we can perceive a gradual reduction of volume, combined either with a fatty metamorphosis or with a compressive condensation of the substance. The Malpighian corpuscles become obsolete in such manner, that in their stead we find small globules, which are exceedingly compact, dense, and perfectly anæmic. These break up into an unstratified nucleus, which corresponds to the compressed vascular coil, and into a thick envelope of connective tissue concentrically stratified around the nucleus in several lamellæ. Now, in the face of these conditions as found, we can, of course, scarcely resist the thought, that an actual strangulation of the rete mirabile had occurred here, and that this was to be ascribed entirely to the spontaneous contraction of the connective tissue having become cicatricial. (Fig. 160, *d*.) But this is also the only fact which speaks for a *qualitative* change of the young connective tissue. Furthermore, the simple theory of crowding would also suffice for explaining the appearances, as already the loss of the urinary tubuli, for example, would make comprehensible the most considerable decrease of volume of the whole kidney. Even in shrivelling of the kidney of high degree, a peculiarly striped or even fibrous nature never becomes evident upon the crowding connective tissue, and even touching the number of the cells, which, in the cicatricial formation appear constantly to be reduced to the utmost, I have never been able to convince myself of any decrease of them worthy of mention.

§ 547. Very interesting, and for the histological significance of the perfectly transparent membranes of the greatest importance, herewith, is the behavior of the tunicæ propriæ of the urinary tubuli. That these in healthy kidneys present a structure in itself, which stands in a more intimate relation with the epithelial lining of the urinary tubuli than with the connective tissue around, is undeniable. In the cellular hyperplasia of the latter, nevertheless, this relation is reversed, and the true nature of the tunica propria becomes manifest. The latter, so to say, makes common cause with the young connective tissue of its neighborhood, it fuses with it, and forms after some time only the boundary, marked by a sharp fine line of the connective tissue, towards the lumen and the epithelium of the urinary tubuli. Simultaneously, we

not at all infrequently observe small contractions, principally irregularities in the rounding of the contour, which correspond to those points where the net of canals in the interior of the connective tissue opens at the surface; at least, just here, we see the young cells coming up close to the lumen. These stomata are, in my opinion, already present in the normal urinary tubuli, still they are much narrower, and just as little to be brought into direct view as the minute stomata of the capillaries. Meanwhile, I have only met with all these changes in very advanced cases of interstitial nephritis, and as yet, only in the medullary substance near the papillæ.

c. *Changes of the Vessels.*

§ 548. In the glomerulus Malpighianus we have a structural element of the kidney, which is so pre-eminently composed of capillary vessels, and therewith, is so well separated from the surrounding parts, that we can comprehend the changes, which exclusively run their course upon them, as little under the changes of the urinary tubuli as under those of the connective substance. Klebs (Handbook of Pathological Anatomy, iv, 644), has described as glomerulo-nephritis, an inflammatory hyperplasia of that small amount of connective tissue which cements the vascular loops of the glomeruli together, and was first seen also in the normal kidney by Axel Key. In glomerulo-nephritis we find the Malpighian coil void of blood, but instead "the whole inner space of the corpuscle is filled by small, somewhat angular nuclei, which lie imbedded in a finely granulated mass." Upon more exact investigation we are convinced that these cell-masses are for the greater part infiltrated between the capillaries, and have caused a compression of their lumen. As glomerulo-nephritis has hitherto only been observed in scarlatina, it at least sufficiently explains the sudden, often total suppression of the secretion of urine, the acute transudations and the uræmia, at times even causing death in twelve to twenty-four hours, in this disease.

If we wish to be completely in possession of the anatomical elements of inflammation of the kidney, we must furthermore not leave unmentioned a histological alteration of the vessels, which, it is true, has nothing to do with the inflammatory process as such, but evidently stands in a very close causal relation to it; I mean the amyloid infiltration of the walls of the vessels. In § 48, *et seq.*, of the General Part, the preferred position which the vascular system occupies in the amyloid disease, was more amply mentioned, and the degeneration of a Malpighian vascular coil chosen as a paradigm. In fact, they are, probably without exception, the Malpighian corpuscles in which the first beginnings of the disease may be demonstrated. The vasa afferentia and the arteriolæ ascendentes commonly follow, while the vasa

efferentia and the vasa recta, therefore the vessels on the far side of the rete mirabile are, for the time being, not attacked. Herewith an exceedingly unequal participation of the glomeruli becomes very perceptible; not only that within the same glomerulus there are not at all infrequently several loops yet completely free, while all the others have already just as completely degenerated, we also very commonly find quite healthy and quite degenerated glomeruli side by side, and one cannot resist the thought that the collateral hyperæmia, conditioned by the partial obliteration of the blood-tract, must be the cause of this longer continuance intact, although it is difficult to give a more exact account of this conception.

After the degeneration of the cortical substance has advanced to this point, the process is wont to pass over to the medullary substance; here, however, as was above shown, they are not the bloodvessels, but the tunicæ propriæ of the urinary tubuli, which first become diseased. If we now take a narrow bit of the cross-cut of the kidney, wash it out, and then place it for a short time in a diluted watery solution of iodine, we observe, even with the naked eye, in the cortical substance numerous mahogany-red points and streaks, which correspond to the glomeruli and to the degenerated arterial vessels, while the medullary substance presents a just as much colored coronet of minute rays, which is the most dense a little above the papilla, but towards the medullary limits rapidly loses in density.

In cases of renal amyloid of very high degree, everything is infiltrated that possesses homogeneous membranes, vessels, and urinary tubules; only the connective tissue and the most of the epithelia have remained free.

2. Individual Forms of Inflammation.

§ 549. Let us now interest ourselves, by the aid of data hitherto obtained of the pathological histology, to bring forward a series of peculiarly characteristic or frequently recurring anatomical appearances which are ascribed to the "inflamed kidney." The frequent combination of doubtless inflammatory and non-inflammatory, for example, retrogressive or simple hyperplastic conditions, which we herein meet with, certainly makes it necessary to mention in this subdivision at the same time the cyanotic kidney and pure renal amyloid, although they do not appear to belong here.

a. *Hyperæmia—Cyanotic Induration—Congestive Nephritis.*

§ 550. We may distinguish at the kidney as well as elsewhere between an active and a passive hyperæmia, since we comprehend the former and others as the initiatory stage of inflammation, the latter as the result of a mechanical obstacle to the return of the blood. Meanwhile the pathological anatomist has for both forms but one phe-

nomenon, varying at most according to intensity,—the accumulation of blood in the venous system, which extends in variable distances into the arterial side of the capillary tract; the arteries themselves up to the glomeruli are constantly but slightly filled. The glomerulus assumes an exceptional position, since only by the direct injury to its blood-capacity by external pressure does it permit a certain amount of blood to escape, which otherwise, under all circumstances, permits it to appear as a red point at the cut surface.

§ 551. Hyperæmia of the highest degree is characterized by a very considerable, perhaps one-third, intumescence of the entire organ. The capsule, in consequence of a serous saturation of the parenchyma, may be easily stripped off. The parenchyma is bluish-red, moist, smooth; the stellulæ Verheynii are very prominent, and may be followed even with the naked eye into their more minute ramifications, the interfascicular veins. Upon a section we find the principal accumulation of blood in the region of the convoluted tubuli; the glomeruli are not always characterized by any particularly strong congestion, and herein, probably, the possibility would be given to distinguish between active and passive hyperæmia. The medullary substance, especially in the region of the vasa recta, exhibits a dark red radiating substance, which is evidently derived from the highly congested veins.

In slighter degrees of hyperæmia, the redness and swelling in the region of the convoluted tubuli are wanting; on the other hand, the congestion of the venous stars, of the glomeruli, and of the vasa recta is only quantitatively less; it also obtains in the quite normal kidney, as already mentioned, and must then not be regarded as something pathological.

§ 552. If the hyperæmia of the kidney is chronic, a condition brought about by venous congestion, further changes are associated; above all the *simple* hyperplasia of the interstitial connective tissue, more minutely described above in § 544. This develops quite uniformly in all regions of the kidney, and thereby distinguishes itself very essentially from the cellular hyperplasia; the whole organ uniformly increases in weight, circumference, and consistence. The most striking is the greater compactness of the tissue, which may so much the more readily cause a mistaking for the inflammatory renal induration, as we actually have here a new formation of connective tissue. Several authors have, therefore, asserted the category, congestive nephritis, although the connective tissue formation in this case is, probably, only the consequence of a better nutrition, and hence, bears upon itself throughout the character of an homologous development. The bloodvessels are just as little altered by this connective tissue as the urinary tubuli; the secretion of the kidney, nevertheless, is wont every now and then to contain albumen, which indicates a periodic increase of the hyperæmia.

I saw the highest degrees of renal hyperæmia in recent cases of Asiatic cholera. It here forms the introduction to a parenchymatous inflammation, and we may assume that all parenchymatous and catarrhal inflammations are introduced in a similar manner. The congestive hyperæmia, and the cyanotic induration following it, are constantly the results of a heart affection, especially of stenosis and insufficiency of the mitral valve.

b. *Acute Parenchymatous Nephritis—Nephritis Albuminosa.*

§ 553. *Slighter degrees.* The kidney is moderately, yet distinctly, enlarged; its consistence is scarcely changed; the capsule is readily stripped off; at the stripped surface the venous stars are prominent; especially does the accumulation of the blood in the veins and the venous side of the capillaries cause a distinct appearance of the lobular division of the kidney. The same is shown by the cross-section. The region of the convoluted urinary tubuli is yellowish-gray, soft, doughy, and is a little elevated above the level of the cut surface. The Malpighian corpuscles are visible therein as red points. A moderate degree of *cloudy swelling of the epithelia* (§ 536) in the convoluted urinary tubuli has been associated to the hyperæmia and complicated its series of phenomena. Otherwise, everything is yet normal, especially the medullary substance.

§ 554. *Higher degrees.* The kidney is enlarged to almost double its normal circumference. Its attenuated capsule is easily taken off. The stripped surface only shows the larger venous stars, which stand in glaring contrast to the yellowish-white parenchyma. Next to the yellowish-white color, the doughy consistence of the parenchyma is the most striking. Upon a cross-section we immediately recognize, however, that both of these qualities belong exclusively to that part of the kidney which lies in the region of the convoluted urinary tubules. This is of course (excepting the small pyramids of Ferrein), identical with the cortical substance in general, so that the customary description of Bright's inflammation, as a yellowish-white, doughy intumescence of the cortex of the kidney beside a hyperæmic, but otherwise less changed medullary substance, suits very well for acute parenchymatous nephritis. The glomeruli Malpighiani are no longer recognizable with the naked eye; they, just as all the bloodvessels which lie in the region of the convoluted urinary tubuli, are found upon section perfectly empty. Without doubt the continued *cloudy swelling of the epithelia* (§ 536) in the convoluted urinary tubules, and the increase of volume of the latter combined therewith, have led in the first place to the tumefaction of the whole organ, afterwards, however, in the constantly exhausting distensibility of the renal capsule, to a compression of the bloodvessels within the changed parenchyma, so that we may actually term the cortical substance anæmic. The blood then appears to have

been principally crowded into the veins and capillaries of the medullary substance. I have already mentioned the striking and most characteristic circumstance, that the medullary substance of the inflamed kidney appears to be rich in blood in the same measure as the cortical substance is poorer in blood. Meanwhile, from this peculiar and certainly very important anomaly of the distribution of blood, as we find it upon section, we must only conclude, *cum grano salis*, upon the distribution of blood during life. If we attempt, with any injection material, to fill the organ from the artery, this does not succeed when the vessels have undergone amyloid degeneration. The amyloid degeneration, however, is an infrequent complication in parenchymatous nephritis. If the vessels are as healthy as ordinarily, no capillary of the cortical substance will remain unfilled. We certainly do experience in injecting, an extraordinary, but still elastic resistance; a resistance that indeed must have undoubtedly made itself felt during life, which, however, is not so great, that we might assume it had made the influx of the blood generally impossible. After death, it is true, as the propulsive power of the heart ceased, this elastic pressure must have obtained a higher significance, and have pressed the blood present completely out of the cortical substance into the veins and into the medullary substance, but I repeat, we must not imagine the blood as unequally distributed during life as we find it post mortem.

To this form of nephritis, in the symptomatology, corresponds the finding of a very scanty, dark urine, thoroughly albuminous and abundantly loaded with fibrinous cylinders, with or without blood, but constantly without pus. The condition develops very acutely, with severe pains, and may, because of the cessation of function of the collective epithelia in the urinary tubuli, which is almost identical with suppression of urine, very rapidly lead to death. Death ensues under uræmic and dropsical phenomena. The acute parenchymatous nephritis is probably constantly the consequence of a poisoning in the widest sense of the word. Acute exanthems, especially, small-pox and scarlatina, poisoning by phosphorus, typhus, cholera, pyæmia, and puerperal processes, produce it.

§ 555. The cure of the parenchymatous inflammation, in the slighter grades, ensues by the resolution of the solid albuminates, which fill the cells of the convoluted tubuli; in the higher grades, a fatty metamorphosis, whose beginning we commonly observe in the fatal cases, causes a complete solution of the epithelial cells. The loss is covered by a new formation, for which probably the connective tissue must without question be looked to. (Compare § 537.)

c. *Interstitial Nephritis.*

§ 556. 1. *Circumscribed purulent form.* *a.* Renal abscesses in pyelitis. The kidney is considerably larger than normal. The capsule

and the cushion of fat are hyperæmic, œdematous. The former cannot always be separated without loss of substance; rather very commonly small shreds of purulently disintegrating parenchyma remain adhering, which covered one of the abscesses soon to be spoken of. The remaining under surface of the capsule also, is not so smooth as ordinarily, but velvety, rough. At various points of the stripped surface of the organ, we see flat, whitish-yellow elevations, which upon closer examination immediately prove to be depots of pus. They are upon an average of the size of half a pin's head, and either stand singly, or united in groups of three to six. If we observe the bounds of the large Malpighian pyramids, marked by the shallow contraction of the surface, it is mostly found that all, or still at least the greater part of the existing abscesses, are united upon the base of a pyramid, while other pyramids are quite free. Each abscess is surrounded by an intensely red area. It has been supposed because of the size, that every abscess corresponded perhaps to a dilated lobulus; this is, however, not correct; the central point of the abscess corresponds, according to position, to an interfascicular vein, emerging from the depth, as is at once seen upon further observation. The other part of the surface shows a moderate hyperæmia; this also prevails upon the whole cut surface; still, everything is of a dull gray color, which is the microscopic expression of a limited but uniform cellular hyperplasia of the connective tissue (§ 546). The cut surface—by this we understand the main section through the greatest circumference of the organ towards the hilus—is at the same time the place for ascertaining more exactly, concerning the seat and the distribution of the abscesses. They present themselves here as long yellow lines of pus, which in the medullary substance correspond to the surroundings of the vasa recta, in the cortical substance to the interfascicular vessels, or more correctly, to the connective tissue lines accompanying them. In the medullary substance they are constantly most densely placed; most of the abscesses of the cortical substance appear as an extension upwards of the medullary suppuration into the cortex; even the points of pus visible at the surface of the organ are occasionally only the extreme ends of abscesses, which reach into the neighborhood of the papillæ. The urinary tubuli of the medullary substance are in the condition of desquamative catarrh (§ 535).

The renal calyces and the pelvis are constantly dilated; their mucous membrane purulently catarrhal (pyelitis), in spots diphtheritic; in their lumen is found an exceedingly disagreeably smelling urine, in ammoniacal decomposition, which yields an abundant deposit of pus corpuscles and triple phosphates. The same condition of the urinary passages is found in the ureters, perhaps in the bladder, nay, even in the urethra, hence the renal affection described is an inflammation conveyed onwards from the larger urinary passages. Originally a superficial affection, in

its transfer to the renal parenchyma it has immediately led to a general participation of the whole renal connective tissue, and this participation itself has in turn increased at various points up to the production of pus. The more abundant accumulation of connective tissue in the environs of the vasa recta and the cortical veins may not have remained without influence in the localization of the suppuration.

§ 557. A renal suppuration is in itself an exceedingly dangerous affection; still, conceivably much depends upon whether only one kidney or both are diseased. In the latter case death is wont to ensue by uræmia. In the former, and if the individual lives, a further series of pathologico-anatomical changes are to be expected. A complete cessation of the process—inspissation, cheesy metamorphosis, nay, calcification of the pus of the abscess and its investment—is only observed in exceedingly narrow limits. The common course is, that the pus breaks through at the apex of the papilla into the renal pelvis. If this has occurred at more than one point, the medullary cone towards the renal pelvis is limited by an ulcerative surface of an exceedingly irregular shape, which rapidly enlarges by the necrosis of the most projecting remains of tissue, and extends deeply into the parenchyma by continued suppuration. If diphtheritis of the urinary passages was previously present, this, without exception, extends itself upon the exposed renal parenchyma. The diphtheritic sloughs are cast off, to be replaced by new ones. The renal parenchyma is destroyed, except a small layer lying next to the capsule.

The rupture of the pus through the capsule of the kidney is much rarer than the rupture towards the hilus. This leads to the formation of inflammatory depots and excavating abscesses in the loose retroperitoneal connective tissue, which may be evacuated externally at various points, for example, under Poupart's ligament.

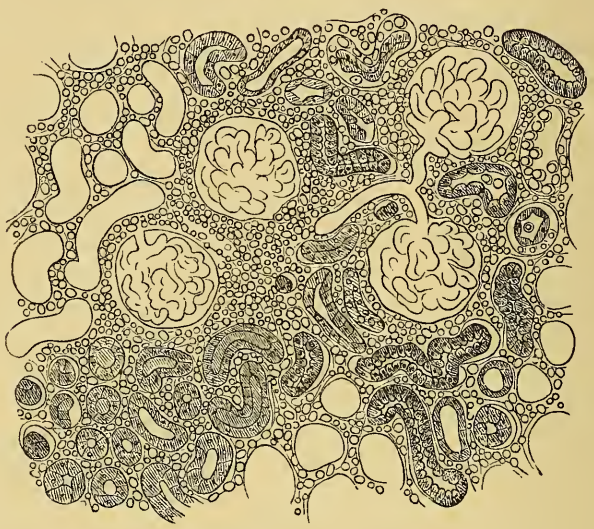
§ 558. β. Embolic renal abscesses. We need make but few alterations in the picture of the pyelitic suppuration delineated in § 556, to obtain that of the embolic. These changes especially concern the first stages of the disturbance, in which, upon the part of embolic abscesses, as in the analogous conditions of the lung, the hemorrhagic element becomes more prominent. The occlusion seldom affects a main branch of the renal artery; they are mostly the arteriolæ ascendentes, or even the vasa afferentia, in which we find the emboli. The size of the depot is naturally determined by the calibre of the occluded vessel. The disturbance begins with an excessive hyperæmia, which increases up to an extravasation of blood into the urinary tubuli. This latter occurs, par excellence, at the central point of the depot; hence the recent depot appears with a deep red centre and faded edges, like a flea-bite upon the skin (Virchow). Afterward the centre becomes yellowish-white; suppuration begins and soon leads to the formation of an abscess, which may no longer be distinguished from the pyelitic

forms. Here, also, we often find a perfect host of abscesses united in one Malpighian pyramid, while the others have remained free. This is explained by the assumption that a larger embolus was broken up at the various points of division of the vessels which it had to pass, whereupon its collective fragments were conveyed into the smaller ramifications of the lobe concerned. But, upon the other hand, what also macroscopically distinguishes the kidney affected by embolism from the pyelitic is, next to the want of a catarrhal diphtheritic disease of the renal calyces, the pre-eminent participation of the cortical substance. There the medullary substance, here the cortical, contains the most of the abscesses.

§ 559. 2. *Diffuse non-purulent form.* 1st stage. The kidney is considerably enlarged; the capsule separates readily; it is often thickened and juicy, so that its participation in the inflammatory processes becomes evident. The consistence of the organ is doughy soft, the color of the surface whitish-pale, excepting some venous stars; if we make the principal section, the peculiar contrast which the cortical substance forms with the medullary immediately strikes the eye. The changes mentioned, of volume, consistence, and color, refer exclusively to the cortical substance; this is throughout its entire thickness whitish-yellow, void of blood, excepting the Malpighian corpuscles, which present themselves as red dots, and swell out, cushion-like, at the cut surface, while under some circumstances the medullary cones are very hyperæmic, but otherwise not further changed. The macroscopic part of the changes, as we see, agrees in a high degree with parenchymatous nephritis. (§ 554.) The volume, it is true, is never so considerable as there, the consistence never so soft and withered, the color never so yellow, but goes more into a milk-white, nevertheless it requires some practice to pass judgment upon such variable criteria. The microscopic investigation can probably never be dispensed with here. It tells us that the affection in question is essentially conditioned by a cellular hyperplasia of the connective tissue in the region of the convoluted urinary tubuli and the Malpighian corpuscles. (§ 546, Fig. 159.) This hyperplasia can generally be designated as diffuse, because in fact no larger section of the renal cortex is entirely spared by it; this, however, does not prevent, that *within a microscopic section* considerable irregularities are exhibited in the accumulation of the young connective tissue, that we here find places where the accumulation has thickened a connective tissue septum to double and three times its normal dimensions, and places close by that are yet normal. (Fig. 159.) For the unaided eye these differences entirely disappear; the numberless young cells here, as wherever they are accumulated in greater amount, cause a whitish tint, which comes out so much the purer, the less blood there is in the vessels. The anæmia of the cortex is produced in quite the same way as in parenchymatous nephritis; what is found post mortem here as there

is not absolute, but only as an indication measuring what the condition may be during life; this kidney also may be injected completely and without difficulty from the artery. I will only bring forward one circumstance, because it has found a direct diagnostic valuation by Traube; namely, the circumstance that here the Malpighian corpuscles exist under external conditions to some extent different from those of the

Fig. 159.



Cellular hyperplasia of interstitial connective tissue. 1–300.

remaining bloodvessels. They lie in the lumen of the urinary tubuli; and although they have apparently experienced a very complete constriction (shrivelling of the kidney), yet they are probably primarily protected from extreme pressure by their intracanalicular position, and hence remain much longer in the hyperæmic condition than in parenchymatous nephritis. Their congestion may even lead to extravasations of blood, and as the track into the larger urinary passages is in this case barred by no swelling of the epithelia of the urinary tubuli, the extravasated blood appears in the urine, and can thus find its diagnostic valuation.

§ 560. Second stage. *Shrivelling of the kidney.* The volume of the kidney is diminished to one-half, nay, below one-half, of the normal; this becomes yet more striking, when the organ is divided by the customary main section, and by this the simultaneous enlargement of the space at the hilus comes into view, which is conditioned by a retraction of the papillæ and the columns of Bertini. If with Henle we imagine the kidney as a disproportionately thick-walled pocket, then its inner and outer surfaces have approximated, which is of course only possible by

a retractive process in the substance of the pocket itself. The capsule may only be stripped off with difficulty in spots; it is whitish, compact, and provided with tolerably wide vessels, which anastomose with those of the layer of fat. The surface exhibits an irregularly tuberous appearance. The half-globular prominences vary in size from 0.1 to 0.5 centimetre in diameter; they are colored yellowish-gray, while the parts retracted have a pure gray or reddish appearance. The leather-like hardness of the whole organ is very striking. Here and there we meet with cysts up to the size of a cherry, with clear yellowish or purulent gray contents. Upon a section we see that principally the cortical substance has lost its thickness. It may go so far, that this only yet forms a covering of a line in thickness over the medullary cones.

§ 561. In the adjoined illustration (Fig. 160), which exhibits to us, under a low power, a segment of the principal section, embracing perhaps three lobuli, the length of the arteriola ascendens (*a*) corresponds at the same time to the thickness of the cortical substance. The vessel is decidedly tortuous, also dilated, and gives off some likewise very tortuous vasa afferentia to the few Malpighian corpuscles yet pervious, while the greater part of the blood (here the injection) has found an outlet in the renal

Fig. 160.

Shrivelling of the kidney. From the section of a shrivelled kidney, embracing about three lobuli from the apices to the bases. *a.* Arteriola ascendens. *b.* Renal capsule penetrated by lymph-spaces. *c.* Boundary of medulla and cortex. *d.* Glomeruli, shrivelled, imbedded in connective tissue, which has also crowded out the other structural constituents of the cortex, except a few urinary tubuli. *e.* Portions of convoluted urinary tubuli within the medullary substance, produced by ectasy of the efferent urinary tubuli. *f.* Gelatinous cysts of the papillæ.

capsule. The latter is considerably thickened and entirely permeated by blood and lymph spaces, which give it a net-like, perforated appearance. (Fig. 160, *b*.) The cortex in its principal mass consists of connective tissue, represented in the drawing by shaded lines. In this connective tissue we observe, 1, the stunted remains of a number of Malpighian corpuscles, which present themselves as larger and smaller concentrically stratified connective tissue globules (*d*), (§ 546); 2, here and there a coil of very much dilated, convoluted urinary tubuli, which have been spared in the general destruction.

At *c* is the boundary towards the medullary substance, which consequently takes up five-sixths of the entire thickness of the organ. The medullary substance, also, is by no means normal. In the first place, the dilatation of the *straight urinary tubuli* and their ramifications strikes us. In the quite peculiar contortions and formation of coils in places (*e*, *e*), I cannot divest myself of the thoughts of a vicarious development. At all events, we have here before us the way in which the known, often very large, amounts of urine, in the second stage of Bright's disease, may be excreted. Of course the compensation can always only be an insufficient one; it depends essentially upon corresponding amounts of urinary constituents also being evacuated with an enormous amount of transuding water of the blood, whereby the simultaneous loss of albumen only weighs not quite so heavy as the benefit which the removal of the urea, &c., affords to the blood. But also for this dearly bought vicarious compensation, ways must be prepared, by which the transudation may arrive externally, and these ways are the tortuous and dilated straight urinary tubuli.

The loop-formed urinary tubuli either exhibit no change, or the cystoid degeneration of the curves, more minutely described in § 540, which is introduced by the colloid metamorphosis of fibrinous cylinders, remain behind. In our illustration (*f*) we see how numerous cysts of this kind, partly arranged as strings of pearls, pervade the immediate neighborhood of the papillæ.

d. *Combination of Parenchymatous and Interstitial Inflammation.*

§ 562. Because of the great conformity of the macroscopic peculiarities which a kidney in the first stage of a pure interstitial nephritis presents with one parenchymatously inflamed, both have been often enough thrown together and accepted as a continuous morbid process, which begins with the parenchymatous swelling, and ends with the shrivelling. It is also by no means my intention to dispute the possibility, nay, the frequency, of a combination of this kind. I only wish to announce that it is a combination of two conditions, which may also occur completely separate. As an anatomical picture belonging to this place, I mention the so-called *spotted kidney*, which arises by

the combination of a medium degree of shrivelling of the kidney and a fatty degeneration of the epithelia of the urinary tubuli.

The kidney is nearly of normal size, rather somewhat under, tolerably hard and inelastic to the touch. The capsule strips off with slight loss of substance. The surface is covered with numberless tuberosities, which are on an average of a millimetre in height, convex externally, not always arranged circularly, but in all kinds of elegant scrolls. An intensely yellow color characterizes them, and distinguishes them very strikingly from the reddish-gray intermediate parts. As the principal section shows, this peculiarly glaring alternation of yellow and reddish-gray is continued throughout the entire cortex. If we place some of the yellow substance under the microscope, we are soon convinced that they are urinary tubuli filled with fat, while the reddish-gray intermediate mass consists of tolerably vascular connective tissue, as also of obliterated urinary tubuli and Malpighian coils.

e. *Combination of Renal Amyloid and Interstitial Nephritis.*

§ 563. An extraordinarily frequent combination, which may be so comprehended, that the amyloid infiltration precedes and progresses perhaps to the degeneration of the Malpighian coils, when the interstitial nephritis is associated. The mechanical obstacle to the circulation in the Malpighian coils causes a gradually increasing collateral hyperæmia of the cortical substance, and thus prepares the soil for the cellular hyperplasia, which enters upon the scene either without further change, or is called forth by some other inflammatory irritation.

The anatomical picture distinguishes itself from that of the simple interstitial nephritis of the first stage, by the treatment with iodine calling forth in the whitish-yellow swollen cortical substance, the Malpighian coils, the known red color, while beside the renal shrivelling we can commonly also distinguish an amyloid infiltration of the papillæ of the kidney. (§ 539.)

f. *Completed Amyloid Infiltration.*

§ 564. This very rarely occurs. I have myself seen it but once; the preparation exists in the Physiological Institute of Breslau. The kidney is enlarged to almost double the normal volume, very pale throughout, waxy, and what appeared to me particularly characteristic, the bases of the Malpighian pyramids were marked out so sharply from each other by deeper furrows between them, such as we otherwise only find in the fœtal kidney. Treatment with iodine proved the amyloid infiltration of all homogeneous membranes, as well of the capillary membranes as of the tunicæ propriæ of the urinary tubuli.

3. Tumors.

§ 565. a. *Cysts.* No organ of the body is so rich in occasional cystic formations as the kidney. It not at all infrequently occurs here, that upon making sections, we are surprised by unexpectedly finding *individual* cysts, which are characterized by perfectly clear, slightly yellow, or even quite colorless contents, and very delicate walls. It is just concerning the origin and nature of these exceedingly simple vesicles we are the least informed. As the renal substance is perfectly normal in other respects, and at the most exhibits the consequences of the mechanical pressure which the cysts exert upon their surroundings, in certain globular impressions upon their immediate neighborhood, we must give up the idea of getting an explanation from this side. Microscopic investigation of the walls shows a thin stratum of fibrous connective tissue, which is covered by a beautiful polygonal pavement epithelium. Chemical investigation of the contents yields *no* urinary constituents; on the other hand, albumen and variable amounts of leucin and tyrosin. All other forms of cysts may be traced back to the urinary tubuli as the starting-point. They are, with the exception of the cystoid degeneration of the fœtal kidney, associate phenomena of inflammatory conditions, and as such were already formerly treated of. (§ 540 *et seq.*)

§ 566. b. *Cavernous tumor.* Analogous to the cavernous tumors of the liver, there also occur at the kidney, tumors from the size of a cherry-stone to a walnut, but unimportant in a medical connection, which are composed of erectile tissue. The seat is principally the outer surface, close under the capsule.

§ 567. c. *Fibroma.* In the interior of a quite normal kidney, we find single lustrous white, very compact and dense connective tissue nodules, of the size of a pea and under. They almost always have their seat in the neighborhood of the larger vascular trunks, at the peripheral parts of the medullary substance. Virchow ascribes their origin to a circumscribed interstitial nephritis, as the urinary tubuli may be traced into the tumor.

§ 568. d. *Leukæmic tumors. Lymphoma.* In peculiarly highly developed cases of leukæmia, beside similar changes of other organs, we also meet in the kidneys, medullary white tumors, which consist of colorless blood-corpuscles imbedded in a most delicate reticulum. These are either globular, and then vary in size from a small dot up to a small cherry; or, in their outer form they are allied to the structure of the kidney, in so far as they more uniformly fill out the interstices of the lobuli, and therefore like these form depots more long-drawn out, also probably wedge-shaped. The view expressed above (§ 524), that we were here dealing with actual extravasations, is particularly confirmed by this, that at the centre of the small tumors we very commonly also

met with red blood-corpuscles, *en masse* (an observation of Virchow, which I confirm).

§ 569. e. *Tuberculosis.* Disseminated form. Miliary, gray, translucent nodules are uniformly but sparsely distributed through the parenchyma of the kidney. They develop in the sheaths of the small arterial vessels, probably also elsewhere in the connective tissue, and only have any significance as a partial phenomenon of a miliary tuberculosis extending throughout the body.

Localized form. *Phthisis renalis.* To the morbid picture of "tuberculosis of the urino-genital apparatus," belongs also an affection of the kidneys, which is allied, as well in its more minute productions, as also in its coarser effects, to the diseases of the mucous membranes already spoken of (§ 383). The irruption of tubercle begins at the renal papillæ, to which it passes from the mucous membrane of the renal calyces. The densely placed groups of gray nodules at first form a continuous infiltrate, then undergo the cheesy metamorphosis, and this often takes place simultaneously for a greater distance, so that we may distinguish zones of cheesy material of a line's breadth. With the softening and casting out of the cheesy masses, a corresponding quantity of renal substance is softened and cast out with it. There arises a genuine tuberculous ulcer of putrid character, which advances its base ever deeper into the organ, first consuming the medullary substance, then the cortex. In cases of very high degree of phthisis renalis the kidney forms a thick membranous sac, with half-spherical projections, which each corresponds to a Malpighian pyramid. A connected ulcer, which occupies the interior of the sac, extends to the surface of the renal pelvis and the ureters, while the projecting ridges which divide the individual renal calyces from each other, are partly destroyed, partly crowded back into the wall of the sac. Of the renal parenchyma, there only yet remains a scanty portion of the cortical substance close under the capsule, or there is nothing at all left; the ulcerating surface lies in the very much thickened capsule itself, which is pervaded by tubercles.

§ 570. f. *Carcinoma.* Cancer exhibits itself at the kidney in all forms, primary and metastatic. The most important are the primary soft carcinomas. They are not frequent, but in part their seat, in part their size, may and must produce the most considerable destruction. Cancerous kidneys may become one foot long, and one-half foot broad. In very uniform and diffuse depositions of the carcinomatous mass, the form of the kidney, at least in approximate outlines, is preserved; in other cases we distinguish single colossal masses, each of which substitutes a Malpighian pyramid, besides smaller ones, which only correspond to groups of lobuli. That the question, however, is about a substitution, and not about a dispossession, is especially proven by the circumstance, that within a carcinomatous mass, we may yet recog-

nize which part of it was formerly medullary substance, and which cortex. For the histology of the production, this marked substitutive character of renal cancer is in so far of interest as it supports the view recently maintained by Waldeyer, according to which the epithelioid elements are said to spring directly from the epithelial cells of the kidney. Waldeyer isolated fragments of a net of cancer-cells, which were beset with sprout-like outgrowths, and which he regarded as thickened cylinders of the epithelia of the urinary tubuli, enlarged by independent growth. Until recently we also held to the production of the tumors of renal cancer from the connective tissue, and explained the retention of the principal forms of the organ by the uniform distribution of the degenerating substance, the connective tissue. (See § 69, A, I.)

§ 571. Renal cancers, like cancers of the liver and testicle, are characterized by their abundance of wide, thin-walled vessels. These vessels are occasionally ruptured; the blood extravasates into larger and smaller lakes; a part of the tumor is entirely pervaded by it. Hence it comes, that just for renal cancers the term "fungus hæmatodes" is so often used. Furthermore, it is worthy of notice that the soft renal cancers have a peculiar tendency to grow into the efferent tubuli, the veins and the renal calyces, a tendency which, under the circumstances, makes itself perceptible by very important clinical signs; thus, if the tumor advances into the renal vein, it finally reaches the vena cava inferior. It then projects into the lumen of the latter by an excrescence, which is easily crushed and conveyed onwards by the blood flowing by. Embolic processes in the lung are the inevitable consequences of this catastrophe. Upon the other hand, if the carcinoma projects into the larger urinary passages, evacuations of blood with the urine are wont to occur tolerably constant, which considerably accelerate the cachexy and death.

IX. ANOMALIES OF THE OVARIES.

1. Inflammation.

§ 572. The physiological activity of the mature ovary is connected with phenomena, which, in other organs, we would not hesitate to place in the category of "inflammatory." The functional hyperæmias, which we observe in the intestinal mucous membrane, the liver, the kidneys, &c., cannot commence to be measured in intensity with the congestion of excitement (Wallungsblutfülle), which the ovaries present during ovulation. The bursting of the follicle, without which the ovum cannot be evacuated, is a spontaneous wounding, the exudation of blood is not wanting, and only by a lengthy process of reparation, which is the physiological pattern of the healing of a wound by granulation, can the solution of continuity be restored. The concomitant processes of menstruation also bear upon themselves the character of a forcible disturbance of the vegetative equilibrium. From all this, however, it follows that it is just as materially difficult for the physician as for the anatomist to determine the limits between the physiological and the pathological, especially inflammatory, changes of the ovary. The relationship of both is just as well expressed clinically in this, that the processes in the discharge of an ovum simply assume an inflammatory character by quantitative excess, as that the actual inflammations appear as "pseudo-menstrual" conditions. In an anatomical relation we must beware of misinterpreting perchance hyperæmic-hemorrhagic phenomena at "individual follicles," perchance thickenings of the albuginea, as also cicatricial retractions of the surface; we must beware of hastily pronouncing an atrophy or hypertrophy, because these things occur up to a certain degree in the plane of evolution and involution of the organ, in conformity to nature.

§ 573. The *suppurative* ovarites, as they especially occur in connection with the puerperal state, are of undoubted inflammatory nature. Meanwhile they have but little histological interest. A strong serofibrinous saturation of the organ leads to often a very considerable tumefaction; upon a section, the stroma appears brawny, œdematous. We observe upon it either streaks of pus, which tend from the hilus, following the course of the vessels towards the periphery, or it has

already here and there come to an accumulation of pus in depots, that is, to the formation of abscesses, which threaten, especially when superficially situated, to perforate into the cavity of the belly. In most cases, moreover, a purulent peritonitis is already present, and has invested the inflamed ovary in a purulent fibrinous mass of exudation. Touching the follicles, these are occasionally marked by a strong hyperæmia and tumefaction, so that it gives the impression that the inflammation had quite specially concentrated itself upon the secretory substance. Under these circumstances, the contents of the follicles are clouded by the admixture of cast-off cells of the membrana granulosa, so that upon the whole the designation of catarrhal inflammation may properly be chosen just for these cases. At all events for judging histologically of all these phenomena, the general points of view on purulent inflammation and that tending to abscess, catarrh, &c., suffice; only we must bestow an especial consideration to the *consequences* which a happily terminated ovaritis must have for the ovary that had been diseased.

An inflammatory new formation, if it pass ever so rapidly over a part, constantly leaves behind a greater vulnerability, which is expressed in a tendency partly to relapses, partly to more hyperplastic processes. The old connective tissue stroma of the organ is in places actually replaced by a young germinal tissue, rich in cells; with the greater abundance of cells there is in itself a greater irritability of the organ given, if we add to this that the ovary is exposed to periodically recurring severe congestions of blood; if we reflect that its physiological changes are, so to say, synonymous with inflammatory conditions, we will find it comprehensible that just at the ovary upon inflammations of an acute course, follow all kinds of hyperplastic processes, which, generally proceeding from the connective tissue constituents, affect individually now more the stroma, now more the capsules of the follicles.

§ 574. The hyperplasia of the stroma of the ovary may appear in the shape of a uniform intumescence, increasing to the size of a man's fist; cases of this sort have also truly been described as hyperplasia of the ovary; a more retractive process diminishing the volume of the organ in all directions is more common, and may be placed parallel to cirrhosis of the liver and granular atrophy. A greater compactness, lustrous white color, and a more or less lobulated surface, here and there beset, probably, also with small, polypous excrescences, prove the simultaneous (often predominating) participation of the cortical layer. According to Virchow, the thickening of the albuginea at the points where the surface is cicatricially contracted, in consequence of a previous ovulation, passes over to the collapsed theca of the bursted follicle. Still, as I have already mentioned above, in judging of this condition the limits between the "normal" and the "inflammatory" are difficult to draw. That the corpora lutea may become the central

and starting point of fibroid tumors, was first seen by Rokitansky, and since frequently confirmed.

§ 575. Hyperplastic conditions in the connective tissue parts, especially in the capsules of the *unbursted* follicle, have, indeed, been frequently enough observed and described, but not referred to the preceding ovarites. Nevertheless, in the often quite obvious concentration of acute ovaritis upon this capsule, it would not be far-fetched to keep in view the possibility of a causal connection of this sort. Herein the circumstance, that thickening of the capsule has been observed par excellence in such follicles, which at the same time have assumed the character of cysts by an abnormal collection of fluid in their cavities, should rather encourage than deter us; for the inflammatory thickened capsule, undoubtedly, opposes a greater resistance than the normal to the forces which otherwise produce the bursting of the follicle. The non-bursting of the follicle is explicable in this way; subsequently the amount of fluid contained in the follicle may continually increase; the increasing pressure in the interior, far from bursting the follicle, rather produces a further reactive thickening of the capsule, so that the disturbance enters upon a circulus vitiosus, whose future effects we most probably may expect to be the ovarian cystoid of form 1 (§ 579).

2. Cysts.

§ 576. Next to the kidney, the ovary is most frequently visited by cystic formations of the most various kind. There we have very large and very small, simple, and composite cysts; cysts with watery, colloid, with fatty, bloody, or mixed contents. The impartial judge, in the presence of this abundance of cysts, will be disposed from the beginning to bring this into connection with the circumstance that the ovary contains the cystic foundations quasi preformed in its follicles. In fact, an exact investigation also proves that at least the majority of all ovarian cysts proceeds from Graafian follicles; while, upon the other hand, until further information, a different mode of origin must be accepted for a group of cysts, although not so large, yet at the least just as important. In the preceding paragraph I have attempted to show in what manner a hyperplasia of the follicular wall, excited by inflammation, may give the first impulse to the cystic formation, that is, must give. Nevertheless, I do not ignore that it therein entirely depends upon an unequal proportion between the forces that should burst the follicle and the resistance of the capsule. The follicle will then also remain unbursted and degenerate into a cyst, when those bursting forces are insufficient, and this case appears to obtain in the hydrops folliculorum, immediately to be spoken of. What, then, bursts the theca of the follicle? Perhaps the transudation from the bloodvessels? Impossible, at least in the sense, that by a transfer of the blood-

pressure upon the follicular contents, a direct increase of pressure took place in them. Ideas of this sort are not compatible with the laws of osmosis. Probably we may, however, think that at the time of menstruation, from the cells of the membrana granulosa of the mature follicle, a chemical body capable of swelling up (colloid ?) is produced, which binds the abundantly present water of transudation in large amount, swells up, and upon this bursts the capsule, as, perhaps, swelling peas are able to burst a skull. It would then probably be imaginable that in certain individuals sufficient amounts of this body would not be formed, consequently the active forces, which should burst the follicle, proved too weak.

So much concerning the still very questionable origin of ovarian cysts from Graafian follicles. Let us now pass to the individual cystic forms.

§ 577. a. *Hydrops folliculorum.* Watery contents, in a chemical relation most closely allied to the serum of the blood, is the most prominent peculiarity of a certain species of ovarian cysts, which are undoubtedly found most frequently, but indeed accidentally, because they do not give occasion to any considerable disturbances and medical interference. Already, in newly-born children, we find not infrequently small examples of these smooth and thin-walled vesicles, poor in bloodvessels; in adults we occasionally have one or several. An ovary so diseased may attain the size of a child's head; it mostly remains below the size of a man's fist. That there is here a dropsy of the Graafian follicles, has been most convincingly proved by Rokitansky, who in a case could still demonstrate the ovum in all cysts not exceeding the size of a bean.

§ 578. b. *Ovarian cystoid.* Under "ovarian cystoid" (cystoma ovarii), we understand tumors entirely composed of cysts, or also consisting of but one cyst, which substitute an ovary, consequently have arisen by a degeneration, cystic at least in its termination. As these tumors are wont, in reference to circumference and weight, far to exceed the ordinary measure of pathological new formations, and to make medical interference of the most dangerous kind necessary, they are correctly accounted among the most important diseases of the ovary. To the anatomist, also, the study of this group of tumors presents a series of interesting phenomena; to him it appears to be especially reserved to establish a conformable classification of ovarian cystoids upon a histological basis. We formerly took much account, whether an ovarian cystoid consisted of one or more cysts, whether it were uni- or multilocular; yet it has been proven that a fundamental significance cannot be attributed to this distinction, very important as it is for practice. For, conformably to proof, the simple cysts are not simple from the beginning, but have arisen only by the continued fusion of adjacent cysts. All cystoids are multilocular at the commence-

ment. Hence we will only allow this principle of subdivision a subordinate place, since we admit that the process of unilocularization mentioned, certainly occurs with special frequency in that form of ovarian cystoid which depends upon a colloid degeneration of the Graafian follicles. (Form 1.)

The macroscopic relations of ovarian cystoids are, in the first place, dependent upon the number and size of the contained cysts. A simple cyst conditions the globular shape; two or more cysts condition a more elongated form, and a surface beset with half-spherical tuberosities. Through the walls of the cysts the contained fluid shines with a yellow, or various shades of brown, color; if we cut or stick it, the originally tense cystic walls fall together, and, indeed, in consequence of communications between the cysts having already taken place often in a more extensive measure than we had expected. The cystic contents obviously are more a subject for chemical than anatomical investigation. The most prominent chemical constituent is the albuminate, still so enigmatical, which has been termed colloid, par excellence (see § 44), and which occurs here in various modifications. The beautiful investigations of Eichwald have proven that in ovarian cystoids in general, two series of chemical transformations go on side by side; since, upon the one hand, the colloids formed by the metamorphoses of tissue are gradually converted into mucus-peptone, upon the other the albuminates transuding from the blood are converted into albuminous peptone. The persistent action, therefore, of the bodily temperature suffices to bring about a kind of slow digestion of those, so to say, raw materials. The larger and older the cysts are, so much the more, therefore, we may expect to meet with the mentioned soluble modifications of albumen; consequently, also, a greater fluidity of the contents. The solid parts, often suspended in the cystic contents in considerable amount, as free cells and nuclei, crystals of cholesterin, fat-globules or detritus, blood-corpuscles, pigments, are collectively, secretory products of the cystic walls, and may in all cases be explained partly by the desquamation and fatty metamorphosis of the epithelial structures, partly by hemorrhages which had taken place.

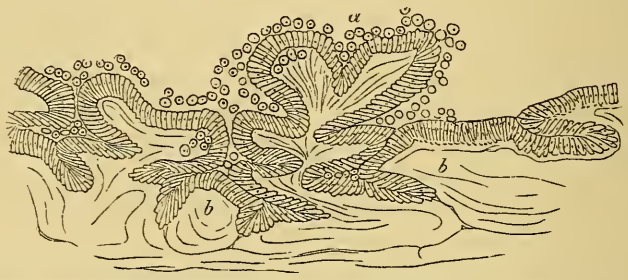
We must leave all further peculiarities of ovarian cystoids to the special consideration of the individual forms, of which we up to the present can distinguish three. (Compare Mayweg's Preisschrift on the Developmental History of Ovarian Cystoids, Bonn, 1868; Waldeyer, Ovarian Cystoma.)

§ 579. 1st form. Multilocular tumors up to the size of a man's head, or unilocular cysts up to two feet in diameter, with smooth, but little-adhering surface, and comparatively thick, fibrinous walls, which are very commonly covered at their inner side with cauliflower-like, or more tuberous papillary excrescences. The contents of the smaller cysts is a very concentrated colloid of yellow amber color; the con-

tents of the larger cysts are more thinly fluid, and supplied with many kinds of fatty and cellular secretory products of the walls (see above). The latter are, without exception, to be placed to account of a simple, non-stratified, cylindrical epithelium, which lines the walls and all its protuberances.

If, for the purpose of microscopic analysis, we make a vertical section through the entire thickness of the cystic wall, we immediately recognize that the latter consists almost throughout of a well-developed connective tissue, stratified in lamellæ. The thickness of the lamellæ amounts on an average to 0.003 mm. Only the innermost subepithelial layer makes an exception to this, at least in all cysts not above the size of a fist. It is formed of germinal tissue, and beset towards the cystic lumen at many points with papillary vegetations of the most various size (Fig. 161). The already mentioned stratum of cylindrical

Fig. 161.



Cross-section through the innermost layer of an ovarian cyst as large as a fist, which was produced by colloid degeneration of Graafian follicles. *a.* Papillary excrescence slightly flattened, clad with cylindrical epithelium. *b.* Stratum of subepithelial connective tissue also split up by papillæ and pervaded by interpapillary clefts lined with epithelia, which are not unlike glandular tubules. 1–200.

epithelial cells is not alone continued upon the surface of the papillæ, but is wont to be here even peculiarly luxuriant. Further, however, there would be but little of special interest to be said of these papillæ if, in their development of form the circumstance did not obtain, that this proceeds in an inclosed, limited space, consequently analogous relations exist to those we learned to know above (§ 70) for the papilloma cysticum. It is manifest that papillæ, which proceed from the inner surface of a spherical cavity, must converge, and hence come into contact upon further growth. This contact will take place so much the sooner the more the papilla has the tendency to ramify, to spread out tree-like. Both exist here, and the consequence of this is that the papillæ grow into each other at their apices and lateral surfaces at an early period and in the most various manner. Hence the larger pediculated tumors up to the size of a fist, which we occasionally meet with in the cysts, have not at all infrequently a smooth, scarcely lobulated surface; while yet, if we investigate it by sections, we can have no doubt that we have before us in fact genuine papillomas. But already

the smaller papillæ, scarcely projecting from the walls, also often fuse together by their ends; hence upon them also we find a phenomenon, which we have learned to know (§ 70) as a frequent consequence of this kind of fusions—I mean the formation of cysts of retention. In my opinion the epithelial-clad gaps which we find in the neighborhood, and partly also somewhat further from the inner surface of these cysts, and which have been already described by Rokitansky, recently especially by Fox, as foundations of the so-called daughter-cysts, are to be understood as former interpapillary spaces. The elevation and thickening of the surface continually advancing towards the interior has, so to say, overtaken these interpapillary spaces ere a complete obliteration could take place; but the small remainder of free epithelial-bearing surface suffices to maintain an independent secretion, and accordingly, to occasion the cystic formation. This is, then, also in fact the only way and manner how, in this first form of ovarian colloid, new cysts arise beside those existing; and if we take into account the very limited occurrence of this kind of daughter-cysts, we will attribute to the whole appearance a more accidental signification, nay, we may emphasize concerning these, that the first form of ovarian cystoids in contrast to the second, is characterized by a certain limitation of the number of cysts, and by the abeyance of all such phenomena as are derived from an increase of this number. The ground for this is no other than that, in the first form of ovarian colloid, a certain given number of Graafian follicles forms the starting-point of the disturbance.

§ 580. The best proof for the correctness of this assumption would undoubtedly be furnished by finding the ovula in the smaller and at the same time primary cysts; we have, however, hitherto succeeded but once in discovering the ovulum in a cyst of perhaps the size of a cherry. In the post-mortem examination of a woman who had died after the operation for the removal of the right cystoid degenerated ovary, I found the left ovary in the early stage of the same disturbance; from this latter the cyst in question was taken. The source of indirect proof is at all events much more abundant. In the first place there is to be alleged that in the form in question we can never demonstrate such small cystic beginnings; that the usual size of the Graafian follicles would thereby be, so to say, underbid. Furthermore, the circumstance that even the smallest cysts are provided with a complete epithelial lining, which, according to the form and stratification of the cells, has the full dignity of an outer surface or glandular epithelium (in contrast to the endothelia), and like this undergoes a periodical renewal. Finally, the far-going analogy with the cysto-sarcomas of certain open-mouthed glands, particularly with the cysto-sarcoma of the testis and mamma. The intra-canalicular papilloma formation, which, for example, characterizes the cysto-sarcoma mammæ phyllodes, again recurs here, with the single difference that in the ovary, because of the closure of the

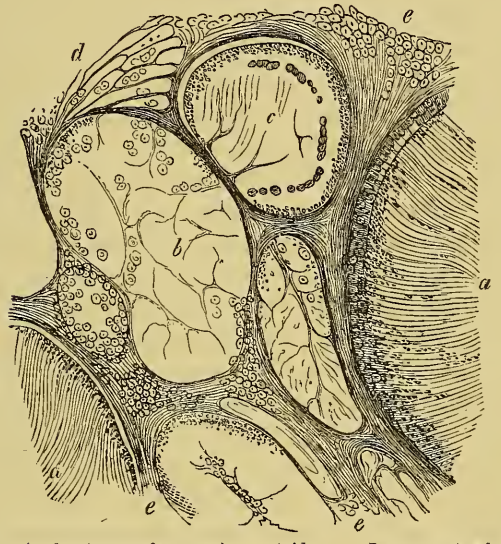
Graafian follicles, the cystic formation comes more into the foreground than in the mammary gland. What, therefore, can be more obvious than that in the ovary also we regard the preformed glandular substance, therefore the follicles, as the seat and point of departure of the disturbance? We will say, in passing, that the more frequent occurrence of unilocular cystoids in this first category finds its explanation just in this, that because of the limited number of follicles, there are from the very beginning a *limited*, although often a tolerably considerable number of cysts, which, when they have attained a certain circumference, flow together by the atrophy of their partition walls, and repeat this confluence until the existing stock of cysts is exhausted; then, however, because of the want of the subsequent formation of cysts form but one, certainly often quite colossal sac.

§ 581. It only yet remains to start the question as to the origin of the colloid substance. Whence comes this material? Is it an excretory product of the epithelial cells? or is it the product of the involution of all older epithelial cells, and do these, with their protoplasms having become colloid, fill up the cavities of the follicles? I decidedly incline to the views of those who regard the colloid as a secretion of the glandular cells similar to mucus. I even believe that the cells of the membrana granulosa, at the time of bursting of the follicle, normally secrete a certain amount of this body, because without the presence of a substance capable of swelling up strongly, the bursting of the follicle would not be well conceivable. Above all, however, sufficiently frequent observations of colloid degenerated cells (Fig. 12) are wanting, while we meet with cast off, but otherwise not degenerated epithelial cells, often in exceedingly great amounts, in the cystic contents.

§ 582. 2d form. At the place of the one ovary (the other, as a rule, is healthy, while in Form 1 the disease is often of both sides), there lies a tumor, not infrequently far above the size of a man's head, which is composed of several large and very many smaller and even the smallest cysts. The larger cysts are often constricted and exhibit, at these places, the remains of former partition walls in the form of fenestrated membranes or ramified vascular strands, which evidently succumb to a gradual maceration. The surface of the tumor is probably always connected with the peritoneum by a large number of inflammatory adhesions upon which larger venous vessels run to and fro. The walls of the cyst are comparatively thin and easily torn, within smooth, often pigmented. The smaller cysts, in their gelatinous contents, show here and there a fibrous something which is expanded in the cavity like a spider's web; the very smallest are only perceptible under the microscope. Moreover, here also, the contents of the larger cysts is more thinly fluid than the contents of the smaller, and only the frequent admixture of blood and blood-pigments has something characteristic for the second form.

§ 583. If, for the purpose of microscopic analyses, we make thin sections at the more compact parts of the tumor, we are soon convinced that uninterrupted accumulations of fibrous, well-organized connective tissue are rare, even where a white, moderately firm substance forms either the outer investment of the tumor, or a broad trabecular work in the interior. All these parts consist, indeed, of connective tissue, but the connective tissue is pervaded by the very smallest cysts which may be traced up to the first beginnings (Fig. 162). The annexed illustration represents to us the interior condition of a trabecula of the stroma

Fig. 162.



Colloid degeneration in the stroma of an ovarian cystoid. *a, a.* Larger cysts whose walls bear an incomplete epithelium of low cylindrical cells whose contents after hardening is split up radiating. *b.* Younger cysts without epithelium permeated by remains of connective tissue fibres. *c.* The same with a wreath of loose epithelia. *d.* Colloid infiltration of the connective tissue which has not yet attained any cystoid appearance and inclosure. *e.* Small-celled infiltration of the stroma. 1–200.

which divides two somewhat larger cysts, *a*, *a*. We immediately recognize that the striped connective tissue, which forms the foundation of the structure, splits up into numerous small trabeculæ, and with these encompasses and penetrates a group of small cysts. Of course we must not imagine these trabeculæ as quite round, they are rather only apparent trabeculæ; in reality, however, the cross-cuts of membranous partition walls of various thickness. Here and there (*e*, *e*) the connective tissue is abundantly infiltrated with young, round cells, a proof that it is in a condition of formative irritation. One might suppose that certain larger aggregations of these cells (*e*) represented the first stage of the cystic formation, the cystic foundation. For certain of the smallest cysts (to the left of *b*) look exactly as if only a certain amount of colloid substance had arisen between the cells of a small group of this kind and had crowded these asunder in all directions.

Such an interpretation has, in fact, been attempted by various authors. Still I would advise caution here. The knife may very well have cut the most extreme point of a larger cyst, and in this manner have produced but the delusive appearance of a very small cyst. Because of this, I will not deny the possibility of a manner of origin of this kind, still I would wish to be more explicit in the definition, and, in general, only speak of a circumscribed colloid softening of the connective tissue stroma as the starting-point of the cysts; for it appears to me, that certain swelled-out and translucent points of the stroma (*d*), which are not exactly round and sharply defined, are also to be regarded as cystic foundations. The colloid substance has here been more diffusely poured out between the fibrous constituents of the stroma; nevertheless this exudation, also, by swelling out further, must tend to the globular form, and the longer this continues, so much the more it is set off from the surroundings as a roundish space permeated by connective tissue septa. If, however, we compare this presumptive fate of the place (*d*) with the actual condition of the smallest specimen of cyst (*b*, *c*, &c.), we must concede that the former assumption gains in probability. The most of the smaller cysts are yet permeated by a system of connective tissue septa, and I can assure, what it is true we do not see in our illustration, that sometimes even capillaries run right through the cystic space. Conditions of this kind by no means agree with the hypothesis that these cysts have also proceeded from Graafian follicles. Only when the cyst has attained a circumference very considerable, in proportion to this fundamental formation, could one be reminded of follicles. Waldeyer (epithelial ovarian tumors, particularly cystoma, Archive of Gynæcology, vol. i, No. 2), has therefore given up the Graafian follicles themselves, as the first points of their development, for certain and small very irregular epithelial sprinklings which he found as well upon the fœtal ovary as in the apparently well preserved remains of a cystomatous ovary. I would gladly join in this view, if my observations, imparted above (Fig. 162, *d*), did not admonish caution; thus, in the larger cysts there is an epithelial stratum, although not always complete, and the colloid substance, without further fibrous admixture is, in hardened preparations, stratified in a manner which indicates a secretion from the wall. That the cysts, especially of a certain size, are to be regarded as secretory cysts, is undoubted also upon other grounds, else whence is this amount of albumen derived, which is present in all large cysts, if it does not transude from the vessels, consequently is secreted at the wall? But in our case, notwithstanding all this, we are not dealing with the follicles, but that transformation of original softening cysts into secretory cysts which I have discussed more circumstantially in § 70.

If finally we sum up the result of our studies it is this, that the second form of ovarian cystoids, which is characterized by the unlimited forma-

tion of new cysts, depends upon a colloid degeneration of the stroma of the ovary, whereby the possibility is to be kept in view that an epithelial proliferation, reminding of embryonal conditions, furnishes the foundations of the cysts. In this case we might correctly designate them as a carcinoma colloides cysticum.

§ 584. 3d form. Both ovaries have equally advanced in a certain form of cysto-colloid degeneration. They have passed beyond the size of a man's fist, are smooth at the surface, and through the albuginea a large number of cysts, from the size of a millet-seed to a pea, are seen, which are all arranged side by side like a mosaic. Upon a section we perceive that this mosaic of cysts extends throughout the thickness of the organ in such manner, however, that the largest specimens up to the size of a cherry, are found at the centre. The whole reminds us of a honeycomb. The contents of the cyst are throughout a clear jelly, so that in this ovarian cystoid, also, the name ovarian colloid, which is particularly customary in Forms 1 and 2, might be not unfittingly applied. Moreover, Form 3 is very rare, and hence it probably comes, that nothing certain is known of the origin of the cysts. The single example, which is at my command, has been macerated in diluted spirits in such fashion that a reliable investigation is impossible. The macroscopic impression speaks decidedly in favor of the Graafian follicles; even the smallest cysts are not smaller than these; moreover, each cyst has a proper firm membrane, and finally the already mentioned arrangement of the cysts, the smaller without, the larger within, very strikingly reminds of the same arrangement of the Graafian follicles. I would designate the degeneration as struma ovarii (according to Virchow's acceptation of struma).

§ 585. c. *Dermoid cysts of the ovary.* By dermoid cysts or dermoids we understand unilocular cystomas, whose walls repeat the textural and structural relations of the outer skin. The skin with its appendages, appears as a closed sac with the surface turned within. The most dermoid cysts which have been observed and described had perhaps the size of a fist, still they occasionally may attain a colossal volume (size of a man's head). Their growth only in part depends upon the processes of new formation, which take place in the cystic walls; to this is associated the accumulation of the secretions of the skin in the interior of the cyst. Hence, as a rule, as *cystic contents* we have a smeary pulp, similar to the vernix caseosa, which consists of cast-off epithelial scales and sebaceous matter. Beside these lie long, mostly light reddish, and very thin hairs, curled and coiled up into a ball.

The *epidermis* shows the typical separation into a horny and mucous layer; hair-follicles are scarcely to be recognized. The same of sebaceous glands.

Papillæ are conceded to the dermoid *cutis* by some authors, denied by others; at all events they do not appear to occur with the same

regularity as at the outer skin. On the other hand, an equivalent for the panniculus adiposus is never wanting, by means of which the dermoid cyst loses itself in the surrounding connective tissue.

Of the more accidental constituents, *teeth* are to be mentioned foremost, which at times present themselves at the surface of the cutis in unprecedented numbers. These teeth do not always have a shape so typical that we might declare them to be molars, incisors, or canine teeth; that they, however, are actual teeth, with fang, neck, and crown, with enamel, cement, and dentine, there is no doubt. Not infrequently we may be convinced that these teeth stick in bony alveoli. Then actual bones have formed in the cystic walls, which may be supplied with a periosteum and vessels, quite like the bones of the skeleton. Henle found in a dermoid cyst a bone 1″ long, of horseshoe shape, which had serrated processes, with which again wedge-shaped bodies of the size of a hemp-seed, supplied with loose articular capsules, articulated.

The higher organized tissues, *muscles* and *nerves*, are more rarely found in the dermoids; yet they have also been repeatedly demonstrated.

The dermoids occur by far most frequently, namely, up to three-fifths, in the ovary; in the next place in the testicle. It is possible that the attributes of the ovaries and testicles as glands of generation play an assistant rôle in the production of dermoid cysts; but it is certainly unjustifiable to regard them on that account as rudimentary fœtuses; for dermoids also occur in other organs. Cloetta described, for example, a dermoid cyst of the lung.

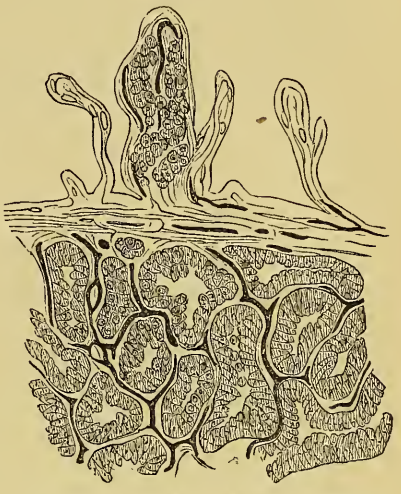
All other cysts of the ovary are only cysts secondarily, for example, by the softening of a solid tumor; yet carcinoma of the ovary may in a considerable degree delusively represent an ovarian cystoid.

3. Carcinoma.

§ 586. Other than medullary carcinomas are exceedingly rare at the ovary. The latter may, although more exact proof of this is still wanting, proceed from the follicles or the foundations of the follicles. In favor of this, the peculiarly adenoid, or let us say at least "regularly alveolar" structure of the round masses, speaks, of which the tumor is composed. Fig. 163 presents the border part of a mass of carcinoma of perhaps the size of a hen's egg. The vessels are filled with a blue material. The tumor touches the thickened albuginea, which latter is covered with a number of papillary excrescences. If, in the first place, we observe the substance of the tumor, we must admit that there is given here a tolerable approximation to the section of a tubular gland, for example, the cortex of the kidney; the trabeculæ of the cancer stroma are collectively vascular and bear the cancer-cells like a low cylindrical epithelium, so that lumina remain free in the centre of the alveoli, which

are like glandular canals. The albuginea itself is not permeated by cancer-nests, but forms a very compact partition wall between the tumor on the one hand and the papillæ upon the other. So much the more striking, and in a certain sense the more demonstrative, is it that one of these papillæ in its somewhat swollen body shows a distinct foundation of new cancer formation. More parallel to than immediately beside the vessels, elongated clefts have been filled with the same large epithelial cells, which in the completed tumor we regard as cancer-cells. It appears to me they are the lymph-vessels, which here, as in the formation of tubercle (§ 115), take the initiative of the development, since their endothelia proliferate to cancer-cells. A sprouting of the follicular epithelia, possibly present, is of course not to be thought of, because of the broad connective tissue barrier, which separates the papillæ from the ovarian tumor. Hence, if the ovarian carcinoma should belong to the glandular carcinomas, it is at least able, when it has exceeded the limits of the organ, to form tumors also in the connective tissue and its inner spaces.

Fig. 163.



Glandular carcinoma of the ovary. The thickened peritoneal covering, provided with papillæ, shows in these papillæ the commencing carcinosis. 1–300.

X. ANOMALIES OF THE TESTICLES.

1. Inflammation.

§ 587. The acute inflammations of the testicle, by which I allude principally to the gonorrhœal and traumatic forms, begin with a very active serous infiltration of the parenchyma, which is constantly associated with a moderate exudation into the sac of the tunica vaginalis propria. The great abundance of lymph-spaces in the testicle, as also their width and distensibility, may play a prominent part in this, for the phenomena are very much the same that can be artificially produced by ligating the lymph-vessels of the spermatic cord. Only certain issues of the acute inflammation are of histological interest. As is known, the complete restitution to the normal condition ensues by far most frequently, more rare are the indurative, most rare the purulent conditions. Both of the latter take their point of departure in the walls of the lymph-vessels. In the indurative inflammation, a hyperplasia of the connective tissue stratum upon the one hand narrows the lumen of the lymph-vessels, upon the other, it more and more thickens the connective tissue tunicæ propriæ of the seminal tubuli by outer apposition, and thereby injures also the lumen of the seminal tubuli and the seminal epithelia. A complete destruction of the latter, and a diminution and flattening of the whole testicle, is therefore the common result of indurative inflammation. It is otherwise in suppuration. The pus-corpuscles separate from the inner surface of the lymph-vessels, and are at once in a free space, which is filled by a continually moving and circulating fluid. Hence, if the pus formation is not intense, the cells furnished will be constantly conveyed away to the vascular system, and the whole is, perhaps, only the quantitative excess of a process, which also occurs normally, and is then called an afflux of lymph-corpuscles from the radicles of the lymph-vessels. Hence, collections of pus in the form of abscesses are rare, and even when it has come to a collection, the resorption of the pus-corpuscles is still to be expected with far greater probability than the rupture externally. If, however, the rupture has happened, the fistulous openings are small and readily close, if a certain proliferation of granulation tissue does not occur about the fistulous openings, which is frequently observed just here, and occasionally leads

to the formation of fungous, sarcoma-like growths, which have the structure of proud flesh.

§ 588. As a chronic inflammation of the testis, Förster correctly regards a condition, which has also been described on the part of others as *atheroma of the testes*. The organ is very considerably enlarged herein. The sac of the tunica vaginalis propria is obliterated by adhesions, the albuginea decidedly indurated and thickened. In the interior we commonly see a large cyst, for example, of the size of the fist, and several smaller, which are quite filled with a semi-fluid atheroma-pulp. Immense masses of crystals of cholesterin, fat-globules of all sizes, granular corpuscles, here and there some yellow pigment, are suspended therein. If we wash out these contents, the walls for the greater part present themselves covered with a layer of densely packed and very vascular granulations, between which are island-like portions impregnated with the salts of lime, slightly roughened and white, a dusting of the surface up to the complete incrustation of a continuous part of the surface, and the transformation of this into a solid plate of lime of the thickness of half a line. The vertical section through the granulation-layer is very characteristic, because this indeed, upon the whole, shows throughout the character of ordinary granulations of wounds, at the most, it is characterized by somewhat larger cellular elements; at the surface, however, no pus is secreted, but fatty granular corpuscles. We can study here very beautifully the fatty metamorphosis in all its stages upon those cells which form the outermost layer of the granulations, and, as it appears to me, arrive here by continual secretion analogous to suppuration. I have never seen an actual production of pus at the surface of the closed cyst; this only occurs where the cavity is opened by the manipulations of the physician.

The smaller cysts, as a rule, permit a sufficing insight into the history of production of this interesting new formation; thus, their lumen is pervaded by certain remains of the normal structure of the testicle, in which we easily recognize larger vascular branches, beside some connective tissue, therefore, the former lobular septa. The intervening spaces have the elongated conical form of the lobuli of the testis, and beside large amounts of fatty detritus, often contain longer fragments of the macerated tunicæ propriæ. Broad masses of very compact, whitely lustrous, poorly vascular connective tissue already invest these smaller cysts and bound them towards the probable remains of the more intact parenchyma of the testicle. The principal cysts also only consist in their innermost parts respectively of granulation-tissue and calcified plates; the principal mass of their walls, likewise, shows a tendon-like substance, which is often collected into skins of two to three lines thick, especially where it passes over continuously into the thickened albuginea.

The question here is accordingly about an orchitis and periorchitis

indurativa, which is distinguished from the ordinary induration of the testicle by its not affecting uniformly the whole testicle, but in the first place puts several principal septa into a hyperplastic condition, and thereby constricts larger sections of the parenchyma of the testicle and compels to fatty degeneration. The abundant cellular production at the surface of the septa, and the immediate conversion of the secreted cells into fatty detritus, the remains of the latter, and the atheromatous degeneration conditioned thereby (§ 29), are the causes, why the parenchymatous spots so constricted subsequently are transformed into atheroma cysts, and as such attain a frequently very considerable size.

2. Tubercle.

§ 589. By tubercle of the testis we understand a certain kind of larger caseous nodules of roundish form, of which, as a rule, several are placed near each other, afterwards run together, and then form a single nodule of very irregular, tuberous, or ramified shape. The cheesy substance is characterized by its elastic springy compactness, which it retains until a central softening leads to the formation of an abscess, which has the tendency to burst externally, and to occasion that known form of fistula of the testicle, which is symptomatically marked by the tediousness of its course, and the occasional evacuation of macerated seminal tubuli. The epididymis and vas deferens are likewise exposed to this kind of disease, nay, the latter is wont to begin by preference in the parenchyma of the epididymis.

If we ask after the origin and extension of the new formation, the opportunity is indeed very rarely presented for studying the first beginnings of the disturbance; on the other hand, very frequently and almost regularly, a histological process is found at the periphery of the nodule, which is evidently intended for enlarging it. The unaided eye perceives there a thin layer of reddish-gray, translucent, and slightly gelatinous substance, which is permeated abundantly by bloodvessels, and forms a small tumefaction towards the healthy parenchyma of the testis. In the adjoining illustration of a vertical section under a magnifying power of 300, *a* represents the relatively normal parenchyma of the testis; *b*, the proliferating layer; *c*, the cheesy nodule. As we perceive, the process has a thoroughly interstitial course. The seminal tubuli remain passive. At *a*, they are yet quite normal, the very thick connective tissue tunicæ propriæ, which play so great a rôle in cystosarcoma (§ 592), scarcely show traces of nuclear and cellular formation in their outermost layers. In the zone *b*, they are pressed asunder more and more by the new formation, without losing their characteristic form constituents; in the zone *c*, they are moved yet somewhat further apart, and here then also begins the vitreous swelling of the tunicæ, and a fatty degeneration of the epithelia; these are the only

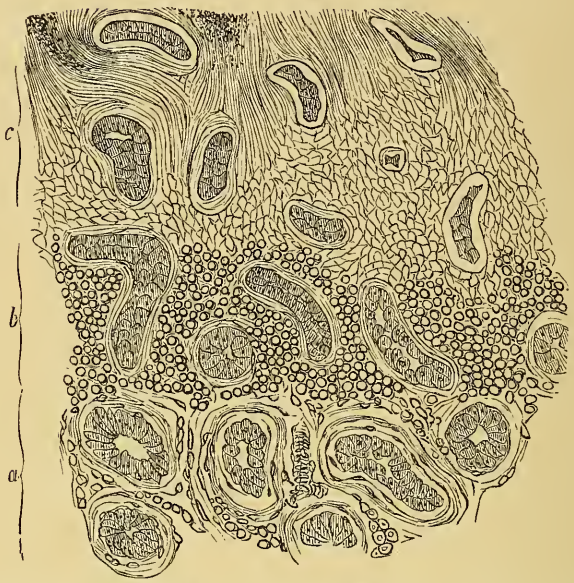
changes of the seminal tubuli, which, however, do not lead to a complete destruction; for, as already observed, the seminal tubuli are again found after the softening and bursting of the cheesy substance; we must therefore accept that they are preserved within the cheesy substance, as we here see them in the illustration.

If we now look at the essential disease, its locality is first of all worthy of notice; thus, it is exactly the region, which according to Ludwig and Tomsa's investigations is pervaded by an exceedingly well-developed system of lymph-spaces, and, if we take counsel of the more recent experiences on tubercle formation, which with so agreeable a uniformity amount to this, that this new formation, so long enigmatical, is produced by a proliferation of the endothelia of the lymph-vessels,* the presumption in fact is not far-fetched, that the question here is also about a process within the lymph-vessels, which is distinguished from the formation of miliary nodules only by its more diffuse appearance. Miliary tubercles of the ordinary constitution are certainly nowhere found here; meanwhile it is to be borne in mind, that in the first place, there are also tubercles (especially upon the peritoneum), which attain the size of a lentil, a flat bean, &c., and that in the second place, the tuberculosis is observed at other organs (especially in the brain) in the same manner as here. The last-mentioned uniformity extends especially also to the further stages of transformation of the new formation. If we follow the latter from the zone *b* towards the zone *c* (Fig. 164), we indeed for a time yet observe the limits of cells, but they become indistinct, and instead of round contours, there arise, as though produced by strong mutual flattening, elongated and many angular, finally, spindle-formed contours, which latter form the transition to a purely fibrous texture. This fibrous texture prevails everywhere in the cheesy nodule. The white color is caused by the massy deposition of dark (highly refracting) fatty granules, the compact, tough consistence, difficult to tear; probably, also, the long persistence may be placed to the account of the fibrous constitution. I was in some degree surprised, as I here for the first time (afterwards, however, in all "solitary" nodular products of tuberculosis) hit upon the fibres of Lebert; I had to confess thereafter, that tubercle need not everywhere and always directly undergo the cheesy metamorphosis, but that between the stage of early infiltration, and that of the cheesy metamorphosis, a third may yet interpose, which expresses the undoubted tendency to a higher organization. I regard the fibrous tubercle as an analogue of the cicatricial, or rather the fibroid tissue, and will return to this view, especially in speaking of the solitary tubercles of the brain.

* Compare, beside § 115 of this work, the more recent works of Langhans and Klebs. (Klebs, Contributions to the History of Tuberculosis, Virchow's Arch., 44.)

Tuberculosis in a disseminated, metastatic form, does not occur in the testis.

Fig. 164.



Section through the border of a cheesy tubercle of the testicle. *a.* Relatively normal substance of testicle. *b.* Small cellular infiltration of the intertubular connective tissue. *c.* Fibrous and cheesy metamorphosis. 1–300.

3. Syphilis.

§ 590. The syphilitic affection of the testis, like that of the liver, permits us to distinguish two principal forms, one simply inflammatory and one gummous. The former runs its course with a considerable induration, destroying the parenchyma of the testis for a great extent. The interstitial tissue forms the starting-point of the disturbance; here upon a hyperplastic production of young connective tissue follows an indurative condensation of the same, and we observe, even with the naked eye, the white fibrous lines, which in proportion to the lobular subdivisions, form conical depositions, whose bases lie at the likewise thickened albuginea, while their apices are directed towards the centrum Highmorianum, and the apices of the adjacent cones are fused together. Finally, we only see a continuous white induration, within which the seminal tubuli, and with them every trace of the old subdivision of the gland, have been destroyed. The testicle is flattened, the tunica vaginalis commonly contains a serous exudation.

The *gummous* syphilis of the testis, as a rule, already presupposes the existence of the induration described. The gummous formation is therefore only to be regarded as a further increase and specification of the process. Mostly there are several nodules of about the size of a cherry-stone, disseminated in the induration. Upon a vertical section,

which embraces the boundary of the nodules towards the induration, we can most distinctly perceive, that the specific process begins with a multiplication of the connective tissue cells, to which a fatty degeneration of the newly formed cells soon follows. The accumulations of the fatty corpuscles, however, flow together, without the continuity of the fibrous intermediate tissue being on that account interrupted, and thus it happens, that these nodules also, like the yellow tubercles, have a very compact consistence, and may therefore be easily mistaken for those.

4. Carcinoma.

§ 591. It is difficult to distinguish, by the naked eye, the soft carcinoma of the testis from soft sarcoma, the medullary cancer from medullary sarcoma. The same soft, in places dissolving consistence, the same kind of propagation from the testis to the epididymis, vas deferens, and retro-peritoneal lymph-glands, the same milk-white color characterize the tumor. In reference to the histological constitution, we are indebted to Birch-Hirschfeld for the proof, that here also, as in cancers of the kidney, the liver, and the mamma, the cancer-cells are derived from the epithelial cells of the glandular tubuli. The stroma is, indeed, richly permeated by young cells, yet the boundary between it and the epithelioid cell-aggregations appears to be clear and distinct; there may be less value to be placed upon the similarity of the cancer-cells with the normal epithelial cells of the testicle; on the other hand, Birch-Hirschfeld has succeeded, by means of fifteen per cent. hydrochloric acid, at the boundary of the new formation towards the healthy parts, to isolate seminal tubuli, which with a smooth surface showed either knotty, less apparent tumefactions, or they passed into the tumor itself with a somewhat more rapid expansion. That we have here the beginnings of the new formation, and that consequently these beginnings consist in a proliferation of the epithelia of the testis, is at least not improbable to me.

In its further growth, the cancer of the testis not infrequently assumes the character of the fungus hæmatodes. A peculiarly rich development of vessels of the stroma, which I have described at § 156, brings about this transition.

None but the soft carcinoma occurs primarily at the testicle. The observations on scirrhus of the testis do not hold good in the face of the more strict requirements of anatomical proof; pigmented cancers are said to have been seen as metastases.

The combination of carcinoma with other tumors is treated of at § 593.

5. Sarcoma and other Histioid Tumors.

§ 592. Not all that the surgeon directly calls sarcoma of the testis, is a sarcoma in the sense of pathological histology. The surgeon

wishes to designate by the term sarcoma only the contrast of a firm, in the widest sense flesh-like tumor, and a tumor with fluid contents, especially hydrocele of the tunica vaginalis. Meanwhile, in point of fact, the testicle is a favorite seat of sarcoma. Sarcoma occurs at the testicle in all its principal species, and that which peculiarly characterizes its occurrence at the testicle, is the combination, almost without exception, not only of the various principal species in one tumor, but of the collective histioid new formations in the sarcoma. The intimate relationship of all histioid tumors comes out very distinctly just in the testis. Cartilaginous, mucous, and fatty tissue, muscular fibres of both kinds, take a more or less important part in the composition of sarcoma of the testicle. The cartilaginous and muscular tissue also forms independent and primary tumors; yet it commonly is not long before, by a rapid peripheral proliferation, the transition follows into round and spindle-celled sarcoma forms.

If already, by these frequent combinations, a great variety is produced in the structure of sarcoma of the testis, this is increased to a still higher degree by the very common appearance of cysts. The cysts are more or less numerous; all the transitions may be traced from the size of a poppy-seed up to that of a pigeon's egg and over; the contents of the smallest is gelatinous, tough, afterward it becomes more thinly fluid and clouded by the admixture of blood, of crystals of cholesterin, and fat-globules. In the large cysts, a synovial-like consistence, capable of being drawn into threads, is also not infrequent, while pure, watery, serous contents are quite rare. The walls of the cysts, especially of the smaller ones, are lined constantly with a continuous cylindrical epithelium; very commonly there are papillary excrescences, which may become so abundant, that they fill up the whole cavity of the cyst (cysto-sarcoma phyllodes). If we trace the origin of these cysts, which more rarely and in individual examples are found also in carcinoma of the testis, we strike upon the seminal tubuli, which, being compressed at one place by the interstitial new formation, degenerate at a part lying immediately behind it, and which had remained free, into a cyst of retention. This is at least the most general view, which I would only wish to modify by this, that we concede also the ectasy of an entire convolution of seminal tubuli, so to say, a circumscribed portion of the parenchyma of the testis, as the starting-point of the cysts. I not infrequently found the smallest cysts, which were penetrated by single strongly macerated connective tissue septa, that I could only regard as the remains of formerly existing, more firm partition walls.

§ 593. The most frequent forms of simple and compound tumors of the histioid series are the following:

a. The soft or *medullary sarcoma* is similar to the medullary carcinoma in its outer appearance. This similarity attains the highest degree

in those "very common" cases, where we actually have a combination with carcinoma. These tumors in their mass are soft, spindle-celled sarcomas, with a broad trabecular work, but in certain small interspaces, which these broad trabeculæ of spindle-cells leave between themselves, or surround, there lie nests of genuine cancer-cells. One might be thereby reminded of seminal tubuli with their epithelium transversely divided, and according to the most recent experiences upon this point, I do not regard it as improbable that we have here the derivative of a seminal tubulus; but at all events these cells no longer resemble the ordinary seminal epithelia, but exhibit that suspicious anomaly of the contours, that multiplicity of shapes, which is peculiar to cancer only. For at other places, also, we see the actual cancer come more into the foreground, and then the whole has the appearance of a carcinoma with a sarcomatous stroma.

Where the medullary sarcoma appears quite complete, or where it is in combination with cartilaginous and mucous tissue, we rather find a round-celled parenchyma with a very perfect intercellular network, also that structure designated as "lymph gland-like," which is distinguished from the ordinary round-cell sarcoma by greater softness, and the abundance of cells easily isolated and scraped off from the cut surface, so that a mistake for soft carcinoma might very easily be made just here, without a microscopic examination.

All medullary tumors of the testis are malignant in the highest degree. If they have arisen in the testicle itself, and not in the epididymis, the albuginea forms for some time an obstacle to the growth of the tumor; but, if the albuginea has been destroyed, the new formation proliferates exceedingly rapidly along the spermatic cord into the cavity of the abdomen, attacks the retroperitoneal lymph-glands, &c., and even after a short time the tumor of the testis itself is the smaller part of the affection.

b. The *cystosarcoma testiculi* is always a complicated tumor. The most constant phenomenon is a relation of the sarcomatous new formation to the seminal tubuli, as Billroth first described it for his adenoid sarcoma of the mamma; namely, the new formation concentrates in the subepithelial connective tissue, *i. e.*, it appears as an enormous thickening and a round-celled degeneration of the tunica propria. To this is joined upon the one hand the ectasy, and upon the other, the phyllodic proliferation into the lumen (compare § 605). Förster, indeed, described here also, a bud-like outgrowth of the seminal tubuli, such as is generally peculiar only to the various species of carcinoma; meanwhile, for my own part I would rather regard the pictures referred to as plications of the enlarged wall. Plications of this sort on the cross-section naturally appear as villiform projections of the epithelium. Here and there, we observe cysts without papillæ upon the walls. In the cystic fluid swim

brownish-yellow globular concretions, which are decidedly characteristic for the mammary glands.

To these changes of the seminal tubuli themselves are associated histioid new formations between the seminal tubuli. We meet there smaller depositions, which consist entirely of hyaline cartilage; the peculiar garland-like form and the ramification here and there exhibited remind us, that these enchondroma formations, as Paget and Billroth saw, correspond to the course of the lymph-vessels and fill their lumen. Larger depots of mucous tissue, even muscular and adipose tissue have been observed in single collections. Finally, the transition into carcinoma threatening at all times, is to be taken into consideration here, as principally just at the glands and apparatus of procreation, there appear to occur, more frequently than elsewhere, transitions from simple, inflammatory irritations, from ulcers, wounds of operations, and catarrhal hyperplasias, into sarcomatous, and afterward into carcinomatous, degenerations. The longer a locality of this kind, for example, the external os uteri, is the seat of a formative irritation, so much the more does it show the tendency to ever a more luxuriant proliferation, finally, to carcinosis.

c. Enchondroma appears as a solitary tumor of the size of a walnut to a hen's egg, and of hyaline constitution. After having existed for some time, perhaps for years, as a painless, sharply circumscribed induration, a more rapid, most painful enlargement sets in, and if we examine anatomically the testicle when extirpated, we find the enchondroma tumor imbedded in a mass of sarcoma, which commonly develops with peculiar abundance towards one direction, and has established large sarcoma masses beside the old cartilaginous tumor.

d. Myoma occurs as a solitary tumor. Rokitansky has described such a one of the size of a goose's egg, which was formed of striated muscular fibre. I myself received from Middeldorpf, in the year 1860, a somewhat smaller tumor, which consisted of smooth muscular fibre and numerous nerve-fibres. The latter formed plexuses with very abundant radiations in the muscular substance. The single fibres were characterized by zigzag curves. A more exact appreciation of their course was not possible to me, because of the unsatisfactory methods of those days.

6. Atrophy.

§ 594. Apart from the secondary atrophies of the seminal tubuli, which occur in inflammation and formation of tumor, I will only mention here the premature occurrence of the senile involution. As is known, the physiological functions of the testicles cease on the far side of the sixtieth year. The seminal epithelia then more and more undergo a fatty metamorphosis. The entire testicle becomes correspondingly smaller, soft, and upon a section shows a yellowish, dark butter yellow, up to a brownish coloring.

XI. ANOMALIES OF THE MAMMA.

1. Inflammation.

§ 595. The tumors of the female mammary gland have been so often, and at already so early a period, the subject of earnest histological investigation, that in this sense, we might not improperly call the mammary gland the nurse of pathological histology. In contrast to this the histology of mastitis is yet as good as unknown. For the time being we are content to transfer ideas which we have actually obtained from other similarly constructed glands, for example, of the salivary glands to the mammary gland, and thereby to explain the various morbid appearances of mastitis.

The acute inflammations which occur during lactation are either diffused over the entire gland, or they form circumscribed tumors of the size of a pigeon's egg and over. Certain diffuse inflammations, which we call mastitis, do not run their course actually in the gland itself, but in the loose connective tissue which encompasses the gland as well behind as in front. These very commonly lead to the formation of abscess, and, in reference to histological processes, fall entirely under the points of view of phlegmon telæ cellulosæ (§ 94). Touching the circumscribed inflammatory depots, here also the interstitial tissue may predominantly participate. The retention of milk in the excretory ducts of the glandular lobules concerned, in the cases where it actually occurs, may be most simply explained by the inflammatory infiltration of the surrounding connective tissue, in like manner as we have spoken of it in the formation of cysts of retention (§ 70). As a rule, the tumor forms abscesses simultaneously at several points; perhaps we may here some time succeed in tracing back the beginning of the purulent fusion to individual glandular lobules. Positive observations are yet wanting concerning the nature and the manner of participation of the secerning parenchyma.

Still more obscure than the relations of acute mastitis, are to us the histological conditions of those painless indurations, which often exist for years in the form of tumors, larger and smaller than a walnut, and either at length decompose or also soften, or finally go over into sarcoma or carcinoma formation. The question here is probably about a plastic cellular infiltration of the connective tissue, which, indeed, as

we know, is a neutral preliminary stage of most pathological new formations.

2. Tumors.

§ 596. When at the start I pointed out that pathological histology had, to a certain extent, taken its degree upon tumors of the mammary gland, the reader might accordingly believe himself entitled to encounter in the following, a representation of the subject unexceptionally methodical. He may, however, find himself deceived if, by a methodical representation, he should imagine to himself a sharply defined system, an exceedingly characteristic subdivision, and the minute dissection of the material. Studies ever becoming more special have led much more to effacing boundaries than to tracing them. I know of but two principal groups of mammary tumors which can be declared, tumors that proceed from the epithelial structural elements of the gland, and those that proceed from the subepithelial or interstitial tissue. Each group extends secondarily over into the developmental province of the other; so much the more must we emphasize the starting-point, and seek in it the proper source of all later peculiarities.

a. *Tumors which proceed from the Epithelial Structural Elements of the Gland.*

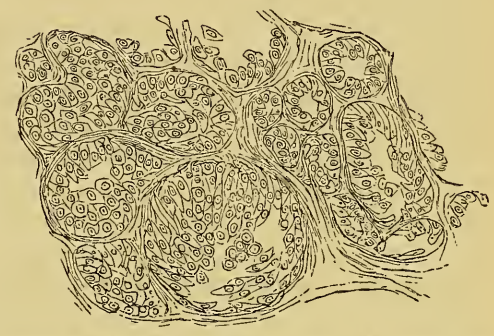
§ 597. The pervading character of all new formations belonging here is a decided projection and pressing forward of the epithelium which lines the inner surface of the acini. This, as is known from normal histology, is formed of a simple stratum of small, low, nucleated cells, which mutually most intimately touch each other, and slightly press together laterally. During lactation these cells multiply to double and threefold the number, but do not therein pile up over each other, but intercalate side by side, so that naturally the surface expansion of the epithelium, and with it the circumference of the terminal vesicles of the acinus, grows considerably. The periacinous and interacinous connective tissue, which is characterized about this time by great succulence and increased abundance of migratory cells, gives way to this active expansion of the acini, and soon the adjacent terminal vesicles of an acinus touch, excepting a very narrow septum, which, however, persists. At length the greatest possible expansion is attained. The epithelia formed thereafter can only find space in that the older cells are loosened from the walls of the acinus; the latter arrive in the lumen of the acinus, and, since they here fall into the fatty metamorphosis, they give rise to the formation of a fatty detritus, which we call milk.

§ 598. These physiological processes present to us many welcome points of comparison for understanding the first series of mammary tumors. The disturbance first coming into consideration, it is true, *the genuine hypertrophy* of the mamma, is too little known that we could

state anything positive about the mode of its origin. According to Birkett, we have here an abnormal number and abnormal size of glandular lobules with simultaneous hyperplasia of the interacinous connective tissue. The rare disease would, therefore, consist in a colossal but uniform intumescence of the mamma, which exhibits a normal texture in all parts.

§ 599. Just as rare, although carefully investigated, is the tumor, which, according to the definition proposed by me (§§ 148, 152), I would rather term *adenoma* of the mamma. A proliferation of the epithelial structures of the acinus forms the undoubted foundation of the neoplasia. This, however, distinguishes itself from the physiological in the first place by this, that the cells are piled up above each other, and that a regular fatty metamorphosis remains absent. Close at the limits of the connective tissue is the germinal place of the young cells (Fig. 165); here we see quite small cell-forms, which most intimately adhere to the walls, and appear to be supplied by a very thin, nucleated layer of protoplasm lining the entire alveolus. The young cells are gradually raised above the level of this layer, and crowd in between the bases of the lowermost epithelial cells. These are themselves gradually lifted off and pushed towards the lumen of the alveolus. Layer follows upon layer, until finally the epithelial masses formed on all sides, touch in the centre of the cavity, and this is itself filled. In the next place begins an ever-increasing dilatation of the cavity, which, indeed, is quite analogous to the physiological dilatation in lactation, but is essentially distinguished from it by not occurring by any means uniformly at all parts of the glandular substance. Individual vesicles rather expand at the expense of all the others, and thus is obtained a degenerated acinus; although we can yet very well recognize it as such, nevertheless it soon presents a foreign appearance. The affection of the gland also is not uniform. The tumor rather forms masses up to the size of a fist, beside which the remainder of the gland becomes atrophic.

Fig. 165.



Adenoma mammæ. Genuine epithelial carcinoma (Billroth). See details in text. 1–300.

The higher development is characteristic, which the single cell-individuals experience. This is accomplished in the specific epidermal direction, although it ceases with the formation of transition epithelia and serrated cells, and never advances to an actual horny metamorphosis.

Afterward the adjacent cell-nests flow together more and more, a fatty metamorphosis also begins at the centre of the larger, which ends in the formation of atheroma-cysts, which may pervade the tumor in great number and in individual specimens up to the size of a pea. Nothing has been made known of an external rupture of these cysts, formation of ulcer, &c.; likewise the future fate of those affected with these tumors is problematical; hitherto a metastasis to the lymph-glands of the axilla has never been observed.

According to all this I see myself obliged to reckon the tumor with the glandular cancroids or adenomas, and would also have no objection to the name of a "true epithelial glandular carcinoma," introduced by Billroth and v. Brunn.

§ 600. The *soft carcinoma* of the mamma follows, in its initiatory stages, characterized by the swelling of one, or simultaneously, several glandular lobules, in a short time, to extensive tumors, which occasion much pain to the patients. The soft carcinoma proceeds no less decidedly from the epithelia than does the form of tumor discussed above. One essential difference, however, already consists in the manner of proliferation. There, "a pushing forward on the part of the matrix," here, "division of the existing epithelial cells." Hence the perfectly sharp boundary is very characteristic which exists between the connective tissue and the epithelium at an early period. A smooth, beautifully undulating boundary outline, with a hyaline translucent outermost edge, limits the connective tissue stroma. It runs exactly parallel to the surface of the epithelial cell-cylinders without anywhere entering with them into an intimate relation. At the first glance we see that the proliferation and the independent growth of the epithelium form here the principal cause of all the changes. The epithelium first forms a solid strand which fills the lumen of the acinus up to the terminal vesicles. The cells herewith assume the stamp of larger cancer-cells, richer in protoplasm, described in § 154. Upon the youngest cells the protoplasm of the single cells appears to flow together, but a distinct separation soon sets in, and therewith occurs the multiplicity of form of the cells caused by the pressure of growth.

We everywhere perceive nuclear division and constriction. Now begins an outgrowing of the cylinder of cells in the form of solid epithelial projections, which push towards the connective tissue. The connective tissue gives back everywhere. The partition walls between the adjacent alveoli are broken through, and soon of the whole very thick system of septa of the acinus, there only remains a delicate network, with wide meshes, which carries the vessels. Meanwhile in the larger accumulations of connective tissue which separate the single acini of the diseased lobule, an abundant infiltration with small round cells, has taken place. The connective tissue has become softer thereby, more yielding, and more capable of participating in the future growth

of the cancer. The cancer mass now already presents a very extensive tumor, upon which, however, we can yet recognize all parts of the old lobule, although very much changed. Now, however, follows a second phase of development.

This is characterized by the ever more numerous springing up of new tumors in the hitherto yet intact substance of the gland. The new tumors grow as did the old, partly fuse with them, and thus contribute to the production of an extensive, irregularly tuberous, and soft tumor, over which the skin is stretched, in order finally to suppurate, and thus permit the eruption of the cancer externally.

§ 601. An entirely new kind of production and growth of carcinomatous new formations has recently become known by a very good work of Köster,—I mean the production of cancer-cells from the endothelia of the lymph-vessels, and the advance, rendered possible thereby and explained, of the cell-cylinders of the cancer into the lymph-vessels of the adjacent connective tissue. Now there is also a cancer of the mamma, which after a moderate multiplication and change of type of the alveolar epithelia, goes over directly into an infiltration of the interacinous and interlobular net of lymph-vessels. In a very compact but moderately large tumor, appearing to the naked eye more whitish than gray, the microscope shows the terminal vesicles of the acini, as also the excretory ducts, dilated up to the larger lactiferous ducts, and filled with a fatty, granular detritus, with granular corpuscles and cells; upon these nests and projections which, as observed, we quite distinctly recognize as the constituents of former acini, the infiltrated lymph-vessels are placed immediately, with a slightly widened base. The net of lymph-vessels is as completely filled with cancer-cells as we only see it in successful injections. The characteristic outlines, with their incurvations, the varicosity, the broad points of intersection of the net, all come out very distinctly and permit no doubt that the question here is actually about degenerated lymph-vessels. Billroth has chosen the suitable name of a *tubular* carcinoma for this form. Meanwhile I do not believe that it is admissible to draw a strict limit between the tubular carcinoma and ordinary scirrhus, as will be shown by the following.

§ 602. The by far most frequent form of carcinomatous disease, the *hard cancer* of the mamma, in the most extended sense of the word, depends less upon a "proliferation" of the existing glandular epithelia than upon an "epithelial infection," which extends from them to the connective tissue cells and the lymphatic endothelia of their neighborhood. As a rule the proliferation of the glandular epithelia is confined to this, that the cells moderately increase by division, that they assume the character of cancer-cells and coalesce into a solid body, which very soon can be no longer distinguished from the nests of cancer-cells arising in the neighborhood. As slight in appearance as this metamorphosis is,

yet, as I believe, there can be no doubt that it gives the first impulse to all further changes; upon larger sections, which embrace the most various stages of the process, we may distinctly see that the cancerous infiltration takes its beginning from the neighborhood of the acini and extends concentrically around these. This extension, consequently the actual growth of the cancer, depends upon a direct transformation of connective tissue cells, and the lymphatic endothelia into cancer-cells, that is, nests and lines of cancer-cells.

It is certainly very important, that we as anatomists, strictly separate the individual constituents of the nutritive apparatus, the blood-vessels, lymph-vessels, and the system of "spaces in the connective tissue lying between the two," because nature itself suggests for this reliable criteria. We will perhaps observe, that in certain pathological changes also, the individual divisions demean themselves independently. On that account, however, we must not ignore the physiological connection of the three parts, which has found its anatomical expression above all in the uniformity and the equivalence of the cells, which line the inner surface of the entire system of canals serving for nutrition. These cells have nucleus and protoplasm; the latter, however, upon the blood and lymph-vessels, has become for the greater part, a thin, homogeneous plate, to which the nucleus, with the still soft, often very small remains of protoplasm, adheres to the outer, *i. e.*, the side turned from the lumen of the vessels. Also, upon the juice-cells there occurs a partial sclerosis of the protoplasm, as is especially visible in the mucous tissue, in the cornea, in the connective tissue layers of the intima vasorum, yet I would not bind myself to trace up the parallel, already now, into the smallest details. The essential unity of these cells comes out much more strikingly and convincingly in pathological proliferations.

For the present, we will continue with our carcinoma. In the frequently and fundamentally studied microscopic pictures which the hard carcinoma of the mammary gland presents, there can be no doubt, that the most of the cell-nests are produced by a direct metamorphosis of single connective tissue cells; the doctrine of Virchow remains undisputed here, if anywhere. We have committed an undeniable error, in that we too prematurely generalized the results which cancer of the mammary gland furnished us; for it has been shown, that cancer-cells may also arise in other ways than from connective tissue corpuscles. For that reason, however, that which we, for example, said above in § 158 *et seq.*, concerning carcinoma simplex in general, now, as ever, retains its complete validity for simple carcinoma of the mamma, from which also the illustrations given *loc. cit.* were taken. The metamorphosis is introduced by an epithelial infection, to be sure still hypothetical, *i. e.*, an incitation to a synonymous individual development, which is exercised by the actual epithelium upon the most contiguous

connective tissue cells. Then follow the abundant accumulations of protoplasm around the nuclei, the nuclear division, the cellular division, as was described at the time, and I cannot avoid seeing, even yet to-day, in the spindle-formed, youngest nests of cancer-cells, a transformed former connective tissue corpuscle. In renewed examination of the subject, I have, it is true, convinced myself that the lymph-vessels may also participate in the cancerous production, still they participate in the most prominent manner only in the hardest forms of the series, called scirrhus, par excellence; we cannot demonstrate their separate participation in the softer ones.

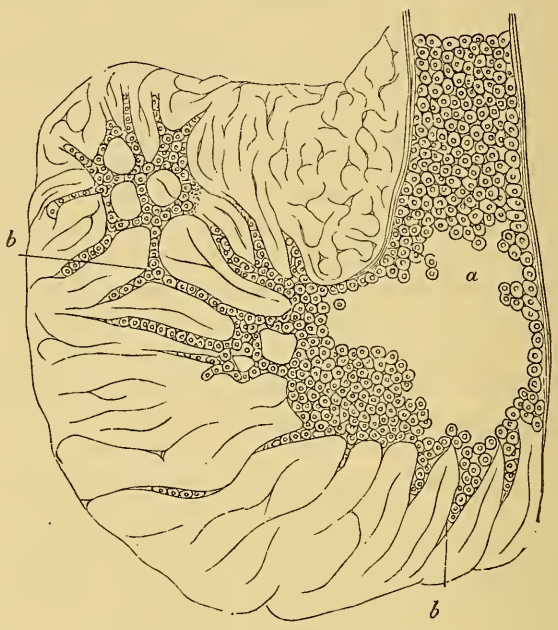
§ 603. We therefore distinguish, as is seen, harder and softer forms in a connected series of hard cancers of the breast. The hardness in general (in contrast to medullary cancer) is conditioned by this, that the known very dense and compact fibres of the interstitial connective tissue are indeed stretched and expanded, perhaps also somewhat thinned by the cancerous infiltration, but never entirely resorbed, so that during the collective phases of development of the cancer, they form a rigid texture, which is expanded throughout the mass of the tumor. Only by the irresistible demand for space of the *growing* cancer-cells, is the intimate connection of the fibres loosened. But if the cancer-cells have passed the zenith of life, the elastic tension of the connective tissue in turn also predominates, and I believe I do not go too far in assuming, that this tension accelerates directly the retrogressive metamorphosis of the cancer-cells. From the preceding considerations, the subdivision of hard cancers becomes self-evident. The more decidedly and the more luxuriantly the cell new formation arises, the larger, and the more space-requiring the single cell-individual becomes, the more without exception each connective tissue cell participates in the degeneration, so much the more will the whole tumor have a softer constitution corresponding to the infiltrate, while, *vice versa*, a moderate production of cells, remaining small, and especially the infiltration of the lymph-vessels, give the connective tissue the predominance, consequently will produce harder forms of cancer.

§ 604. All cancers of the breast are apt to arise in the form of nodule; when there once occurs an exception to this rule, when also diffuse infiltrations of one or several lobules, nay, of the whole gland occur, these are regularly somewhat softer connective tissue cancers, which are characterized by large many-formed cells. For the much more frequent occurrence of this species in the nodular form, what was said in the General Part on *carcinoma simplex*, may be brought to remembrance again at this place.

Let us treat of the genuine *scirrhus* somewhat more particularly. Billroth has designated this as the small-celled, tubular connective tissue cancer. His experienced eye has at once pointed out the two most important criteria of the new formation; namely, the cells of scirrhus

in fact scarcely attain the third part of the size of a common cancer-cell. But they, nevertheless, have a decidedly epithelial character, as may best be seen where the interstitial new formation joins the epithelium of the acini and excretory ducts (Fig. 166). What further

Fig. 166.



Scirrhus mammæ. *a*. Lactiferous duct with hyperplastic epithelium. *b*. Cellular infiltrated clefts of the connective tissue (lymph-vessels?) after Waldeyer.

characterizes the cell is its great durability. A retrogressive metamorphosis can scarcely be demonstrated upon these cancers. The cut surface of the nodule is compact, white in places, like the sheen of satin, without the yellow reticulation which the zone of fatty metamorphosis shows in simple cancer. The second criterion of Billroth, the tubularity, depends in the first place upon the infiltration of the lymph-vessels, in the second upon this, that the connective tissue cells in their proliferation and change of type, fill up the clefts of the connective tissue more uniformly in long rows, instead of concentrating upon more than one point, as in simple cancer, and forming a nest. The illustration referring to this (§ 601) belongs to Waldeyer, who has made himself meritorious particularly about the proof of the connection of the interstitial proliferation with the epithelium of the acini. This shows at *b*, as appears to me, a fragment of the infiltrated net of lymph-vessels, yet I have since received pictures, in which the lymphadenoid character of certain tubular infiltrates came out very much more distinctly, nay, in which the lymph-vessels were quite exclusively the seat of the new formation (compare above, § 601). The connective tissue

cells appear here to participate but little. This, however, is decidedly not the ordinary case. In order to form a conception of the ordinary relations, we must imagine all the minute lines, which exist beside the infiltrates, beset with rows of cells but little interrupted.

The gelatinous cancer also occurs at the mamma, although rarely. I have seen it as cancer en cuirasse.

In conclusion, I will yet give a table of synonyms, which must certainly be very desirable to the beginner in the widely expanded literature of cancer of the breast:

Simple hypertrophy of the mamma. True adenoma (Billroth).

Adenoma or cancroid hypertrophy according to my terminology. True glandular epithelial carcinoma (Billroth).

Medullary carcinoma. Soft cancer of the breast, acinous large-celled glandular carcinoma (Billroth).

Carcinoma simplex (Förster). With the following, designated by practitioners as scirrhus. The most common cancer of the breast. Large-celled (?) tubular cancer (Billroth). Carcinoma reticulatum (Müller).

Scirrhus. Fibrous cancer. Small-celled tubular cancer (Billroth). Retracting, atrophying, cicatrizing cancer.

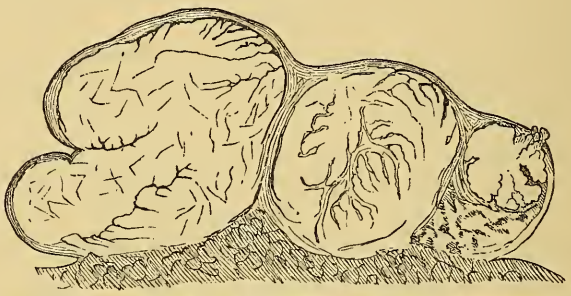
b. *Tumors which proceed from the Connective Tissue of the Gland.*

§ 605. In this second group of tumors of the mamma, we find the most representatives of the histioid new formations, the sarcoma, the fibroma, the myxoma, &c. Tumors which mostly proceed from a circumscribed part of the gland, and growing in the nodular form often attain colossal dimensions; tumors which only exceptionally relapse and form interior metastases after a fundamental extirpation. The most important of these tumors, undoubtedly is the *cystosarcoma mammæ*, a tumor which deserves our entire attention, because under an exceedingly characteristic macroscopic form it brings before us the various species of the histioid new formation, whether single or combined, and thereby proves their close relationship and intimate connection.

The expression cystosarcoma is hence by no means to be conceived as the designation of a definite, perhaps round-celled, sarcoma with cysts, but it only tells us that a new formation with the textural character of histioid tumors has attacked the mamma and dilated its preformed cavities. The nature and manner of this dilatation, however, has such prominent peculiarities that there result therefrom an exceedingly strange macroscopic appearance of the tumor. Round cysts filled with mucus are met with but rarely, and only singly. On the other hand, we everywhere observe upon the cut surface shallow clefts, which here and there communicate with one another; upon the whole, however, are dispersed more parallel or concentric, and thereby impart to the mass of the tumor a peculiar foliated structure, which Virchow has

very appropriately compared to the structure of a divided head of cabbage (Fig. 167). If we are to speak of cysts here, these—as we must say to ourselves from the commencement—have either been pressed

Fig. 167.



Usual macroscopic appearance of a cystosarcoma mammæ upon section.

flat or filled up with the constituents of the tumor to such an extent that the vesicular character is entirely unrecognizable. Both is the case to a certain degree. In the first place it may be regarded as settled, that those clefts are the altered excretory ducts of the gland. Upon a sufficiently thin section (Fig. 168) we observe a continuous covering of multiple stratified cylindrical epithelium, which secretes in the lumen of the clefts a viscous, clear, synovia-like mucus. The epithelium accordingly, in contrast to the normal, is in a luxuriant hyperplastic condition, which is quite conformable to the abnormal enlargement of the surface covered by it. This enlargement of the epithelial-clad surface, *i. e.*, of the subepithelial and interstitial connective tissue, is, however, the proper central point of the process. It either ensues in the manner of a more uniform distension and thickening of the tubular walls, or by the growing in of papillar and dendritic vegetations into the lumen of the tubuli. More rarely, and mostly only as a complication, there arise solid, globular tumors, removed from the surface of the tubuli, in the midst of the broader layers of the interstitial tissue. If to the multiplicity of the external appearance resulting herefrom, we yet add the multiplicity of the material forming the tumor, we cannot wonder that almost every cystosarcoma mammæ has its peculiarities. We here only adduce the anatomical appearances of those most frequently recurring:

Fig. 168.

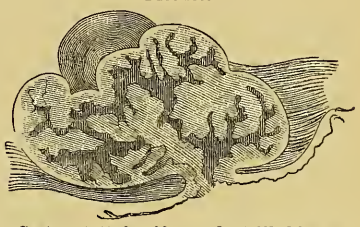
Dilated and distorted lactiferous duct clothed with cylindrical epithelium. 1–200.

1. Cystosarcoma fibrosum. (Fibroma intracanaliculare papillare mammæ, Virchow.) A roundish, mostly lobular tumefaction of the mamma, of very considerable hardness. Upon a section, we partly see larger nodules, up to the size of a hen's egg, of the color and constitution of genuine fibroids, partly just such leaves and partition walls;

finally, smaller and larger groups of papillæ, which probably have also at single places broken through the integument and are then exposed free.

2. Cystosarcoma mucosum. (Myxoma intracanaliculare arborescens mammæ, Virchow. Cystosarcoma proliferum, or phyllodes, Müller.) The most frequent form; it is distinguished from the fibrous by the more rapid growth and luxuriant proliferation of foliated and papillar excrescences into the lactiferous ducts. This relation comes out most clearly, when beside the distension and distortion of the lactiferous ducts, a collection of a mucoid secretion goes along with it, and now actual round or half round sacs arise, into which the papillary proliferations project (Fig. 169). The material of the tumor is mucoid tissue mixed with round-celled sarcoma tissue.

Fig. 169.



Cysto-ectatic lactiferous duct filled by papillary excrescences of the walls. After Meckel von Hemsbach.

3. Sarcoma pericanaliculare; adenoides, Billroth. A tumor appearing as roundish nodules, which, upon sections, exhibits leaf-like sinuosities of a white or reddish-gray substance, that upon microscopic investigation is recognized as round- or more rarely spindled-celled sarcoma tissue. The new formation has here been limited to the subepithelial connective tissue stratum, and as we see is a monstrous copy of the mode of ramification of the normal glandular parenchyma.

4. Sarcoma pericanaliculare diffusum. An entirely uniform, yet mostly spindle-celled sarcoma mass, within which the lactiferous ducts are distorted and distended into widely gaping clefts. This tumor also begins in the surroundings of the ducts, then, however, passes over the entire interstitial tissue.

§ 606. Beside the cystosarcomas, the remaining histioid tumors of the mammæ form a comparatively small number. Most frequently there occurs a round-celled sarcoma composed of several nodules; the most interesting may be a spindle-celled sarcoma of limited malignity, which is characterized by its peculiarly radiating structure (carcinoma fasciculatum Mülleri). Still the tumor is too rare to report more accurately concerning it. Smaller enchondroma nodules have been repeatedly found in the mammæ, likewise lipomas, yet the latter may probably always be regarded as degenerated fat-lobules of the neighborhood.

XII. ANOMALIES OF THE PROSTATE GLAND.

1. Hypertrophy.

§ 607. More recently the view has been advanced, and especially defended in England (Thompson), that the prostate is to be regarded as the analogue of the female uterus. The great abundance of smooth muscular fibres, by which the stroma of the gland is distinguished, the circumstance, that the recognized equivalent of the womb, the so-called utriculus prostaticus, is sunk pretty accurately into the centre of the gland, in fact, give this parallelism something attractive, yet, it must not be overlooked, that upon the one hand the glandulæ utriculares, with which the prostatic tubuli must have been compared, are not imbedded in the muscular structure of the uterus, upon the other, the mentioned utriculus prostaticus not only possesses a cavity, but also, a proper wall distinctly set apart from the substance of the prostate, which thus has yet a nearer claim to be compared with the womb. It is always interesting, that just the most frequent form of disease of the prostate, the hypertrophy, presents in many points similarities not to be mistaken with a disease of the womb, likewise very frequent; namely, the fibroma formation.

§ 608. We can distinguish two forms of prostatic hypertrophy. In the one, the rarer form, there is a uniform enlargement of the organ in all directions, considerable increase of consistence by the arising of a thoroughly compact, stretched, whitish fibrous tissue, which pervades the whole gland. The collective muscular bundles here are in the condition of progressive hyperplasia, while the glandular tubuli perish atrophic. In very marked cases of this degeneration the glandular constituents are completely destroyed; there is no longer a trace of them to be demonstrated; the prostate has been converted into a homogeneous fibro-muscular tumor.

The relations are otherwise in the second, by far more common form of prostatic hypertrophy, which is characterized even for superficial observation, by the existence of more distinct nodules. The latter are of round, or at least, roundish shape, and vary in diameter from 0.5 mm. to 15 mm.; the smaller are constantly soft, reddish-gray and project cushion-like from the cut surface, while the larger for the most part, although by no means always, are of somewhat harder, more fibrous constitution, and pass more into a whitish coloring, but in other respects

likewise form protuberances at the cut surface. Where these nodules are less numerous, we can say, that they appear set into the parenchyma of the prostate; as a rule, however, they are present in such large amount, that the gland is actually composed mosaic-like of them, and the remains of the relatively unchanged glandular parenchyma disappear beside them. The numerous varieties, which are observed in the external form of the hypertrophic prostate, the circumstance, that at one time the left, then the right lateral lobe, then again, the superior portion of the posterior circumference of the gland (the so-called middle lobe) is attacked, the most manifold distortions and displacements, which the prostatic portion of the urethra experiences, all is explained by the varying numbers and the unequally rapid growth of the nodules.

§ 609. Let us, therefore, enter more minutely upon the histological constitution, and the history of the origin of this so important constituent of the hypertrophic prostate. All nodules, the smallest as well as the largest, show in their composition glandular and muscular elements. The former resemble the tubuli of the normal prostate just as much by their low, more pavement-like cylindrical epithelium, as by the kind and the manner of ramification, which ensues at almost right angles. I have been able to discover nothing of a tunica propria in the ordinary sense, but probably the fibro-muscular tissue, the nearest investment of the tubuli, is stratified parallel to the surface of the tubuli, and may thus to a great extent be regarded as a "proper investment" of the lumina lined with epithelium. We should do violence to facts, were we to ignore, that the glandular tubuli, in so far, at least, play the most important rôle in the entire new formation, as it is their form and ramification which lie at the base of the whole structure of the nodule. Whether a sprouting of the glandular epithelium in the form of solid cell-projections, therefore genuine glandular hyperplasia, furnishes the first point of departure for the new formation, I have not been able to decide; more probable to me is the primary participation of the *subepithelial tissue*. This becomes hyperplastic, and swells from a scarcely measurable thickness to a stout layer from 0.05 to 0.2 mm. of young tissue, consisting entirely of spindle-cells. Most authors regard these spindle-cells as muscular, and therefore, designate the new formation, as also the common fibroid of the uterus as fibro-muscular. I have several objections to this nomenclature, still I would avoid entangling a thing in itself very simple, by disputes as to its designation (§ 128). A single glandular tubulus with its terminal ramifications gets, by the enlargement spoken of, of the subepithelial stratum, the form and size of a pin's head, and to that extent is elevated from the remaining parenchyma as the smallest nodule. The continued enlargement of the nodule ensues upon the one hand by the participation of the most contiguous glandular tubuli, upon the other from the interior by the outgrowing of the existing fibro-tubular elements of the tumor. The more the latter

mode of growth prevails, so much the more is the nodule isolated when it becomes larger, and finally, even comes to lie in a special fibrous envelope.

If we now sum up what has been said, we must designate the ordinary hypertrophy of the prostate as a fibro-muscular hyperplasia of the peritubular stroma of individual sections of the gland, with the simultaneous elongation and multiplication of the tubuli themselves. A similar affection has been observed by Billroth in the mammary gland, and described as an adenoid sarcoma (§ 605, 3).

2. Inflammation.

§ 610. The prostate in respect to acute inflammations, behaves to some extent like the outer skin. As there the intimate interweaving of the fibres of the cutis, so here the great compactness of the stroma forbids the rapid extension of the process. Hence, we find the acute inflammation in all stages limited to single, although often numerous small depots. I, of course, do not speak here of traumatic suppurations, which are guided in the extension by the læsio continui which has occurred, but of those acute parenchymatous swellings, which in rare cases are protopathic, but which are mostly produced by the sympathy of the prostate with the remaining urino-genital system, above all with catarrhs of the urinary passages.

I consider it proper to distinguish two stages of acute inflammation. A considerable hyperæmia and œdematous saturation of the entire organ characterizes the beginning of the affection, and continues during the entire first stage. Unfortunately but little has become known of the more minute anatomical conditions. Thompson observed "points of thickish pus, which, however, were not actually small abscesses, but glandular cysts." According to this, the process appears therefore, already at an early period to be localized in the tubuli. The second stage, whose occurrence is mostly prevented by medical skill, is the formation of abscess. There develops a luxuriant secretion of pus-corpuscles at the inner surface of the glandular tubuli; the pus-corpuscles mix with the normal secretion of the gland, and form with it a glue-like, greenish-yellow fluid, capable of being drawn out into threads, which to some extent is distinguished from common pus. The pre-existing cavities are distended, afterward single ones fuse together, and we then find the prostate pervaded by a variously large number of larger and smaller abscesses. Very rarely a single larger abscess cavity occupies the centre of a lateral lobe. Generally, weeks and months pass ere the inflammation has advanced to this point, because the tense fibro-muscular stroma of the gland is not favorable to the progress of the suppuration. The abscess, as a rule, opens towards the urethral surface; less frequently the pus bursts through externally and occasions fistulous openings towards the rectum, the intestine, or penis.

3. Tuberculosis.

§ 611. At the prostate, tuberculosis only occurs in that form which leads to phthisis of the organ. The originally gray nodules, afterward becoming cheesy, are imbedded in the surroundings of the tubuli. Their softening and breaking down leads to the formation of multiple abscesses, which enlarge by the progressive formation of new tubercles, and finally perforate towards the bladder. The whole process is analogous to phthisis renalis and testiculi (§ 569 and § 589).

4. Cancer.

§ 612. Cancer of the prostate is a disease not very frequent, and constantly protopathic. Medullary cancer forms very extensive knotty tumors, which mostly protrude towards the lumen of the urethra, afterwards break through and form ulcers. According to the statement of Oscar Wyss, carcinoma arises by a primary degeneration of the glandular substance, especially of the tubular epithelium, while the stroma remains passive. I have no observations of my own to report. To the melanotic cancer, which likewise has been observed at the prostate, the medullary form may be annexed.

XIII. ANOMALIES OF THE SALIVARY GLANDS.

1. Inflammation.

§ 613. The advances worthy of recognition which the normal histology of the salivary glands has most recently made, have by no means yet been turned to profit for the pathological relations. This depends especially upon this, that the diseases of the salivary glands in general are rare, and that inflammations particularly are wont to come under investigation at too advanced a stage. Experimental study has hitherto found its greatest difficulties in the insensibility of the salivary glands of animals to traumatic influences, so that it is to some extent to be excused, if our acquaintance with the histological processes in inflammation of the salivary glands is as yet based upon a limited number of better investigated cases of parotitis (Virchow and C. O. Weber). I have myself kept to the very well-preserved material of the Pathological Institute of Bonn, used by C. O. Weber.

§ 614. The inflammatory irritant is conveyed to the salivary gland probably in all cases from the mucous surface upon which its excretory duct opens. Even in the so-called idiopathic parotitis, a perhaps insignificant stomatitis is wont to be primary; and touching the dyscrasic forms, the most important among them, the mercurial, has already shown itself likewise as conveyed onwards from the oral mucous membrane; only the parotitis of infectious diseases (typhus, pyæmia, acute exanthems, &c.) has, in our opinion, the right to a direct origin from the diseased blood which flows through the gland. The anatomical changes correspond to these etiological presumptions, in so far as they bear in essentials the character of a catarrhal inflammation of the secerning glandular parenchyma, combined with a catarrh of the salivary ducts.

In the first place, touching the parenchyma, to Virchow is due the merit of having set aside the formerly generally diffused error, that parotitis was essentially an inflammation of the glandular connective tissue. It is true that in acute parotitis, as well the connective tissue investments of the gland as particularly the connective tissue septa in the interior, experience a considerable, primarily œdematous, afterwards perhaps, even a purulent infiltration. Nevertheless, every in-

flammation of the salivary glands, in the first place, concerns the secerning parenchyma in the narrowest sense of the word, *i. e.*, the salivary cells which line the short terminal tubuli of the gland as their epithelium. The so-called glandular lobules, distinguishable by the naked eye, which normally have perhaps the size of a large pin's head and a pale yellowish-gray color, come out upon the inflamed gland as dark red, tensely swollen bodies, of the size of a lentil. We see that the inflammatory hyperæmia has concentrated quite specially upon these lobules. Even effusions of blood are observed here and there upon the surface of the lobules. If we then pass to the microscopic examination of well-hardened preparations, we recognize, only after some practice certainly, on the tolerably variegated picture the following:

The terminal tubuli have become diseased to various extents groupwise, according to their combination into single acini. Beside single, yet fully normal acini, we find, 1, those whose epithelia are much enlarged, dark-granularly clouded and loosened in their connection. The enlarged cells, which here and there exhibit nuclear division, fill out the entire space; they have widened it comparatively to double its size, and still more; Weber has also observed endogenous pus formation in these large cells. 2. Those whose alveoli contain in their lumen numerous pus-corpuscles, while a continuous epithelium yet lines the walls. (Fig. 170.) This pus has the significance of a catarrhal superficial secretion, and the question only is, whence is it derived? Several possibilities exist here. In the first place, we might think of the just mentioned endogenous pus-formation described by Weber, and see its final result in the existing pus; in the second place, we might think of a migration of young cells from the subepithelial connective tissue. The existence of a continuous epithelial layer I would not regard as an obstacle to the migration; finally, in the third place, the possibility is to be considered, that the epithelia still existing at the walls, produced the young centrally situated cells by division; for, just here we see regularly active processes of division, and if we reflect that this cell-layer is most probably also the matrix of the normal epithelial cells, the conjecture comes of itself, that an excessive participation of the physiological regeneration may play a rôle in the inflammation. Upon the acini filled with recently swollen epithelia, we already observe nuclear division in those cells which are crescentic upon a cross-section, *in toto* stellated and anastomosing, and rich in protoplasm, which form a proper layer between the connective tissue alveolar wall and the actual and fully formed salivary cells. According to Pflüger, these cells stand in the

Fig. 170.

From the transverse section of an inflamed parotid gland. Terminal glandular tubulus filled with pus-corpuscles, the walls lined with epithelial cells, which are in active proliferation, the surrounding connective tissue infiltrated with small cells. 1-500.

most intimate connection with the nervous system. It does not, however, appear to be incompatible herewith, that they at the same time provide for the restoration of the epithelial stratum above them, as Heidenhain particularly has demonstrated. If now we compare the variously changed acini with one another, we soon arrive at the conviction, that they are just these cells which still persist after the loss of the remainder of the epithelial stratum, at the same time, however, have fallen into a morbid proliferative process. 3. Those acini, in which no trace is left of an epithelium, and which only yet resemble connective tissue meshes filled with pus. These completely purulent acini flow together into ever larger abscesses, which by degrees occupy entire lobules, nay, entire lobes of the gland. 4. The interstitial connective tissue is in the beginning œdematously puffed up, and thus serves the anatomist by distinctly separating from each other, and making known the individual inflamed lobules. Afterward, at first in the environs of the inflamed acini, there begins a cellular infiltration, which the longer it continues so much the more advances, partly towards the lumen of the acini, partly outwards into the broader connective tissue septa, giving occasion, on both sides, to suppuration and the formation of abscess. 5. The salivary ducts, in the entire extent of the inflammatory depot, likewise produce pus at their surface, as C. O. Weber has demonstrated; still their epithelium remains intact for a very long time, and only perishes together with the complete suppuration of the gland.

After all this, we may imagine the inflammatory process of the salivary glands running its course, perhaps, in such manner that in a first stage, hyperæmia of the glandular lobules and cloudy swelling of the salivary cells go hand in hand with an œdematous saturation of the connective tissue; in a second stage, a purulent catarrhal secretion is maintained, partly by the epithelium of the acini, partly by the surrounding connective tissue, while at the same time a cellular infiltration of the glandular connective tissue takes place; in a third stage, which, however, as a rule, is not attained, the connective tissue pus, upon the one hand, breaks into the alveoli, upon the other forms abscesses in the connective tissue, and thus brings about the destruction of the entire organ. The never-failing active participation of the salivary ducts in the purulent catarrh suggests the thought, that most of the inflammations of the parotid are in fact conveyed from the oral cavity through the excretory ducts. The so decidedly catarrhal character of parotitis would at the same time find its explanation thereby.

2. Tumors.

§ 615. The *soft carcinoma* of the parotid, a rare new formation, according to all that has become known of the histological detail of it, appears to be a genuine glandular carcinoma, *i. e.*, it appears to pro-

ceed from the epithelial linings of the glandular acini themselves. A luxuriant and intractable proliferation of the latter, in the form of solid cell-cylinders, which incessantly advance in all directions, partly breaking through the connective tissue, partly distending it, is the principal impulse to its growth. The stroma consists of thin and smooth connective tissue trabeculæ, which are expanded between a vascular net, richly developed in places. The cancer-cells in general only lie loose upon the stroma, yet an observation of Sick deserves mention, according to which the cancer-cells are more firmly adherent to the veins and the venous capillaries, nay, appear to be produced there, by division of the adventitial cells. C. O. Weber also emphasizes a more intimate relation of the connective tissue to the cancer-cell production, since he calls attention to the not infrequent occurrence of papillary excrescences, which project into the lumen of the acini. I have also seen something similar in the soft carcinomas of the mamma. The separation of the cancer-cells from the connective tissue was indeed generally exceedingly sharply defined, yet *single points* existed, at which directly the opposite, namely, a continuous transition of the connective tissue cells into cancer-cells was visible. They were mostly points of intersection of the thickest of the trabeculæ of the stroma, yet I could not ascertain more minutely concerning their position and significance.

The melanotic carcinoma is yet more rare than the simple medullary cancer; nothing whatever is known of its histological relations.

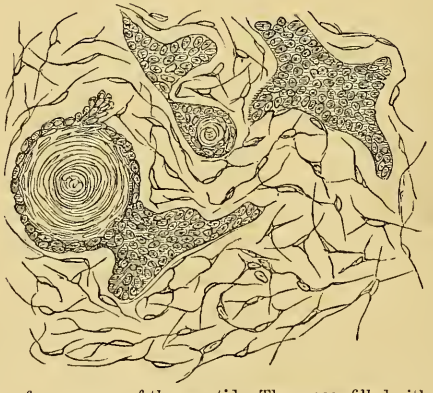
§ 616. C. O. Weber has given some statements on *scirrhus* of the parotid. According to them this tumor presents important analogies to scirrhus of the mamma, yet the participation of the glandular epithelium is still far more decided than there; the small-celled infiltration of the connective tissue has more the character of a reactive inflammation and an indurating hyperplasia. The glandular epithelia form tubes and cylinders, which penetrate the compact white mass of the tumor in all directions.

§ 617. An adenoma of the salivary glands has as yet not been described; the *epithelial carcinoma* likewise does not occur primarily, yet we not infrequently find it as an intruder, when the peripheral proliferation of a cancroid of the lips or tongue is continued to the parotid or submaxillary gland. If anywhere the investigations of Köster (§ 167) have a prominent significance, it is for this intrusion of the cancroid projections into the structure of a contiguous organ. Just as it prescribes the course and the mode of ramification of the lymph-vessels, we here see the cell-cylinders extend in the first place into the connective tissue investment, then penetrate upon the broader septa into the interior of the gland, in order finally from this point to attack the single lobules of the secerning parenchyma itself. The single alveolus participates in such manner, that first of all the spindle or crescentic border cells, which we have learned to know as the matrix of the salivary cells,

divide actively and multiply. There arises a cushion of larger epithelial cells, which surrounds the older salivary cells circularly, and expands the alveolus perhaps to double the normal extent. If the change has advanced yet somewhat further, we can upon the one hand no longer recognize the former salivary cells as something peculiar, upon the other we cannot distinguish the epithelial cells produced by the alveolus, from the epithelial cells of the adjacent cancroid projections, with which they now also appear in direct connection. Touching this latter point, the direct communication of the epithelial production of both sides, it does seem to me as though the question therein was about the disclosure and extension of preformed processes. Of another (perhaps simple atrophic) destruction of the glandular cells, there is nothing to be seen; we will only yet mention the enormous small-celled infiltration of the connective tissue, which everywhere precedes the described epithelial proliferation, without however having directly participated in it.

§ 618. Beside the carcinomas proper, we must yet mention the frequent occurrence of a compound epithelial proliferation, which is wont to be peculiar to certain mixed histioid new formations. The salivary gland, as was mentioned, is a favorite, next to bone the most favorite seat of *enchondroma*. Perfectly pure, nay, I might say, the purest forms of this tumor are observed just here. Besides this, however, there are tumors in which the cartilaginous tissue only presents the acme of the individual development of tissue, while beside it mucous tissue, as

Fig. 171.



From the cut surface of a myxoma of the parotid. The spaces filled with epithelial cells and pearly globules, are probably lymph-vessels. Compare text. 1–300.

also spindle- and round-celled sarcoma tissue, represent the chief mass of the tumor (Billroth). These tumors constantly proceed from the interstitial connective tissue and form nodules, which may attain the size of a fist, but because of their thoroughly central growth, commonly become unbearable to the patient already when they have

reached the circumference of a walnut. I have very commonly found upon them a radiating structure, at the centre, a compact fibrous place, and proceeding from this rays of sarcoma tissue, into which, here and there, portions of mucous and cartilaginous tissues are inserted. In other tumors, the mucous tissue has decidedly the predominance, and these are probably then directly designated as myxoma of the parotid. Just with these Billroth has observed the above-mentioned compound epithelial proliferation. Whether they proceed from the glandular acini, is doubtful; on the other hand, it is not doubtful that according to their principal bulk, they are metamorphosed lymph-vessels. A glance at the beautiful preparations of Billroth, of which one is also at my disposal, teaches this. The entire net of lymph-vessels, with its characteristic contours, appears filled with epithelial masses, and even the small fragment of it which I delineated ere I knew Köster's work (§ 167), shows the unmistakable contours of three transversely and obliquely divided lymph-vessels. It is striking, that just herewith the development of pearly nodules is observed, which is not once the case in secondary cancroid of the salivary glands (§ 617).

XIV. ANOMALIES OF THE THYROID GLAND.

THE searching studies of R. Virchow (Morbid Tumors, iii, I) have so considerably cleared up and promoted the pathological anatomy of goître, which hitherto had labored under a certain want of connection and vagueness, that I may venture to include the tolerably difficult theme also, in a short and compendious manner.

1. STRUMA.

§ 619. The thyroid gland is subjected to but few diseases; the most important of these is goître, struma, an enlargement of the organ often very considerable, which occurs sporadically almost everywhere, but in several mountainous regions so frequently, that especially among the female portion of the population, we scarcely meet with a healthy thyroid gland.

We may indeed set up a whole series of variously modified goîtres; there are cystic, vascular, gelatinous, follicular, amyloid goîtres, but they are all grouped around a common point of departure, the *struma hypertrophica*. In other words, every goître, though afterwards it bear an impress ever so deviating or peculiar, begins with a genuine and simple hypertrophy of the glandular substance, which in itself alone, *i. e.*, without the supervention of any other, secondary metamorphoses, occasions the condition of struma hypertrophica. Now what do we understand by struma hypertrophica?

§ 620. I will rehearse the structure of the thyroid gland in few words. Upon it, as upon a gland with open duct, we distinguish two substances, 1, the glandular follicles, the analogue of the secerning glandular substances, for example, the tubuli of the kidney, the acini of the mucous glands, &c., and 2, a framework of connective tissue, which incloses the follicles, and unites them in smaller groups to "grains" (Körnern), in larger to lobules and lobes. The follicles are vesicles closed all around, consisting of a simple pavement epithelium, and each inclosing a drop of a clear fluid very rich in albumen. The connective tissue is at the same time the bearer of an exceptionally rich vascularization, which is supplied by the four large thyroid arteries. The development of the struma begins in every case by the follicular

cells multiplying by division. But because this multiplication takes place more abundantly at individual points of the follicular walls than at others, the follicles receive villiform projections, which when they have attained a certain length, ramify, become constricted, and form new follicles. Billroth succeeded in isolating in connection, follicular structures thus ramifying and projecting. The whole process, as we see, is a genuine hyperplasia of the proper glandular substance, and as long as it continues so exclusively in this sense, we speak of struma hypertrophica.

The external appearance of a hypertrophic struma, is first of all dependent upon the circumstance, that the hyperplasia very rarely attacks the gland uniformly and in its entire extent, but that single lobes and lobules, or even certain sub-lobules, that occur at various points of the periphery, predominantly participate. Thus arise sharply defined, round nodules (goître-nodules), projecting cushion-like at the cut surface, which, when they have their seat at the periphery of the organ, occasion the most striking deformities. Further distinctions are based upon the relative participation of the connective tissue and the vessels in the hyperplastic processes. A very frequent form of struma is produced by this, that the development of the stroma quite strikingly remains behind that of the follicles. The goître-nodules then have a very soft, almost fluctuating constitution; they are yellowish-gray with a reddish tinge, and cut off from the surrounding parts by a compact layer of connective tissue, a so-called capsule, out of which they can be more or less easily peeled (struma mollis). In other cases, the development of the vessels predominates, especially of the arteries and capillaries, to such an extent, that the term struma aneurismatica is justifiable, which is derived from Philipp von Walther. The arteries are dilated, tortuous, and thickened up to the smallest ramifications; the tumor pulsates, and the increased temperature also tells of the enormous amount of blood which flows through the gland in a given time. A third modification of hypertrophic struma is caused by this, that the connective tissue participates in the hyperplasia in more than a sufficient manner. Broad, white connective tissue septa, then penetrate the entire organ; in the interior of the nodules are established depots of compact fibrous tissue, which expand peripherally, and smother the follicular new formation. Here and there, nodules and septa come into contact, finally the connective tissue prevails so very much, that we begin to overlook the hyperplasia of the follicular structures, which nevertheless was primary (struma fibrosa, fibrous goître).

§ 621. When thus, already in the ascending series of development of struma hyperplastica, we can prove a certain multiplicity of the anatomical picture, this will be yet considerably increased when we consider their later history. Here, in the first place, we hit upon the

gelatinous goître (struma gelatinosa or colloides). It is known that the unenlarged—I do not say the normal—thyroid gland contains certain amounts of colloid substance. We can occasionally press out from the cut surface amber-yellow, translucent globules, of compact elastic consistence, or also of more fluid constitution, and easily convince ourselves that these globules are derived from the interior of the follicles. Whether they come there by secretion on the part of the walls, or whether they arise by a chemical metamorphosis of that albuminate which is contained in the follicular fluid, has indeed not yet been definitively decided, yet the beautiful discussions thereupon by Virchow which we read, may move many a one to agree more with the latter acceptation. Now the gelatinous formation spoken of, is complicated with very peculiar readiness with the hyperplastic enlargement of the follicles, and thus results that well-known form of goître which is characterized by the uniform, often colossal, enlargement of the whole gland. The appearance of the numberless alveoli, filled with a yellowish, viscid jelly, the peculiarly tense, doughy consistence, are very characteristic.

Of course the more abundant the gelatinous masses become, so much the more will the pressure exerted from alveolus to alveolus bring about an atrophy of the connective tissue septa, and thus the confluence of the follicles, of the lobules and lobes into larger common cavities. In these, however, the jelly more and more liquefies; it finally becomes as thin as an ordinary albuminous solution, and is also not chemically to be distinguished from such a one. The whole has become a cyst, and the number and size of the cysts which the struma contains are now directed according to the number and size of the glandular sections, which have entered upon the metamorphosis just described. There are goîtres which are altogether composed of larger and smaller cysts (struma cystica). At this stage, however, the change does not long continue. What originally was only a softening cyst becomes a secreting cyst, and by this a very vigorous impulse is given to further enlargement. Blood-serum, even blood is deposited in the interior of the cysts in considerable quantity; individuals among them attain a colossal extent (giant goître). Upon the other hand the increased interior pressure may lead to further resorption of the partition walls in the interior, the cystic goître becomes unilocular; and the final result, perhaps, is, instead of the thyroid gland, a simple, moderately large, but very thick-walled cyst.

§ 622. We finally have yet to mention the struma ossea and struma amyloides. Each of these represents a peculiar kind of retrogressive metamorphosis, which in the one case the glandular parenchyma and the vessels experience; in the other, the connective tissue stroma. Commonly they are only divisions of larger strumas, which calcify or are impregnated by the amyloid substance. Yet the petrifaction may go so far probably, that, after maceration, a completely connected

skeleton, a cystic wall, as a bony drum and the like, remains behind. Upon the other hand the amyloid infiltration also of single goître nodules may attain so high a degree that a perfectly wax-like constitution results (§ 48), and the chemist finds the opportunity just here of obtaining very large quantities of amyloid substance as chemically pure as possible.

2. Cancer.

§ 623. What in its time was called scirrhus thyroideæ, is nothing but the above-described connective tissue induration of the hyperplastic struma. There accordingly remains only the carcinoma molle as an occasionally occurring affection of the thyroid gland. This idiopathically forms tolerably extensive tumors, which have the tendency to burst towards the œsophagus or the trachea. Metastatic carcinomas are tolerably rare; we have no histological data in reference either to the one or the other form.

XV. ANOMALIES OF THE SUPRARENAL CAPSULES.

§ 624. That the suprarenal capsules also are subject to a series of pathological changes, has only been more intimately known and appreciated in medical circles for a few years back. In the year 1855 Thomas Addison made the assertion that a certain constitutional affection, consisting of anæmia, beside a debility proceeding to fatal marasmus, and a continually increasing dirty brownish, not quite uniform, but in spots a darker coloring of the outer skin, was produced by the complete disorganization of the suprarenal capsules. This assertion has in the meantime been pretty much confirmed in its entire extent, especially, however, has the coloring of the skin, the melasma suprarenale, acquired an unquestioned standing in science. Upon the details of the causal connection, the greatest disagreement certainly prevails among authors; Virchow, who especially occupied himself with the question in Germany, after mature reflection has arrived at the opinion that the destruction of the suprarenal capsules is to be taken as an injury to the nervous apparatus partly of the suprarenal capsules themselves, partly of the suprarenal region (for example, of the solar plexus), and that the remaining symptoms are to be explained from this basis through the instrumentality of the nervous system. According to this, the nature and the manner in which the suprarenal capsules are destroyed, would be a matter of indifference. Still conformable to experience it is certain that in the great majority of cases *tuberculosis* of the suprarenal capsules causes Addison's disease.

§ 625. Hence let us in the first place continue with this by far most frequent affection of the organ. It begins with the irruption of gray nodules, over the size of a millet-seed, in the medullary substance. The particulars concerning their seat, whether in the sheaths of vessels, in those of the nerves or in the lymph-vessels, are not known. The nodules fuse together, and thus form ever larger tumors, soon becoming caseous, which finally may grow to the size of a pigeon's egg and over. Herein a small-celled infiltration of the connective tissue septa, which I regard as inflammatory, plays a chief rôle. The medulla and cortex in like manner perish in the degeneration. Only the capsule bids defiance to the destruction, nay, it is converted by reactive inflammatory hyperplasia into a juicy induration, from one-half to two lines thick, which

bounds the caseous depot externally. I have several times seen it in connection with the adjacent surface of the liver, the pancreas, &c., and believe that just this continuation of the inflammation to the surroundings of the suprarenal capsules may produce the disturbances of the nervous plexuses so emphasized by Virchow.

§ 626. Upon the soft *carcinoma* of the suprarenal capsules, which occurs even as a primary disease, mostly it is true with simultaneous carcinoma of the sexual glands, no histological statements have as yet been made. What was formerly called sarcoma has recently been described by Virchow as *glioma.* Virchow is convinced that the medullary substance of the suprarenal capsules, which is so rich in nerve-fibres and ganglion-cells, is also not wanting in the nervous cement substance, the neuroglia, and hence regards certain not very rarely occurring, roundish, pale reddish, compact tumors of the medullary substance, of the size of a pea to a cherry, as partial hyperplasias of this neuroglia, consequently as glioma (compare Tumors of the Nervous System). To be well distinguished from this is another more uniform hyperplasia of the entire glandular substance, which Virchow has recently described as *struma suprarenalis.* This term is well chosen because of the great resemblance which the cortex of the suprarenal capsules has in structure to the thyroid gland. We here likewise have closed follicles which are filled with cells of an epithelial kind; the follicles in the outermost part of the cortex are roundish; farther inwards elongated, tubular; at the limit towards the medulla they are very small, and their follicular cells filled with black, and brown granular pigment (intermediate pigment layer, Virchow). Struma suprarenalis is produced by a proliferation of the follicular cells, and accordingly as this process extends over the whole gland or remains confined to individual parts, we have knotted or more uniform intumescences of the organ. The nodules may become as large as a walnut, and then show very much elongated and ramified follicles twisted to and fro, with fatty breaking down of the cell-protoplasm. Where the interstitial tissue participates more actively in the hyperplasia there arise compact, sclerotic places. We see the analogy with struma thyroideæ is certainly very profound; we may give in our adhesion to the analogy, as brought forward by Virchow, with full conviction.

XVI. ANOMALIES OF THE OSSEOUS SYSTEM.

§ 627. As a principal result of the medical investigations of this period, we have correctly laid down the axiom of the identity of pathological phenomena with the phenomena of physiological life. The relation of the various individual sciences to this axiom was, and naturally is, somewhat different. While it is comparatively easy for a teacher of clinical medicine to make plausible to his students, that fever is only a quantitative excess of normal heat, that the most tormenting dyspnœa is produced by want of oxygen, and an excess of carbonic acid, quite like the normal need of respiration, on the other hand pathological anatomy has a much more difficult position, although it only wishes to draw a parallel with some probability, for example, between the pathological and physiological new formations (see §§ 60, 67). Under these circumstances it is peculiarly pleasant to the pathological anatomist that, in the diseases of the osseous system, he has at least *one* paradigm which is fitted to make this conformity evident also to an unpracticed eye and to a reluctant mind.

He to whom that interesting series of histological phenomena is familiar which accompanies the normal growth of the bony system, he who is exactly informed of what is known concerning the formation of bone from periosteum, and of the transformation of cartilage into bone, he knows also the foundation of the pathological histology of the system, and will with ease find his way in the slighter qualitative deviations which yet exist as accessories. A large number of diseases of bone depend upon a simple plus or minus of the normal growth, a far greater depend upon the excessive prominence of individual anatomical forces which play a subordinate rôle in normal growth; everywhere, however, we can demonstrate at least an analogy of the pathological phenomenon with some normal one. We will take these relations into account as much as possible in our subdivisions.

1. Diseases of Development.

§ 628. Whether it is correct to trace back the general over, or under development of the whole body, the so-called *dwarf* and *giant growth*,

so exclusively as we are wont to do, to a more or less intense growth of the skeleton, I will not investigate here, and as a *negative* answer to this question will only adduce the one circumstance, that at least the excessive growth of single members, which is here and there observed, does not alone proceed from the ossifying skeleton of the part concerned; thus, if we remove the soft parts of such an extremity, compare their weight with the weight of the bones which remained behind in development, and proceed likewise with the other unchanged extremities, it is shown that the great total weight of the diseased extremity is by no means exclusively to be placed to the account of the bones, but that the muscles, skin, vessels, &c., have increased in an equal measure.

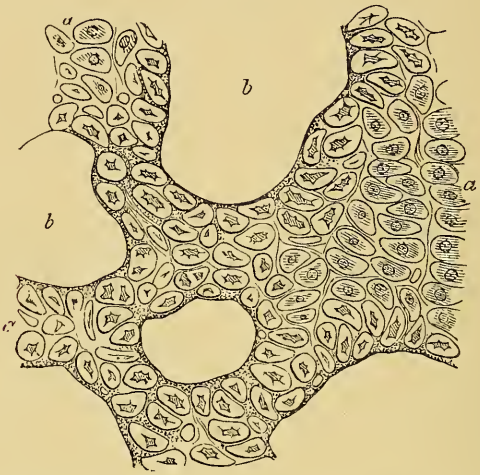
§ 629. An actual disturbance of normal growth takes place in the *premature ossification of the sutures and the synchondroses.* By the early ossification of the longitudinal sutures of the skull, those long-extended forms of the skull, with narrow forehead, arise, which we term dolichocephalic; by the pre-eminently rapid ossification of the coronary and lambdoid sutures the brachycephalic round skulls are produced. Prognathic formation of the face results from the accelerated ossification of the cartilaginous joint which exists in the foundation between the bodies of the occipital and sphenoid bones (in the os tribasilare, Virchow). Premature ossification in the synchondroses of the pelvis (synchondrosis sacro-iliaca dextra, sinistra; symphysis pubis), cause "permanency of the pelvic curves concerned, at a youthful standpoint," and consequently obliquely and transversely contracted pelves. All these things may under proper circumstances have, or occasionally obtain, a pathological significance, yet they still fall so very much within the bounds of health that among others the forms of skull and face of the diverse races of men show varieties quite similar to those above touched upon.

§ 630. *Rachitis*, English disease. The numerous anomalous conditions of the osseous system, that large number of curvatures and swellings of the bones, which we see arise in the English disease, have their ultimate ground in a morbid acceleration of the processes, which *introduce and prepare* the conversion of cartilage into bone, as also the production of bone from periosteum. The proper formation of bone ensues at slower paces, and hence it comes, that the substance accumulates in disproportional amount, which in normal ossification being scarcely produced, already advances again to conversion into bony tissue, and hence is of but very short, temporary continuance. It is this transition substance, which occasions the mentioned tumefactions, and furthermore, gives occasion to fractures and curvatures. Still I will not anticipate.

§ 631. In the *formation of bone from the cartilaginous foundation,*

as is known, the cartilage, immediately before the advancing bony boundaries, slowly fuses, layer by layer, into a relatively soft material, consisting of cells; the cartilage-cells divide, and as a rule, the division is twice repeated, namely, with the daughter and granddaughter cells,

Fig. 172.



From the proliferating layer of a rachitic cartilage of the epiphysis. *a.* Several columns of cells each of which has been produced from one cartilage-cell. *b.* Direct ossification of the cartilage. See § 631. 1–500.

so that in the place of one original cartilage-cell there are present on an average eight, which until further change are inclosed by a common cavity. This cavity is the former cartilage-cavity. The transparent, tolerably thick membrane, which lines it, is the former cartilage-capsule. Both are distended, dilated, enlarged corresponding to the multiplication of the occupants, and corresponding to a peculiar puffing up, which each of the newly formed cells of the third generation experiences. The hyaline basis-substance of the old cartilage is consumed excepting a small remainder, so that the large ovoid capsules of the adjacent cell-groups come immediately into contact. A single, at most, double, layer of such cell-capsules forms the normal zone of growth of the cartilage.

Just these first processes, so to say the preparations for the osseous growth, experience in rachitis a decided disturbance. It must probably be accepted, that in rachitis the chemical (?) irritant, which induces the cartilage-cells to division, is present in greater quantity, and consequently causes a more frequent division of the single cells, as also a more rapid engagement of ever new cell-layers in the proliferative process. This assumption corresponds in a high degree with what is found anatomically. Ten to twenty, and more layers of cartilage-cells have

entered simultaneously upon the proliferating process. The granddaughter cells also have again divided, and thus cell-groups of thirty to forty elements have arisen, which are placed in long-drawn columns, somewhat bent and compressed here and there by the mutual flattening, vertically, towards the surface of the bone. (Fig. 172, *a*.) While upon normal bone we scarcely observe the proliferating zone of the cartilage with the naked eye, as but an exceedingly narrow, reddish-gray stripe, upon the rachitic bones (Fig. 173) it pushes as a broad, translucent gray, and very soft cushion, *b*, between the cartilage, *a*, upon the one side, and the completed osseous structure, *d*, upon the other.

Fig. 173.

Section through the upper half of a rachitic humerus, moderately magnified. *a*. Hyaline cartilage of epiphysis. *b*. Its proliferating layer pervaded by medullary spaces. At *c*. A large piece of cartilage actually ossified. (See Fig. 174.) *d*. Limits of the bone. *e*. The medullary cavity. *f*. The compact substance. *g*. Proliferating layer of the periosteum.

§ 632. That which takes place here in the cartilage, is repeated in a perfectly analogous manner in the periosteum. The young, vascular germinal tissue, which is produced by the periosteum at its surface lying towards the bone, under normal circumstances only presents a thin stratum, which is scarcely perceptible to the unaided eye. The rapidity with which, though just produced, it is transformed into bone, does not permit a larger accumulation to take place. It is otherwise in rachitis. Under the influence of this morbid process, this transition substance often accumulates in very great layers of a line in height. Older authors speak of a hemorrhagic exudation between the periosteum and the bone, and because of its color compare the deposit with the pulp of the spleen. More accurately observed, meanwhile, there is here nowhere found an extravasation, but the great abundance of thin-walled and wide capillaries occasions the pronounced coloring of the young connective tissue. (Fig. 173, *g*.) The deposit, as a rule, is drawn in the form of broad, flat, bed-like elevations over the surface of the bone. Upon the flat bones of the cranium these are wont to be sharply circumscribed, which is not the case to such an extent at the extremities.

§ 633. If we now ask, how the bone itself behaves in presence of these luxuriant products of the cartilage and periosteum, does it make use, so to say, of the opportunity presenting itself to more rapid growth, and does it grow more rapidly or not? That, in general, it does not do this, is already proved by the fact of the "accumulation of the

transition tissue." But in face of the peculiar histological phenomena, which proceed in just those accumulated transition tissues, we might at least get the idea, that nature was fully conscious of her duties towards the bone, that she attempts to accomplish the difficult task at least by her ossifying powers, and although with her limited stock of lime-salts, limited vascular and medullary space formation, she is not able to furnish an actually solid bone, yet she distributes these to the best advantage over the entire proliferating zone, as though she would remind us, how far already the bone actually should reach, if all had proceeded correctly.

§ 634. Setting teleology aside, the fact remains, that the process of ossification is not entirely absent within the proliferating layers, but that it is at least indicated in its individual anatomical energies. If, first of all, we continue with *cartilage*, there the *occurrence of well-developed medullary spaces* within the layer *b* (Fig. 173) is to be registered in the first place. We know what an important part the formation of medullary spaces plays in the ossification of cartilage. Those roundish groups of proliferated cartilage-cells are transformed by a further, and, as it appears, very suddenly occurring division, each into an equally large depot of very much smaller, but very much more numerous cells (medullary cells); by the partial melting down of the basis-substance, this depot enters into connection with the immediately contiguous medullary spaces of the completed bone; almost simultaneously ensues the formation of a capillary loop for the annexed territory, and a new medullary space with all its attributes is complete. In order to make this transforming process, the only one of its kind, more comprehensible, I cannot resist defining it also as a growing-in of the medulla of the bone into the cartilage. The medullary tissue perfectly resembles the tissue of granulation. Therefore, like as the granulations shoot up from the surface of a healing wound, thus here, vascular proliferations of the medullary tissue rise up from the surface of the bone, out of the open standing medullary spaces, which vascular proliferations project with their clubbed ends into the cartilaginous tissue. If we were not accustomed to keep in view, in this case, more the production of the spaces for the young tissue, so to say the negative picture of the whole phenomenon, we might just as well call the *medullary spaces*, *medullary papillæ*, and with this new conception we would, perhaps, be more fortunate in the interpretation of individual phenomena.

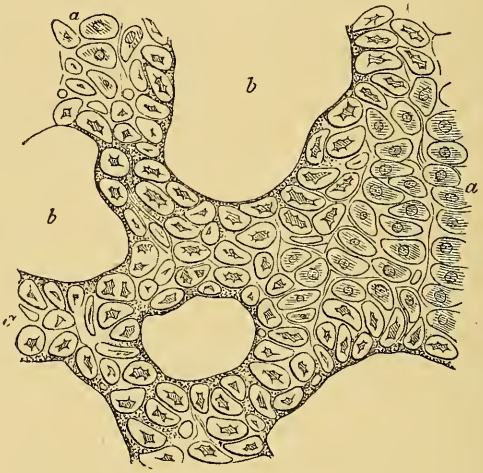
In the normal osseous growth the formation of medullary spaces and the advance of the medulla of the bone into the cartilage take place simultaneously and uniformly upon the whole borders of ossification. Between the adjacent medullary spaces the cartilage is completely dissolved, the capillary loops anastomose, and at the limits of the territory of nutrition (§ 52) begins the development of the first osseous trabeculæ, sclerosis of the basis-substance, transformation of the medullary cells into bone-corpuscles, calcification, &c. A single glance at Fig. 173 shows us that

we cannot speak of a uniform advance of this sort, of the formation of medullary spaces in rachitis. We rather see that, while as a whole the medullary spaces remain in rank and file (at *d*), individuals of them have extended their processes far into the proliferated cartilage, nay, have advanced up to the border of the unproliferated cartilage (*a*). If we investigate the thing upon a horizontal section (Fig. 17), carried through the cartilage (perhaps at *b*), we observe that, notwithstanding this, these sporadic medullary spaces are not distributed without rule, but that rather each medullary space forms the central point of a larger territory of cartilage, which is assigned to it with reference to its nutrition. Consequently, it does not appear improbable to us, and it is indeed in unison also with the general laws of nutrition and vascularization, that this entire preliminary formation of medullary spaces has the significance of a vascularization, a nutritive arrangement for the proliferated as for the non-proliferated part of the cartilage, which latter is elevated disproportionately far from its nutritive soil, by the interposition of so mighty a layer of young non-vascular tissue.

Beside the formation of medullary spaces, a number of calcified places within the proliferated cartilage reminds us of the processes of normal ossification. In the latter the *calcification* shows itself, upon the one hand, as a provisional incrustation of the cartilage at the osseous limits, upon the other, as a definitive impregnation of the basis-substance of the permanent bone. In reference to the provisional calcification of cartilage, and the peculiar disturbance which it experiences in rickets, I may only refer to § 54, where I have made use of the case in order to demonstrate thereupon the principles of calcification in general. By far the most of the rough, white disseminations, grating under the knife, which the rickety proliferated cartilage contains, are provisional calcified cartilage. Beside these, however, there occurs also a definitive deposition of lime-salts, and indeed in the sense of normal bone-formation. Kölliker was the first who observed upon rachitic cartilage the direct transition from cartilage to bone (§ 54). The annexed illustration (Fig. 174) is intended to give the reader an idea of this highly remarkable cartilaginous bone. As we see, it consists of medullary spaces, *b*, *b*, which are separated by broad bridges of a tissue, which according to the stellate form of its cells, and according to the completed lime-impregnation of the basis-substance, inclusive of the cell-capsules, is no longer to be regarded as calcified cartilage, but as osseous tissue. It is true we cannot doubt that, excepting the impregnation with lime-salts, only a very moderate change of position of the single cells has led to the transformation of the proliferated cartilage into the texture in question. At *a*, *a*, the latter passes over uninterruptedly into the above-mentioned columns of cartilage-cells, and the persistence of a peculiar zone for the capsule of the cell, spite of the calcification,

would be something unprecedented for the normal bone. But upon the other hand, the behavior which nature itself retains towards the cartilaginous bone, proves that she wishes it regarded as the equivalent of genuine bone. For as the illustration, Fig. 173, proves, in the gradual advance of the line of ossification, *d*, *d*, the cartilaginous bone is quite simply included, and taken up into the system of genuine bone. The homogeneous, limy constitution, and the great abundance of medullary spaces, make the sharply-circumscribed portion, *c*, of the proliferated cartilage known to us as cartilaginous bone. From this portion, also, our section, Fig. 174, was taken. If, however, we glance at the nearest

Fig. 174.



Same as Fig. 172. 1-500.

contiguous region of the diaphysis complete up to that point, we observe a smaller piece constituted quite like this, which is out of continuity with the former, and already quite surrounded with regular medullary spaces. Virchow has expressed the conjecture, that pieces of cartilaginous bone of this kind remaining, may probably in after years condition a predisposition to enchondromatous degeneration.

§ 635. The "incomplete ossification of the transition tissue" on the part of the *periosteum* assumes a much simpler aspect. All complications which the non-vascularity of cartilage brings with it, the formation of medullary spaces, the provisional calcification, &c., are done away with; the question only is, how much of genuine bony tissue is produced from the young vascular connective tissue. This amount, which may probably correspond to the normal amount, is distributed in rachitis over a very much larger space than in normal circumstances; hence the individual osseous trabeculæ are very thin, and the total result is the transformation of the subperiosteal "exudation,"

described in § 632, into an exceedingly loose, vascular osteophyte, which lies upon the bone in an undue thickness, and at the same time remains an undue time in the condition of osteophyte, while the apposition of compact bony substance entirely ceases for the time being.

§ 636. Herewith we have throughout accompanied the rachitic process up to the acme of the disturbances. Let us now ask, in what manner the latter are fitted to bring about the various deformities of the rachitic skeleton. In this connection the circumstance, first of all, comes into consideration, that the broad layers of proliferated cartilaginous tissue, which push in between the epiphyses and the diaphyses of long bones, give way to the mechanical actions to which the skeleton is at all places exposed, swell out laterally, and form *roundish rolls surrounding the bone.*

The name "Zwiewuchs" (double growth), which rachitis bears in some regions of Germany, is derived from this, that the tumefactions of both sides of the epiphysis cartilage belonging to one joint were rated as two joints (articuli duplicati), placed immediately side by side. The swelling of the collective costal cartilages, at their points of contact with the bone, is termed "rachitic garland." Naturally, displacements of the bone at the cartilage are not excluded. The well-known chicken-breast (pectus gallinaceum) arises from this, that the collective sternal extremities of the ossifying bodies of the ribs are drawn inwards by the movements of respiration, while the sternum, together with the costal cartilages, is pressed out of the level of the thoracic framework. An almost right angle curvature of the costal cartilages is necessary for this, which only becomes possible by the greater capability of displacement inwards of the proliferated cartilage. The deformities of the pelvis, which are caused by a too great mobility of the cartilages of the synchondroses sacro-iliacæ, are yet more important to the physician; namely, as the sacrum under the whole burden of the trunk, head, and the upper extremities, is naturally pressed downwards, and is not sufficiently hindered in the movement by the yielding synchondroses sacro-iliacæ, the promontory projects forwards to a greater or less extent into the pelvic strait, and narrows it from above and behind in such manner, that in the subsequent fixing of the abnormal condition a kidney-shaped configuration of it results.

The disturbance of the periosteal growth is principally answerable for the manifold curvatures and fractures which the bones of the extremities experience. We might indeed ask, whether then the superposition of a new formation upon the surface of the bone must not rather contribute to give the bone a greater firmness? This is in itself unquestionable; we must, however, reflect that the growth of the bone in thickness, the continual apposition of compact substance at the periphery, is constantly and everywhere accompanied by a resorption of the compact substance at the inner surface towards the medullary

cavity, a resorption which keeps equal pace with that apposition, and which also does not stand still during the rachitic process. If now, as we saw, even this rachitis interrupts the peripheral apposition of compact substance, the necessary consequence is a decrease of thickness of the bony shell, which cannot be overcome in its consequences even by the thickest osteophytic layers. Hence the bones bend, or, what is likewise very frequent, they break, like a cracked roll of paper, at one side, while the other side extends over the place of fracture, and the medulla at the centre is crushed (infractio). The most typical in this connection is the behavior of the leg and thigh, which constantly curve outwards under the burden of the body, while at the same time the tibia moves inwards at its lower epiphysis (bow-leg, genu varum).

§ 637. The effects of rachitis upon the growth of the occipital bone deserve an especial consideration. The occipital bone, more than all the other protecting bones of the cranium, is exposed to mechanical influences. The pressure from within of the superimposed brain meets together just at the occiput with the counter pressure of anything supporting the head of the patient, as a pillow or the like. If it now comes to a luxuriant proliferation upon the part of the periosteum, the young tissue, but little capable of resistance, must perish atrophically under this pressure from opposing sides, ere yet it can advance to ossification; a thickening of the occipital bone by apposition on the part of the periosteum is hence not accomplished, while upon the other hand the resorption of the vitreous table, connected with the growth of the brain, makes the usual progress. The consequence is, that the shell of the occipital bone here and there gets thin places, finally actually holes, which are only closed by the dura mater and the periosteum (soft occiput, craniotabes).

§ 638. In what degree, in individual cases, the changes of the skeleton described eventuate, depends partly upon the intensity, partly upon the continuance of the rachitic process. If this becomes extinct, the layers formed in excess subsequently ossify, and in their stead arises an exceedingly dense, hard, and heavy osseous tissue. The existing curvatures and swellings are fixed thereby, and are maintained so much the longer, as the bones after the cessation of the rachitis are wont to cease in their growth. It is as though the material and the capacity for the regular formation of bone had been exhausted in the tempest of the disease. The individual remains small, at least below the normal medium, and the deformities of the extremities of the chest cavity and the pelvic ring remaining behind, become to him still continually a source for many sufferings and discomforts.

2. Inflammation.

a. *General Remarks.*

§ 639. If we survey the entire province of the disturbances which is embraced by the term "inflammation in the osseous system," we will be disposed just as much to admire the great multiplicity of the morbid processes in the clinical sense, as the great monotony of them in the sense of the pathological anatomists. The majority of all osseous inflammations run their course after the manner of a partial, acute growth; the most striking deformities of the exterior outlines, the most profound changes in the quality of the bone, are produced by the same anatomical means which are active in the physiological enlargement, namely, with the formation of bone by the periosteum and cartilage, with the formation of medullary spaces and their enlargement in the interior of the bone. In § 627 I already made a remark alluding to this. Here is the place to test its bearings. The only, it is true, very important and pregnant deviation from the physiological type, is the production of pus. If suppuration ensues, the whole course of the inflammatory disturbance becomes far more complicated; healing can only be accomplished by indirect ways, which, because of the peculiar constitution of the domain, I mean the osseous structure, leads much less certainly to the goal than does the second intention of the soft parts.

§ 640. If in the next place we consider the histological apparatus of the *non-suppurative* inflammations, we first of all touch upon a *bone-forming periostitis* (periostitis ossificans). The inflammation of the periosteum discovers itself in an exalted activity of its physiological function. According to the known scheme of the normal periosteal growth one layer of bone is superimposed after another; we have inflammatory hyperostoses, periostoses, and exostoses (see § 673). Here and there, under normal circumstances, a transitory stage of development is maintained an undue length of time; thus, in the healing of fractures, we will meet with an often very considerable accumulation of osteoid cartilage, under the name of callus; the requisite transformation of the spongy osteophyte into compact substance is also occasionally delayed for a very long time (spina ventosa), yet otherwise everything proceeds in its usual course as far as concerns the bone itself. It is somewhat different with the surroundings of the bone. Virchow's careful studies have established the fact that, in connection with well-pronounced cases of ossifying periostitis, bone may also form outside of the periosteum (parostosis). As by a local contagion, the disposition and the capacity "to form bone" is continued to the connective tissue, which stands in continuous connection with the periosteum, to the intermuscular connective tissue, to the sheaths of the nerves and vessels.

The objection might be made that we were dealing with exostoses considerably pushed forward, but still always clothed by the periosteum; but, although the periosteum in such cases passes over uninterruptedly into the parostotic bone, yet, by carefully following its contours from the healthy parts, we can arrive at the sure conviction that the parostotic bone is actually situated beyond the last lamella of the periosteum.

I cannot say, from my own observations, in what manner the parosteal connective tissue forms bone, yet the conjecture is admissible that herein exactly the same phenomena are repeated, as they are known from the periosteal growth.

§ 641. The second factor of non-suppurative inflammation of bone is the *sclerosing ostitis* (ostitis ossificans), an excess of the ossifying processes, which the growth in length of the long bones condition; at the same time, however, shut off their medullary cavity towards the cartilaginous epiphysis—that is, towards the articular cartilage.

We know that, under normal circumstances, a narrow-meshed, spongy tissue only is formed at this place; the sclerosing ostitis yields a compact substance, which is even not infrequently characterized by very narrow Haversian canals, consequently presents a very dense, ivory constitution (eburneatio ossium). The histological process is entirely a further continuation of the deposition of new lamellæ of bone at the inner surface of the medullary spaces; by this the gradual diminution of the latter is caused, excepting the lumen of the capillaries.

§ 642. The third very important factor is the *rarefying ostitis* (O. carnosa or fungosa); a process which has exactly the opposite effects of the two preceding, and which, therefore, finds its analogy in that centrifugal widening of the medullary cavity which follows upon the footsteps of the periosteal growth as well as the growth of bone from the epiphysis, and thereby maintains the thickness of the compact part of the bone and the spongy epiphysis constant, at a determined measure, corresponding to the size and age of the individual. Inflammatory irritants may partially accelerate this process, destroy this compact substance, and make the bone to a greater or less extent soft, fragile, flesh-like.

§ 643. Touching the histological process, the physiological rarefaction is indeed generally the model of the pathological; yet small peculiarities are not to be overlooked, which occur as well upon the part of the melting-down osseous tissue as upon the part of the enlarging medulla, and find their interpretation essentially in the greater rapidity of the pathological process. Under that head belong—1, *certain peculiar changes of form which the osseous tissue presents immediately before its resorption.* While under normal circumstances the border of resorption of the disappearing osseous tissue, for example, the contour of a medullary cavity, forms a smooth, uninterrupted line, in rarefying ostitis the

so-called lacunæ of Howship arise; *i. e.*, the border of resorption is composed of a number of shallow curves or deeper semicircular excisions which are concave towards without, consequently let the portion of the edge of the bone situated between each two of them project as protruding angles (see Fig. 175). A somewhat rarer occurrence is the

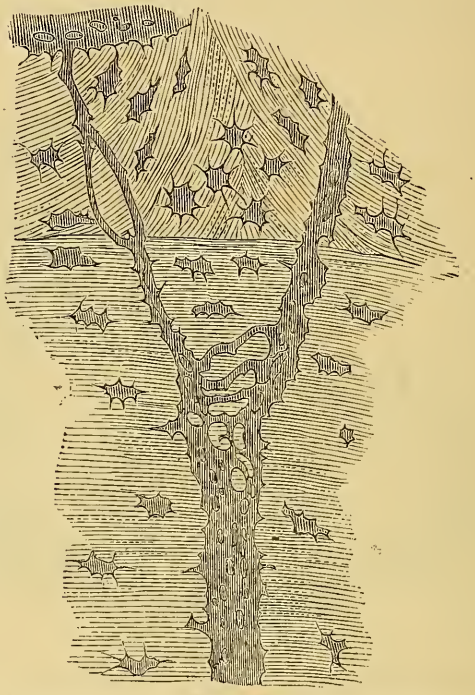
Fig. 175.

Caries fungosa. A fragment of bone with Howship's lacunæ and bone-corpuscles infiltrated with fat. 1–300.

preceding canaliculization of the osseous tissue which Volkmann first described, and, indeed, as "vascularization." Fig. 176 is a repetition of the illustration given by Volkmann. As we see, an osseous trabecula is here broken through transversely by a canaliculus, which begins at one side by a somewhat broader lumen; in the middle of its course, however, divides into two main branches, while a greater number of small side branches expands a rich anastomosing net between the two main branches. The collective canaliculi are provided with serrated contours, that at certain places correspond too distinctly to the known contours of bone-corpuscles, that we could even entertain but the slightest doubt as to the origin of the canaliculi from anastomosing bone-corpuscles. For the remainder, the distance and arrangement of the adjacent unchanged bone-corpuscles also declare that just in the direction which the canaliculus now holds a row of bone-corpuscles has been abolished. The question only is, whether we actually have to do with capillary vessels as Volkmann insists. I doubt it, because I have not succeeded either in filling the canaliculi from the bloodvessels, nor in discovering the attribute of a capillary tube—a nucleated membrane—

in the interior of the canaliculi. To judge according to the refractive conditions, the contents of these tubuli are no other than the contents

Fig. 176.



Rarefying ostitis. Canaliculization of the osseous tissue. After R. Volkmann. 1-500. See text.

of the lacunæ of bone; hence I can only perceive in them a higher unfolding of the nutritive arrangement put into practice in the system of anastomosing osseous lacunæ.

Both the lacunæ of Howship as well as the canaliculization of the osseous substance, are a consequence of the increased supply of fluid nutritive material to the bone. We may and must represent to ourselves, that the normal nutrition of osseous tissue is connected with a conveyance of fluid, which proceeds from bone-corpuscle to bone-corpuscle. If the amount of fluid passing the osseous tissue in a given time increases, the bone-corpuscles made use of and their anastomosing connections dilate, and I have grounds for believing that this dilatation depends upon a direct solution of the intercellular substance in the quantity of fluid itself passing through (see § 656, canaliculization of cartilage). The solution and dilatation naturally ensue sooner in the directions of the strongest current than in all the others, and with this it may then be connected, that upon the one hand, the liquefaction advances variously rapid at the border of resorption itself, that consequently at one point an inlet is formed, while alongside a point re-

mains (Howship's lacunæ), upon the other hand, however, the bridges between adjacent medullary canaliculi are broken through in the most direct and shortest way, which naturally passes transversely through the layers of the lamellæ (canaliculi). I consider it advisable, ere further investigations afford more positive points of support, to continue in this general conception of the thing, and hence, agree neither with Billroth, who traces the production of Howship's lacunæ to the compressing granulations and vascular loops, nor do I consider those correct who would regard the lacunæ once for all as enlarged cavities of bone-corpuscles. Both may be the case under circumstances, but while in the former case, I keep in view, perhaps, the more abundant secretion of nutritive fluid just at the apices of the granulations, at the curves of the capillary vessels, in the other case I consider the cavity of the bone-corpuscles as a preformed reservoir for the same fluid, and refer to this the accelerated solution of the nearest lying basis-substance. A Howship's lacuna may be filled with cells, it may contain a giant cell, and it is my firm conviction, that these elements have proceeded from a pre-existing bone-cell, but also, that these changes could not be thought of without a more abundant afflux of nutritive fluid; in short, in all cases we come back to these latter premises, and are not surprised, if we ever (in osteomalacia) meet with the lacunæ of Howship at that boundary line of the normal and the already decalcified osseous tissue, or if we see that even the dead ivory peg, which was driven into the bone for the cure of pseudarthrosis, presents the same mode of melting down, since we may everywhere regard the far more rapid progress of a fluid dissolving either only the lime-salts, or both the lime-salts and the osseous cartilage, as the cause of the appearance.

§ 644. A second series of peculiarities, which distinguished the pathological from the physiological rarefaction, is yielded by the behavior of the *medulla.*

According to a very generally received acceptation of Virchow, the condition of the (non-purulent) inflamed medulla is identical with that of the fœtal, or red marrow of bone; by this the imaginable great approximation of what is found pathologically to the physiological model would be given, for we know, that it is just that species of marrow of bone, which first of all arises in the physiological enlargement of the medullary cavity, in order afterwards to be converted, perhaps, into fatty medulla. The histological constitution in itself is likewise quite calculated to support the comparison. Here, as there, we find a small-celled tissue of granulation, which is richly permeated by capillary vessels. But, notwithstanding all this, it appears necessary to me, to place the inflammatory character of the whole metamorphosis more in the foreground. Rarefying ostitis begins, and runs its course from beginning to end, with a very considerable active hyperæmia of the medulla of the bone. To this associates itself a new formation on the part of the medullary

parenchyma, which leads to a direct increase of volume, and indeed, at the expense of the compact substance. The cells of the fatty medulla part with their fat; they divide repeatedly, and just here, the more interior thoroughly heterologous increase of the medulla is palpable.

But the external increase also, the advance of the medullary cylinder towards the osseous tissue, must be considered more from the positive than from the negative side. The surface of the medullary cylinder is beset with fungous granulations, which push forwards in all directions, grow through the bone, elevate the cartilage, and likewise grow through it, in order, finally, having reached the surface, to expand as a fungiform proliferation. This independent, boundless outgrowth of the medulla occurs in a certain opposition to the modest rôle of a stop-gap, to which the medulla is sentenced in the physiological rarefaction, and deserves to be specially characterized as an "inflammatory" phenomenon.

§ 645. *Purulent* forms of inflammation are observed partly at the same points as the non-purulent, partly at those free surfaces which are inclosed by the articular cavities. At the periosteum and medulla, suppuration presents a too luxuriant production of young cell-forms, which in the former case form the inner osteoplastic layer of the periosteum, in the latter, the medullary granulations. The consequence in both cases is a liquefaction of the tissues mentioned, and a more or less abundant accumulation of pus. The pus production at the surface of articular cavities is to be judged of under essentially different points of view. The articular cavity is an inner space, or one for motion in the connective tissue (§ 265 *et seq.*), and as such is closely allied to the serous sacs; upon the other hand, the structure of the synovial membrane, because of its thick stratum of connective tissue and double layer of epithelium, reminds of the relations of mucous membranes. The pathological, especially the inflammatory changes, in so far reflect this hybrid position, as we observe upon the synovial membranes upon the one hand sero-fibrinous exhalations, like as upon serous membranes, upon the other purulent catarrhal secretions, as upon mucous membranes. The serous and sero-fibrinous transudations (hydrarthrus), as also the purely fibrinous exhalations (arthro-meningitis crouposa) present no sort of histological interest. The purulent inflammation of the synovial membrane (arthro-meningitis purulenta) according to the assumption of R. Volkmann, to which I incline, is at least in its first stages an acute purulent catarrh, a blennorrhœa of the joint. After the normal epithelial cells are cast off, the stratum of connective tissue, without the continuity of the surface being disturbed, produces large amounts of pus-corpuscles, which cloud the originally clear contents of the articular cavity and convert it, the longer it continues, the more into a thickish pus, drawing out into threads because mixed with synovia. In the further course a turn for the worse sets in, especially by this, that the articular cartilage is irritated by the stagnating pus, thereby under-

going a kind of decomposition, and is excited to a kind of superficial ulceration, which destroys the cartilage layer by layer, and after this may pass over to the bone itself. In this case the cartilage perishes by a process, which begins with cellular division, and ends with the complete dissolution of the cells, as also of the intercellular substance. If we make a vertical section through the cartilage, we discover the first nuclear and cellular divisions, perhaps, in the tenth to the twelfth cell-layer counting from above. These primarily go the way of simple hyperplasia of cartilage; we see groups of four to ten cells, which yet distinctly bear the character of cartilage-cells, in a common capsule. Further towards the surface, the ordinary pus-corpuscle takes the place of the cartilage-cells, together with very considerable dilatation of the cartilage cavities, and the capsules gradually becoming indistinct. The basis-substance has meanwhile become finely granular, cloudy, towards the surface it more and more disappears, and finally, liquefies in the contents of the articular cavity. Simultaneously with this complete liquefaction of the basis-substance is produced the opening of the most superficial of the cartilage cavities. The pus-corpuscles, which have mostly been converted by retrogressive metamorphoses into a fatty or fatty granular detritus, mingle with the pus in the articular cavity ; a semicircular erosion of the free edge remains behind yet for a time, but with it vanishes the last trace of the cartilaginous structure.

We have no grounds for withholding the name of a genuine ulceration from this kind of destruction. The terms preferred by many authors, "softening of cartilage," or "maceration of cartilage," express but one part of the change and neglect the evidently active participation of the cellular elements. The cartilaginous ulcer appears to the naked eye as a sharp-edged, mostly very shallow deficiency, as a corrosion of the surface which is found by predilection at the points of mutual contact, but gradually extends over the entire articular head, and as has already been mentioned, penetrates into the depth, layer by layer.

§ 646. I said above that the formation of pus introduces a very critical force into the course of changes in inflammations of the osseous system. This depends essentially upon the circumstance that the structure of bones is not favorable to a rapidly occurring expansion. The suppuration, however, like every excessive cell new formation, in the first place requires space, under certain circumstances very much space, and the mechanical force which is developed in the continued division and multiplication of cells, is one so considerable, that against it the integrity and turgidity of vessels cannot maintain themselves if both are to exist side by side in a given but insufficient space, and one not capable of further expansion. In this manner, *i. e.*, by the compression and rupture of vessels, suppuration gives occasion to a series of the most manifold and profound disturbances of nutrition,

which, as far as they affect the osseous tissue, fall entirely into the province of necrosis. The osseous tissue at one time dies in larger, at another in smaller portions; the sequestra, as foreign bodies, require a new process of inflammation and dissolution. This, however, leads, if at all, but very slowly, to its purpose, because the firmly put together osseous substance only allows a very gradual separation of its continuity with the healthy parts. Hence, therefore, the endless course of every inflammation of bone or joint when it has once come to suppuration.

After this general review of the histologically important phenomena which accompany the inflammations of bones, we will attempt to trace their results in *several* pregnant and frequently recurring morbid appearances.

b. *The Individual Forms of Inflammation.*

1. *Traumatic Inflammation.*

§ 647. The office of the osseous system is to afford protection and security to the entire organism against external influences. How many a blow and knock breaks against the bones of the cranium, and of the extremities, which without their interposition would have destroyed or injured the most vitally important organs. But on that account wounds and fractures are also peculiarly frequent in the osseous system, and in respect to the great importance which the restoration of the interrupted connection has, deserve the entire attention of the physician. Does nature share this attention? It almost seems so, when we observe how every injury to bone, in its *property as an inflammatory irritant*, conditions a series of histological processes whose necessary final result is the reunion of the solution of continuity. This may best be demonstrated by several examples. For this I choose a case of fracture of the femur, with longitudinal displacement, such as is presented with peculiar frequency for surgical treatment.

§ 648. Let, therefore, the thigh of a well-nourished adult be obliquely fractured at the middle third. The plane of the fracture runs from within and below, outwards and upwards. The broken end overlaps; the lower end, having glided the distance of an inch upwards, the upper end for the same extent downwards, they are now fixed in this abnormal position by the contraction of the large muscular bellies which surround them on all sides. The medullary cavity is exposed at both broken ends, numerous vessels, among others a larger branch of the nutritive artery, are torn, in consequence of this a recent coagulum fills all spaces which have arisen between the broken surfaces and the adjacent soft parts. The periosteum and medulla are partly crushed, partly displaced and loosened. They answer the severe irritation by an ossifying periostitis and a sclerosing ostitis, setting in at an early period.

§ 649. The ossifying periostitis, in the course of a few weeks, yields a layer of osteoid tissue of 4 to 6 lines thick which is termed callus or callous cartilage (§ 139). This proliferation is greatest immediately at the edges themselves of the fracture, and from here extends two to three inches on every side, gradually passing over to the level of the normal bone. As far as the fragments override each other, and come into contact with their respective periosteum, the periosteal proliferation of both also fuses into a whole, and thereby the principal task of the cure is undoubtedly accomplished; for it is only necessary now that the osteoid tissue be converted into genuine bone to make the very intimate, but for the time being yet soft connection, a very solid and lasting one. This ossification is wont to be completed certainly only after a considerable time (in four or five months). It begins at the periphery, where the inflammatory irritant has had the least intense action, and advances towards the fractured surfaces. The osseous tissue thus produced is primarily very loose and porous; its bone-corpuscles yet resemble the plump cells of the osteoid cartilage; they are large, provided with few and short processes, not infrequently the capsular contours which surround the bone-corpuscles like an area, even remind us of the similarity to cartilage of the basis texture. Only subsequently ensues a deposition by layers of perfectly typical osseous tissue at the inner surface of the medullary spaces; the medullary spaces become constantly smaller, finally the Haversian canals only yet remain, and a compact substance of faultless texture and faultless hardness has taken the place of the spongy callus.

§ 650. The effects of sclerosing ostitis are less striking, nay, if we regard the restitution of a nearly normal bone, as the aim of the healing efforts, it almost appears as though the sclerosing ostitis effected anything else than what is promotive of this end. To the restoration of bone finally belongs also the restoration of a proper medullary cylinder; here it is, however, as though each end of the fracture wished to exclude itself, since on both sides a primarily cartilaginous, afterward an osseous new formation fills up the medullary cavity, which appears to be not to the purpose, at least in fractures without displacement. The filling-up mass in its earlier period of development has been termed interior callus, which is only to be approved of in face of the perfect conformity in the histological relation. The transformation into genuine osseous tissue, finally into compact substance, ensues entirely as we saw it in the outer callus.

§ 651. The state of the seat of fracture is now the following: A considerable, upon the whole, spindle-formed, very firm swelling, to be felt even through the soft parts. Upon cutting in, first of all we touch upon a juicy, here and there already compact, indurated connective tissue, which passes over towards the interior into the periosteum. Then follows the callus, with irregularly tuberous outlines, its ossifica-

tion more or less completed. The callus fills up both the angles pointing inwards, which the lower surface of fracture forms with the upper fragment of the shaft, and the upper surface of fracture with the lower fragment, so that the transition from the upper to the lower portion of the epiphysis is accomplished by a closed S-formed osseous bridge. If we saw through the seat of fracture, at the plane of this S, we distinctly recognize the fractured surfaces of the compact substance, and this condition is maintained yet for a long time. Only after some years a *rarefying ostitis* perforates this double layer of compact substance, which pushes in between the two ends of the interrupted medullary cylinder. The latter is accomplished by this in order to approximate the united bone as much as possible to the normal. To this purpose also the peculiar smoothing-off leads which the seat of fracture experiences when the inflammatory irritation has ceased and the excess of periosteal proliferation, which has given the seat of fracture the above-mentioned irregular contour, has fallen into a secondary resorption.

§ 652. The circumstances naturally prove far simpler, when displacement has either not at all taken place, or when it has been readjusted by surgical skill at the proper time; more difficult when the displacement was combined with a separation of the broken ends. In the latter case, either no union at all takes place (fracture of the patellæ), or a so-called false joint is formed, in that each fragment terminates in itself, and opposes to the other a rounded end, often even clothed with a permanent remainder of osteoid cartilage. Only very insignificant separations do not prevent the accomplishment of a firm union. It was for a long time believed that this was owing to the capacity for organization of the extravasation of blood, which without doubt exists immediately after the fracture between the broken surfaces. By Virchow's studies, however, it has been proven, that just here the parostosis ossificans (§ 640) interferes as an auxiliary, and by the independent new formation of bone from young connective tissue, fills up the gaps which have arisen.

Wounds of bone also close in a perfectly analogous manner to the union of fractures. In both cases a profound disturbance of the healing process is brought about only by this, that larger or smaller fragments of bone become *necrosed*, whether they were broken off in the very beginning, or were placed beyond nutrition only in the course of the inflammation. We will have to mention this case among others in the next section.

2. *Necrosis.*

§ 653. The complete cessation of nutrition within a certain, mostly circumscribed portion of bone, is followed by a series of inflammatory processes in the neighborhood, whose final result is the loosening and

separation of the dead from the living parts. The course of these changes is mostly determined by the particular cause of the necrosis. In traumatic necroses, under certain circumstances, the loosening of the dead portion of bone from the living is already effected (comminuted fracture), but the concealed situation makes a rapid extrusion impossible for the time being. In injuries also, a purulent periostitis is mostly the force bringing about the necrosis, as it is present, as the first and only cause, in by far the most cases of necrosis. The *purulent periostitis* culminates, as has been mentioned, in a collection of pus between the periosteum and the bone. A preformed cavity capable of dilatation does not exist here, but probably the cambium layer of bone (M. Schultze), especially in youthful still growing bones, is so soft, that comparatively slight resistance is offered to its loosening. Only the vessels which pass tolerably numerously from the periosteum to the cortex of the bone, must be ruptured, and it depends upon the intensity of the inflammation, that is upon the quantity of the pus, to what extent this is accomplished. This laceration of the vessels is not incorrectly looked upon as a principal cause of the frequency of peripheral necroses after purulent periostitis. It is in fact very obvious, to designate the direct interruption of the supply of blood to the outer third of the compact substance, which properly belongs to the periosteum, as the cause of the complete cessation of vital processes in just this third. Nevertheless, although necrosis does not follow upon purulent periostitis, by any means in all cases, this must not determine us to reject, without more ado, this so evident etiological relation, but invite us to seek the causes of the exception in peculiar relations, for example, in a substitution, still possible at the right time, of the cortical circulation by the vessels of the medulla. Only the pus itself is to be regarded from the beginning as something excreted from the organic unity, in this sense "dead." Its presence excites a sequestering inflammation as well in the periosteum as in the bone. The periosteum is very soon converted into a pyogenic membrane, which protects and excludes the organism against its own secretory product. In the bone there develops a rarefying ostitis, whose office it is to exclude the organism from this side also, by a layer of granulation-tissue from the dead part. This rarefying ostitis is nourished from the medulla, and reaches as far into the compact substance as its vascular tracks have remained open and in circulation. There are cases where it develops upon the outer surface, where the Haversian canals dilate, and the tissue of granulation springs up in numberless vascular villosities, and unite into a continuous layer, which then connects with the elevated periosteum into an abscess-membrane inclosed all around. More frequently, it is true, the outer layers of the compact substance have been too long deprived of circulation and the exchange of material, that their re-vitalization could be possible by the medulla, and

then our rarefying ostitis appears as a sequestering inflammation, which separates the lamellæ that have perished and ends in pus, which fills the abscess-cavity. The dead bone is called sequestrum, the rarefying ostitis, which separates it, demarcation. The demarcation may occupy months and years. During this time, the suppuration continues uninterruptedly; the elevated periosteum, however, again returns to its ossifying capacity, and forms under the pyogenic surface a layer of new osseous tissue, which in time may attain a very considerable thickness. The bony capsule, called coffin (Todtenlade), which is thus produced, lodges the more or less loosened sequestrum in its interior. The adjacent not elevated periosteum also participates by ossifying periostitis. For a distance of several inches upwards and downwards, osteophytes and exostoses arise in varying form and number. All these phenomena of inflammation, extending to some distance, disappear as soon as the sequestrum is successfully removed. Even the bony capsule diminishes, and by the obliteration of the cavity of the abscess, is again applied to the surface of the bone, the exostoses disappear, and the bone again assumes its normal form.

3. *Caries Simplex.*

§ 654. Above, at § 645, I took the opportunity to describe the relations of cartilage in purulent articular inflammations. We saw at length a genuine cartilaginous ulcer formed, which, penetrating into the depth layer by layer, threatened to destroy the entire thickness of the articular covering. When I broke off my description at this point, I did it because I did not wish to anticipate the description of another process, which is wont to develop from the primary articular suppurations, but which could only be indicated in those general preliminaries. This is simple caries of bones.

There was a time when the conception of caries was very comprehensive. Wherever, by pathological changes a corroded, disorganized condition of bone had been occasioned, the term caries was applied; in this sense we might speak of cancerous, syphilitic caries, we might term the deficiencies of bone caused by aneurisms, carious, &c. At present we confine ourselves more and more to calling two forms of actual ulceration of bone, the one simple, the other fungous caries. Simple caries corresponds to what upon the skin we would call an indolent ulcer. A loss of substance at the surface of a bone, slowly going deeper, upon the whole, however, shallow, upon whose base small amounts of pus, together with breaking-down remains of tissue, are continually separated. The pus, as in general all fluid constituents of the secretion, is produced by the exposed medullary tissue. This, at a certain distance from the surface, is in a hyperæmic hyperplastic condition, which towards the surface gives place to an extraordinarily dense cellular infiltration. The cells fill up all the pores of the osseous

structure completely, they leave no space for blood and bloodvessels; the latter are compressed, and then together with the cells themselves go over into a molecular detritus. The latter not infrequently forms an uninterrupted, most superficial layer, which naturally only obtains support and adheres, because it is penetrated by the trabeculæ of the spongy substance, not yet destroyed and connected net-formed. The interference of the osseous tissue in the inflammatory process has consequently a decidedly injurious influence upon its course. It is the osseous tissue which, upon the one hand by refusing space, makes impossible the free development of a healthy granulation-surface, and lets the cell-formation smother in its own exuberance; upon the other hand, however, by the persistent connection with the healthy bony trabeculæ of the deeper layers, holds fast the breaking-down, putrefactive material, which had better have been separated and cast off long ago, like a slough upon the surface of an ulcer, and thereby impresses upon the entire process the character of an indolent ulceration.

§ 655. As has already been remarked, the articulations are the most common seats of this simple caries. It sets in as soon as the cartilaginous coverings are definitively destroyed, and the bone now projects uncovered into the articular cavity filled with pus and communicating with the air by fistulous passages. Herewith the dependence of the proper destructive process upon the pressure and the friction, which the articular surfaces exert upon each other, is characteristic. Not by an inflammatory sequestration, as in fungous caries, but by mechanical violence, the smallest fragments of the osseous trabeculæ are continually loosened simultaneously with the detritus which envelops them. We find and feel them, like grains of sand, in the thin ichorous pus which the articular cavity secretes. This destruction, to which Volkmann very properly applies the term molecular necrosis, advances, indeed, slowly, but still in the course of time produces very extensive deficiencies upon the condyles, the articular cavity, &c., and therewith considerable shortenings and deformities of limbs. The ulcerating surface is constantly distinguished by its superficial character. It is sharply circumscribed, relatively smooth, and the infiltration extends at the most one-half to one line into the substance of the bone. According to R. Volkmann, who, in his excellent work upon Diseases of Bones, has also had consideration to the histological detail in the most thorough manner, under the zone of the actual inflammation and suppuration, there not infrequently follows even a layer, often of a line in thickness, of abnormally dense osseous tissue. It is as though the bone would protect itself by a sclerosing ostitis against the further progress of the destruction. In truth, the significance of a somewhat less intense inflammation of the tissue, contiguous to the actual inflammatory depot, might be ascribed to the sclerosis.

The non-articular forms of simple caries proceed from circumscribed

purulent periostitis; the most are of a syphilitic kind, and are apt to be complicated with the gumma formation (see below).

4. *Caries fungosa.*

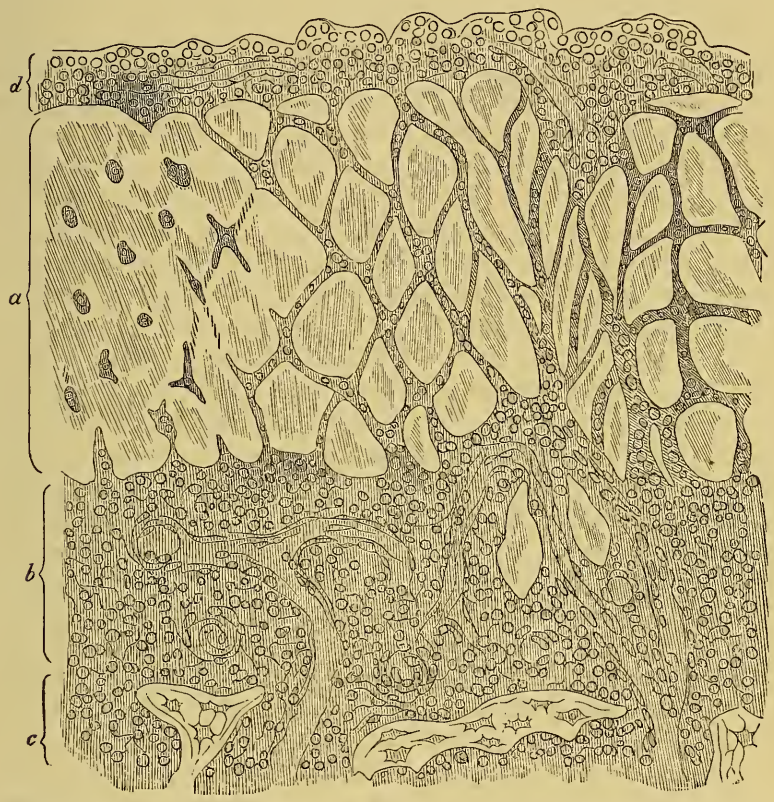
§ 656. While simple caries is essentially an osseous ulceration and nothing else, in fungous caries we have presented to us a much more comprehensive morbid picture, in which ulceration only plays a secondary part, while in the first place the question is about a non-purulent inflammation, which either affects one bone in its totality, or what is more frequent, the epiphyses of contiguous bones meeting together in one joint. Perhaps it is admissible to comprehend caries fungosa in every case as a periarticular osseous inflammation, in so far as the total diseasing is only observed in the short bones of the carpus and tarsus, as also in the vertebral column; these, however, are, as a rule, beset on several sides by joints and semi-joints, and are at the same time too small to be able to represent more than the epiphyses of these joints. Upon the basis of this close relation to the articulations, a relation which, in the course of the process, becomes ever more prominent, caries fungosa is comprehended by most surgeons as chronic articular inflammation. With Volkmann I would regard the articulation only as the local central point of the disturbance, but seek its point of departure, as before said, not at the surface, but in the deeper situated parenchymas of the individual parts of the joint, especially, however of the bones.

A *rarefying ostitis*, as I have delineated it in §§ 642–643 in its histological detail, attacks, for example, simultaneously the lower epiphysis of the femur and the upper epiphysis of the tibia. The hyperæmic medulla enlarges there, the osseous trabeculæ of the spongy substance melt down more and more, while the compact cortical layer indeed becomes likewise thinner, but yet never so thin that it would be incapable of preserving the contours of the epiphysis and give it some external support. The growth of the medulla of the bone is from the beginning directed more towards the cartilage-bearing surface. The medullary spaces and the Haversian canals, which lie close under the cartilage, open, so to say, and the proliferating granulations of the medulla press forward and soon form a continuous cushion, which is intercalated between the under surface of the cartilage and the upper surface of the bone (Fig. 177, *b*). The cartilage accordingly is somewhat elevated from the bone. The interspace, that is the thickness of the cushion of granulation, may amount to near a line.

That an inflammatory movement so considerable in the substratum of the cartilage distributing nourishment must have the greatest influence upon the nutrition of the bone itself, is manifest. The cartilage is better nourished, if we will call it a better nutrition, as it is now permeated by a larger quantity of the fluid constituents of the blood. In

this hypernutrition, however, the cartilage itself is in the worst plight, since it gradually perishes as cartilage, although its cellular elements may still exist in a numerous, but degenerated progeny. The unaided eye, in observing the vertical section, has the impression as though the car-

Fig. 177.



Arthritis fungosa. Vertical section, which reaches from the surface of the joint to the bone. *a*. The last remains of articular cartilage. *b*. Layer of granulations between the bone and cartilage. *c*. Rarefied osseous structure. *d*. Superficial granulations proceeding from the border of synovial membrane. 1-300.

tilage were penetrated by the osseous granulations. The microscope judges somewhat different, since it recognizes an active participation of the cartilage in the work of its own destruction. Fig. 177 is intended for elucidating the process. The zone *a* contains the last remains of a disappearing articular cartilage. To the left we yet see some ordinary cartilage-cells distributed in the customary alternating interspaces in the hyaline basis-substance. Further to the right begins a rarefaction of the basis-substance in the directions which indicate the straight way from one cartilage cavity to another. These evidently are the same routes upon which also physiological nutrition takes place through the intermediary transportation of fluid. By the increased demand upon them a kind of washing-out, softening, and rarefaction sets in,

which finally leads to the formation of a complete network of canals in the cartilage. The points of intersection of this net are determined in their position by the former cartilage-cavities. Shortly before the definitive opening of the canals, the cartilage-cavities enlarge in the directions referred to, and we may very well be convinced that about this time, therefore, yet before the possibility of a migration of mobile cells of the granulation-tissue, the cartilage-cells themselves have multiplied by division. The cells by division are very much smaller than the mother cells; the contents of the cartilage-cavities, even before direct contact with the tissue of granulation, perfectly resembles this in its histological quality, so that when finally the last remains of the separating basis-substance have disappeared, the products of the cartilage-cells simply unite with the existing amount of granulation-tissue. By degrees, then, the cartilage-canals widen more and more at the expense of the basis-substance. Vascular loops arise in them, and seek to accomplish union with the bloodvessels penetrating from above.

§ 657. Thus, while in the manner described the cartilage is penetrated from within outwards, a perfectly similar destruction in the reverse direction from without inwards has been in preparation. I brought forward above purposely the participation also of the non-osseous contiguous parts of the joint in the entire inflammatory processes. Hereby was meant, above all, the synovial membrane, then the subsynovial connective tissue, then the ligaments of the joint, finally all the connective tissue which is in direct continuity with the parts named, up to the skin. A general hyperæmic and hyperplastic condition of the synovial membrane, which needs by no means be connected from the beginning with suppuration (caries sicca), concentrates upon that delicate, commonly somewhat projecting border, with which the synovial membrane embraces the cartilage. From this border a young connective tissue membrane develops, which covers the cartilage from the edge. In the beginning it lies upon the yet whitish translucent cartilage, like a delicate, vascular veil. Gradually, however, the most superficial layers of the cartilage participate in the inflammation, the cells multiply, the capsules open, and the young connective tissue, with its vessels, penetrates everywhere. The dissolution of the cartilaginous structure ensues upon this side precisely as from the opposite. Finally, the proliferations of both sides melt down, and the cartilage is broken through.

As soon as this latter catastrophe has ensued at a sufficient number of points, the proliferation advancing from the bone gets the upper hand, and flat, fungiform vegetations spread out unhindered, which entirely cover over the cartilage and hide it from view, so that the articular surface is in fact already entirely formed of granulation-masses, although considerable remains of cartilage yet exist below it.

§ 658. The process may cease with the preceding phenomena, as de-

scribed. There are cases of fungous articular inflammation—and the cases, thanks to a seasonable diagnosis and the rational treatment of modern surgery, become more frequent from year to year—in which it does not generally proceed to suppuration at all, where the granulations decompose, and the mobility of the joint is retained; for, the granulations of the bone, even when they form the articular surface, do not necessarily secrete larger quantities of pus. They also rather have in their texture a great similarity to the persistent connective tissue formations, especially to the so-called adenoid tissue of the lymph-follicles and of the intestinal mucous membrane, and their limited disposition to secretion from the surface also appears to be connected herewith. (Compare § 105.)

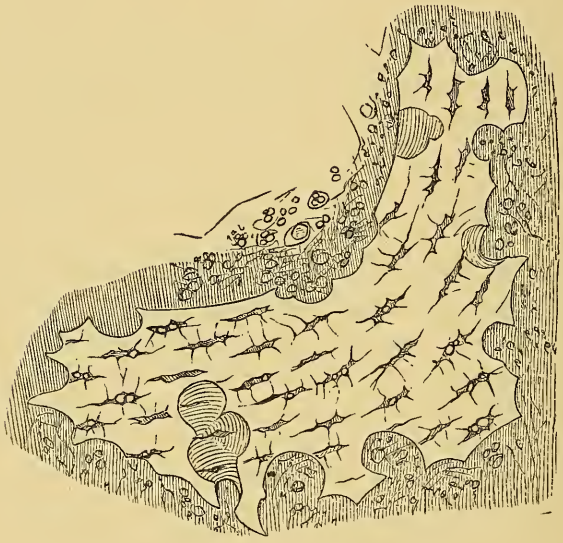
.As will already have become apparent from this, all depends upon, when, how, and where *suppuration* complicates the delineated inflammatory phenomena. In general, it must be acknowledged that in all the parts attacked there exists an extraordinary predisposition to the formation of pus. In the next place, in all stages of the disease, an increased production of pus and its accumulation in the *articular cavity* may happen. The disease may even begin with a purulent articular inflammation, and only in the course of time unfold the true character of the affection in a fungous degeneration of the deeper parts of the joint. In this case the surface of the synovial membrane is covered with spongy granulations, which flow together and form a connected cushion. If the pus bursts externally, these fistulous passages are also soon covered with the caro luxurians fungosa; this happens when abscesses form beside the joint, burst, and then continue for some time as sinuous ulcers. Of the numerous openings which exist in the skin above the diseased joint, as a rule but the smallest minority actually lead into the articular cavity, nay, it may happen that not a single one leads into it, because the articular cavity has not yet been opened.

Moreover, the occurrence of *periarticular abscesses* presupposes a preceding inflammatory infiltration of the total connective tissue surrounding the joint, an inflammatory infiltration which probably always sets in when the affection is of long continuance. It has a peculiarly hyperplastic character. The connective tissue degenerates to a firm, white, indurated mass of relatively large, even of colossal extent, a mass which finally behaves more as an independently growing tumor, which stretches the skin about the joint and shines through it with a white color (tumor albus). Here and there the inflammation increases to a special height, then follows suppuration, and one of the just-mentioned abscesses forms, which opens externally, and is wont to delusively represent articular fistula.

Finally, suppuration also with predilection sets in in the boundaries of the inflamed *bone* itself. This caries proper, as a rule, begins at the surface directed towards the joint, with a purulent breaking down of the

granulations and rapidly extends, penetrating deeper through the entire thickness of the epiphysis. Upon sections we see irregular yellow stripes and spots arising in the midst of the hyperæmic osseous medulla. The more luxuriant the previous proliferation, so much the more rapid and thorough the disorganization. The osseous trabecular work is so rarefied that we can pass through and through it with the probe without any considerable resistance. The secretion which flows from the articular fistulas assumes a more ichorous character, and contains numerous fragments of the osseous trabeculæ, upon which we yet distinctly perceive the traces of the preceding rarefaction (Fig. 178). A peculiar

Fig. 178.



Caries fungosa. Same as Fig. 175.

filling with fat has been repeatedly observed upon the bone-corpuscles of carious bone. Ranvier (Archives de Physiologie Normale et Pathologique, Janvier, 1868, page 69) distinguishes a first and a second period in the death of osseous tissue. In the first period the bone-corpuscles show the phenomena of fatty degeneration; in the second ensues the actual devitalization of individual osseous trabeculæ. Why should we not let this acceptation obtain, although we may not agree with the valued author in this, that he will have the death of the osseous tissue to appear as the central point of the entire disturbance, and the inflammation to appear as something accessory?

It would also lead too far were I to describe here the extensive destructions which fungous caries may occasion in the osseous system. Not infrequently, all the short bones of the carpus or tarsus, including the contiguous bones of the forearm or leg, are diseased, the tumor albus

grown to the size of a man's head, and amputation only remains to the surgeon for saving the life of the person.

§ 659. Touching the cure of the inflammatory process, apart from the above-mentioned arrest at an early period (§ 658), there is some hope in such cases where the articular surfaces participate at an early period in the process, in consequence of which, the articular cavity fills up relatively rapidly with granulations, and we thereupon succeed in moderating the inflammation in general, especially by derivation to the skin. Under proper circumstances we hereby attain a complete obliteration of the articular cavity, since the production of granulation-masses from all sides fuse together and are converted into fibrous connective tissue strands. The mobility of the joint is then of course lost, though in forcible bending we have recently found a means to afterward again set aside this defect also.

§ 660. I can only regard the so-called *scrofulous caries of the vertebral column* as a subdivision of fungous caries. A rarefying ostitis here as there. The spongy substance of the bodies of the vertebræ forms its seat; if we observe this upon sections we see how the net of osseous trabeculæ has here and there roundish gaps more or less running into each other which are filled with a perfectly soft, pale reddish, gelatinous substance. This substance also extends into the adjacent medullary spaces, evidently undergoing a progressive enlargement, and may without more ado be regarded as hyperplastic medullary tissue. Only the limited development of an actual inflammatory hyperæmia is striking. Is this, in general, never found? It rather appears to me as if the early occurrence of an œdematous condition, or of a mucoid softening of the young connective tissue, compressed its bloodvessels, and thereby occasioned anæmia and further nutritive disturbances. These further nutritive disturbances consist in a cheesy metamorphosis, which sets in in the midst of the depot of granulations, and gradually extends further. The "crude tubercles" (§ 33) which make their appearance in this manner within the vertebral column must naturally have imposed far more upon the unassisted eyes of the older authors, than the insignificant palish gray infiltration at their periphery, and thus it has happened that even to the present day the term tuberculous is given to the process. That it may lead to tuberculosis, I mean to constitutional miliary tuberculosis, may not be doubted, yet it does this only in its property as cheesy inflammation, upon the whole infrequently, and only in children.

The further course of the affection justifies the term caries. The cheesy depots, which develop at the anterior perimeter of the vertebral bodies, soften into a pus-like fluid, and this seeks and finds an outlet, since by stripping off the periosteum, and the longitudinal ligaments of the vertebral column, it collects and gravitates downwards at their anterior surface. Of course all the pus which is afterward evacuated

externally at some remote point, for example at Poupart's ligament, is not a product of the vertebral caries, but its principal bulk is yielded by the inflamed membranes, periosteum, tendons, and fasciæ, along which the abscess has made its way outwards.

§ 661. It is striking and appears to speak especially against accepting fungous caries as a primary articular inflammation, that the *intervertebral discs*, which are regarded correctly as incomplete joints, are drawn into the inflammatory process, either not at all or at a comparatively late period. They are generally destroyed by suppuration from without, rarely by this, that the fungous proliferations of the osseous medulla grow into them. It is otherwise with the articulations of the transverse processes and the heads of the ribs, which, if they have generally become inflamed, participate entirely in the manner of ordinary fungous caries. Moreover the suppurations of the joints and semi-joints have a high clinical interest, because they destroy the connections of the vertebræ and make possible those dangerous displacements, of which I will only mention the so-called Pott's curvature, and the almost always fatal luxation of the atlas, that is of the processus dentatus against the spinal cord.

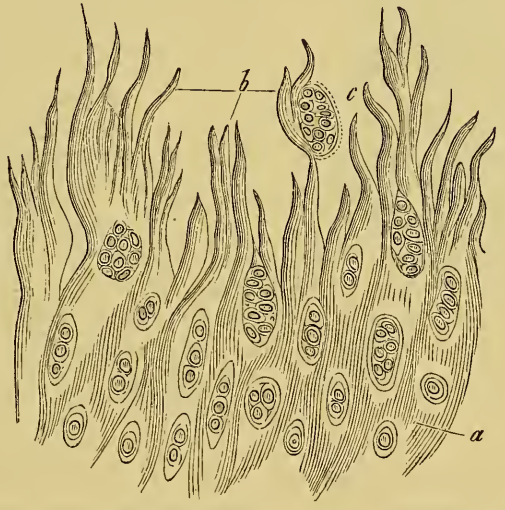
I. APPENDIX.

Arthritis Deformans.

§ 662. What I have designated in the superscription as deforming articular inflammation, is also known by the name of malum senile articulorum, because only older, mostly actually very old persons are wont to suffer with it. The process, according to its nature, is one of those lingering inflammations of the period of involution of the body, which we have also learned to know in atheromatous processes of the inner arterial tunic. The inflammatory irritant, which affects the articular surfaces, is not strong enough to call forth a suppuration, but probably a hyperplastic new formation, in which all the parts forming the joint participate, the articular cartilage and the synovial membrane in equal manner. The synovial membrane sends out partly larger, pediculated adipose and connective tissue polyps, partly more minute dendritic vegetations, villi and fringes, which impart a peculiar roughness to the surface, aptly compared by Volkmann to a sheep's hide. The cartilage falls into a perfectly homologous proliferation, already known to us in rachitis and from the General Part (§ 79). This affects in the first place the outermost, most superficial layers of tissue, and successively penetrates deeper. The cells divide, there arise those groups of eight to twenty larger cartilage-cells, between which, if nothing prevents the continued formation, the remains of basis-substance become ever narrower and narrower, until finally, an exceedingly large-celled, or if you will, large vesicular tissue results, which has only retained

in simultaneously enlarged cartilage capsules a remainder of support-giving basis-substance. We have often already seen (for example, in rachitis), that this texture is not able to withstand the mechanical influences to which the osseous system is exposed. Hence, we are not surprised, if we see it break down and perish at those points of the articular surface, which, in the movements of the joint, are exposed to the most rapid displacement, and in repose to the strongest pressure of the articular condyles acting against each other. The hyperplasia maintains itself only at the edges of the articular cartilage. Here the level of the surface is raised, and indeed, not into a uniform swelling, as we might expect, but in the form of a small tuberous proliferation, *i. e.*, numberless ecchondroses fusing into a wreath. Concerning the detail as well of this proliferation, as of the disorganization at the points of contact (Fig. 179), I beg a reference to the anticipated representa-

Fig. 179.



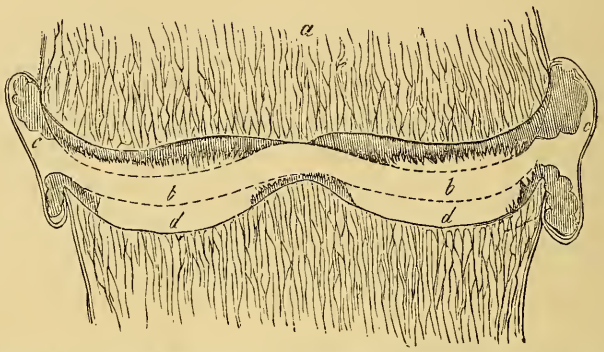
Arthritis deformans. Vertical section through an articular body disintegrating superficially. 1–300.

tions in §§ 79 and 41. The further consequences will occupy us here, to which that peculiar union of formation and destruction, which our process contains, must of necessity lead.

§ 663. The adjoining illustration (Fig. 180) shows us upon an ideal section the coarser effects as well of the peripheral hyperplasia (*c*), as of the interior softening of the cartilage. The dotted lines (*b*, *b*) are intended to denote the normal limits of the latter. The articular head, *a*, is according to this, yet covered with a thin layer of superficially fibrillated cartilage, while upon the opposing articular head the destruction of the cartilage has already penetrated to the bone, and the latter is exposed at two places. A caries of the exposed portion of the articulation is not wont to occur in malum senile. The bone rather shuts out its

medullary spaces by a sclerosing ostitis against the articular cavity, so that to the naked eye it appears to be covered with a smooth, very dense and white plate of bone. In this osseous plate we commonly see the distinct traces of the mechanical violence to which it was exposed.

Fig. 180.



Semi-diagrammatic section of a knee-joint in malum senile. *a*. Lower epiphysis of the femur. *b*. The former boundary line of the cartilage. *c*. Border proliferations. *d*. The smooth surfaces.

The inequalities of the one side engrave corresponding furrows upon the other (friction surfaces). And it does not only conclude with superficial loss of substance. But here we touch upon a new force, which is of the greatest importance for the further course of the affection. The brittle osseous tissue can oppose just as little resistance to the continual grinding and friction, as perhaps, two pieces of pumice-stone which we rub together. The bone diminishes more and more, and hereby, the door is opened to the most profound deformities of the joint. Entire epiphyses are gradually destroyed, the neck of the head of the thigh bone disappears, and if we, nevertheless, yet find a head attached to the femur below the trochanter, this is only apparently the old head of the femur, in reality, however, a cast of the cotyloid cavity, which is formed at the centre from the last remains of the neck of the femur, at the edges, by that intermediate calcified proliferation of the edges of the articular cartilage. It is interesting, that the latter retains its originally active rôle during the whole process, lasting for years. As we also see this indicated in Fig. 180, it actually swells out beyond the edges of the articular surface, because there scarce remains space for it between the hostile vis-à-vis articular heads mutually destroying each other. It swells out and then proliferates, down the outer side of the bone, pressing the capsule before it, and squeezing it between itself and the periosteum. As, however, it is a plastic material, in cases like the one previously mentioned, it will easily fill out the ring-formed gap, which remains between the evenly cut off neck of the femur and the spherical surface of the cotyloid cavity. A vertical section instantly exhibits the true composition of the apparent articular head.

The hip-joint is the favorite seat of deforming arthritis. Next to it the sterno-clavicular articulation, the knee-joint, and the phalangeal joints of the hands and feet are exposed to it.

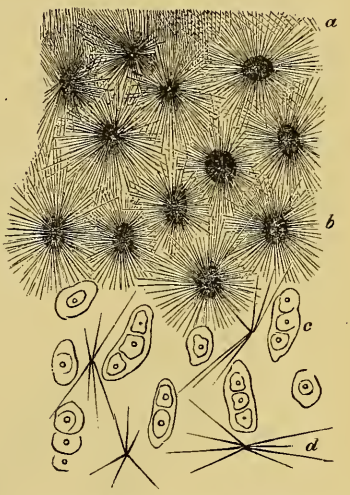
II. APPENDIX.

Arthritis Uratica.

§ 664. The presence of a superabundance of uric acid in the blood, which is the chemical expression of a general disease, gout, still obscure in its nature, leads to abnormal exudations of urates, among others also, into the articular cavities and into the parenchyma of the cartilage, bones, and the membranous parts, which bound the joints. From a histological standpoint we may place this uric acid infiltration of solid parts by the side of the infiltrations with the salts of lime, amyloid substance, fat or pigment, but its occurrence limited alone to gout deterred me from considering it more minutely in the General Part.

Most worthy of notice is the nature and the manner in which the uric acid infiltration presents itself in cartilaginous tissue. The cartilage-cells here prove to be the principal depositories of the urates of lime and soda. They regularly form the central point of the stellate tufts of crystals, which pervade the cartilage. I am not, indeed, of the opinion, that there is herein an active participation of the cells, but the deposition ensues the soonest just where there is the most room for it, in the cartilage cavities, at all events, the microscopic appearance is very characteristic (Fig. 181). In the membranous parts of the joints, as also in the medulla of the bone, the crystalline tufts are distributed without respect to the texture. They here form regular knots up to the size of a pea and over, at the sight of which we involuntarily ask, whence the space was obtained for so voluminous a deposition.

FIG. 181.



Arthritis uratica. Vertical section through a superficial articular body infiltrated with urate of lime. *a*. The surface. *b*. Cartilage cavities with tufts of crystals. *c*. Cartilage cells not yet infiltrated, in division. *d*. Isolated needles of crystals in the basis-substance. After Cornеil et Ranvier.

The uric acid infiltration is self-evidently a considerably mechanico-chemical irritant to the affected parts. Tedious hyperæmias of the synovial membrane and of the periarticular connective tissue, now and then acute inflammatory œdemas, finally, partly superficial, partly deeper going actual suppurations, leading to caries, are the ordinary consequences.

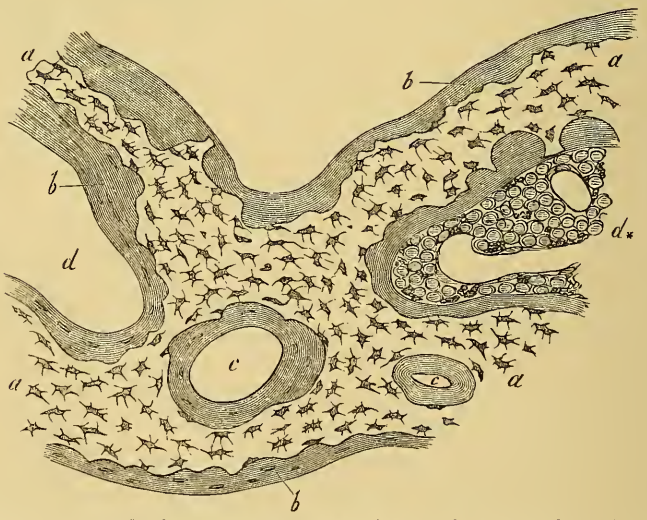
III. APPENDIX.

Osteomalacia.

§ 665. The expression, softening of bone, is very indicative of a morbid process, whose principal and almost only anatomical sign consists in an abstraction of lime and gradual liquefaction of the osseous tissue, therefore precisely of that which is solid in bone. Softening of bone has been regarded at one time quite generally as a chemical disturbance of nutrition, at another as an inflammation; we could perhaps still more correctly accuse a venous hyperæmia as the cause, or speak of a premature senescence of the bones—in one word, the etiology of osseous softening is yet unknown to us, on which account we would do well, in the first place, to go through the anatomical changes as free as possible of prejudice, and only subsequently seek out leading points for the classification of the disease in that system.

§ 666. As was just observed, the softening of bone is essentially a softening of the osseous *tissue*. If we break off with the forceps one of the smallest of the osseous trabeculæ from the spongy substance of an osteomalacic bone, treat it with carmine, and then place it under the microscope, with a power of three hundred, there is presented to us a highly characteristic picture (Fig. 182). The osseous trabecula con-

Fig. 182.



Softening of bone. Spicula of bone from the spongy substance of an osteomalacic rib. *a*. Normal osseous tissue. *b*. Decalcified osseous tissue. *c*. Haversian canal. *d*. Medullary spaces. *d**. A medullary space filled with red medulla. The lumina of the capillaries open. 1–300.

sists of two kinds of substances, and accordingly shows two distinct and sharply defined zones, an exterior one lying next to the medullary spaces (*d*), and to the Haversian canals (*c*), and an inner one, which follows the axis of the osseous trabecula. The inner one (*a*), contains

a perfectly normal osseous tissue; the bone-corpuscles, with their numberless anastomosing processes, and the strongly refractive, thoroughly colorless basis-substance are intact. The outer one, on the other hand (*b*), shows us a minutely striated basis-substance, colored deep red by the carmine, which only here and there exhibits small shaded lines as the last remains of formerly existing bone-corpuscles. We can no longer speak of processes of these bone-corpuscles; it rather appears that a certain swelling out of the intercellular substance is taking place, to cause the collective lacunæ of the bone and their processes to disappear. The change which we here see before us, reminds us too much of the known changes which osseous tissue undergoes in removing the lime by means of hydrochloric acid, that we could for one moment doubt that here also a decalcification of the osseous tissue (halisteresis, Frey), had taken place. This decalcification progresses upon every osseous trabecula from without inwards; we may observe its progress at the time upon the sharp line which separates the decalcified osseous tissue from the normal. Herewith it is interesting to see that this line does not run perhaps parallel to the outer contour of the osseous trabecula, but in just such indented curves, such as we otherwise only perceive upon the line of resorption of the osseous tissue in inflammations, caries, &c. (Howship's lacunæ). From this we conclude that the decalcification advances more rapidly in certain directions, and at certain points than at others, and that the lacunæ of Howship owe their production to this unequally rapid progress of the decalcification. But, if in the face of all these impressions and considerations, we ask after an explanation of the process, many a one will probably agree with me, when I defend the opinion, that an acid proceeding from the medullary spaces and the Haversian canals, robs the bone-tissue of its salts of lime. The great conformity of the outer zone of the osseous trabecula with a bone-tissue artificially decalcified by acid, speaks most convincingly for this assumption; but to this yet belongs, that we can particularly well imagine, how an acid proceeding from the medullary canals advances more rapidly or more slowly in places, in a territory not uniformly and everywhere pervious, but only perforated by canals, always according to the width and number of the canals.

§ 667. The decalcification is the first act of the bone softening. Some time afterward follows the second act, the dissolution of the decalcified bone-tissue. This also advances from the medullary spaces towards the axis of the osseous trabeculæ. The latter, for some time, consist only of bone-cartilage, then they become more and more thin at the centre, finally melt down and disappear from view. The product of their solution, a slimy, not more intimately known material, mingles with the contents of the medullary spaces, and may in part yet play a further rôle as intercellular substance of the enlarged medullary tissue.

§ 668. To what extent the process delineated is fitted, by the gradual

enlargement of the Haversian canals, to form out of the compact substance of bone a spongy substance, and out of the spongy substance a cavity without osseous trabeculæ, is manifest. In order, however, to obtain a correct conception of the coarser phenomena of osteomalacia, it is to be remembered that the melting down of the bone advances constantly from within outwards. Accordingly, first of all, the medullary cavity enlarges; upon the long bones it encroaches from the diaphysis to both the epiphyses, while in the interior of such bones as originally possess no medullary cavity, generally only medullary spaces form; thereupon the compact cortex diminishes in thickness to that of an ordinary playing card; certainly not below it. I have not seen that this last remainder had also disappeared, which is probably connected with the circumstance, that the outermost layer of the bone is not nourished from the medullary cavity, but from the periosteum, and consequently also participates less in a disturbance of nutrition which so evidently proceeds from the medullary cavity.

I purposely say "from the medullary cavity," because it would already be a step beyond the matter of fact were I to say, "from the medulla." The medulla of the bone has, it is true, been often enough proclaimed as the focus of the whole disturbance, yet its changes are so ambiguous that we have never yet succeeded in basing thereupon a unanimous acceptation of the process of bone-softening. The medulla is found very vascular in all recent forms of bone-softening. Where there are larger accumulations of fat, the fat gradually disappears, so that finally a dark brownish-red and thinly pulpy mass, very like the pulp of the spleen, fills up everything that is called medullary cavity and spaces, or Haversian canals. Virchow was wont, at least formerly, to emphasize the identity of this red pulp with the fœtal medulla of bone. Upon the ground of my own investigations, I must turn against this acceptation. I have met with a medullary tissue extraordinarily rich in cells, like that of the fœtus, only in a certainly exceedingly interesting case of softening of all the bodies of the vertebræ in a child of five years. The medulla here presented an appearance, which immediately reminded of the genuine splenic pulp (Fig. 182, *d*). The medullary cells densely crowded and imbedded in a stroma, which was woven out of the most delicate trabeculæ of connective tissue; between them red blood-corpuscles, and various yellow and brown pigments. The bloodvessels only contrasted with the parenchyma by a sharply defined contour; hence almost without proper walls, gaping, comparable to bored holes and canals, reminded of the pulp-tubes of the spleen. Yet I sought in vain for more close analogies. In all other cases of osteomalacia the medulla is to be called directly poor in young medullary cells. Extravasated blood-corpuscles are often present in large amount, and are apt to cover up the tissue into which they have penetrated contrary to rule. But where they are wanting, we find a gelat-

inous, transparent basis-substance, with few, but tolerably large, roundish-cornered cells, which, if we saw without previous knowledge, must impose on us as small epithelial cells. These cells are either former fat-cells, as we perceive by the occasional occurrence in them of a larger fat-globule, or they are actually younger elements, concerning whose origin nothing is at present known. Their limited number, however, in contrast to the abundant basis-substance, by no means admits of concluding upon an active, perhaps even inflammatory process of proliferation.

Much more striking than the behavior of the parenchyma is the very considerable dilatation and congestion of the medullary vessels. I have already mentioned that parenchymatous hemorrhages are constantly found. Now this extravasated blood and the congested capillaries are they which impart to the medulla its dark color. But I cannot conclude to regard this hyperæmia as an active congestion. The atrophic constitution of the medulla denies this, as also the want of all inflammatory infiltration or new formation. The anatomical condition found, agrees much better with the acceptation of a congestion by stagnation, which goes to the border of a stasis, and hence with all the surplus of blood occasions want of nutrition, and afterward retrogressive metamorphoses. I might even represent to myself, that a more abundant development of carbonic acid ensued in the stagnating blood of the medulla of the bone, and that this carbonic acid perhaps served to dissolve the salts of lime of the bone. Perhaps just here a bridge were possible between the conditions of the medulla, upon the one hand, and softening of the bone-tissue upon the other. But even granted that the causal connection between the stagnating congestion and the softening of the bone were to be sought in the direction indicated, whence the passive congestion itself? We are yet by no means sufficiently acquainted with the relations of the circulation in the interior of bone. Are, perhaps, certain anomalies of the periosteum able to alter the circulation in the medulla; are the vasomotor nerves implicated? It has been observed that the periosteum thickens in older persons, that it becomes more vascular, and that especially the vessels which pass from the periosteum to the surface of the bone, become hyperæmic. With these changes, a peripheral (so-called concentric) liquefaction and resorption of the cortex of the bone goes hand in hand. The whole would be a useful pendant to the resorption of bone from within, which takes place in osteomalacia; this comparison moreover is so much the more permissible, as we in fact know of an osteomalacia senilis, which distinguishes itself not essentially from the ordinary form. Shall we now from this standpoint define the osteomalacia of younger individuals as a premature senescence of the osseous system? I venture to answer this question just as little affirmatively as negatively, and will agree with the reader to wait for the results of further investigations. Let us only yet mention, that lactic acid has several times

recently been successfully demonstrated (Weber, Mörs) in the urine and bones of osteomalacic persons. An older investigation, also, of C. Schmidt found the contents of fully formed softening cysts of the bones acid. Nothing is established concerning the place where this acid is produced; perhaps, however, we here stand at the commencement of a solution of the difficult problem.

§ 669. Let us now consider, in a short review, the manifold curvatures and fractures which the osteomalacic skeleton is wont to experience. The favorite seat of osteomalacia is the vertebral column, and the bones of the pelvis and thoracic cavity. The vertebral column, under the burden of the body, curves S-formed, in such manner, indeed, that a kypho-scoliosis [convex curvature] of the dorsal portion corresponds with a lordo-scoliosis [concave curvature] of the lumbar portion, while the cervical portion presents itself concave at the junction with the dorsal region. The ribs curve and break partly by the tractions of the respiratory organs, partly under the burden of the upper extremities, in such manner, that a line of fractured places directed outwards runs down not far from the heads of the ribs; a second series of points of fracture is turned inwards in the axillary line; a third series of points of fracture again, turned outwards, is situated in the parasternal line. Thus tray-like gutters (upon the walls of the chest) are produced for the arms; the entire thoracic cavity, however, is pushed forwards, the sternum, often itself fractured several times, stands in a line with the chin, to which under certain circumstances it may be so approximated as to touch. The pelvis alters its shape under the threefold actions of both the heads of the femurs from below, and the sacrum from above. Consequently, the promontory and the points of the linea innominata corresponding to the acetabula approximate, while at the same time the symphysis and the points corresponding to the greatest curvature of the ossa ilia are pushed outwards, that is, anteriorly. The pelvic outlet becomes trefoil-shaped, thereby beaked anteriorly. If the change is of very high degree, the true pelvis scarcely offers room enough for the undisturbed passage of the intestinal and urinary evacuations, to say nothing of the passage of a child's head.

The bones of the extremities are wont to exhibit numerous fractures, which only heal slowly and incompletely by callus-masses. Simple curvatures, such as so frequently occur in rickets, are rare in osteomalacia; where a bone appears angular, the angular position is regularly the consequence of a complete or half fracture, an infraction (§ 636) such as also occurs in rickets.

§ 670. The cure of osteomalacia is so rare that we can only entertain conjectures concerning the anatomical process of cure. That we would be justified in regarding the so-called *cystic degeneration* of bones as such a one, I would not like, indeed, to assert positively, but probably point out, that in the first place the production of cystic cavities

in the medullary cavity represents a more advanced stage of development of the osteomalacia, and secondly, that with this stage of development an arrest of the morbid process is also attained. In relation to the first, we will mention that the total liquefaction of the red pulp of softening in depots, which is the first factor of the cystic formation, may very well be regarded as a further consequence of the deep disturbance of nutrition of the diseased bone. The detail of the process, it is true, is not known; there is finally produced a fluid, clear as water and rich in albumen, and only the yellow and red pigment-bodies, which are abundantly present especially in the smaller cysts, remind one of the vascularity of the former stage of softening. The second factor is the formation of a compact white connective tissue membrane, which incloses the fluid mentioned, and bounds it towards the adjacent bone. I have shown above (§ 41) that the osseous tissue itself is capable of a fibrous metamorphosis, and I do not hesitate to lay claim to this capacity in the present case. The cystic membrane is provided only with very few and small vessels, hence these cysts never assume the character of secreting cysts, but continue in this state unchanged for years.

The cystic degeneration, as a rule, affects all the bones of the body which were previously osteomalacic. What the osteomalacia for its part has spared, for example, that last subperiosteal remainder of compact substance (which is wont to maintain at least the contours of the bone by a layer thin as paper), beside this, however, many of the short bones of the hand and foot, the entire cranium, also remain untouched by the cystic degeneration. The cysts themselves, however, are no longer progressive, consequently, with the development of a certain number of cysts, an actual cessation of the process is reached.

3. Tumors.

§ 671. In accordance with our programme (§ 609), for the subdivision of the very numerous tumors of the osseous system, we use the greater or lesser deviation of the neoplastic process from the normal growth of bone. Accordingly the various osseous and cartilaginous outgrowths, the exostoses and ecchondroses will have to be placed at the head, next to them we would range the histioid growths, the syphilitic new formation, and finally, the carcinomas.

§ 672. The hyperplasias of the fully grown, so-called permanent cartilage are constantly partial. They mostly proceed from a small circumscribed spot of the surface, and push above the level as warty, afterwards fungous or polypous formations (*ecchondrosis*). Thus we occasionally find them upon the costal cartilages of older individuals, where meantime they never attain any considerable size. To these joins a group of outgrowths of various synchondroses, and of the intervertebral discs, especially studied by Virchow, of which the ecchondrosis

spheno-occipitalis is especially interesting, partly because of its seat upon the centre of the clivus Blumenbachii, partly because of its histological constitution. The tumor seldom attains the size of a small cherry, and consists of a soft, trembling jelly, which by microscopic investigation, proves to be a cartilaginous tissue, whose basis-substance is softened mucoid, and whose cells are degenerated into large vesicular cavities (physalides).

More important is the occurrence of ecchondrosis upon the cartilaginous coverings of the articulations. At a former place we have learned to know the marginal outgrowths of articular cartilage in arthritis deformans.

In most intimate connection with this cartilaginous hyperplasia in arthritis deformans stands, upon the one hand, the formation of *cartilaginous free bodies in the articulations*, upon the other, the exostosis cartilaginea. The former are constricted, warty outgrowths of the articular cartilage (more rarely of the synovial membrane), of the size of a pea and over; they arise at the same place, and are formed of the same large-celled cartilaginous tissue as the senile ecchondroses. They readily calcify, and thereby become arthrolithes, which may cause the individual affected the greatest inconveniences.

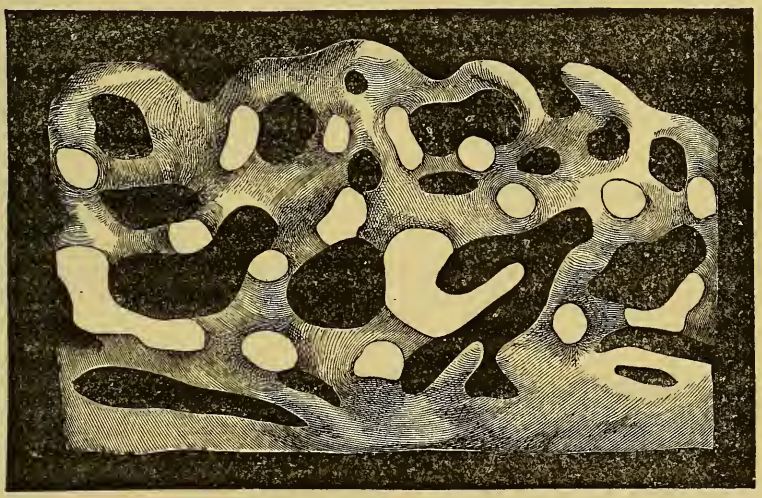
Somewhat more complicated is the production of *exostosis cartilaginea;* we thus name certain tuberous outgrowths of the long bones in the neighborhood of the joints, which are osseous in their principal bulk, but are provided with a more or less complete cartilaginous covering and occasionally with a proper synovial membrane. According to the precedent of Virchow they are derived from a disturbance of the development of the bone. Here also an ecchondrosis forms the point of departure, but a tolerably large ecchondrosis, which arises either from the edge of the articular surface, or from the cartilaginous stripes between the epiphysis and the diaphysis, is not loosened, but continues to grow in permanent connection with the bone, and thereby determines the latter to enlarge not only in the normal chief direction, but also in the lateral direction given off from it. It is easy to comprehend how such an ecchondrosis, provided it proceeds from the articular surface and not from the under edge of the epiphysis, primarily lies in the articular cavity itself, by a further removal from the joint comes to lie in the first place in an excavation, then in a recess of the synovial membrane, and finally in a proper synovial sac (exostosis bursata).

§ 673. The example of exostosis cartilaginea shows us how impracticable it would be to divide the hyperplasias of the osseous system into hyperplasias of the cartilaginous and osseous tissue. The bone only enlarges, in that it follows its mother structure in its proliferations. These are the actually producing parts, this the seat of the pathological irritation, not the bone itself. In the *exostoses*, also in the more contracted sense, *i. e.*, in the circumscribed osseous outgrowths of the

bony system, we must maintain this standpoint unmoved. The question therewith is throughout about excesses of the *periosteal* growth of bone, and if this relation remains unconsidered in the nomenclature, it only comes from this, that the periosteum, in comparison to its almost unlimited osteoplastic capacity, is a very thin, delicate membrane, which attracts but little attention and is easily stripped off.

The histological processes, excepting several subordinate variations, are the same as in the normal and in the inflammatory periosteal growth of bone. The innermost layer of the periosteum yields a vascular germinal tissue. Upon another occasion (§ 52) we have already amply discussed how genuine bone is formed from this germinal tissue by the deposition of a homogeneous, dense, strongly refractive basis-substance, calcification, &c. The newly formed bone consists primarily of an exceedingly porous mass, which adheres but loosely to the old surface of the old bone, and is designated as *osteophyte* (Fig. 183);

Fig. 183.



Osteophyte. Formation of bone from the periosteum in the primary spongy stage.

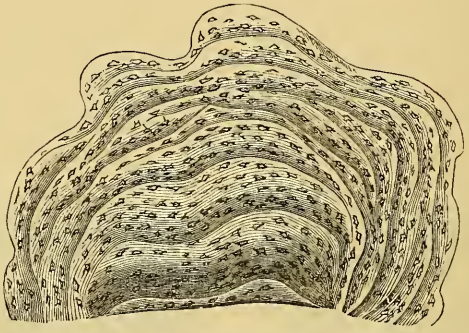
afterward this connection becomes firmer, and then by the concentric apposition of new bony lamellæ to the trabeculæ of the osteophyte, ensues the transition into compact osseous substance. It must meanwhile be observed that the latter metamorphosis may set in very late under certain circumstances; indeed, it need not occur at all.

Finally, quite as in the normal growth of bone, upon the compact stage, a porous, or, as we now say, a spongy stage is wont to follow anew, nay, after some time it follows so regularly and so frequently, that we might almost believe the compact substance, like cartilage, can generally only exist in a certain thickness of deposition, if the history of *exostosis eburnea* did not prove the contrary. This exostosis is so

remarkable a phenomenon, just because, quite divergent from the usual schema, namely, without regard to the vessels and their course, the osseous tissue is deposited layer by layer, about one of the smallest of tubers as a nucleus. This gradually becomes a warty, polypous, cauliflower-like, therewith lustrous white formation, which may attain the size of a man's fist, and nevertheless consist throughout of compact bony substance (Fig. 184).

This entire kind of growth undoubtedly reminds us of the formation of dentine, and that this comparison is not inapt is shown yet more

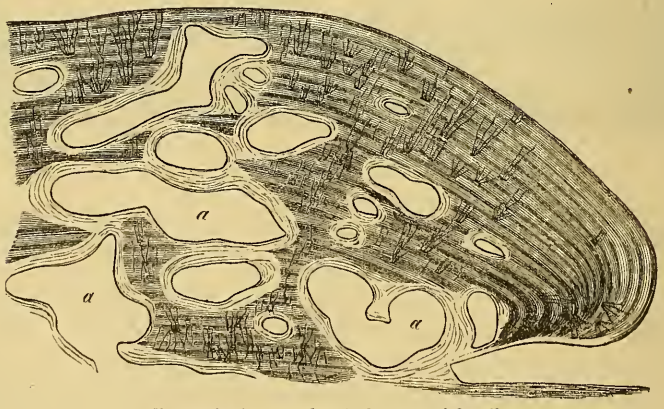
Fig. 184.



From an exostosis eburnea of the shoulder-blade.

strikingly by those peculiar, small, flatly-roundish outgrowths of the roof of the cranium, which look like ivory shirt-buttons, and hence have been designated by Virchow, as *button* exostoses. A vertical cut through the centre of such a new formation (Fig. 185) shows us as the

Fig. 185.



Exostosis eburnea clavata from cranial walls.

foundation of the design, an exceedingly finely striated substance, in which a bone-corpuscle is only here and there set in, which has developed its very long processes only in one direction, namely, towards the

exterior and vertical to the line of striation. Is a greater similarity necessary to declare as dentine, this basis-substance of the exostosis, which is evidently only subsequently interrupted by the formation of medullary spaces?

§ 674. Under the etiological forces of periosteal osseous hyperplasia, the inflammatory irritation comes more decidedly into the foreground beside the simple, *i. e.*, hitherto inexplicable anomaly of growth. It is correct, that the growing bone is also peculiarly disposed to these changes, but a greater age and hereditary influences also bring with them a like predisposition, and in but few cases of exostosis eburnea is this force the only one which we can adduce in explanation. Mostly general diseases, especially syphilis, rheumatism, and rachitis, are implicated, and if it is already known of these that they easily excite inflammations of the periosteum, we can still less exclude this acceptation, where we see an external, mechanical irritant causing the hyperplasia. Frequently enough a knock, a blow, is stated as the first cause of a formation of exostosis; more than once (the last by Virchow, l. c. ii, 84) has the case of *the formation of multiple exostoses* been observed at the points of insertion of the muscles. But this latter case also teaches us, how closely here the inflammatory growth from external irritations and the non-inflammatory normal growth are related. For even the normal skeleton shows at the points of insertion of many muscles, rough elevations, which are known in descriptive anatomy as crests, tubercles, eminences.

§ 675. Whilst now, as we have seen, the exostoses and ecchondroses only present unessential deviations from the normal growth of bone and cartilage, in the histioid tumors of the osseous system we must already be satisfied with bare analogies. We may adduce, that these, corresponding to the two physiological places of growth, proceed either from the periosteum, or from the medulla of bones, and therefore distinguish between central and peripheral sarcomas, enchondromas, &c. Moreover, upon all the peripheral, we can establish an initiatory stage, while the pathological proliferation of these does not distinguish itself externally from the periosteal proliferation introducing the formation of bone; in the decided tendency of just these tumors to ossification, we can also recognize a correspondence to the physiological function of the periosteum. Finally, the above-described chondroma osteoides (§ 139), evidently comes very near the physiological paradigm. In other respects, however, we must let the entire stress rest upon the heterology of the new formation, and regard all sarcomas, enchondromas, myxomas, &c., occurring upon bone, as qualitative deviations in the functions of the vascular connective tissue system.

§ 676. In the next place, we consider the *peripheral osteosarcoma*, then that soft layer of the periosteum turned towards the bone, which Max Schultze has so aptly designated as the cambium layer of bone,

undoubtedly participates primarily in the production of this tumor. We may even represent to ourselves, that a quantitative excess of the normal phenomena of growth, which proceed at this place, espècially the production of a larger amount of embryonal formative tissue, introduces the sarcoma formation at a circumscribed spot of the surface of the bone. In all later stages, the peripheral osteosarcoma is nothing else than a sarcoma placed between the periosteum and the bone. Apart from the clinical course, the formation of metastases and reproduction which are observed, off and on, in a vivid manner, the most superficial histological analysis already suffices to reveal to us the sarcomatous nature of the tumor. As a rule, every species of sarcoma-tissue is found side by side, yet in most of the tumors the spindle-cell tissue predominates. This especially obtains of those colossal tumors which develop at the ends of the large bones of the extremities (femur, tibia, humerus, &c.), and are characterized by an incomplete radiated structure. These lift off the periosteum, grow around the contiguous cartilage, and but slightly penetrate into the compact cortex. Afterward they pass over to those structures which are in continuous connection with the bone, muscles, parosteal connective tissue, articular capsules, ligaments, &c.; while the more loosely superimposed parts, for example, muscular bellies and tendons passing over, occasion corresponding impressions.

In all sarcomas of the osseous system, whether they proceed from the medulla or the periosteum, we occasionally find larger or smaller portions of bony substance of secondary formation; as a permanent sign, however, ossification is only found in a portion of the peripheral osteosarcomas, which on that account have been designated by Joh. Müller, as osteoid. Joh. Müller distinguishes a benignant and malignant osteoid. The latter is identical with the cancer of bone to be spoken of by us in the next place. The former will now occupy us. The benignant osteoid, which is probably most frequently observed upon the bones of the face, shows, as a rule, a most remarkably radiating structure. From a point, or rather from a relatively small surface, fibrous lines, which we may perceive even with the naked eye, proceed uniformly and in straight lines towards the periphery; the tumor is also more readily torn in this direction than in any other. The cause of this lies in an actual papillary organization

Fig. 186.

Transverse section through the middle of an ossifying sarcoma of the periosteum of the lower maxilla. Round-celled sarcoma, the basis-substance calcified in places. The calcified places form elongated spiculæ, which stand vertical to the surface of the bone, but are cut across here. 1-300.

of the tumor; long, thin papillæ, ramifying at very acute angles compose it. In Fig. 186, a cut surface shows us, that the papillæ are, taken altogether, roundish, and formed throughout of germinal tissue with little intercellular substance. Lines of loose connective tissue pervade the interspaces between the papillæ and fill them up. It is interesting, that cleft-like gaps are visible here and there between the connective tissue sheaths and the surfaces of the papillæ. The connective tissue sheaths here present smooth surfaces to the papillæ, and the papillæ to the connective tissue sheaths; these gaps may readily be filled by injection and are connected with adjacent lymph-vessels.

§ 677. Touching now the ossification, this is nothing else than a calcification of the scanty intercellular substance. For every cell there remains a circular, not always radiating cleft (Fig. 186); merely from the texture I would be but little disposed to speak of an actual ossification, if beside this the circumstance did not remind us of true ossification, that the deposition of the salts of lime within the papillæ occurred in zones, which surround the vessels mantle-like, and thus betray their analogy to osteophytes. After maceration the ossified parts present themselves as a radiating framework, which is loosely put together by delicate osseous trabeculæ.

In a typical case, whose preparation is preserved in the collection at Zurich, I saw a peripheral osteosarcoma, round-celled throughout and nowhere ossified. At the most various points of the osseous system, especially however at the sternum, at the inner surface of the skull, and at all openings of the skull and cavity of the vertebral column, through which nerves passed in and out, the periosteum was lifted off by a flat layer, mostly of a line in height, but at the sternum of the thickness of a finger, of a substance like the roe of fishes. The superficial expansion of this multiple sarcoma was very various, fluctuating between the size of a lentil and that of a silver dollar; at the openings for the nerves the sarcoma formed a ring-shaped cushion, especially at the foramina intervertebralia.

The polyps of the nasal cavities, proceeding from the anterior surfaces of the bodies of the upper vertebræ and the os tribasilare, are to be regarded as thoroughly fibrous sarcomas of the periosteum. (Compare Virchow, Tumors, i, p. 354.)

Whether the giant-celled sarcoma may also proceed from the periosteum of bones, is, according to my judgment, yet an undecided question. Virchow has recently designated that compact-elastic, more rarely soft sarcoma of the alveolar processes, attached by a broad base, and protruding with roundish contours, which in former times was called epulis, as peripheral osteosarcoma in the sense of periosteal proliferation. He did this in opposition to Nélaton, who indeed also places over against each other two groups of myeloplaxic tumors (giant-celled sarcomas), the epulides periosseuses and the epulides intra-osseuses, but

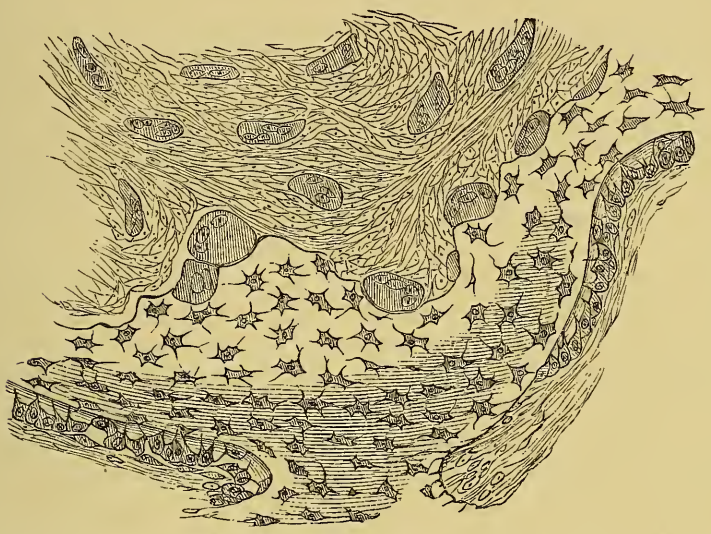
does not let the former proceed directly from the periosteum, but from the perivascular medullary cells of the dilated Haversian canals, which open at the surface of the bone. Nélaton, namely, would like to see the giant-cells universally recognized as medullary cells. Virchow replies to this, that many of the epulides periosseuses are attached to a bony elevation, according to his opinion a preceding periosteal proliferation of the bone, which pushes in between the soft parts of the tumor with its giant-cells and the bone. It is true he, upon the other hand, acknowledges even the great tendency and capacity of the epulides to penetrate destructively into the bone, and I would like to ask whether this osseous base might not be regarded as an ossified part of the tumor itself. It would then bring about more the continuity than the division of the tumor and the bone, and might serve for supporting the views of Nélaton. I am cautious on this account, because, in respect to the giant-celled sarcoma proceeding from the medulla, I have convinced *myself* that the giant-cells are bone-cells, which have become free in the resorption of the bone, and have thereupon gone over into the peculiar hypertrophic state. Of course it is not intended to say by this, that giant-cells in general can only be produced in this manner. (Compare § 67.)

The sarcomatous epulis contains giant-cells of quite colossal dimensions. If these fall out of thin sections, which were made parallel to the border of the jaw, there arise gaps, which are not unlike the alveoli of cancer. The quasi stroma consists of the various species of sarcoma tissue; and, accordingly, as one or the other predominates, the tumor is softer or harder. The firmest ones contain predominantly connective tissue fibres, the softest round cells, the intermediate ones, and at the same time the most common, spindle-cells.

§ 678. The *central osteosarcoma* (myelogenes osteosarcoma, Virchow) is observed in three different species. The most frequent are the giant-celled sarcomas of the lower jaw, designated by Nélaton as epulides intra-osseuses, the more infrequent of the upper jaw. These proceed from the red medulla of the spongy substance, and by continued central growth form irregularly roundish knobs, up to the size of a child's head. It is manifest that therewith they must come in conflict with the compact osseous cortex. The osseous cortex is—as we say, and as also the first glance seems to confirm—*puffed up* by the central tumor. It is as though the bone possessed none at all of the hardness and firmness peculiar to it, and must adapt itself unresistingly to the central distension. This is a phenomenon which recurs everywhere when a slowly-growing tumefaction has its seat in the interior of bone; it not only recurs in all sarcomas myelogenes, but also in the central enchondromas and myxomas. Volkmann has attempted to prove that an interstitial displacement of the osseous substance actually takes place herein, but as sagacious as are his reflections, and as readily as I ad-

mit that every individual case of distension of bone touched upon by him must first be thoroughly investigated ere we can speak of a final judgment, so certainly does at least the distension of the cortex of the bone by central osteosarcoma depend upon apposition and resorption. Apposition externally, by the continual apposition of bone on the part of the periosteum; resorption within, by the continual melting down of the osseous tissue at the surface of the growing tumor. Fig. 187 was

FIG. 187.



From the border of a spindle- and giant-celled sarcoma of the lower maxilla, of the size of a fist. Osseous trabecula which disappears at the one side by resorption, and grows at the other by apposition. See details in text. 1–500.

taken from the vertical section of a myeloid of the size of a fist. It embraces the edge of the tumor and an osseous trabecula, which, together with three or four others just so constituted, presents the last remains of the osseous cortex of the lower jaw. Upon these trabeculæ we see both the processes in action. The periosteal side is beset almost entirely with the known osteoblasts of Gegenbaur. We here probably have the most favorable opportunity of seeing osseous tissue produced; each individual force of the process is presented with unsurpassable clearness. (Compare § 52.) Upon the opposite side resorption is in progress. A sharp, tortuous line bounds the bone towards the tumor. At several places we see polynucleated giant-cells imbedded in the contours of Howship's lacunæ; we distinguish larger and smaller elements, the smallest are but little larger than the adjacent bone-corpuscles, and would not deserve the name of polynucleated giant-cells, if they were not characterized by the same finely granular quality of the protoplasm and the gradual transitions as the future myeloplaxes. The situation of the youngest myeloplaxes is so constantly at the inner edge of the

bone, that we cannot avoid thinking that the myeloplaxes may have their original seat just here; are perhaps produced by a metamorphosis of the bone-corpuscles, which become free from time to time, in the progressing solution of the osseous basis-substance. If thereupon I consider the distribution of the giant-cells in the sarcoma and compare it with the position of bone-corpuscles in bone, I cannot exclude the perception that they are placed in both tissues in certain alternating interspaces. This uniformity however might, in my opinion, be very unforcedly explained by accepting, that in the growth of the tumor, the bone-corpuscles becoming free and immediately degenerating to myeloplaxes, are crowded off from the bone with a certain uniformity by layers of cells, and are incorporated into the tumor. The strict proof that the giant-cells of central osteosarcoma are former bone-cells, is thereby certainly not yet furnished. Meanwhile I am glad to be able to state, that recently the physiological occurrence also of giant-cells has been explained in the same manner. (Bredichin, Centralblatt, 1867, 563.)

Thus far the histological processes in the swelling of bone. It is manifest that, although apposition and resorption keep even pace, yet in time an attenuation of the cortex of the bone must be produced. There must be more added than resorbed, if the bone is to suffice to clothe the tumor becoming ever larger with a layer of compact substance of always the same thickness. Now, inasmuch, however, as the contrary rather occurs, *i. e.*, less is added than resorbed, we cannot be surprised, if finally, the shell becomes defective at individual places, the tumor therefore breaks through the bone.

The intra-osseous epulides of the jaw, of which we have been hitherto speaking, consist mostly of spindle-cell tissue. The tendency of recently cut surfaces in lying exposed to the air is remarkable for assuming a reddish-yellow tinge, even merging into greenish.

§ 679. The second species of central osteosarcoma is observed par excellence at the lower end of the femur, at the upper end of the tibia, and at the upper end of the humerus. It is characterized by great softness and vascularity. The tissue is originally round-celled, but goes over at one point into mucoid tissue, at another into adipose tissue, at a third spindle-celled and fibrous, so that we can here speak of a mixed tumor (sarcoma mixtum). The vascularity generally leads to hemorrhages, and the partly recent pools of blood filled with clots, partly older depots of softening stuffed out with reddish-brown pigment, may so predominate at the first glance, as to cause the impression of aneurism of the bone, or of fungus hæmatodes. Of course, only the latter term is to be used, and indeed with circumspection. The amount of poly-nucleated giant-cells contained here is also characteristic; the tumor likewise belongs among the giant-cell sarcomas.

§ 680. Thirdly, there is a central osteofibroma, which proves its close

relationship to the epulides intraosseuses by its favorite seat, the maxillary bones, and the completely analogous distension of the cortex of the bone. Giant-cells cannot be demonstrated in it. On the other hand there is shown a decided tendency to ossification, either by finding therein numerous, but small spiculæ of bone, which in passing the finger over the cut surface feel like a sandy roughness, or more extensive ossifications gradually convert the tumor into an osteoma.

§ 681. The pure *myxoma* of bone is described by Virchow as a tumor proceeding from the medulla, distending the bone, and finally breaking through it, which in its substance, resembles the flesh of oysters, or the gelatinous disc of sea-nettles. Because of the near relationship of enchondroma with myxoma, it is difficult to draw a strict boundary between the two. The most of gelatinous, soft osseous tumors are enchondromas.

§ 682. That the osseous system is the main seat of *cartilaginous growths*, was already mentioned when we were occupied with its histological relations in general (§ 135). We will yet state, that of the various parts of the skeleton, the phalanges of the fingers and toes, then the upper arm, femur, and tibia, then the maxillæ, the bones of the pelvis and the scapula are most frequently attacked, the ribs and the bones of the base of the skull more rarely, the vertebral column, clavicle and sternum most rarely. Joh. Müller first made a distinction into external enchondromas, proceeding from the periosteum, and internal ones proceeding from the medulla. It is here, however, as with the epulides, the internal are unquestioned; in reference to the external we cannot very positively say, in how far the compact substance, how far the periosteum participate in their formation. Even Virchow is doubtful. The whole affair becomes still more questionable by this, that recently the direct transition of osseous into cartilaginous tissue has been several times asserted. (Weber.)* In consequence of this, the compact substance would deserve a greater consideration, and especially if it should be confirmed, what Virchow, it is true, has expressed more by way of conjecture, that in the compact substance, remains of cartilaginous tissue may give the impulse to enchondromatous degeneration.

The internal enchondroma behaves like the central osteosarcoma, and myxoma only in so far, that it distends the bone to a shell, and only

* This process can only be studied upon very thin lamellæ of bone, which are taken from the border of the bone and the tumor. The osseous texture experiences a kind of uniform fusion; the basis-substance becomes translucent from the edges, while the cells lose their processes and come to lie in a roundish cavity, which appears to be caused only by a softening of the basis-substance proceeding from the lacunæ of the bone, and affecting their immediate surroundings. To an osseous tissue which has attained this stage of metamorphosis, we cannot deny a great similarity with cartilaginous tissue, still the whole process does not give the impression of a proliferating new formation, but of an organic metamorphosis, which, of course, is not yet synonymous with disorganization.

after longer growth breaks through at single places. In other respects, the growth of the enchondroma by adjacent foci, is the cause of several peculiarities worthy of note. To this place belongs especially the stronger inflammatory irritation, which is produced by the occurrence of disseminated nodules in the environs of the tumor. Beside an often very considerable ossifying periostitis, we find a genuine sclerosing osteomyelitis especially frequent. The medullary cavity in the neighborhood of the enchondroma is at times as though closed by an exceedingly hard, minutely porous, compact substance. The periostitis ossificans ever yields new lamellæ of bone, and therewith, as well building material for the tumor, as also a bony capsule, which remains complete longer in enchondroma than in any other central osseous tumor.

The enchondromas of bone are maintained longer and become larger with an unchanged internal constitution than the enchondromas of soft parts. Afterward they show those secondary metamorphoses, which have been mentioned (§ 137), calcification, ossification, conversion into mucoid tissue, mucoid softening, and cystic degeneration. It only yet remains for us to mention here several varieties of enchondroma, which, up to the present time have been observed only upon bone. *a.* The enchondroma hæmatodes. Upon the right fibula of a boy, who had been under treatment in the surgical clinic at Bonn, I found a tumor of twice the size of the fist, which was undoubtedly cartilaginous in its border portions, and by its lobular structure betrayed throughout the structure of enchondroma. The internal lobules, however, showed a gelatinous swelling-out of the basis-substance, and were pervaded by quite peculiar blood-conveying canals, of which only so much could with certainty be said, that they had been produced by the anastomoses of adjacent cartilage-cavities. Together they formed a network with strongly projecting, concavely contoured points of intersection. But whether they actually were bloodvessels, or whether these were only extravasations modified by the structure, we were not able to decide. The softening went hand in hand with a simultaneous sarcomatous degeneration of the connective tissue framework. (C. Hösterman, Inaugural Dissertation. Bonn, 1868.) *b.* The enchondroma pseudopapillosum. A peripheral enchondroma of the upper maxilla, which likewise was obtained from the surgical clinic of Dr. Busch, had a distinctly papillary, cauliflower-like surface. The massy proliferations, after having filled the cavity of the upper maxilla, broke through the bone at the anterior surface. The tumor owed its singular structure to the peculiarly central growth which characterized it, quite contrary to the manner of enchondromas. The smallest nodules always again originated in the connective tissue of the larger. Finally, the independent growth of the latter caused a partial loosening from the neighborhood. Cleft-like and shallow expanded gaps accordingly subdivided the tumor and split it up into groups of nodules, which were very similar to the

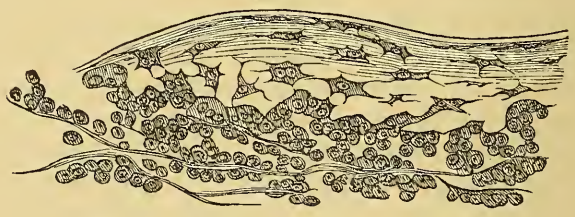
ramified papillæ of a cauliflower growth. (C. Hopmann, Inaugural Dissertation. Bonn, 1867.)

§ 683. Cancer of the osseous system will become in the next few years an absorbing question of pathological histology. If it is true, what according to Thiersch's precedent has recently found such ardent defenders, that all genuine cancers proceed from external or glandular epithelia, all osseous cancers could be produced only by contiguous infiltration from adjacent cutaneous-, mucous membrane-, or glandular cancers. That this is actually so, in fact, cannot be doubted in certain cases. If, for example, we see an epithelial cancer of the face pass over to the maxillary bone, or just such a cancer of the leg pass to the tibia, and a kind of cancerous caries produced there, then we have here an advance of the cancerous cell-cylinders into the vascular pores of the osseous substance, which in correspondence with this, enlarge and cause the intervening nutritive territories of the osseous tissue to disappear. Also when in the diploë of the cranial bones or in the spongy substance of the ribs or elsewhere in the medulla of bones, metastatic nodules arise and flourish, we might at least admit the possibility of an "epithelial infection" of the medullary cells there existing, although in this case I, as an anatomist, would have simply to prove the fact of the transformation of connective tissue cells into epithelial cells, and with the possibility of this transformation, therefore to concede the development of cancer from connective tissue. What excuse, however, could we devise when we must acknowledge that there are also primary cancers of bone, which in addition recur with a certain predilection at the same place and in the same histological species? First we have there those soft, rapidly growing cancers which so readily proceed from the upper ends, as well of the humerus as of the femur, and occasionally flourish to quite an extensive circumference. These, at one time, develop predominantly from the medulla, then predominantly from the periosteum; as soon as the periosteum has been drawn into the affection, upon the one hand the growth of the tumor advances more rapidly, upon the other ossification sets in in the form of an exceedingly delicate framework, either spongy or more radiating. They are everywhere the thicker trabeculæ of the cancer-stroma which calcify and thus furnish a kind of spurious osseous tissue (carcinoma osteoides). A second, likewise frequent seat of development of primary osseous cancers are the bones of the head. Soft, rapidly growing nodules arise in the diploë, and in a short time perforate the cortex of the bone towards both sides. Or the central tumor grows somewhat slower and the periosteum has time to introduce at least the peripheral formation of a shell. This we occasionally see upon the upper maxilla. A third more rare, but so much the more characteristic form, is the diffuse carcinosis of the pelvic and the adjacent vertebral bones, which presents itself clinically as an osteomalacia. The question here also is about a

soft carcinoma, which is characterized by a degeneration of the medulla, dispersed in numberless small depots. In all these primary osseous cancers we cannot speak of an epithelial starting-point, and yet our entire definition of what comprehends cancer would have to be overthrown if we did not regard these things as genuine cancers.*

Exact statements are indeed yet wanting at this time, upon the origin of the first cancer-cells; still the analogy with the other myelogenous osseous tumors aids us in thinking of a metamorphosis of the medullary cells. I, however, add with emphasis, also of the adventitial vascular cells. The osseous tissue melts down without resistance before the advancing new formation. A decalcification is wont to precede resorption, as in osteomalacia. The osseous trabeculæ are, therefore, up to a certain time, elastic, pliable, cartilaginous. The bone-corpuscles, probably, do not behave the same in all cases. It is, indeed, comparatively easy to break a spicula of bone out of the centre of a carcinoma, and to examine upon this point, wherefore I can point to a tolerable series of such investigations. The result is that a more active participation of the bone-cells, in the new formation, is only exceptionally to be established. The adjoining illustration (Fig. 188), presents to view the mode of participation. We have here the border of a soft cancer of the ribs.

Fig. 188.



Osseous trabecula in cancerous degeneration. 1–500.

An osseous trabecula, which bounds the tumor, has been involved in the disease, and is already completely dissolved upon one side, while upon the other it still shows smooth contours. The bone-corpuscles, which are yet normal at the side turned away from the tumor, successively increase in size, while the basis-substance loses its salts of lime and decreases in inverse proportion to the enlargement of the bone-corpuscles. At this edge of the osseous trabecula we only yet observe scanty remains of it. The cells, on the other hand, by division of the nuclei and enlargement of the protoplasm, have been converted into larger, more nucleated elements, which thereupon immediately break up

* According to a very recent publication of Billroth's, in Langenbeck's Archives, certain soft carcinomas are not to be regarded as such, but as "alveolar" sarcomas, produced by a higher development of the lymphadenoid type of tissue; an acceptation which would please me extraordinarily, especially for the sarcomas of bones and nerves.

into an amount of smaller cells corresponding to the number of the nuclei. Whether these cells afterward go over into cancer-cells, or whether their whole production is only a concomitant consequence of the intense irritation of the tissue, I must leave undecided. At all events it is not constant.

The gelatinous cancer also has been repeatedly, although always only secondarily, observed upon bone. Still we have no histological statements concerning the manner of their origin and diffusion.

§ 684. The *syphilitic gummous tumor* appears in the so-called tertiary period of the disease upon the osseous system. The term gumma is probably derived from the peculiarly elastic resistance which the palpating finger encounters upon investigating the flat, circumscribed tumefactions of the cranial bones through the integuments. The soft, rapidly proliferating tissue, which composes this tumor is primarily furnished by the inner layer of the periosteum; yet once again we are here reminded of the physiological growth, but already the finer structure of the product next furnished is thoroughly heterologous. A delicate, gelatinous, in places fibrous basis-substance contains numerous round and spindle-cells, arranged in elegant concentric rings around the vessels, which penetrate the new formation in all directions. I regard these vessels as the periosteal vessels of the bone, as those which normally pass over between the periosteum and the bone, and go to the surface of the latter. The adventitia of these vessels is the proper matrix of the syphiloma. Here arise cells and basis-substance in repeated layers, of which the younger press before them the older, and thus produce a concentric arrangement of the entire new formation. The mucoid swelling up of the basis-substance develops mechanical forces which neither the periosteum nor the bone are able to encounter. The former is lifted off from the bone, the latter disappears under the tumor, becomes rough, and finally extensively defective (caries syphilitica). The syphilitic infiltration herein creeps along the Haversian vessels into the compact osseous substance and causes the osseous tissue to disappear in territories, as also occurs in like manner, in rarefying ostitis, on the part of the medullary granulations. If then all the osseous tissue between each two vessels has been destroyed, the syphiloma-mass from both sides fuses together, and only the concentric grouping yet reminds one of the primary participation of the vascular sheaths. We see exactly the same relations recur upon gumma cerebri.

The syphiloma of bone is, upon the one hand, itself to be regarded as a heterologous, syphilitic inflammation of bone; upon the other, it excites in its surroundings all kinds of ostitis and periostitis, by which then the bone becomes more distorted and destroyed than by the tumor itself. The syphilitic inflammations, caries, necrosis, &c., are not histologically distinguished from the simple affections bearing these names.

Syphiloma is subject to a metamorphosis peculiar to it (caseous metamorphosis); moreover, a direct liquefaction into pus is observed. Under the effects of antisyphilitic medicaments, the mucus of the basis-substance experiences a further chemical metamorphosis, which makes it capable of resorption; the cells are converted into a detritus likewise capable of resorption.

§ 685. If from *tuberculosis* of bone we exclude the formerly mentioned cases of cheesy ostitis, there only remains as genuine miliary irruption an occasional, but tolerably rare occurrence of them in the environs of the caseous depots. The tubercles, according to Virchow, arise from the red medulla, and behave as the ordinary miliary nodules. I myself have not yet had the opportunity of seeing genuine osseous tubercles.

XVII. ANOMALIES OF THE NERVOUS SYSTEM.

§ 686. One of the most striking of the phenomena in the province of the pathological histology of the nervous system, is the limited, and constantly but passive participation of the special nervous elementary parts, in all the changes which affect the brain, spinal marrow, or the peripheral nerves. The more we were formerly at pains to trace back to anomalies of the ganglion-cells and nerve-fibres, particularly the mental disturbances and other essential neuroses, so much the more surely may we now assert the thesis, based upon the negative results of all these investigations, that the causes of, "perhaps," all nervous diseases are to be sought in anatomical disturbances of the non-nervous constituents of the system. With reference to this, however, it appears to me advisable to make introductory reflections upon the diverse ways and modes, in which the nervous and non-nervous elements participate in the composition of the various sections of the nervous apparatus.

§ 687. We may start from this, that the minutest ramifications of the peripheral nervous system, the nerve-fibres running isolated, are implanted in that continuity of connective substance, which fills out all interspaces between the organs, and constituents of organs, of the body. The first unions, also, of nerve-fibres up to groups of perhaps twenty, yet exhibit no perceptible modifications in the quality of the connective tissue. To this corresponds the unconstrained course of the individual fibres, the numerous curves to and fro, the peculiar slackness which characterizes the structure of these smallest nerve-bundles. As soon, however, as we pass to the larger branches and trunks, we find a distinct differentiation of the connective tissue *between* the nerve-fibres, and of that *around* the nerve-fibres. The softer and the more delicate the former, the so-called perineurium, becomes, so much the more does the latter condense into a compact sheath, which is well fitted to protect the nerves against mechanical violence. The perineurium contains no proper connective tissue fibrils, its intercellular substance is homogeneous, and without the addition of the cells would be invisible. The cells have elongated nuclei, and beside these a very small amount of finely granular protoplasm. Whether the sheaths of Schwann of the medulla-containing nerve-tubes are to be reckoned with this latter or with the perineurium, I will leave undecided, at all events the struc-

tures, occasionally designated as nuclei of the sheaths of Schwann, are identical with the cells of the perineurium, as they participate in every pathological proliferation of the interstitial connective tissue, and consequently identify themselves with the connective tissue.

The outer sheath of the peripheral nerves is, at the same time, the bearer of the larger vascular branches intended for the nerves, and sends inward a certain number of fibrous connective tissue processes, which subdivide the nerve-fibres into larger and smaller bundles, and at the same time serve the smallest arteries and veins as bridges, while the long-meshed capillary net expands in the perineurium.

In the central organs we meet with a yet more profound specialization of the non-nervous structural constituents. In the brain and spinal marrow, upon the one hand, the perineurium assumes a peculiarly delicate constitution; upon the other hand, in the connective tissue investment, a new separation takes place, namely, into an outer, peculiarly dense, thick, and compact membrane (dura mater), which only contains a few small vessels, on that account, however, can serve so much the more as a protection of the central organs, and into a very delicate sheathing of loose connective tissue (pia mater), which is to be exclusively regarded as the conductor of the larger vascular branches. The connective tissue processes, conveying the smaller vessels inwards, only exist in the spinal marrow, as generally the white substance of the spinal cord distinguishes itself qualitatively but little from a peripheral nerve. In the brain, on the other hand, the smallest arteries and veins, as we commonly say, pass naked into the most sacred parts of the nervous system. This "naked" is, of course, to be taken *cum grano salis*, and least of all has an expert in the pathological conditions of the brain, occasion for overlooking the mantle of connective tissue, though ever so delicate, which surrounds these vessels. This same thing has been designated here, at one time, as connective tissue adventitia; at another, as a perivascular lymph-vessel. Kölliker was the first to strip off a homogeneous membrane with inward-lying nuclei from the vessels of the brain; afterward, the injections of His taught, that between this membrane and the brain there existed a space, which is connected with the larger perivascular spaces of the pia mater. His regards this space, and those spaces as lymph-passages. I let this hypothesis hold good, but with the expressed reservation, that these lymph-passages want many things pertaining to genuine "lymph-vessels." The endothelium is, at the least, incomplete, the inclosure as to space imperfect; we can in general only speak of gaps in the connective tissue, and could scarcely go amiss, if we classified the whole arrangement more with those cells of authors, on whose account we formerly designated the intermuscular and subcutaneous connective tissue as cellular tissue. The connection with the system of lymph-vessels, of course not yet fully proven, would then only be peculiar.

In conclusion, one word concerning the perineurium of the brain, the neuroglia Virchovi. As well the quality, as especially the quantity, of this substance have not yet been sufficiently ascertained. Touching the quality, we are wont to make a distinction between the neuroglia of the white medullary layer, and that of the gray nuclear, and cortical layers. Of the neuroglia of the medulla we can assert with certainty, that to it everything is to be reckoned which is found here beside the nerve-fibres and vessels; on that account all granules and nuclei of the white substance are neuroglia-cells and nuclei; on that account that soft, finely granular and spongy material, in which the nerve-fibres are imbedded, is basis-substance of the neuroglia. The estimation of the relations in the cortex of the brain is much more difficult. At the border towards the medulla, in the cerebellum, less pronounced also in the brain, we touch upon a packed accumulation of the so-called "granules," *i. e.*, small, pale, round and homogeneous nuclear bodies, which, according to more recent investigations, have collectively the value of small cells, because they are collectively provided with protoplasmatic appendices, which were formerly overlooked. Upon this, that these appendices occasionally run out into minute fibrils, is based the assumption that the granules are connected with the nerve-fibres, consequently are themselves nervous. These granules farther outwards decrease in numbers, although they always yet remain frequent, and are wont to lie together in small groups of three to five; beside them arise the known pyramidal ganglion-cells; the principal bulk, however, of the gray cortex is formed by a continuity of very finely granular and—as is now, according to M. Schultze's precedent, generally accepted—also sponge-like, finely reticulated substance. This substance, which evidently functions as the supporter of the nervous elementary parts, is the basis-substance of the neuroglia, and the question only is, which of the coexisting cellular elements we shall regard as cells of the neuroglia. If it were permitted to transfer without more ado the experiences of the white substance, the granules could at least in part be approximated to it. In fact, I know no difference between the "connective tissue" granules of the white substance and those of the gray substance. Here, however, the above-mentioned convictions of important authorities oppress us, who regard the granules of the cortex of the brain as small nerve-cells. The pathological facts, likewise, do not satisfactorily solve the riddle for us, for although we can demonstrate, that certain tumors arise and grow by a hyperplasia of these cells (the gliomas), yet these also are only such tumors as do not occur in other localities, excepting the allied retina. All the other new formations, carcinoma, sarcoma, tubercle, even pus, arise in other places, and can be adduced in only a subordinate manner for deciding what is connective tissue, and what is nervous in the brain. In other respects, I believe that every one who views the processes of the formation of

glioma, yellow softening, and some others, with unprejudiced eyes, will incline more to the conviction that the collective granules of the brain have the same significance, and, indeed, the significance of connective tissue cells.

1. Hyperæmia and Inflammation.

§ 688. Inasmuch as we have seen that every larger section of the nervous system possesses its peculiar vascular arrangement, it cannot surprise us if just in the province of hyperæmia, hemorrhage, and inflammation, we meet with a large number of individual pictures of disease in themselves peculiar. Dura mater, pia mater, brain and spinal marrow, peripheral nerves, all have their peculiar forms of hyperæmia and inflammation. Nay, these peculiarities are so great that we do not succeed satisfactorily in explaining them by the mere differences of vascular distribution and of vascularity. The whole relation of parenchyma to vessel, their significance for each other, is a different one in the dura mater from what it is in the pia mater, different in the pia mater from what it is in the brain. The ordinary schema, that every organ receives its corresponding amount of arteries and veins, which ramify *in it* into capillaries, suits properly only to the peripheral nerves. In the spinal cord, but still more in the brain, it appears to be the intention that only the smallest vessels, actually serving for nutrition and subject to no variations of calibre, penetrate into the nervous substance. Accordingly there exist in the brain and spinal marrow everywhere only *small nutritive territories*, from which results, for the hyperæmias and inflammations of the proper central organs, the double peculiarity that from local causes (for example, traumatic) they have a tendency to limit themselves to a small space, and that they are produced in a certain diffusion, generally only in consequence of intense *functional* irritations (psychoses). On the contrary, in the pia mater we have an enormous amount of large vessels, beside a parenchyma scarcely needing nutrition, which, however, possesses wide spaces, which present the most favorable opportunities for taking up inflammatory products and for extending an inflammation. Hence, just here the tendency of all hyperæmias and inflammatory processes to diffuse extension, which in acute cases are only checked by the limited space of the cranial capsule, to which in chronic cases, however, and in the still open cranial covering, an almost unlimited field is opened (hydrocephalus externus). The dura mater, because of its disproportional compactness and the intimate interweaving of its connective tissue bundles, cannot satisfy its contingent inflammatory desires in its parenchyma, hence hyperæmia and exudation appear at its inner surface, and here lead to one of the most interesting sequences of histological phenomena, with which we at the same time will begin our more special considerations.

a. *Pachymeningitis.*

§ 689. The *acute circumscribed suppurations* of the dura mater, which occur upon the occasion of penetrating wounds of the head and erysipelas, in caries of the petrous portion of the temporal bone, as also in the environs of softened thrombi of the venous sinus, are but little productive for histological studies, and only this one fact is to be brought forward, that the changes easily assume a gangrenous character, which is probably connected with this, that the narrow and few vasa propria of the dura mater easily become thrombotic, and thereby disproportionately large parenchymatous islands are placed beyond nutrition.

§ 690. The non-purulent, internal, also hemorrhagic *pachymeningitis* begins with a hyperæmia, which, according to a classification of Kremiansky, embraces in by far the most cases, in the first place, the territory of distribution of the arteria meningea media, the regio bregmatica, and from here gradually extends anteriorly, posteriorly, and downwards. The arteries are dilated, more tortuous than normal, and surrounded by an exceptionally thick, felty adventitia. The hyperæmia of the capillaries is expressed by a scarcely perceptible rosy tinge of the formerly so white and smooth inner surface, continues also during the continuance of the entire process at this inconsiderable acme of development. So much the more worthy of notice is that which is developed upon the basis of this hyperæmia, in and upon the surface of the dura mater. For the naked eye this, in the first place, is a loose, veil-like, yellowish coating, which is sown broadcast with numberless blood points and dots. This can be torn off with the forceps without difficulty; and if in doing this we carefully direct our view to the line of the separation, we here and there perceive red threads, which stretch between the dura mater and the pseudo-membrane; these immediately afterwards tear. These threads are nothing but vessels, which pass out of the dura mater into the pseudo-membrane and here ramify stellate. If we examine the membrane under the microscope, we are astonished especially at its great richness in very wide and thin-walled vessels. The walls of these vessels, scarcely to be called capillaries, appear with a simple, furthermore very delicate contour; the calibre however is, upon an average, three to four times as large as the calibre of ordinary capillaries, therewith irregularly curved out and distorted now to this side, now to that (Fig. 189, *c*). The substance in which the vessels are imbedded, and which forms a continuity throughout the whole pseudo-membrane, I would most prefer to call mucoid tissue. It is true, because of the various other depositions, there is no correct judgment to be had as to its quality, but I believe I have recognized this with certainty, that the cellular elements of the substance are spindle-formed and stellated, and are in connection by means of anastomosing processes of protoplasm, that the number of the cells is, upon the whole, limited, and the

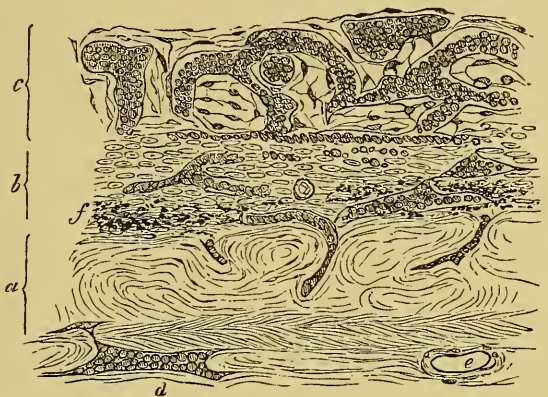
basis-substance perfectly homogeneous and transparent, but is clouded by acetic acid.

Touching the production of the so constituted neomembrane, probably no one will require of me, that I at this place expressly reject the views of Lancereaux, so meritorious in regard to this disease, who assumes, that a generatio æquivoca of cells takes place here; just as little can I approve of the older conceptions of German authors, according to which a superficial effusion of blood forms the first given substratum, consequently the neomembrane would be an organized extravasation. I rather place myself upon the standpoint first introduced by Virchow, and since then almost universally accepted, who regards the neomembrane as an efflorescence of the dura mater, and every hemorrhage, which happens in the course of the process, as conditioned by the peculiar constitution of this neomembrane. The latest investigations of Kremiansky have taught, that the epithelium of the dura mater readily thickens at the borders of the neomembrane, and then passes over continuously into the substance of the membrane. Kremiansky believes, that according to this condition, we must accept a participation, though ever so limited, of the epithelium in the formation of the membrane. Should this acceptation be confirmed, it would come into consideration at all events only for the very first beginning of the process. In other respects the subepithelial layer of the dura mater is undoubtedly to be regarded as the main source of the new formation. Out of the vascular pores, which open, first of all the formative cells (perhaps migratory colorless blood-cells?) press forward, then vessels; the former furnish the loose connective tissue parenchyma, the latter are themselves the vessels of the new membrane. The main stress consequently falls upon the development and dilatation of the vessels, for we may correctly imagine, that the newly developed capillary net acts like a valve towards the blood pressure, increased by the active hyperæmia, in the interior of the dura mater. The less here the unyieldingness of the fibrous tissue allows of a persistent enlargement of the calibre of the vessels, and the deposition of young tissue beside the vessels, so much the more marked becomes the ectasy of the newly formed vessels, which is only opposed by the general intracranial pressure.

§ 691. Before we speak of the hemorrhages, which are wont to complicate the further course of the process, I will bring the history of the pseudo-membrane by itself, to a conclusion. If we come to view the disease at a later stage, we find the membrane composed of several distinctly discriminable layers (Fig. 189). The one situated most inward (*c*), if moreover the process has not ceased, has the characters of the "first tinge," delineated in the preceding §§. It is at the same time the youngest, last produced layer. The next following (*b*) is distinguished from it by the far greater richness in cells of the parenchyma, and somewhat narrower vessels; the third (*a*), and all the follow-

ing, are woven of compact, lustrous connective tissue fibres, almost as densely as the dura mater itself, so that with the naked eye we cannot distinguish it from this. As we see, the question here is about a true analogy with the processes of organization, as we principally know

FIG. 189.



Pachymeningitis chronica hæmorrhagica. Vertical section through the dura mater, and an efflorescence of the same of several layers. The dura mater, which contains a venous vessel without proper walls and an artery, is not more minutely designated. It is intimately connected with the oldest layer of new membrane *a*. The latter simulates it even histologically. *b*. Next oldest layer consisting of spindle-celled and round-celled tissue, separated from *a* by a stripe of pigment *f*. *c*. Most recent efflorescence very vascular, separated from *b* by a thin layer of blood-corpuscles. 1–300.

them from the inflammatory new formation, about young, older, and the oldest connective tissue. Interesting and full of significance only is the circumstance, that here the cicatricial formation furnishes ever anew the same favorable soil for the superficial efflorescence that the structure of the dura mater presents from the beginning. It appears to me, that in this, there lies a ground as well for the rare cure, as especially for the desultory progress of the disease. As soon as the organization has brought about a certain measure of diminution of the vessels, the blood pressure in the inflamed membrane requires a new valve, which is thereupon provided for it by the efflorescence of a new membrane, furnished with wide bloodvessels.

§ 692. We come now to the intercurrent hemorrhages already several times mentioned, which play so prominent a rôle in the clinical and anatomical disease-pictures of pachymeningitis. That a vascular arrangement, as is presented in the pachymeningitic neomembrane, must almost necessarily give occasion to rupture of the vessels, is manifest. Hence, already the most delicate pseudo-membranous incipience is regularly pervaded with points of blood up to the size of a small lentil. The thicker the pseudo-membranes become, so much the larger also do the effusions of blood become; finally, we meet with pools of blood as thick and broad as the hand, which were formerly designated as hæmatoma of the dura mater. All these hemorrhages, the hæmatoma not excepted, are interstitial. The smaller blood points have their seat in the tissue of

the neomembrane itself, the larger constantly ensue between the youngest telangiectatic layer of the neomembrane upon the one hand, and the older layers of the neomembrane, or, if these are yet wanting, the surface of the dura mater on the other. The telangiectatic layer is lifted up by the effused blood and forms a sac, which in larger hæmatomas is expanded like a delicate cobweb over the coagulum of blood. This was once regarded as a peripheral, encapsuling coagulation of fibrin. Here and there, we probably also find some blood in the arachnoidal sac, which has then oozed through the delicate connective tissue membrane.

§ 693. Larger hæmatomas easily become fatal by pressure upon the brain. A more rare occurrence is diffuse suppuration of the whole neomembrane as a reactive inflammation against the hemorrhagic effusion, as in wounds. I have seen this once. On the other hand, we very frequently have the opportunity of seeing the decomposition of the effused blood, and the formation of numerous pigment bodies in the interior of the neomembranes. For these things, the most instructive are the older pseudo-membranes no longer developing, which we occasionally, although rarely find beside recent irruptions, and which are characterized by their peculiar brick-red, or light rust color. The vessels are completely obliterated in these membranes; we can, however, distinctly recognize and follow their ramifications by tracing up the accumulations of pigment, which accompany them on both sides. The pigment appears here in red and reddish-yellow granules, of which three to seven are united in large round cells. Pigment-cell lies close to pigment-cell, only the width of the vessel itself and the centre of the parenchymatous island remains free, so that an elegant picture results.

b. *Leptomeningitis* (*meningitis*, *arachnitis*, *hydrocephalus*).

§ 694. The anatomical substratum, whose hyperæmic inflammatory condition will occupy us in the following, forms indeed a connected whole, but its individual parts, arachnoidea, properly pia mater, networks of vessels, and the ependyma of the ventricles, have so pronounced an anatomical individuality, that we must not be surprised if each of them takes part in the disturbances of the whole, in its own manner. To this is to be added, that seldom or never is the entire system simultaneously diseased, but at one time it is the pia mater over the convexity of the hemispheres of the brain (meningitis convexa, hydrocephalus externus), at another time it is the pia mater of the base and of the Sylvian fissure (meningitis basilaris), the third time they are the plexus choroidei and the ependyma of the ventricles (meningitis ventricularis, hydrocephalus internus), and as these localizations also about correspond to the mentioned subdivisions of the system, the peculiarities of the latter give at the same time occasion to charac-

teristic local modifications, which characterize each of the different morbid pictures which we have to specify here.

§ 695. Meanwhile, ere we penetrate further into the subject itself, it appears to me judicious to assert several more general considerations concerning the changes in the amount of blood contained in the brain, and its vascular membrane. In this connection we encounter, above all others, the effects of the firm limitation of the organ as to space by the bony cranial capsule. "For every quantity of fluid which enters this space, a like quantity of fluid must leave the space, and *vice versâ*." This necessity would form the basis for a very uniform circulation within the cranial cavity. As the blood-pressure in the vessels would be directly transferred upon the parenchyma by the continuity of the surrounding fluid, the parenchyma, however, finding a support in the firm cranial capsule, the interior of the cranium (including the blood) would necessarily stand everywhere under the same pressure, and the circulation would be entirely maintained by the difference of pressure in the carotids, and the vertebral arteries *before* their entrance into the cranial cavity, and in the internal jugular vein. The flowing of the blood within the cranium would thereby be identical with the flowing of fluids in unyielding tubes; nothing whatever could be said of variations of calibre; the significance of the walls of the vessels as an elastic membrane would be done away; a somewhat larger part of the propulsive force would have to be converted by friction into heat; a variation of pressure, especially an increase at any one place, a hyperæmia, not to say a hemorrhage, would be not at all possible, &c. All these consequences are, in fact, realized up to a certain degree; it is known that the walls of the arteries in the brain are exceptionally thin in comparison to their lumen (the lumen of the basilar artery, for the sake of example, is not smaller than the lumen of the brachial, while its walls are scarcely one-third part as thick); the larger cerebral veins, the sinuses of the dura mater are actually rigid tubes. If, nevertheless, the realization of our consequences is not complete, this can only have its cause in this, that the closure of the cranial capsule is not complete; and this, in fact, it is not. The spinal marrow fills up the foramen magnum somewhat more than one-half, and in this interspace the liquor cerebro-spinalis can freely interchange; it may pass out of the cranial cavity when a greater filling of the cerebral vessels requires it; it may return thither in the contrary case; in short, we have here a valve with some play, and we must also from this point of view admit the possibility of variations of pressure in the interior of the cranial cavity. Of course, increases of pressure by hyperæmia and exudation can occur constantly only in a limited region, and only up to a certain point. If the play of the valve is exhausted, no increase of pressure can now any longer be reached by the further supply of blood; this is possible now only by the irresistible pressure of a firm new-formation, and takes place con-

stantly at the expense of the vascularity of the brain. The blood is then pressed out, or not at all admitted; and in the latter instance the death of the individual is brought about thereby. In very many cerebral diseases we will have occasion to remember these circumstances. For the hyperæmias and inflammations of the pia mater system there results meanwhile only an explanation of that limitation to certain sections, which I stated as characteristic in the preceding paragraph.

§ 696. The *acute hyperæmia and purulent infiltration* of the pia mater over the convexity of the cerebral hemispheres, will be the next object of our studies. This is at the same time the non-specific, very commonly traumatic, more rarely spontaneous, the so-called by the laity, inflammation of the brain; a tolerably decided congestion of the collective vessels coursing in the pia mater, with purulent infiltration of the subarachnoid lymph-spaces. The most striking phenomenon herewith is, that the purulent exudation is strictly confined to the parenchyma of the pia mater, and nowhere passes beyond its outer limits, the arachnoid. The formerly so favorite drawing of an analogy between the arachnoidal sac and a serous sac, which received a heavy blow already by Luschka's studies* upon the parietal layer of the arachnoid, appears to have lost even its last adherents by this glaring deviation from the superficial character of serous inflammations. It does appear to me, as though the deviation has its cause simply in the presence of cavities very capable of dilatation in the nearest surroundings of the vessels. If anywhere, then, will the theory of inflammatory exudation set up by Cohnheim (§ 89) find its application in this case. For even with the naked eye we can establish, that the production of pus everywhere follows the course of the vessels. The pus accompanies the outer surface of the vessels, and indeed quite peculiarly the large and small venous trunks, which empty in the region of the vertex into the longitudinal sinus, as a yellowish-white, primarily narrow double band, afterward becoming ever broader. The longer the process continues, so much the more do the stripes of pus of adjacent vessels come in contact with each other, the pia mater swells up in toto, not infrequently attains a peculiar rigidity, which is derived from the tense expansion of its fibres, perhaps also from the coagulation of lymphatic constituents of the exudation, and may then, inclusive of the processes which fill the sulci, be lifted off from the compressed and anæmic, rarely somewhat softened brain-surface, of which it presents a solid cast.

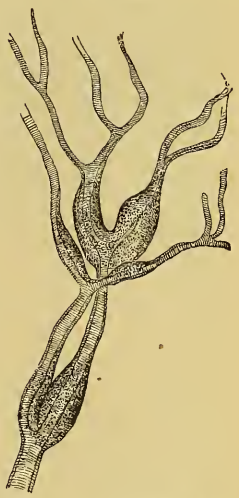
If we place a still transparent bit of the pia mater, which contains a small vein, under the microscope, we see, especially after previous coloring with carmine, the picture of inflammation, which Cohnheim learned to know from the peritoneum of the frog, in the most pregnant manner. The paving of the intima with colorless blood-corpuscles may be best

* Luschka has proven that the so-called parietal layer of the arachnoid is only the epithelium of the dura mater.

seen upon cross-sections of hardened preparations, likewise the constantly very moderate infiltration of the tunica media; but what makes the superficial picture quite specially valuable to us, is the conviction we get here, that each pus-corpuscle infiltrated into the pia mater has actually migrated from the vessels. Close to the media the cells lie densely packed, the further removed from the vessel so much the fewer do the pus-corpuscles become, until we finally meet with connective tissue meshes, in which only one pus-corpuscle or so swims, or which are yet entirely free. After this the explanation of the total picture can scarcely be doubtful. The pus-corpuscles are migrated colorless blood-corpuscles.

§ 697. A morbid picture, different in many respects, is presented to us by the *acute basilar meningitis*, which, because of the never-failing complication with miliary tuberculosis, is also termed tuberculous meningitis. The proper central point here is, in fact, not formed by the inflammation of the pia mater, however this may also be replaced by a multiple hemorrhage and red softening of the cerebral cortex; this is the fatal force of the entire process, yet only a secondary one. As the most essential phenomenon, we must rather regard the development of numerous tubercles in those parts of the pia mater which line the furrows and sulci of the base of the brain. The nodules are most abundantly found in the region of the fissure of Sylvius, and here again the sheaths of the arteries are the preferred seats of development. This was already minutely explained in § 115, together with the whole history of development of tubercle. The *injury to the lumen of vessels* by the miliary tubercles was less emphasized there. (See Fig. 190.) The latter protrude as round, or at least roundish tumors, not only outwards, but also push the media and intima inwards, so that at the place where a tubercle is situated, a projection is formed into the vessel. Afterward, both tunics are directly broken through by the tuberculous proliferation. If we cut open a tuberculous vessel longitudinally, and observe the inner surface, at the point where a perforating tubercle is seated, instead of the known longitudinal folds of the intima and the transverse striæ which are produced by the muscular fibres, we observe a sharply-circumscribed cleft, through which the small-celled tissue of the tubercle projects. Consequently, by the tuberculosis not only is the lumen of the vessel narrowed, but its durability is also directly changed and brought in question. We may imagine that by this alone are already brought about the most

FIG. 190.



Tuberculous degeneration of a branch of the artery of the Sylvian fissure, with its ramifications. The miliary nodules which have developed in the adventitia partly compress the lumen of the vessel.

considerable local disturbances of the circulation. The increase of the blood-pressure before the narrowed spot may give occasion to diffused collateral congestions, and currents, the destruction of the intima and media to hemorrhages; all this, however, in a higher degree, if an acute active congestion is added. I, therefore, so comprehend the course of the inflammation, that I assume a longer stage, in which the tubercles gradually come to development, and in this manner a best possibly prepared soil is produced for the inflammation, while, in a second stage, the addition of an active hyperæmia brings about in a short time the total picture of basilar meningitis.

§ 698. In taking out the brain, we almost regularly find free fluid in the cranial cavity, which has run out of the system of ventricles. The collective ventricles of the brain, especially, however, the two lateral ventricles, participate in the disease by a serous effusion (hydrocephalus acutus), and small sugillations in the ependyma. The depressions at the base of the brain are covered with a gelatinous exudation, which fills and distends the meshes of the pia mater; here and there we probably also find a yellowish coagulum free upon the surface. The sero-fibrinous infiltration is continued to the Sylvian fissure, here

FIG. 191.

Vertical section through the pia mater and the contiguous portion of the cortex of brain in tubercular meningitis. *a, a.* A larger vessel of the pia mater whose entire sheath is inflammatorily infiltrated. *b, b.* Lymph-spaces of the pia mater with commencing tubercular proliferation of the endothelia. *c.* Miliary tubercle of the pia mater. *d.* Outermost layer of cortex of brain infiltrated with round cells. *e.* Normal brain-substance. *f, f.* Proper cerebral vessels in a state of tuberculous degeneration.

assumes "in spots" a purulent character, without, however, at any time a pregnant picture of purulent meningitis being developed. The pus only appears in narrow yellowish stripes, which accompany the vessels, and for the naked eye flow together with the much more striking tuberculous proliferations. The latter, upon the artery of the Sylvian fissure, are often a line in height and breadth, caseous, friable; while upon the smaller ramifications they are commonly grayish, translucent, and less striking. We find a special peculiarity of tuber-

culous meningitis in the participation of the cerebral cortex. This is brought about, upon the one hand, by the irruption of tubercles upon all those vessels which penetrate "naked" from the pia mater into the cerebral cortex; upon the other hand, there is a continuous transition of the inflammatory infiltration of the pia mater to the surface which it covers. The most external, white layer, or poor-in-cells of the gray cortex is in spots most densely infiltrated with cells that have penetrated (?). If we strip off the pia mater, these infiltrates remain adhering to it, and the surface appears rough, as though corroded. The tuberculous degenerations of the vasa propria of the brain are at all events much more important. These advance up to the borders of the centre of Vieussens, and not only by the puffing up of the vessel, but especially by the numerous hemorrhages which they occasion, lead to the mechanical injury and destruction of the cerebral cortex.

An observation is at my command, where the cerebral cortex, all around the fissure of Sylvius, was in the condition of red softening, which could without difficulty be traced back to numberless dotted ecchymoses of tuberculous cerebral vessels. Rokitansky also speaks of hemorrhages which were occasioned by the tubercle-formation.

§ 699. *Venous hyperæmia and œdema of the pia mater. Hydrocephalus externus.* In consequence of long-continued or of frequently recurring irritative hyperæmias of the brain (psychoses, alcoholism), the veins of the pia mater fall into a persistent relaxation and distension, which with all its phenomena and consequences falls under the category of stagnant hyperæmia and of phlebectasy. That this is actually so, proceeds from the perfectly analogous development of the morbid pictures in mechanical obstacles to the efflux of blood from the cranial cavity, in thrombosis of the sinuses, &c. The seat of this disease, therefore, is the region of the cerebral veins, the region of the vertex along the longitudinal sinus. The longitudinal sinus is either not capable of dilatation, or the pressure from both sides of the softer edges of brain capable of tumefying, prevents this dilatation; in short, the longitudinal sinus itself shows anything else than an abnormally large calibre. So much the more does the ectasy occur in those well-known six to eight pairs of large veins, which collect the blood at the whole surface of the great hemispheres, and convey it to the longitudinal sinus. These become both wider and longer. The elongation shows itself in a greater, and often very great, expression of the spiral and zigzag turns, which their course at least indicates already under normal circumstances. Upon the small branches, the most wonderful convolutions, curves backward and the like, occasionally occur probably under the co-operating influence of the compression between the brain and the arachnoid. The next consequence of the venous dilatation is the effusion of serous fluid, the œdema of the pia mater. This fluid is perfectly clear as water, but little albuminous. It collects in the meshes

of the pia mater, and pours out freely and completely as soon as we split the arachnoid by a cut at a dependent place. The great amount of fluid often surprises, particularly if we reflect that the space which it occupies is properly taken up by quite different things, and that this can only be accomplished by the crowding aside and compression of the brain. Herewith everything depends upon the length of time; we also know of sudden effusions of serum into the meshes of the pia mater, an acute œdema of the pia mater, which either again rapidly recedes, in that the fluid returns to the veins, or proves fatal by compression of the brain. It is different when the accumulation of water slowly increases, when the brain has time to accommodate itself to the abnormal condition. It is astonishing to what degree of compression, as to space, the accommodative capacity of this highly organized structure may go. Not only that the gyri are gradually pressed asunder, the sulci dilated tray-like, a quite uniform decrease of thickness of the hemispheres also takes place in the direction from the surface of the ventricle to the surface of the cortex of the brain. The hemispheres lose up to one-third, nay, up to one-half of their normal volume, and as it was not easy for the older authors to believe in so extensive a diminution of the brain, they discovered an explanation of hydrocephalus from vacuum, *i. e.*, they took the atrophy of the brain as the primary, and let the effusion of water appear for the purpose of filling the vacancy.

Only one, and indeed, never very important phenomenon of hydrocephalus externus is properly of histological interest. I mean the so-called milky clouding, which the tissue of the pia mater experiences in the immediate surroundings of the vessels. This milky clouding has not incorrectly been regarded as an induration of the connective tissue. It begins with an infiltration of colorless cells, and in so far, has something analogous with purulent arachnitis. The degree of the milky clouding also, depends in the later stages directly upon the amount of infiltrated round cells, although, besides, or rather after this infiltration a fibrous transformation, consequently a new formation, takes place of connective tissue. Finally, the outer layer of the pia mater, inclusive of the arachnoid, is converted into a tolerably compact film, from whose under surface the vessels penetrating into the brain proceed and leap over the often tolerably broad space up to the surface of the brain, either naked, or only accompanied by some connective tissue adhering to them. The brain-substance itself is leather-like, compact, dry, here and there also macerated, *i. e.*, softened without any development of pus or other formed constituents.

§ 700. *Hydrocephalus internus.* Upon the occasion of tuberculous basilar meningitis we mentioned quite transitorily the participation of the ventricles of the brain in this process. Almost constantly we find a moderate dilatation of the lateral ventricles, produced by an evidently acute effusion of pure, slightly yellowish serum of the blood into them

(hydrocephalus acutus). For this effusion the immediate connection of the pia mater basalis with the choroid plexus must be made answerable. I find in many cases of this sort the branches of the choroid artery beset with tubercles. The tubercles will just as well lead to circulatory disturbances, hemorrhages and serous effusions here, as they do upon the other branches of the internal carotid, especially upon the artery of the Sylvian fissure (§ 697); it only remains for us to comprehend, how the exclusion as to space of the pia mater towards the brain has the consequence, that the effusion is not poured out into the parenchyma, but upon the free surface of the choroid plexus, *i. e.*, into the ventricle.

§ 701. Far greater difficulties present themselves for understanding chronic hydrocephalus. A slowly increasing collection of water in the ventricular spaces of the brain (and "of the spinal marrow" we must add in reference to the analogous conditions of hydrorhachis, spina bifida, &c.), leads to a corresponding dilatation of them, and to a centrifugal decrease of thickness of the cerebral hemispheres, as also the other cerebral parts immediately bounding the ventricles. The swelling out of the central nervous organs is also imparted to the osseous envelope, naturally, only so long and in so far as no osseous connections by suture, yet exist between the cranial parts. In the latter case—the acquired hydrocephalus—the substance of the brain, indeed, suffers a greater centrifugal pressure, the decrease of thickness, however, proves to be of less degree than in congenital hydrocephalus. In congenital hydrocephalus there are then again two cases to be distinguished, accordingly as the hydrocephalic effusion sets in in the very earliest periods of development of the fœtus, when it bursts the cerebral vesicles and generally lets neither brain nor cranium come to development (anencephalus, hemicephalic abortion), or accordingly as the effusion is first produced towards the end of pregnancy, where we then have—a happily terminated labor presupposed—the comparatively most favorable chances for the continuance of the life of the individual, since the yet unclosed sutural connections of the cranium give way to the dilatation of the brain without a too great and injurious counter pressure, while upon the other hand the great accommodative capacity of the brain to abnormal positions makes possible the psychical functions.

Into the province of hydrocephalus fall also those partial projections of the ventricular spaces of the brain and of the central canal of the spinal marrow, directed to one point, which are known as hydrorhachis, spina bifida, encephalocele, myelocele, encephalo-myelocele.

§ 702. If we now ask: whence these effusions? What is the nature of hydrocephalus? we must unfortunately acknowledge, that we are yet far removed from a generally sufficient explanation. Virchow would like to maintain, based upon the relations of the ependyma ventriculorum, an inflammatory process; in the same sense we might find a

parallel with acute hydrocephalus. For my own part I would likewise appeal to acute hydrocephalus, but only generally to obtain a basis for the investigation. We have seen, that there, anomalies of the distribution of blood in the choroid plexus occasion the effusion. It was a matter of indifference how these anomalies of the distribution of the blood were produced, they sufficed for explaining the exudation, and our next duty is, therefore, to examine the choroid plexuses also in chronic hydrocephalus, in order, perhaps, there to make the source and the seat of the disease discoverable. Now, in fact, the plexuses are constantly hyperæmic, and if we place parts of them under the microscope, we furthermore find that the surface is beset with numberless, small and unbranched, but very vascular papillæ. Each of these papillæ consists of a thick mantle of epithelial cells and a central part, which is occupied almost only by lumina of vessels. The epithelium in all its two to three layers shows the known forms described by Henle, roundish polygonal cells with manifold, prickly processes, which extend into the interspaces of the nearest contiguous cells and reach down to the connective tissue of the papillæ. I should, perhaps, only say, to the vessels of the papillæ, for the vascular membrane appears, in fact, to be the only connective tissue that generally exists in these papillæ; I have nowhere seen the picture of epithelial-bearing vessels so beautifully as here. Farther below we will be aware, that the production of epithelial-bearing vessels is a characteristic peculiarity of the locality, *i. e.*, not so much of the choroid plexus, as principally of the "brain-surface of the pia mater," of which the surface of the plexus is only a part. Exceedingly interesting tumors, which will be more minutely spoken of under the myxomas and psammomas, depend upon this, and the history of cerebral cancer will teach us, that the heterologous production also of epithelial cells is confined to the same situations, consequently is not heterologous to that degree that it might appear at first sight.

If we now return to our theme, the finding of papillæ of the kind described, especially at certain places of the choroid plexus, is also so constant in healthy individuals, that we can only place a value upon the quantitative excess of this proliferation, and we can only afar off imagine the increased secretion of the liquor cerebro-spinalis in connection with the increase of these papillæ. I would at all events place a greater value upon each, even the smallest active or passive hyperæmia of the plexus, and especially direct attention to this, that just these hyperæmias and exudations, because of their direct relation to the liquor cerebro-spinalis, to the valve of intracranial pressure, might more easily carry the day than the hyperæmias in other regions of the cranial contents.

In my opinion an exaggerated value has been placed upon the changes which the ependyma of the ventricle experiences. The epen-

dyma becomes thicker and denser in certain regions, for example, above the optic thalamus; at the fornix and at the stria cornea, moreover, partial thickenings are raised up in the form of small translucent nodules like beads of dew above the level of the surface. But as well the general as the partial thickening ensues without any participation of the vessels; the ependyma—taken apart from the epithelium as the boundary layer of the neuroglia—lets indeed the vessels of the contiguous parts of the brain with their main ramifications shine through, but it itself never contains vessels, and hence must be regarded as a partition wall ever becoming thicker between the free surface and the cerebral vessels. In much thickened ependymas we find the most beautiful nets of stellate cells; the single cells often with double nucleus, longitudinally ramified, and especially in the longitudinal direction; the intermediate substance is finely fibrous and stratified in numerous layers, so that upon a cross-section, the fibres of the deeper layer meet the fibres of the upper at acute angles. The thickenings also, like beads of dew, which are observed at the fourth ventricle even without hydrocephalus in very varying clinical morbid pictures (epilepsy, masticatory facial convulsions, disturbances of speech), consist entirely of fibrous connective tissue with very few cellular elements.

§ 703. In conjunction with hydrocephalus internus, we must mention the so-called *white softening*, since it has by no means yet been established that this is to be exclusively regarded as "a post mortem" maceration of the cerebral substance in the hydrocephalic fluid. In the thing itself there is, of course, but little changed thereby, only the occasional punctiform hemorrhages could scarcely be explained without a *vis a tergo*, *i. e.*, without circulation and life. Moreover, the question is about a softening and dissolution, which, in the first place, the neuroglia, afterward also the nerve-fibres, fall into. Thus arise at various points of the surface of the ventricles, by preference in the posterior horn, superficial cleavings of the white substance, which extend to the depth of one to two lines into the walls of the ventricle. Formed constituents, pus, &c., are not developed therewith.

c. *Hemorrhage.*

§ 704. Ere we take into consideration the hyperæmic inflammatory conditions of the cerebral substance itself, we will yet continue upon the bridge which leads over from the pia mater to the brain, *i. e.*, we will discuss several changes of the cerebral vessels and the various cerebral hemorrhages, since these stand in manifold and very close relation to those inflammatory processes; a knowledge of them, indeed, precedes the study of cerebral inflammations proper.

Apart from traumatic hemorrhages into the so-called arachnoidal sac, which are produced by the tearing of the veins of the pia mater from the longitudinal sinus, and apart from those more rare cases,

where aneurisms of the basilar arteries rupture, intracranial hemorrhages are accomplished only by the bursting of proper vessels, *i. e.*, running in the cerebral substance.

Pathological anatomy is wont in general to distinguish a hemorrhage in bulk, from the punctated form, according to the quantity of the extravasated blood. This distinction, however, is also etiological and, indeed, in so far justified, as the bulky hemorrhage is probably exclusively produced upon the basis of a preceding diseased condition of the vessels, while the punctated hemorrhage owes its occurrence to a greater number of etiological causes. The extravasation of blood in small punctiform portions is in the first place observed in every acute inflammation of the brain; we have, indeed, hemorrhagic hyperæmias and inflammations also in other organs, upon the serous membranes, mucous membranes, &c., but nowhere is the sugillation so constant an accessory as just here. Furthermore, the embolic occlusion of a small cerebral artery, together with a hyperæmia proceeding even to a stasis, brings about punctiform hemorrhages in the territory of the ramifications affected. Thirdly, the endoarteritic process (§ 215) next to the large arterial trunks of the base, attacks also the medium and smallest ramifications of them. By the fatty usure (§ 220) of these medium sized branches of the artery of the Sylvian fissure, which run through the substantia perforata lateralis to the corpora striata, the majority of large hemorrhages are brought about. But punctated hemorrhages may also be conditioned by endoarteritis, of course in a somewhat different manner. The hemorrhage occurs here from the arterial transition vessels. These are considerably dilated, so that they present actually spindle-formed aneurisms. Herewith I naturally do not think of those dissecting aneurisms, which are themselves a frequent form of punctated hemorrhage (see psychoses), but of a distension affecting the total walls, which is analogous to the aneurisma verum of large arteries. The vessels are converted into wide, slack, thin-walled tubes; there is scarcely yet an indication existing of the histological elementary parts of the walls and their arrangement into three tunics. Instead of the inner and middle tunic we observe a number, not large, of flat nuclei, which permit us to conclude upon a process of division taking place, by the duplicity of the nucleoli, and the known indentations and constrictions. The endothelium, intima, and media have also been destroyed by a demonstrable process of proliferation, with them, however, and especially with the media, just that constituent of the walls of the vessels, which guarantees above all their capacity of passing from distension to contraction, and thus to render resistance to the pressure of the blood. The walls of the vessels, distended beyond the normal measure, finally give way at places and the extravasation of blood follows. Finally, in the fourth place, the morbus maculosus Werlhofii* also occurs in the

[* Purpura hæmorrhagica.]

brain in the form of numerous punctiform hemorrhages. As the cause, therefore, of the bulky hemorrhage, we have to adduce the atheromatous process; as the cause of the punctated hemorrhage, beside that, also the simple inflammatory hyperæmia, embolism and the morbus maculosus.

§ 705. The histological changes, which come into question in cerebral hemorrhage, can be far better studied in the punctated hemorrhage than in the bulky. We continue, therefore, in the first place, with the former. In the punctated hemorrhage there always appears but a small quantity of blood at the outer surface of the vessel, which collects in the form of a globular drop. The cause of this is to be sought in the rapidly occurring equalization of the intravascular blood-pressure and the resistance, increased by the extravasation itself, which the surrounding nerve-tissue opposes to the effusion of the blood. This explanation applies still more closely to those punctiform extravasations occurring especially in psychoses, in which the blood does not at all reach the outer surface of the vessel, but, being held back by the elevated and bellied adventitia, forms a so-called dissecting aneurism (see § 714). That herewith the counter-pressure of the extravasated blood, supported by the tension of the adventitia, furnishes the principal force for stopping the hemorrhage, can scarcely be doubted. But also in the free hemorrhages the small opening which the vessel had received by the momentaneous giving way of its walls, again closes immediately. It is that form of hemorrhage which was formerly called diapedesis.

The view which the constantly multiple punctated hemorrhage affords the naked eye is partly characterized by the name, is partly dependent upon the etiological causes. In morbus maculosus and the diffuse inflammations of the cortex of the brain (psychoses) we see the blood-points uniformly distributed over the whole brain-substance—that is, the cortex of the brain; in all other cases we have depot-like affections. Upon the central region, diseased in the highest degree, we can distinguish a zone from one surrounding it, in which the disturbance decreases in intensity from within outwards. Therewith the singular mystification rules, that the very first morbid picture, the condition immediately after the occurrence of the hemorrhage, is the same, whether the question be about a circumscribed inflammation, about an embolus, or a degeneration of the vessels. We find the substance of the brain pervaded with blood-points in a circle of $\frac{1}{4}$–$\frac{1}{2}$–1 square inch and more, which blood-points vary little among themselves in size; increase, however, in number towards the centre, till finally the centre itself is composed of exceedingly numerous, densely crowded blood-points. The partly pressed aside, partly compressed brain-substance, in the immediate surroundings of each individual blood point, shows a slightly reddish discoloration; where the blood-points are quite densely crowded, these reddish areas run into each other, so that for the most

superficial observation the entire depot presents itself as a reddish-yellow spot beset with a large number of intensely red blood-points.

§ 706. If we now occupy ourselves with the further fate of the effused blood, we first of all touch upon distinguishable phenomena of coagulation. In the first place, in the interior of each blood-drop we find the known minutely filamented net of rigid fibrin, in whose meshes the blood-corpuscles lie; furthermore, however, our interest is excited by the formation of a membrane inclosing, encapsuling the drop of blood. This is of various, never very considerable thickness, and consists of a soft, originally homogeneous, clearly translucent substance. We are evidently dealing with a secondary excretion of an albuminate at the periphery of the extravasation, which has nothing to do with the coagulation of the fibrin primarily present; and the question only is, how this is to be accepted and explained. Now, in this connection, the simple application recommends itself, as I think, of that experience made by Alexander Schmidt upon the formation and separation of fibrin, which I have already imparted (§ 186). According to that, the encapsuling of the extravasated blood would have to be regarded as a separation of fibrin, for which the fibrinogenous substance of the circumfluent nutritive fluid, the fibrino-plastic substance of the blood-corpuscles is furnished. This fibrinous capsule is a quite constant phenomenon, but I lay especial stress upon it on this account, because I believe that it has frequently experienced misinterpretation; thus, if we make sections through the hardened substance of a punctated apoplectic depot, we might readily feel called upon to regard the capsules as the walls of a transversely divided vessel filled with blood, and thereupon especially to extend the region of the interparietal hemorrhage unduly. Hence it is necessary to convince ourselves by teased out preparations, which are treated with glycerine, that the blood-points may actually be isolated in the form of globules, each of which is surrounded by a capsule closed all around. By moderate pressure upon the covering glass we may burst the capsule and press out the contained blood-corpuscles. The empty capsule then remains behind, in whose centre we now recognize the minutely filamented framework of the primary fibrin.

§ 707. Up to this point the course of the changes in all cases of punctated hemorrhage is the same. Now, however, the way separates and deviates in three directions—to yellow softening, to suppuration, and to the direct organization of the apoplectic depot. For this variety is answerable, partly the etiological cause, partly the behavior of the cerebral substance. Of the new morbid pictures, however, which meet us upon this occasion for the first time, the cicatricial formation only is exclusively the consequence of the apoplexy; the others, because they may be occasioned also in other ways, stand upon a broader base, and are hence treated of, partly in the inflammation of the brain (red softening and suppuration), partly by themselves (yellow softening). Con-

sequently there only remains for us to mention yet at this place the direct organization of the apoplectic depot. This divides at each single blood-point into the organization of the capsule and that of its contents.

If, in the first place, we continue with the latter, I made at the proper time the statement, that colorless blood-corpuscles gradually take the place of the red ones. This occurs without the capsule being opened at any place; hence it appears as though the red corpuscles were converted into colorless ones. I must yet hold fast to this statement, which I have proved experimentally, although I admit that, by the meanwhile established migratory capacity of amœboid cells, the possibility of the migration of the cells mentioned through the fibrinous capsule, lies close to our thoughts, and is to be further considered. If all the red blood-corpuscles are replaced by colorless cells, there is nothing to oppose a direct transformation of this germinal tissue into fibrinous connective tissue; this is then also accomplished, and indeed in such manner, that a concentric stratification of the fibres is produced.

Meantime the capsule has also organized; we see cleft-spaces which run parallel to the surface, and divide the capsule into multiple layers or lamellæ; in these cleft-spaces connective tissue corpuscles (probably migrated cells) become visible; finally, the inner connective tissue fuses with the outer completely to a relatively small compact nodule.

A modification of this process only occurs where the blood-points are so densely seated, that the adjacent ones touch with their capsules. In this case I have observed an intimate growing together and adhesion of the capsules; as a final result, however, a kind of cavernous tissue, whose meshes were filled with clear serum. As these meshes previously contained the extravasated blood, the question is, What has become of it? Upon this I can impart no definite information.

§ 708. Thus far the metamorphoses of the punctated hemorrhagic depots. Let us now attempt to apply the experiences just obtained to the phenomena of the *bulky hemorrhage*. Let us assume that one of the larger branches of the artery of the Sylvian fissure, which advances from below towards the corpus striatum, is torn; the blood has been effused in a large body, and has disrupted the substance of the brain in all directions. It has advanced outwards as far as the centre of Vieussens. It has pushed the thalamus opticus inwards, first lifted up the corpus striatum itself, then however broken through it at various points, in order to be poured free into the lumen of the lateral ventricle. A lake of blood, two inches long, and half an inch wide and deep, has been established in the region of the extra ventricular portion of the corpus striatum (Linsenkern). The considerable demand for space which such a condition brings with it, is satisfied partly by the complete displacement of the cerebro-spinal fluid, partly by the emptying of the cerebral vessels; in case we make a post mortem, if the dura mater is lifted from the surface of the brain, we find the sulci effaced, the gyri flattened,

and all the veins of the vertex so completely emptied, that we cannot recognize their smaller branches with the naked eye. The question certainly is, whether in extravasations of so high a degree, death must not inevitably occur. Still I would have it considered, that just in the bulky hemorrhages, the curability of the individual affections has very wide limits. If once the first injury has been happily withstood, the occurring coagulation of the extravasated blood already brings about a direct relief to the brain; the blood clot contracts vigorously and from all sides, and although the functional disturbances, which the tearing of so many important connections between the centre and the periphery has brought with it, last yet for a long time, still the blood relatively soon again finds access to the vessels, and thereby the danger of death, threatened by the want of nutrition of the organ, is turned aside. The cure of the condition thereupon immediately begins. Here, also, it comes, in the next place, to the separation of a fibrinous capsule at the whole periphery of the blood-clot, which, of course, turns out thicker in the measure that a larger amount of fibrinogenous and fibrino-plastic substance is at disposal. This capsule is confirmed by all authors. Originally it has the thickness of a line and more, is gelatinously soft and yellowish translucent. Afterward it passes through a metamorphosis analogous to that of the capsules of the punctiform depots; it becomes a far thinner, but also more compact layer of fibrillar connective tissue, which separates the apoplectic depot towards all sides from the surrounding parenchyma of the brain. Upon the whole, but little is known of the changes which the effused blood undergoes. The hæmatin is dissolved in a diffuse manner, and often permeates the surroundings of the depot for a considerable distance, until it is absorbed by the vessels and removed. A part of it goes through the pigment-metamorphosis, and becomes the occasion of the deposition of yellow pigment granules and hæmatoidin crystals into the cicatrix. In other respects the blood undergoes a connective tissue metamorphosis, whose result, of course, as in arterial thrombus, is a diminishing small quantity of connective tissue. This small quantity always suffices to seal the walls of the capsule, and to produce from the entire depot a simple connective tissue stripe, therefore a cicatrix in the ordinary sense. Meanwhile this happens only in the rarest cases. The ordinary result is not a connective tissue stripe, but a so-called "apoplectic cyst," *i. e.*, the walls of the secondary connective tissue capsule do not collapse, but the space between them fills with a clear, slightly yellowish, or quite colorless fluid, in which the connective tissue production, of the organization of the blood, floats as a delicate, loose texture. For explaining this peculiarity we must probably point out the necessity, that the large gap of the brain-substance be compensated by a corresponding filling up of the space, with which then it also agrees, when these cysts are only found in the interior of the hemispheres, where any other mode of filling the

space is not possible, while the rare apoplectic depots of the surface form simple cicatrices, and the depression of the level arising therefrom is filled up with a little meningeal serum.

Touching the changes which the cerebral substance contiguous to the apoplectic depots experiences, that part of it which is actually broken up and torn, is liquefied by fatty metamorphosis and removed, and we will have to recur to this in yellow softening. It would be interesting to learn the process of sequestration, the separation of what has remained intact from what was destroyed, more accurately, yet for the present all statements are wanting hereupon.

d. *Encephalitis—Myelitis.*

§ 709. At another place I have already adduced the grounds, which are fitted in some measure to explain to us the peculiar phenomenon, that the inflammations of the substance of the central organs, with the exception of those which are conditioned by functional irritation, have a tendency to limit themselves to as small a space as possible (§ 688). Here I may content myself with once more stating the fact, and therewith to announce the glaring contrast, in relation to extension, acuteness, and symptomatology of the affection, which exists between what is popularly called "inflammation of the brain" (meningitis), and that which actually is inflammation of the brain. Cerebral inflammation proper owes its origin to traumatic influences in the most extended sense of the word, that is to say, to a local irritation attacking the brain from without. Either a stroke or a blow has actually encountered the cranium, a stab or cut perforated it and injured the brain, or a depot of inflammation and suppuration, which originally lay beside the brain, has infected the brain at the point of contact, or finally, the occlusion of a vessel, atheromatous inflammation, &c., have led to a circumscribed punctated hemorrhage, which then brings after it the inflammation as a secondary production.

§ 710. The main stress in encephalitis and myelitis rests upon the behavior of the parenchyma of the brain proper; we commonly say, this experiences a purulent melting down, and thereby, probably also not tell an untruth, for the result is: a depot of pus in place of the cerebral substance. But, unfortunately, by this the mode of this melting down is not by any means yet established. In the present state of the teachings on suppuration also, we can probably least of all expect an exhaustive detail just here. Only conjectures can be expressed, and individual points for guides may be maintained. To these latter I reckon the non-active participation of the nervous elements in the production of pus, and the intense participation of the vascular system in the entire process. The nerve fibres in the territory of the inflammatory depot are partly suspended as disconnected fragments in the pus, they partly adhere to the walls of the depot in a condition of advancing

maceration and dissolution. I could demonstrate in them, neither fatty, nor granular degeneration; the white substance separates at their surface in drops, the axis-cylinders may gradually become finer and then break down. The ganglion cells "in the depot" become darkly granular and experience a kind of crushing; I could several times demonstrate very characteristic fragments of them. Of the behavior of the ganglion-cells of the immediate neighborhood of the depot we will speak farther below.

Of the greatest importance for the macroscopic portion of the morbid picture, but probably also for the more minute appearances, is the manner in which the vascular apparatus participates. The intense hyperæmia, which opens the circle of disturbances, has without exception numerous small hemorrhages as a consequence, and these, indeed, are not wanting where the hemorrhage is the primary, and the inflammation secondary. If subsequently, it comes to softening and purulent melting down of the depot, the extravasated blood mingles with the pulp of softening, and imparts to it a more or less intense red color. Hence, the name "*red softening*," which is so apt to be employed for the encephalitic and myelitic depots, but which would naturally recur wherever the same result, although from varying conditions, has been arrived at. The purulent substratum is characteristic of the inflammatory form of red softening, and the circumstance, that the depot of softening is surrounded by an area of one, to one and a half, to two lines broad, within which the parenchyma is pervaded by numerous blood-points, and swelled up by commencing purulent infiltration.

The most important of all questions, which interest us in encephalitis, the question, whence the pus itself? has not yet been satisfactorily answered. Meynert assumes, based upon his microscopic investigations, a suppuration of the ganglion-cells by division, and the formation of a brood by their nuclei. My own investigations have taught me, that the accumulation of pus first ensues about the same vessels, which had bled. Upon transverse sections of hardened encephalitic depots (red softening) we find these surrounded by a comparatively broad area of pus-corpuscles; we may also succeed, with some care, in drawing out vessels covered with pus provided with actually purulent sheaths, from recent preparations. Finally, upon cross-sections we likewise see, that these masses of pus have pressed asunder, and away from the vessels the extravasated, but still fluid blood, so that instead of a drop it forms a ring, which surrounds the pus. According to this, therefore, the pus would be yielded by the adventitia of the vessels; we might also think of migratory colorless blood-corpuscles. Notwithstanding all this I would not like to deny to the neuroglia entirely, the capacity of producing pus; that it is generally able to produce cells is indubitable to me (solitary tubercles, glioma), and I regard my own just communicated results as indeed certain, but not as exhaustive.

Beyond the proper depot of pus, although not always, we meet with a zone of œdematous saturation, in which, according to the investigations of Meynert, the nervous, as well as the non-nervous elementary parts experience a series of changes, which lay claim to a heightened interest, since Meynert does not seem indisposed to ascribe to them an important rôle also in chronic cerebral inflammations, as which he correctly accepts the psychoses. Meynert describes upon these ganglion-cells a vesicular transformation of the nucleus, a simple and multiple nuclear division, a dropsical swelling up and a sclerosis, finally a molecular disintegration, and an obsolescence of the cell-body. Of these metamorphoses, the dropsical swelling up of the nucleus and the cell, may probably exclusively pertain to the red softening; the sclerosis was already described by Rokitansky by the name of colloid transformation. The protoplasm is considerably increased, and of a homogeneous, strongly refractive constitution; the entire cell appears of a very plump contour, the processes knottily tumefied. The nucleus has become invisible, before that the nucleolus. Meynert thinks to explain the condition as an infiltration with protagon, the principal constituent of the white substance of the nerves discovered by Liebreich. Moreover, all these changes, with the exception of the nuclear division in the ganglion-cells, which I could never establish with certainty, are of a retrogressive kind; the calcification and excessive pigmentary infiltration described by Förster might yet be added, of which the former is likewise found around old encephalitic depots; it is, however, here also confirmed that the nervous elements participate only passively in the disturbances.

§ 711. We have no positive observations upon the possibility, and the nature and manner, of healing of a recent encephalitic depot. Meanwhile I regard it as probable that certain forms as well of yellow softening as also of the so-called apoplectic cysts, may appear as productions of encephalitis. The yellow softening would then indicate a cessation of the process, the apoplectic cyst a cicatrization, both, however, would have to be regarded as healings in contrast to the much commoner continued development of the inflammatory depot into a *cerebral abscess*. How this further development is accomplished, we have received some hints in the preceding paragraph; if, however, I left the question as to the participation of the neuroglia open, it was done principally with reference to the cerebral abscess. The most essential part in the production of that which is called cerebral abscess, namely, is a compact connective tissue capsule which incloses the pus upon all sides from the cerebral substance. This capsule, which may attain one-half line in thickness, passes over so uninterruptedly upon the surrounding nervous parts that the thought of a spontaneous production of the connective tissue on the part of the nerve-substance is brought very close. The definitive answer of the interesting question we will

have to leave to experimental investigation, which has already been active in this province (Leidesdorf and Stricker), up to the present time, however, has not yet touched the kernel of the affair; namely, the derivation of the inflammatory cells. For my own part I can accurately state, what in an older abscess is seen upon cross-sections, which embrace the abscess-membrane and the nearest adjacent nervous parenchyma even into the healthy parts, and therein I will proceed from within outwards. The cerebral pus has a greenish-yellow color, synovia-like consistence, reacts mostly acid, is odorless, and evidently of a very bland nature, without tendency to decomposition. The pus-corpuscles are mostly polynucleated, which is perhaps, a consequence of the continued maceration in a slightly acid medium. The surface of the abscess-membrane is smooth. An uninterrupted, tolerably thick layer of fatty-degenerated cells gives it a yellowish-white, opaque appearance. Upon the latter follows a layer of regular germinal tissue, which by its irregular thickness causes wave-like inequalities of the surface. The germinal tissue towards the exterior goes over into a very loose spindle-cell tissue which is stratified distinctly parallel to the surface, and only here and there sends up a fibrous line obliquely into the apices of the villosities of the germinal tissue. We see here everywhere the most beautiful spindle-cells; each apparently simple fibre upon more accurate observation may be recognized as a fibre-cell, so that here the appearance actually is as though all the connective tissue fibres following in the nearest outer layer were produced from spindle-cells. Little is to be said of the proper fibrous layer of the connective tissue capsule which conditions the varying thickness of the entire membrane. Beside the fibres it yet always contains numerous partly round, partly caudate cells. The latter always become more numerous towards the outer surface; at the surface itself they get the upper hand of the fibrous parts, and at the same time assume for the greater part the character of fatty-granular cells, so that here, for the second time, there follows a zone of fatty degeneration, which denotes the boundary of the abscess-membrane towards the nerve-tissue. I imagine that the pressure of the growing depot of pus, upon the one hand, as an inflammatory irritant, brings about a certain reaction of the surroundings, which makes itself known in the proliferation of numerous young cells, that however upon the other hand, the same pressure interferes with the normal fulness of the vessels, which is very possible in the peculiar relations of the intracranial circulation. The result is a fatty degeneration of the newly formed cells, *i. e.*, a zone of yellow softening at the boundary of the abscess-membrane towards the brain. Of course the softening is never a complete liquefaction of the parts, but we are soon convinced that through the depot of softening a network of coarse fibres is expanded, which is connected with the abscess-membrane upon the one hand, and with the nerve-substance upon the

other. These fibrous lines are bundles of primitive nerve-tubes, which also inclose ganglion-cells, where the question is about gray substance; they run in a compressed condition parallel to the surface of the depot, and can only have been placed in this situation by the pressure of growth of the abscess itself. Only when we lift off the abscess-membrane from the brain-substance do they expand as a network. The maceration in the fluid of softening has moreover most beautifully isolated the individual fibrils, the ganglion-cells are pressed flat, here and there converted into long spindles and bands; the process of the axis cylinder is mostly maintained; I could recognize a process of atrophy only in the gradual decrease of volume (obsolescence, Meynert), not in a fatty, colloid, or other metamorphosis. The neuroglia in its old form has disappeared, since it is just it which has been converted into the young cells and their equivalent, the fluid of softening. If we attempt to follow the beginnings of the disturbance farther yet into the nerve-substance, we will seek in vain at most of the points of the surface; only here and there I was fortunate enough to observe the first divisions of the neuroglia nuclei hereupon, and upon the ground of analogous experiences in other processes, I do not hesitate, until further information, to believe that the entire connective tissue production separating the depot of pus, inclusive of the fatty degenerated transition cells, proceeds from the neuroglia.

The phenomena of acute and abscess-forming myelitis are perfectly analogous to those of encephalitis. The form of the depots is determined by the kind of injury. Fractures of the vertebral column are wont to produce, in the first place, contusions and then demarcating inflammation and suppuration of the surroundings of the contused spot, &c.

e. *Hyperæmia and Inflammation in Psychical Disturbances.*

§ 712. The studies of Meynert,* which have attracted attention, upon the pathological histology of the psychoses, vindicate for the nervous elements of the cortex of the brain a prominent rôle in the anatomical course of the morbid processes. Meynert is at pains to prove that the various forms of excitement correspond to demonstrable alterations of definite groups of ganglion-cells, and we can only wish that in this track ever more certain data will be found again and again.†

* Dr. Theodore Meynert: The structure of the cerebral cortex and its local differences, together with a pathologico-anatomical corollary. Vierteljahrsschrift der Psychiatrie, 1867, I Heft, page 77 ff.

† Meynert places at the foundation of his observations a certain number of exceedingly valuable data upon the structure of the gray substance of the cerebrum. He shows that the involuted edge of the cerebral cortex, which is enveloped on both sides in white substance, and forms the corpus fimbriatum and the hippocampus major, contains only multiple pyramidal so-called motor ganglion-cells, that the olfactory bulbs (very much less developed in man than in many mammals) contain only round-

No one will *à priori* dispute the physiological title of the nervous substance to appear pre-eminently as the material substratum of the psychoses. But, unfortunately, all that pathological anatomy has collected in experience yet amounts to this, that the essential anatomical foundation of all psychical disturbances are to be sought in an anomaly of the distribution of blood and its consequences. Only that the individual authors, who have applied their activity to this province, have at one time particularly brought forward this, at another time that point of the anatomical picture of the disease, and hence the ensemble, and the reciprocity of the single forces does not yet appear with sufficient clearness.

§ 713. Hence, the almost exclusive object of our considerations is a persistent hyperæmia of the cerebral cortex, which forms the general basis of the disturbances. In most cases, and from a certain period in all, we may regard this hyperæmia as functional, accordingly, as identical with that active hyperæmia of the glands and the membranes which characterizes these at the time of their heightened activity. For every functional hyperæmia, is characteristic its seat in the capillaries which immediately surround the functioning elements, and its periodicity; in the latter is reflected the functional exhaustion of the organs, the decrease of their susceptibility to irritation, their need of rest and reparation. But how, if an artificial or violent excitement does not permit the apparatus to attain rest? There is an over-excitement of the organs, to which the central nervous system also is quite peculiarly exposed. Who does not know in his own person the process, that is popularly called "passing away of sleep, to get beyond sleep" (Uebersprungen des Schlafes, über den Schlaf wegkommen). This may recur several times at shorter intervals. The question here therefore is about a super-excitation of the brain, which is produced at one time by emotions, at another by overworking the intellect or the imagination, then by corporeal irritant means. Without doubt a likewise prolonged

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ish and smaller, so-called sensitive ganglion-cells, that the medullary capsule of the nucleus tæniæformis, the amygdalum and the walls of the Sylvian fissure especially, have spindle-formed nerve-cells connected with the bow-shaped fibres of Arnold, &c. He refers these local differences, in which every one will agree with him, to differences of function, and gives expectation of important elucidations which the pathological anatomy of the psychoses has to look for, from this direction. Unfortunately, the first step which Meynert himself has made, can scarcely be called a happy one. He starts from this, that in a normal ganglion-cell the nucleus is to a certain extent continued into the processes and is contained by these, that consequently by nature it is not round, but must be supposed angular and with points. That the round form is already something pathological and forms the first link of a chain of changes, which afterwards leads to the division of the nucleolus and of the nucleus, &c. Against this it is to be objected that in the most recent possible ganglion-cells, the nuclei are all found round, that hence, if after hardening preparations in chromic acid, the nuclei are generally not round, but spindle-formed or pyramidal, this change of form is probably to be explained entirely by the shrinking of the surrounding protoplasm, *i. e.*, of the fibrous substance (Schultze) of the ganglion-cells.

hyperæmia of the cortex of the brain corresponds to the condition of over-excitement; here now the point appears, from which we may gain an insight into the etiology of the psychoses.

It is customary to divide hyperæmias into active and passive. Both forms have numerous points of contact however, they often directly pass over into each other, as for example we saw in § 510, or they at least interfere incidentally, the one in the course of the other. This latter occurs among others, when an ordinary fluxion has attained its culminating point by a considerable and uniform congestion of the capillaries. The *absolute excess of blood*, which now exists in the capillary territory concerned, is an obstacle *to its own* movement by its *weight*, and if on the other hand, we invoke the strengthening of the *vis a tergo* by the dilatation of the arteries, the unhindered efflux through the easily dilatable veins, the means are thereby probably given whereby this obstacle is, as a rule, removed. Nothing, however, is changed in the fact itself, that in the course of the active congestion, a static force is developed, which opposes the readjustment of the disturbance. This will fall into the scale so much the heavier, the stronger and more persistent the hyperæmia is, the more exclusively it concentrates upon the capillaries, finally, the more delicate and yielding the walls of the capillaries are. Now the capillaries of the cerebral cortex, like all intracranial vessels (§ 695), are of a quite disproportional delicacy; just in the cranial cavity also, because of the peculiar relations of pressure and counter-pressure (§ 695), we can very well confide in the thought of an exclusive, or at least very predominant concentration of the congestion upon a definite section of the vascular system, here, therefore, where the question is about a functional irritation of the cerebral cortex, upon the capillaries and transition vessels of the cerebral cortex.

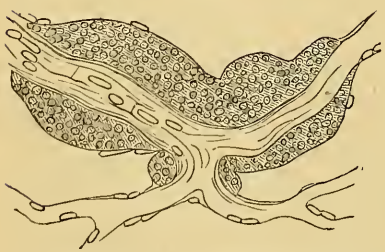
Hence we are not surprised, if in the hyperæmias of the cerebral cortex, an influence as detrimental as possible of the static tendency spoken of becomes perceptible. A long-continued or frequently recurring, or finally, a very severe hyperæmia will produce just here a kind of stasis, which upon its part brings forth in the first place an excessive distension; in the second place, a relaxation of the vascular walls. As a strip of India-rubber, which has been too strongly stretched, regains its old form but slowly and incompletely, thus it occurs here also with the elastic and contractile elements of the small vessels. If the distension has once become the habitual state, corresponding organic changes take place in the vascular walls, which make the return to the normal calibre, which in the beginning is only a question of time, an impossibility, and thereby the first step is accomplished towards the incurability of the disturbance.

This is my conception of the origin of the acute psychoses as it is unfolded to me in the histological investigation of the cerebral cortex.

Naturally I must leave it to the clinical teachers to trace back the remaining known etiological causes, as age, hereditary influences, cranial formation, and variations of calibre of the emissory veins, constitution, acute diseases, dipsomania, immorality, need, and poverty, tumors in the brain, injuries to the head and the like, either to an exalted irritability of the cerebral cortex, or to an exalted irritation of it, or finally to a more limited capacity of resistance of the vascular walls. I now turn to the statement of the histological changes themselves, and will here maintain the customary two stages of acute and chronic insanity.

§ 714. I. *Acute Conditions.* These are either to be recognized at the first glance, or they are comparatively difficult, but they *may* still be demonstrated. It is at the present time yet a thoroughly unexplained fact that the capillaries of the brain post mortem, are found to be emptier of blood than the capillaries of any other organ. Even hyperæmic congestions may entirely disappear after death. Hence from the very beginning we must not place too much weight upon the direct demonstration of hyperæmias. Slight rosy coloring of the white substance, a slight red tinge, which is mingled with the usual gray of the cerebral cortex, must be esteemed here already as very significant symptoms; where, however, they are wanting, it is not to be concluded that they were also wanting during life. Hence we must keep to the indirect means of proof. Herewith above all the circumstance assists us that the cerebral vessels bleed easily. Hence the principal task of the histologist would be to demonstrate whether the vessels had bled. Now there are cases of acute insanity, especially cases of mania, where the cerebral cortex is pervaded with numerous punctated hemorrhages, in spots, has even passed over into red softening already. Under these circumstances it is of course not difficult to establish the hemorrhage, and to conclude upon a hyperæmia having existed during life, although no trace of this itself has remained behind, as is quite usual, and the vessels are found as empty as though a drop of blood had never circulated in them. As I have already extensively treated of punctated hemorrhage and red softening, I will at this place only mention some peculiarities which are characteristic of their occurrence in the psychoses. In the first place touching punctated hemorrhage, this mostly appears here as dissecting aneurism of the smallest veins (Fig. 192), *i. e.*, the blood, after rupturing the inner and middle tunics of the vessel, has made room for itself between the latter and the uninjured adventitia, and now presents a spindle-formed, dark blood-red tumefaction

Fig. 192.



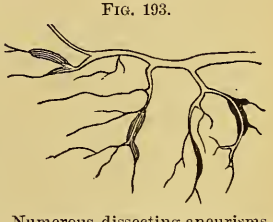
Dissecting aneurism of a small vein just before its breaking up into capillaries. The adventitia, provided with nuclei and designated by a simple sharp contour, is lifted up by an effusion of blood from the inner vascular tunics. 1-300.

of the vessel. Upon a cross-section this depot of blood likewise appears as a round drop; and, as the elevated adventitia may very well be regarded as a peripherally encapsuling coagulation of fibrin, the proof of the central vessel is unconditionally necessary to assure us from mistaking it for a free hemorrhage. It is true much does not depend upon it; free and interparietal hemorrhages mostly occur intermingled, only that, as pointed out in circumscribed encephalitis, the free hemorrhages predominate; in diffuse encephalitis, as which we will for the present regard the psychoses, the interparietal predominate.

In reference to the red softening of the cerebral cortex which occurs in maniacal patients, the peculiarly stratified appearance is to be emphasized. Most frequently the middle layer of the cerebral cortex is softened; hence, in attempting to strip off the pia mater from the surface of the brain, the outer layer is wont to come away with it; more rarely the softening affects the outer layer itself, where then in tearing off the pia mater the surface remains rough, as though ulcerated; most rarely a layer of softening forms at the boundary of the cortex of the brain with the white substance. I believe that this peculiar localization is connected with the manner of ramification of the vessels of the cerebral cortex in three tiers, one above the other, discovered by Arndt, a mode of ramification which corresponds to the phases of growth of the brain; at the same time, however, it probably stands in closer relation to the distribution of function to the various layers of the cerebral cortex thus definitely characterized, as we meet it, as is known, in a similar manner in the most complicated organs. Were the conjecture correct, the place of the softening might at the same time be regarded as the place of the highest functional irritation. Still this can only serve as a guide for further investigations.

§ 715. If we pass to the usual forms in which the hemorrhagic condition is less pronounced, I repeat, that less pronounced is not yet synonymous with wanting. Let us only attempt to isolate the vascular trees of the cerebral cortex not by simply tearing them out, but by carefully stripping off the pia mater under a very gentle stream of water, and we will be frequently astonished at how many dissecting aneurisms are overlooked, when we are contented with merely vertical sections, but still more at how many less extended, but still surely hemorrhagic infiltrations of the walls occur. Horizontal sections through the gray substance are likewise to be recommended. The red blood-corpuscles actually extravasated penetrate directly, but to various depths, into the adjacent brain-substance, and thus form small red areas around the vascular gaps, which terminate towards the exterior with indistinct limits. Upon the cortex

Fig. 193.

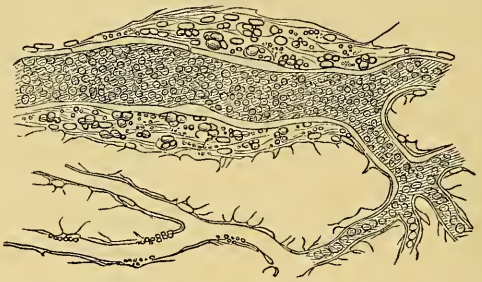


Numerous dissecting aneurisms upon the ramifications of a small cerebral vein.

of a brain which presented absolutely nothing to a superficial examination, I found many single blood-corpuscles lying free in the parenchyma, and I thereby first had my attention called to the great diffusion of minute hemorrhages.

§ 716. Moreover yet during the acute stage, the transformation of the extravasated blood-corpuscles, that is of their hæmatin into pigment and some connective tissue, begins. The pigment appears in variously sized round or elliptic lumps, which are found in small groups of two, four or more, in the adventitia of the vessels (Fig. 194). Free

Fig. 194.



Small vein and capillaries from the brain of an imbecile. The vein shows the remains of former adventitial hemorrhage, pigment bodies, &c. Concerning the capillaries, see the text of Fig. 195. 1-300.

in the parenchyma of the brain, we also find individual pigment-corpuscles, yet this is a rarity, while again a stronger pigmentation of the ganglion-cells occurs often enough. Thus then we find in many acute cases of insanity, recent hemorrhagic processes, beside traces of hemorrhages which took place formerly, side by side in variegated change.

§ 717. Extravasated blood and blood-pigment are criteria of hyperæmias which had taken place, fortunately difficult to be effaced, but therefore so much the more credible. That they are not the only ones, I indicated already above, since I hinted, that certain disorganizations of the vascular walls occurring in the course of time, rendered the return to the normal state difficult. Only one of these disorganizations of the vascular walls yet belongs to the province of acute conditions. This is that so-called "fatty degeneration" of the capillary vessels, which moreover is by no means constant in psychoses, but is furthermore yet found after other severe and persistent agitations of the cerebral substance, for example, after typhus, small-pox, &c. It is an accumulation of fat-globules in the immediate surroundings of the nuclei. A small remainder of softer protoplasm yet constantly continues here, this lets the fat-globules arise in its interior, and thus are produced at the outer side of the vessels, small three-cornered tumefactions, which lodge the dark fat-globules, and each a nucleus, and give the vessel a very elegant appearance (Fig. 194, Fig. 196). The question only is, whether we are correct in interpreting this condition

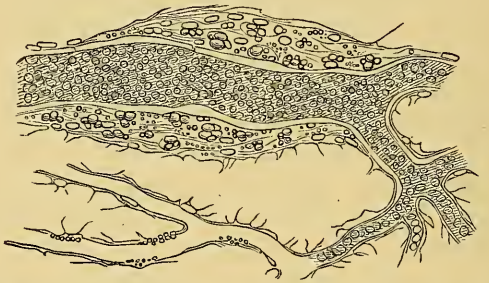
as a retrogressive metamorphosis. Just here the possibility is so great, that the fat-globules are taken up from another place, for example, out of the cerebral substance itself, into the protoplasm; the immediate contact of the fat-containing cells with the nutritive fluid moreover, permits us to think of a disturbance of nutrition; finally Leidesdorf and Stricker have proved with great certainty in traumatic inflammations, that the fatty degeneration mentioned agrees very well with an active behavior of the cellular parts, with nuclear division and cell-formation, so that they immediately struck upon the thought of placing the granular cells upon a parallel with the cells of the formative yelk. Against this, I have only to make the objection, that the fatty metamorphosis is a recognized more frequent mode of decomposition of senescent or badly nourished cells, or of those cast out of the organic union; that even the most abundantly presented nourishment, alone cannot prevent the disorganization, as the fate of many colorless blood-cells and the fatty usure of the vessels (§ 220) proves, and that the same fatty metamorphosis of the vessels is an essential constituent of yellow softening, which usually arises by the direct stoppage of the circulation and nutrition in a circumscribed section of the brain. Let now the signification of the fat in the present case be what it will, in this the conditions found by me at all events agree with those of Leidesdorf and Stricker, that, nevertheless, in all fat-infiltrations, the question may be about a progressive process. For what is the more built up at the outer surface of the vessels the longer it continues, and what contributes the most to the permanent disorganization of the latter, is an effective new formation of connective tissue cells and fibres, as a glance at the second stage of the disturbance will prove.

§ 718. II. *Chronic Conditions.* The later phases of the anatomical disturbances accompanying the psychoses, are very much better known than the earlier, probably principally because they are more obvious. They may be traced in two directions; namely, upon the one hand, the hyperæmia of the brain having become chronic, causes that venous stagnation in the pia mater, which I described in § 699 *et seq.*, as hydrocephalus externus. The dilatation and undulations of the veins, the cellular infiltration of the arachnoid, the œdema of the pia mater, the atrophy of the brain, unite into highly characteristic morbid pictures. Upon the other hand, to the hyperæmia of the cerebral vessels, there is associated a perivascular development of connective tissue, which extends to the brain itself, and in the latter instance also causes thereby a disappearance of the nervous elementary parts.

§ 719. Let us in the next place view the vessels. Stricker assumes, that at the outer surface of the capillary vessels there exists a continuous layer of protoplasm, which among other things is answerable for the development of the vascular system, furthermore, however, for other new formations also proceeding from the vessels. The behavior of the

capillaries in acute and chronic inflammations of the brain, agrees strikingly with this assumption. I refer partly to the already mentioned purulent encephalitis, partly to the scleroses of the brain to be spoken of hereafter, and the gray degeneration of the spinal marrow. In the psychoses also, a moderate increase of the perivascular protoplasm shows itself; new nuclei are shown, which have been produced by the division of the old, somewhat enlarged capillary nuclei, finally the thickening of the walls, and the greater abundance of cells becomes distinct even to the unpracticed eye. What, however, above all assures the diagnosis, is the springing up of numerous minute, slightly refractive processes of protoplasm, which impart to the vessel, a strange, prickly appearance (Fig. 195). These processes are in connection with

Fig. 195.



Small vein and capillaries from the cerebral cortex of an imbecile. The capillaries have thickened walls provided with processes radiating towards all sides. The processes mostly proceed from the nuclear places. 1–300.

a system of juice-cells, which has formed in the meantime in the cerebral substance itself, and upon vertical sections is recognized especially when the preparations are recently taken from the brain. Treating with Canada balsam, turpentine, even glycerine, mostly makes the network invisible; what we still see thereafter of it, are sclerotic, and therefore more strongly refractive fragments, which occur tolerably frequent. This net of juice-cells in its diffusion, *i.e.*, in the number of stellate cells pertaining to a vascular territory, corresponds so very much to the usual relations in other vascular connective substances, that we unwillingly cast aside the thought, that a physiologically preformed arrangement might lie at the foundation here; still up to the present time, this proof has not been attained. Hence I believe, that an actual outgrowth on the part of the surface of the vessels has taken place here, for which indeed a so useful point of support is at our command also in the vascular new formation by processes (§ 71). L. Meyer, who has acquired the greatest merit for his study of these changes, even speaks of an actually occurring vascular new formation in the cerebral cortex. The vascular new formation would then be a step further upon the path that is trodden by the sprouting of protoplasmatic processes at the surface of the capillaries, nuclear formation, and the

development of an anastomosing net of connective tissue cells. The essential part of the affair is the exclusive participation of the vascular connective tissue, in contrast to the neuroglia, which remains unchanged. We will have occasion to return to quite similar relations in tumors of the brain.

The changes which the ganglion-cells and the nerve-fibres experience, in contrast with the process upon the vascular apparatus hitherto described, are only of a secondary and passive nature. The most frequent is a certain atrophy of the ganglion-cells, connected with the already mentioned brownish-coloring, which is probably caused by attracted hæmatin. The definitive granular disintegration, the dropsy and sclerosis, especially, however, the nuclear division which Meynert has taught us (see § 712), according to my experience occur only in a very limited extent. More frequently there is a division of the neuroglia granules; still this appears to be without further consequences. We only see somewhat numerous granules where we normally expect but few; here and there also small chains and nests of granules. They are guiltless of the formation of the net of connective tissue cells mentioned.

Touching the macroscopic relations, the most of them are explained by the outer pressure, which is exerted on the part of the œdematous pia mater upon the surface of the brain. The leather-like consistence, and the whitish decoloration of the cerebral cortex, where they exist, may also be placed to the account of the intergrowing of connective tissue. I need scarcely add, that the latter is regarded by me as the proper disorganizing disturbance, making the machinery of thought useless.

2. Yellow Softening.

§ 720. By yellow softening we understand the complete solution and liquefaction of circumscribed parts of the central nervous system in the way of fatty degeneration. For the production of yellow softening the injury and suppression of the circulation is the most important preliminary condition; hence we principally meet with it in consequence of acute inflammatory, embolic, and hemorrhagic conditions, as we learned in the previous section. That embolism can directly, *i. e.*, without the middle link of a punctated hemorrhage, produce yellow softening, is, according to my judgment, not yet sufficiently proven, still for the time being we may admit the possibility. Yellow softening everywhere presents the final result, whether the sequence of the preceding disturbances have shown themselves in this or that manner. The following series are the most frequent: 1. Embolism, punctated hemorrhage, yellow softening. 2. Punctated hemorrhage, thrombosis of the capillaries, yellow softening. 3. Punctated hemorrhage, inflammation (red softening), yellow softening. 4. Encephalitis, punctated hemorrhage, red,

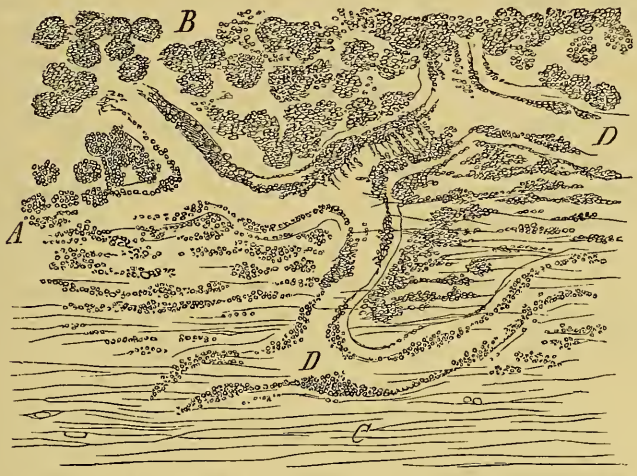
then yellow softening. Yellow softening only tells us so much, that, in the present stage of the process, regular nutrition has been permanently interrupted. Hence we also find it upon quite a number of other occasions. It has appeared to me, that the white substance in the anterior lobe of the right cerebral hemisphere was completely softened yellow, because the gray substance was degenerated gliomatous all around, and consequently the circulation of blood through the cortex was impeded. Around most tumors of central growth we find a zone of yellow softening, produced by the pressure of the tumor upon the bloodvessels of the neighborhood; it is absolutely impossible to give an exhaustive summary of these cases; it is rather left to the sagacity of the individual to explain the production of yellow softening in each single case.

§ 721. If we now pass to the histological detail of yellow softening, this is composed of two factors, of the solution and liquefaction of the nervous parts, and of that of the connective tissue and the vessels. The former takes place without the development of new-formed elements; the behavior of the white substance therein only is characteristic. This first of all coagulates about the axis cylinders (§ 32); it then extravasates, and is yet maintained for a time in certain drops and fragments, which are sufficiently characterized by the variety and the oddity of their outer shape. Some are knobbed, club-shaped, others lobulated, rolled up coil-like, or drawn out in a great number of knobbed processes. By moderately warming the object-glass, globular drops are formed; by the addition of water peculiar phenomena of swelling and cleaving are exhibited upon them, which can again be checked by a solution of salt. Finally, however, these things also disappear, and we get a homogeneous albuminous fluid; perhaps the white substance decomposes into fat and albumen, and the fat-granules, which become free therein, in the next place come together with the other fatty detritus.

The connective tissue and vessels behave differently in their liquefaction. Here the fatty degeneration plays a principal rôle, here it becomes an actually destroying process. The collective cells of the neuroglia are transformed into granular corpuscles. Upon vertical sections, through the border of the depot of softening (Fig. 196), we can follow the accumulation of the smallest aggregations of fatty granules between the nerve-fibres up to the formation of quite colossal granular corpuscles. The latter are suspended in the fluid of softening, and impart to it the peculiar coloring from which the process has received its name. Over a black ground we can see the granular corpuscles, even with the naked eye, swimming as small atoms. The vessels also perish by the fatty metamorphosis. We see spindle-formed heaps of fatty granules at the nuclear places of the capillaries, larger confluent masses of fat-granules under the adventitia of larger vessels. I found

the latter (Fig. 196, *D*) universally lifted off, as though an interparietal lymph-space had made its appearance. The homogeneous tunics of the vessels and the basis-substance of the neuroglia are, without doubt,

Fig. 196.



Yellow softening of the white substance of the brain. *A*. Border of the depot of softening, *B*, and of the brain-substance, *C*, not yet softened. *D*. A fatty degenerated vessel. 1–300.

really dissolved, although quite gradually, so that only the fatty granules and the fatty granular corpuscles are found in the fluid of softening.

§ 722. Thus far the histological detail. The macroscopic effect will naturally prove different, according as the situation of the depot is favorable or not to a resorption of the products of softening. Depots of softening, which lie within the hemispheres, cannot be obliterated because their walls cannot collapse; the fatty granules are, perhaps, resorbed afterward, the fluid clears up, there arises a cyst, but there the process also ceases. If the depot, as occurs frequently in the corpus striatum, lies near the surface of the ventricle, there is produced probably a slight depression of the separating layer, and the layer of softening is completely obliterated. This depression, however, presents itself more pregnantly, when the destructive process affected the cerebral cortex itself. We find cases, not very infrequent, of extensive, usually multiple deficiencies of the surface, above which the pia mater is either collapsed or filled with a simple œdematous fluid, or finally with yellow fat emulsion. The brownish coloring, which the nearest contiguous cerebral substance presents, in general points to hyperæmic-hemorrhagic conditions as the cause of the deficiency, though the primary affection has up to the present not yet been ascertained with certainty. Only that the final removal of the destroyed parts of the cerebral cortex is due to yellow softening appears certain; likewise that the quite superficial situation of the depot of softening has made the traceless resorption of the fluid of softening possible.

§ 723. In our representation of the inflammatory affection of the central nervous system, indications have here and there occurred which made us believe that we must concede to fatty degeneration, especially to the fatty granular corpuscles, a position beyond the province of the retrogressive metamorphoses. To this place belong the numerously adduced experiments of Leidesdorf and Stricker upon traumatic inflammations of the brain; here would also belong a fatty metamorphosis of the neuroglia-cells diffused through the entire white substance of the brain, which Virchow has recently described as encephalitis of a newly-born syphilitic child. To the same place we will have to reckon the finding of granular corpuscles in certain parts of the spinal marrow in paralytic insane persons (Westphal), and the fatty degeneration of single fibres of the spinal marrow, which Türk has described as a consequence of central disease in depots. At all events we must maintain so much, that fatty degeneration formation of granular corpuscles is not identical, without further ceremony, with yellow softening.

3. Gray Degeneration.

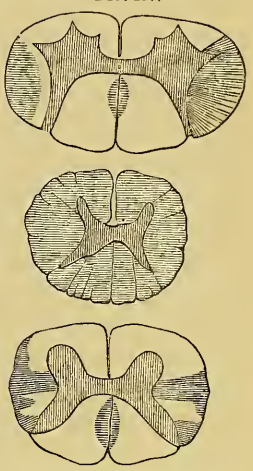
§ 724. The white substance of the brain, of the spinal marrow and of several peripheral nervous trunks, corresponding to certain typically recurring clinical morbid pictures, is found in circumscribed depots, stripes or spots, not white but gray, similar to the gray of the cerebral cortex, and this is the reason why all these cases have been comprehended under the common name of gray degeneration. In this we have been guided by an instinct correct in itself. For if we consider the gray discoloration alone, this certainly everywhere, and in the first place, owes its production to one and the same anatomical force, namely, to the loss of the sheath of white substance of Schwann on the part of the nerve-fibres. Nerve-fibres containing white substance look white *en masse*, those without white substance look gray. Rarely, however, is the loss of white substance the only and the primary affection. The loss of white substance is a secondary phenomenon; it is the first step towards atrophy, nay, towards the complete destruction of the nerve-fibres, and is wont to precede this latter in the same manner as, perhaps, the resorption of the lime-salts precedes the dissolution of the osseous tissue.

§ 725. Since the gray degeneration has most recently been the subject of repeated scientific investigation, I name particularly the works of Leyden, Frommann, and Charcot; it has been shown that we must strictly separate two forms of gray degeneration, which we may designate as the simple non-inflammatory, and as the indurating-inflammatory, or plainly as gray degeneration and sclerosis.

The simple gray degeneration is especially observed in the spinal marrow. Here they are principally the posterior columns, more rarely

the lateral and anterior columns, which are affected. (Fig. 197.) If, in the post mortem, the spinal marrow has been taken out of the sac of the dura mater and washed off, we see—to use Leyden's language—already shining through the pia mater, in place of the posterior columns, "a band of gray or grayish-white color, which mostly extends throughout the whole length of the spinal cord." Upon a cross-section we perceive that the gray discoloration of the surface depends upon a transformation of the white substance extending deeply. Usually the entire posterior columns have been converted into a reddish-gray, somewhat brawny mass. If there yet exists an unchanged remainder of normal tissue, this is sharply defined from the degenerated portion; the latter also sinks a little below the level of the cut surface, and upon pressure a small amount of clear fluid appears. The degeneration generally progresses from the cauda equina upwards, and extends—as seen upon a cross-section—from the periphery and the posterior fissure towards the axis and the lateral portion, so that in incomplete degeneration the remains of white substance forms a lamella, which is closely joined to the posterior commissure, and from thence extends along the posterior horns towards the periphery. The posterior roots of the nerves of the spinal marrow probably always participate in the degeneration, though this appears to be overlooked in many carefully described cases.

FIG. 197.



Unusual localization of simple gray degeneration. In the cervical and lumbar portion of the spinal marrow (the upper and lower figures), the lateral columns particularly are affected; in the dorsal portion (the central figure), the entire medulla. After Frommann. Natural size. Cross-sections.

§ 726. In the histological process which lies at the foundation of the simple gray degeneration, an increase of the interfibrillar connective substance of the white fibres plays the principal part. Whether this substance, under normal circumstances is finely granular, or finely fibrillar has, up to the present time, not been quite established. Both the one and the other are asserted with great confidence. Granted now that those are correct, who like myself, hold a finely granular, protoplasm-like constitution as normal, then a transformation of the amorphous cement into a fine-meshed fibrous network would, at least, be the first step to gray degeneration. This fibrous network is, it is true, not so finely spongy as the reticulum normally assumed by Schultze. It rather is brought about by this, that as in treatment by reagents, the originally uniformly distributed cement draws together into certain branching lines. In the three-cornered prismatic interval, between each three contiguous nerve-fibres, there forms a stouter rod running parallel to the nerve-fibres; from this, however, numberless

smaller processes proceed, which, penetrating transversely and obliquely between the fibres, enter into connection with each other, so that an exceedingly elegant plaited work is produced.* After this first, so to say preparatory stage, there ensues a peculiar outgrowing of the fibrils; according to Frommann small protuberances spring up here and there which elongate and again ramify. The process makes the impression of a crystallization, at least of a coagulation, and can only be comprehended by our accepting at the same time a continual separation of the coagulating substance, I mean a soft preliminary stage. Thus are probably explained the observations of older authors who found here and there larger quantities of amorphous interstitial substance. If we tease out small portions of the gray degenerated parenchyma with needles, the fibrous felt breaks up without remainder into a number of roundish balls, which upon more accurate examination exhibit at their centre, a more solid nucleated spot, from which all the numberless fibres appear to proceed (Fig. 198). Each of these spots corresponds to one of those branched and anastomosing connective tissue cells which are distributed at certain interspaces through the nervous substance. We know that these cells are placed most densely at the periphery, and that they decrease in number the deeper we penetrate into the parenchyma of the cord. With this agrees the condition found upon the cross-section of the gray degenerated cord in so far as after lengthened moving about of the thin glass cover we can, without using needles, achieve a certain disengagement of single balls from each other, whereupon these appear to be smaller towards the periphery, more voluminous towards the centre of the spinal cord. Those cells are connected at the periphery with the innermost layer of the pia mater, and may be regarded as a kind of radiation of supporting fibres into the nervous substance (Henle and Merkel). The gray degeneration also proceeds demonstrably from the periphery as a basis, and gradually advances from here towards the centre. According to all this the conjecture forces itself upon us that the most important part of the morbid process develops in close connection to this preformed system of fibrous connective tissue, proceeds from it. The fibrous metamorphosis of the nervous connective substance appears as a chemical and morphological identification of the formless intermediate substance with the fibrous; the physiological relationship

Fig. 198.

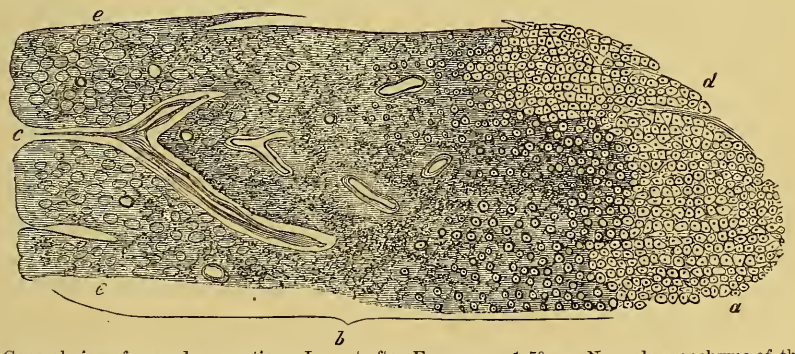
Nucleated connective tissue cells beset all around with fibrous tufts obtained by teasing out gray degenerated spinal marrow. 1–300.

* Frommann first demonstrated this elegant network. He also finds it in the normal spinal marrow, but I regard it here as the consequence of a reactional shrinking.

of both is confirmed hereby, and the conviction grounded that the neuroglia is a connective substance, and not, as is always yet asserted from several sides, of a nervous nature.

§ 727. If we now pass to the second factor of the simple gray degeneration, the disappearance of the nerve-fibres in the attacked columns of the cord, then the fact proves that this stands in exact relation to the progressive diffusion of the interstitial tissue, indeed to the causative connection of both phenomena; for the time, however, it continues doubtful whether the disappearance of the nerve-fibres brings after it the hyperplasia of the nerve-connecting substance, or *vice versa*, whether the hyperplasia of the nerve-connecting substance causes the disappearance. I confess that I cannot well imagine the decomposition of the nerve-fibres as primary; in peripheral nerves, artificially produced atrophies of the nerve-tubules never exert a similar effect upon the perineurium; on the contrary, however, we are acquainted with very much as to how an external pressure induces atrophy of the nerve-fibres. According to Frommann, whom I indorse here with full conviction, the growing connective tissue network penetrates into the space which is destined for the nerve-tubules, narrows it, and finally brings the nerve-tubules themselves to disintegration. By this it would appear to me as though the neurolemma identified itself at an early period with the advancing connective substance, the sheath of white substance of Schwann crumbled, and only the axis cylinder resisted for a longer time. The thicker axis cylinders are maintained remarkably long, and may often be demonstrated yet in such parts as according to all appearances have already been degenerated for a very long time (Fig. 199).

Fig. 199.



General view of gray degeneration. In part after Frommann. 1–50. *a*. Normal parenchyma of the spinal marrow. The light figures are the cross-sections of nerve-fibres. *b*. The territory of the gray degeneration. *c*. A vascular cleft with a vessel. *d*. Boundary towards the gray substance (posterior horn). *e*. Periphery of the column of the spinal cord richly infiltrated with amyloid corpuscles.

§ 728. The behavior of the vessels is of subordinate significance in simple gray degeneration. They are, indeed, never normal, but the changes which they show are neither considerable nor constant. Most

usually there is upon the larger vessels a very much extended adventitia, consisting of wavy and stratified connective tissue; in this case the adventitia has participated in the hyperplasia of the neuroglia; here and there is observed a superposition also of fatty and pigmentary granules upon the smaller vessels; at the same place a peculiar sclerotic, homogeneously lustrous constitution of the vascular walls, similar to the amyloid infiltration, but without the iodine reaction.

The longest known, but in its histological significance yet quite obscure phenomenon, in simple gray degeneration, is the never-failing, often massy deposition of corpora amylacea, into the degenerated parts. These lie most densely in the longest degenerated border parts (Fig. 199) and along the larger vascular branches; but they also are not entirely wanting at such places where the degeneration is just beginning. Rokitansky derived the corpora amylacea from the fragments of disintegrated sheaths of white substance; the view also recently communicated by me, that the corpora amylacea are degenerated cells, has gained ground. The uniform size and the occasional perception of an unchanged nucleus, the entire distribution of the corpora amylacea, lets it almost certainly appear that they are formed by an amyloid infiltration of the round neuroglia-cells, of the granules of the normal medulla.

§ 729. The second form of gray degeneration, which we named above the *indurating inflammatory*, has a far greater extent of diffusion than the first. The total white substance of the central organs, therefore, not alone the white columns of the medulla, but also the centre of Vieussens of the brain, the corpus callosum, the fornix, and the fimbria, the septum lucidum, the optic tract, the corpora geniculata, the peduncles of the brain, the pons and medulla oblongata, are exposed to it. It appears in numerous depots of disease, of which the smallest are perhaps the size of a pin's head, while the larger extend over whole sections of white substance; for example, over the entire fornix or over a piece of the lateral columns of an inch long, nay, over the entire spinal cord. As the process which lies at the foundation here has in the second place constantly a considerable reduction of volume, as a consequence, the strata of white substance of the central organs are deformed in a corresponding manner; by depots of disease of the lateral columns, which are situated alternately right and left, the spinal marrow receives a series of outward curves and retractions, which actually cause it to appear tortuous; if the process extends through the whole thickness of the organ it appears contracted at this place, which then especially produces the impression of a considerable deformity, when there is a perfectly normal part close beside it (compare the beautiful illustrations by Cruveilhier).

§ 730. If we attentively consider the smaller and smallest of the gray depots, we are certainly struck with the peculiar phenomenon that in the midst of each of them there is a red point or streak, the trans-

versely or obliquely divided lumen of a vascular branch filled with blood. The microscopic investigation of these vessels shows that they together with all their more minute ramifications are in a condition, which at every other place we would designate as chronic inflammatory. The adventitia consists of an often fivefold layer of round cells stratified above each other. Therewith the lumen of the vessel is not perhaps contracted, but considerably dilated, which is partly to be referred to an alteration of the media. I have several times convinced myself upon vessels of this kind that the smooth, muscular fibres of this membrane, no longer existed in the characteristic form and arrangement. Changes of a progressive kind are also perceptible upon the capillaries. Their walls are beset all around with cells, which are either migratory, or have originated by division of the cells of the vessels.

In these changes of individual vascular trees I perceive the first link of the anatomical process. The second is a fibrous metamorphosis and hyperplasia of the neuroglia, which is perfectly analogous to that described in § 726, and only differs from it in this, that here the cellular elements of the connective substance play a more important part. The stellated supporting cells, which here also show themselves as the central point, so to say, as the centres of crystallization of the formation of fibres, assume the form of polynucleated giant cells, while the numberless, often very long and shining fibres, which proceed from their periphery, impart to them an exceedingly strange, monstrous appearance. The round cells of the neuroglia also multiply, and at the border of the depot form a more dense infiltration. Their future fate, however, is destruction by the fatty metamorphosis. They swell up into tolerably extensive granular corpuscles, are found distributed as such in large amount in the fibrous felt of the depot; finally, they break down into fatty detritus, which is resorbed. The destruction of the nerve-fibres ensues in a manner similar to that in the simple gray degeneration. Corpora amylacea are either not at all formed, or still only in inconsiderable number. The final result is a fibrous felt, which is saturated like a sponge with a slimy fluid, containing but few free nuclei and small uninucleated cells. This fluid appears upon every recently cut surface, upon making lateral pressure; if subsequently the fibrils of the fibrous felt contract continually, the fluid disappears, the fibres draw closer together, until they finally touch immediately and without any intervals, and form that exceedingly unyielding, compact, dry tissue, that composes the cicatrices or indurations, which remain behind after the cessation of the process.

§ 731. At the conclusion of this section I cannot avoid stating that there is also yet a simple, not fatty atrophy of the peripheral nerves, which depends entirely upon a loss of the medullary sheath of Schwann, and hence likewise brings after it a gray discoloration. We observe this, for example, upon the optic nerve, after disease of the retina,

after extirpation of the globe of the eye, upon the optic tract in gliomas of the thalamus, and other cerebral tumors, which compress the tract, &c.

The gray degenerations which we perceive in all kinds of disturbances in the territories of distribution of the cerebral nerves in the medulla oblongata, have not yet been sufficiently investigated. In a case of masticatory facial convulsions I found a sclerosing development of connective tissue, which proceeded from the floor of the fourth ventricle; in several cases of epilepsy I proved an indurating thickening of the pia mater at the anterior circumference of the medulla oblongata, which, however, had not penetrated into its substance. There was at the same time present a strong brownish pigmentation.

4. Tumors.

§ 732. Throughout the Oncology of Virchow, that imperishable monument of German science, the effort of the author shows itself now more, now less prominently, to accustom his scholars to a less abstract conception of the individual species of tumor, and to show us what an important influence upon the anatomical and physiological quality of a new formation, its seat, *i. e.*, the tissue from which it proceeds, has. Every one, who does not only care for a superficial definition and nomenclature, but who has accustomed himself to test tumors thoroughly as to their structure and texture, and to compare these with their vital properties, will, with Virchow, hope the best from this point, for the final adjustment of that pitiable disunion, which yet exists at the present time, between the justifiable demands of practice, and the limited knowledge of pathological anatomy. Medical instinct itself points us to this route, since it bases its prognosis just as much upon the seat of the new formation as upon its histological quality and habits. Meanwhile it would be foolish, for the sake of a knowledge which yet beckons to us from the distance in uncertain outlines, and which must be gained only by laborious investigations for years, to give up the possession which we have in hand. Be it now permitted me to make an attempt in the present chapter in the direction indicated, in that I divide the tumors of the nervous system, according to their starting-points, into the three following groups: *a*, tumors, which proceed from the free surfaces of the envelopes and interior cavities of the system; *b*, tumors, which proceed from the sheaths of vessels; *c*, tumors, which proceed from the neuroglia (perineurium).

a. *Tumors at the Free Surfaces of the Interior Cavities of the Nervous System.*

§ 733. The sac of the arachnoid, the dura mater spinalis, and the cavities of the brain, present expanded surfaces, upon which a series of

histioid tumors occur under the general form of flat, roundish protuberances. The conformity in the external form is explained by the uniform mode of development of all these new formations. They are collectively efflorescences, in the more contracted sense of the word. Only the most superficial layers of the wall participate in their production. For some time even the endothelium only may be affected by the morbid irritant; thus, we find its cells in the environs of all these tumors in active nuclear and cellular division. The actually effective force, however, of the new formation, is an "exudation of germinal tissue from the pores of the surface." I intentionally choose this somewhat ancient-sounding term, because it characterizes the derivation in actually a pregnant manner. The cells arising at the surface, which immediately come together to small elevations of germinal tissue, are migratory. We have no right to assume that they have been formed by a formative irritation of the connective tissue cells upon the spot. Against this speaks, apart from the deficient proof of a division of the connective tissue cells, the entire behavior of the connective tissue, whose fibrous lines remain quite intact for a long time where the new formation is seated, and only when the tumor attains a more considerable volume do they begin to separate and loosen. The latter takes place through an infiltration with the substance of the tumor, penetrating from without; it is as though the tumor, whose growth in the beginning is only directed outwards, afterwards grew inwards. The true relation of things may be this, that the cell-masses intended for exudation, upon their way to the surface, therefore, in the interstices of the connective tissue, are held back, because the adjacent organs present a too considerable resistance to the growth of the tumor. The adjacent organs can only gradually accommodate themselves to the altered condition, which takes place, especially by this, that at the place of the greatest pressure they become atrophic, and present deficiencies, which correspond to the form and size of the tumor. The more time allowed them for this, so much the more completely will they accommodate themselves. Hence the infiltration constantly turns out so much the larger, the more rapidly the tumor grows (spindle-celled sarcoma), so much the smaller, the slower it grows (Pacchionian granulations, lipoma, &c.). It would be entirely wanting, if the tumor met with no resistance from the adjacent organs, if it grew up into the open air; it is, in fact, wanting in tumors which project into the cerebral cavities.

§ 734. The *Pacchionian granulations* of the arachnoid, to a certain extent, form the physiological model of the entire group of tumors. According to L. Meyer, the development of these small, but numerous, milk-white protuberances, which develop by preference along the longitudinal sinus, over the edges of both hemispheres, stands in direct relation to the so-called respiratory movement of the brain. The hemispheres

are displaced in being more copiously filled with blood [at each pulsation of the heart], like the lungs upon being filled with air. The displacement is zero at the base, because the brain is fastened here; it is greatest at the edges of the brain, because these are furthest removed from the place of fastening. Under a low magnifying power now, the Pacchionian granulations present themselves as groups of papillæ, which are either simple or branched once or twice, which become pediculated in continued growth, without ever being entirely dissevered from their mother soil. They are absolutely non-vascular, and in their chief bulk consist of a striped connective tissue, poor in cells, which proceeds directly from a thin, but continually renewing layer of subepithelial germinal tissue. The epithelium, which covers them, appears in contrast to the normal epithelium of the arachnoid to be several times stratified; Meyer even discovered actual epithelial granulations in the environs of these tumors, so that the active participation of this structural element is without doubt, although the connective tissue occupies the dominant position in the entire production.

Far more multifarious are the superficial tumors of the dura mater. In the first place, we must mention here a *spindle-celled sarcoma*, which proceeds by predilection from the dura mater of the base, forms in the neighborhood of the clivus and of the sella turcica, tuberculated-tuberous, often right extensive protuberances directly compressing the nerves passing out, and the contiguous parts of the brain, thereby first irritating, then paralyzing, and finally destroying them. The same form of sarcoma is found upon the dura mater spinalis. It is characterized by very large, beautifully developed and nucleated spindle-cells, which lie together in bundles; upon teasing them out, however, easily separate. To this tolerably rapid-growing sarcoma, two other slower-growing forms of tumors are closely allied, which were first known in their peculiarity through Virchow's Treatise on Tumors, the myxoma and the psammoma of the dura mater. The *myxoma*, especially upon the spinal portion of the dura mater, is of eminent clinical significance, because, upon the one hand, it most frequently occurs here; upon the other, becomes dangerous by pressure upon the spinal marrow; while at the brain it mostly proceeds from the convexity, and hence belongs to those tumors to whose presence the brain accommodates itself in a great degree. The *psammoma* is a tumor with a connective tissue, or even with a mucoid tissue substratum, which distinguishes itself by its contents of globular lime-concretions. At the pineal gland, where these lime-concretions are almost physiological, we are accustomed to call them brain sand, hence the name (psammos, sand). According to Virchow, in the grains of sand of the psammoma, the question is about a concentrically stratified, non-cellular, organic foundation, into which the lime-salts are precipitated, at first into the centre, and then progressing ever further outwards. We would consequently

have to reckon a series of quite similar tumors, in which the sand-formation depends upon cell-incrustation (Fig. 200), not among the psammomas.

Finally, in rare cases, small lipomas have been observed upon the inner surface of the dura mater and upon the ependyma of the ventricles, which from the beginning protrude above the level, and never penetrate deeper into the cerebral substance.

b. *Tumors which proceed from the Sheaths of the Vessels.*

§ 735. Let us next consider somewhat more accurately the soil upon which the development of this large and important group of tumors takes place. In the inflammatory processes and in miliary tuberculosis (§ 115), we have already learned to know the sheaths of vessels as the favorite germinal places of the pathological neoplasia. We saw as well pus-corpuscles, as tubercle-cells arise upon the surface of the vessels and form tumefactions. Therewith the possibility that the question might be about migratory colorless blood-corpuscles, made us careful in our judgment, and we decided to regard the pus-corpuscles in general actually as emigrants, the tubercle cells, however, as autochthonous elements. The latter was done upon the ground of direct observation. We could prove, that in the formation of miliary tubercles the adventitial cells multiplied by division, and that in this manner the substance of the tubercle is formed. The adventitial cells of the vessels are, therefore, the proper supporters of the neoplastic function. What exactly are these adventitial cells?

The adventitia of the cerebral vessels is a homogeneous membrane with nuclei placed alternately. By treating with nitrate of silver we can demonstrate upon it the known lines of Recklinghausen, which subdivide it into lozenge-shaped fields, in whose centres the nuclei are situated. The outside of the cerebral vessels is, therefore, clothed with an endothelium which corresponds to the epithelium of the lymph-vessels. Were the opposing cerebral substance likewise clothed with such an epithelium, there could be no doubt whatever in the correctness of the assumption of His, that the cerebral vessels were contained in lymph-spaces. Notwithstanding this want, I regard the doubt unjustifiable, because I find that in the pathological new formations the adventitial epithelia unfold all those peculiarities in a high measure, which we lately learned in the epithelia of the lymph-vessels; namely, after having multiplied by division, they furnish a ready formative material for the various tumors. Herewith the tendency is certainly predominant, to the formation of a contrast between epithelium and connective substance; we will see how benignant and malignant epithelial tumors, cancers, and papillomas of the most various kind, form upon this base; beside these, however, the gumma syphiliticum and sarcoma occur as perivascular tumors, although in my opinion the proof for the latter is not yet furnished.

The outer surface of the cerebral vessels passes over at the periphery into the under surface of the pia mater, at the ventricles into the surface of the choroid plexus. The under surface of the pia mater is clad with the same lymph-vessel epithelium as the vessels, hence it falls completely under the same category as they. The surface of the plexus bears a well-developed and characteristic epithelium, which I have already spoken of in § 702. In the epithelium of the plexus we manifestly meet with the tendency to the production of higher forms of epithelium. I can add, that the forms which we see here serve in a certain measure as the type in all epithelial tumors, which proceed from the under surface of the pia mater, or the surface of the cerebral vessels.

The dura mater only shows analogous relations at its side turned to the cranium, since from this numerous vessels leap over the boundary line between the dura mater and the cranium, and sink into the Haversian canals of the surface of the bone. Will we ever discover lymph-spaces here also? For the present I can only state the great conformity in the behavior of these and the cerebral vessels in the formation of cancer and syphiloma, of which we will treat variously in the following.

The mode of growth of this group of tumors now is generally this, that at the surfaces mentioned the new formation establishes itself in its characteristic way, and then spreads out along the surface in a uniform manner; the growth in thickness is exhausted by the complete filling up of the space which exists between the producing points of the numerously and in all directions curved surface. This space is originally filled by the parenchyma of the nervous organs; for example, by the parenchyma of the brain. The parenchyma of the brain, however, does *not* participate in the new formation, but perishes atrophic, so that the tumors constantly appear as something foreign, separate, set into the nervous system. They cause death either by the destruction of parts of the central nervous system important to life or by this, that they excite inflammation and hemorrhage in their neighborhood. Meantime they may attain a very considerable size without proving fatal, which is not surprising in the great accommodative capacity of the brain for slowly growing local atrophies.

§ 736. The first tumor belonging here is the *carcinoma cerebri simplex*. This most frequently proceeds from the under surface of the pia mater. Such tumors, also, as appear to be isolated in the centre of Vieussens, are wont to be in connection at some place with the pia mater lining of an adjacent sulcus; yet quite isolated tumors only adhering to the vessels, also occur, which of course are but small, and constantly of a metastatic kind. The production of the cancer from the cells of the producing surface can be best traced at the borders of the nodule, especially there where the tumor, following the vessels, pene-

trates into the brain-substance. The zone of growth is about a line broad. Outwardly it borders upon the normal brain, inwardly upon the tumor as far as completely formed, and appears to the unaided eye as a zone of liquefaction, because a greater part of the cerebral substance is destroyed by fatty metamorphosis. By treating with chromic acid, as is known, we can make the parenchyma of the brain retract from the vessels, and the vascular openings appear larger than they are. Hence this method best accomplishes our purpose here, where all depends upon distinguishing the vessels and their belongings from the parenchyma of the brain. By means of it we can follow the changes of the vessels step by step.

The formation of larger cell-heaps out of each adventitial cell may be the first link of the process. The newly-formed cells are large, rich in protoplasm, have a nucleus and nucleoli, and bear an unmistakable resemblance to the epithelial cells of the choroid plexus. They are less stratified than conglobate; at the centre of the ball they are globular, at the surface spindle-formed. The spindles of adjacent cell-heaps come together into incomplete fibrous lines, and thus form those finer septa which are wont to subdivide the larger alveoli of every carcinoma. The trabeculæ of the stroma of the first order are formed here as everywhere by the remaining portion of the parenchyma which is destroyed by the cancer. It has been already mentioned that a greater part of the brain-substance perishes by fatty metamorphosis. What remains is, between each two considerably widened openings for vessels, a narrow bridge of fine and parallel fibrous tissue, which contains a moderate number of smooth nuclei. Whether in the round, shining fibrils, we have before us axis cylinders that have remained over, or metamorphosed neuroglia, I will not decide, though I believe I ought to assume the latter. If we trace up these fibre-lines deeper into the cancerous tumor, we observe how they always become homogeneous, finally to pass directly over into the principal trabecular network of the stroma.

In the further increase of volume of the tumor, the cell-proliferation predominates. The stroma disappears, in places, into very delicate threads and lamellæ, while the cells, rounded into colossal nests, fill the intervals. It is interesting, that the vessels, from which the new formation proceeds, are for the greater part corroded; always only the larger of them may be injected, while the others are obliterated to thin lines of connective tissue. The vessels, moreover, if they are not completely dissolved, form a second trabecular work, which interweaves in the characteristic manner, with the system of stroma-trabeculæ, without entering into connection with it. Any one, who has ever occupied himself in brushing out preparations of cerebral cancer, must have been struck by this, so to say, double stroma, although I do not find it even casually mentioned anywhere.

§ 737. We might call the cerebral carcinoma, as it presents itself as

a primary tumor, a fungus of the pia mater, and be reminded hereby of the completely analogous production of the *fungus of the dura mater.* Both tumors are alike not only in their histological constitution, but they also occur side by side, nay, in direct continuity with each other, so that every doubt of their relationship must vanish. The fungus of the dura mater arises at the side of this membrane turned to the bone, penetrates with the vessels into the compact substance, destroys the vitreous table, thereupon spreads out somewhat more easily in the diploë; finally, however, also breaks through the external compact lamella of the cranial bones, to lift up the integuments of the cranium as a fungoid proliferation. The dura mater is likewise not infrequently penetrated towards the interior, whereupon, after the preceding fusion of the arachnoidal lamellæ to the fungus of the dura mater, there is added a fungus of the pia mater.

§ 738. Nearest to genuine carcinoma there stands one of those oncological curiosities, in which the brain is so rich, a tumor which unites the structure of an epithelial carcinoma with the innocuity of a wart or an induration: the *cholesteatoma* of authors, or the *pearl-cancer.* This is a pavement epithelium, whose cell-cylinders have been entirely converted into a mass of pearly globules, shining like satin, and is most frequently found at the base of the brain, where it pushes forward out of the depressions between the more central parts of the brain (pons, medulla oblongata) and the lateral parts (the hemispheres of the cerebellum, the lower lobes, &c.), and occasionally forms a tumor above the size of a walnut. It is covered upon its surface by the arachnoid, while upon the opposite side it directly touches the cerebral substance, according to which its origin would have to be sought in or under the pia mater. The more rare occurrence of the pearly cancer in the midst of the cerebral substance indicates that its base of development is the same as in simple carcinoma, namely, the lymph-spaces and the sheaths of the vessels. In reference to the more minute detail of the development, Virchow speaks of blunt-ended, outgrowing cell-cylinders, of a deposition of epidermis globules into the meshes of the pia mater, &c.; both of which very well agrees with the assumption that the inner surface of the lymph-spaces, referring to their epithelium, produces the cells of the nodules of the tumor.

Closely related to the pearly cancer there is a rare tumor of the third ventricle, which contains the epithelial cell-cylinders and the nodules imbedded in a very voluminous stroma of mucoid tissue. (Fig. 200.) The tumor, at first sight, makes the impression of a thoroughly soft myxoma, which is only characterized by the amount contained of milk white, very hard atoms and granules. The milk-white granules are calcified pearly globules. If we place them under the microscope, and exert a moderate pressure upon the covering glass, they burst into scaly pieces, which correspond to the calcified cells. In their surroundings

we see then the more recent epithelial proliferations forming tubules and nests, as in all genuine cancers.

Only it is striking, that all these cancers have only a local significance, and that even the fungus of the pia mater seldom or never forms metastases.

Fig. 200.

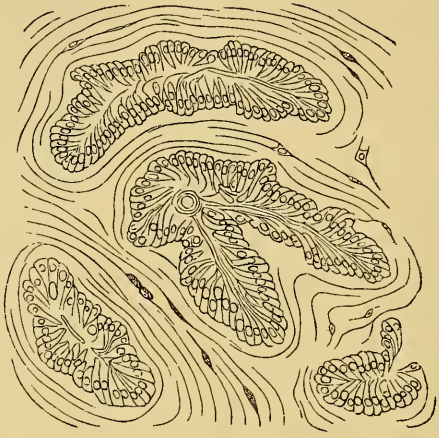
Epithelioma myxomatodes psammosum. See details in text. 1–300.

§ 739. In the series of tumors now following, the most prominent phenomenon is an "outgrowing of the producing surface in the form of genuine papillæ." I met with the *papilloma* of the pia mater and of the vessels, for the first time, upon the cerebellum. A roundish tumor, of the size of a pigeon's egg, had insinuated itself between the pia mater and the left hemisphere, and had caused in the latter a deficiency corresponding to its form and size. The substance of the tumor was reddish-gray, translucent, tremblingly soft. Upon teasing it out it broke up, without remainder, into an enormous mass of richly branched papillæ, each of which had a central vessel, very little connective tissue, and a doubly stratified epithelial mantle. The outer cell-layer consisted of short and thick cylindrical cells. If we followed the stroma of the papillæ, we at last touched upon the bloodvessels, which pass from the pia mater into the cerebellum, so that no doubt could arise as to the origin of the tumor.

Another closely allied papilloma appears to have been held by most authors as a myxoma. It is far more frequent than the simple papilloma, and is distinguished from this only by the abundant production of mucus at the surface of the papillæ. The epithelium (Fig. 201) consists of very long, well-formed cylindrical cells, and these are they which secrete here, as at the surface of a mucous membrane, layer upon layer of a tough, vitreous mucus. As mucus is a substance very capable of swelling up, it demands a proportionally large space. Thus, it is explained, why these tumors, in their principal bulk, in fact consist of mucus, wherefore, the papillary excrescences of the vascular walls standing almost individualized in the mucus might actually be overlooked. This form of tumor, which we may call *papilloma myxomatodes*, mostly occurs multiple upon the brain. In a case under my observation, a tumor of the size of a hen's egg was seated in the region of the pes hippocampi, where it had developed from the vessels of the choroid plexus here penetrating into the substance of the brain, and had filled up the entire cavity of the middle cornu. Several smaller ones were distributed over the entire surface of the hemispheres, and were imbedded in the cerebral cortex in the same manner, as I described above of simple papilloma.

§ 740. The gelatinous degeneration of the cortex of the cerebellum, described by Billroth, is to be regarded as a pure *myxoma* of the sheaths of the vessels. What is macroscopically found has the greatest resemblance to the cerebral papillomas described in the preceding paragraph. Microscopically there is a simple degeneration of the adventitia, the for-

Fig. 201.



Papilloma myxomatodes proceeding from the vessels of the cortex of the brain. The vascular papillæ are separated by broad, interposed bands of stratified mucus. 1-300. (Compare with this and the preceding illustration the dissertation of Le Blanc: Contributions to Pathological Anatomy of Cerebral Tumors. Bonn, 1868.)

mation of a relatively thick sheath of mucoid tissue around all of the vessels entering into the brain from the pia mater. The nervous parenchyma lying between the vessels is destroyed. But after all this has happened, the thickened vessels flow together into a common, vitreously transparent, slightly reddish-gray body of a tumor, which therefore, fits into a deficiency of the surface corresponding to its size.

§ 741. Whether this gelatinous degeneration of the vascular sheaths stood in relation to a constitutional syphilis, may, according to what was found in this one case, be answered neither affirmatively nor negatively. This much, however, is certain, that the genuine *syphiloma* of the central nervous system histologically stands so near to no tumor-formation as to this. The composition of the gumma syphiliticum, out of a germinal tissue rich in cells with abundant mucoid basis-substance, has been so frequently spoken of, that I need not again return to it here. It is less known, that the cerebral syphiloma develops from the sheaths of the vessels exactly according to the type of the group of tumors here in question. We see the gummata most frequently at the circumference, especially at the base of the brain, more rarely in the interior. They reach the size of a walnut, even of a hen's egg. While as a rule, they contain in the interior a caseous spot, the periphery shows a soft, gelatinous tissue, which is richly pervaded by blood-con-

veying vessels. Sections of hardened preparations show, that the parenchyma of the tumor rich in cells is arranged in concentric layers around the vessels; Virchow could even yet demonstrate this arrangement in the caseous parts. Upon the other side, where the new formation advances towards the brain or its membranes, we may convince ourselves, that this advance takes place along the sheaths of the vessels, into the spaces for the vessels, without the neighboring parts actively participating in the process. It is true, we rarely have the opportunity of studying the process in perfectly unequivocal pictures, because almost always all kinds of inflammatory, apoplectic, and softening processes exist in the neighborhood of the gummata, which disturb the investigation.

c. *Tumors which proceed from the Neuroglia.*

§ 742. As I fully expressed myself at another place (§ 687) upon the histological peculiarities of the neuroglia, I can at present content myself with the statement, that the tumors of the neuroglia proceed essentially from its cells. Those small, round, and still enigmatical elements, which we shortly call the granules of the nervous cement, are able by continued division to produce larger connected cell-masses, which present themselves to us under the form of tumors.

§ 743. Of these tumors let us first consider that called *glioma* by Virchow. Glioma formerly went under the designation of sarcoma, and at the present day I would not hesitate to continue the old name, if the influences of locality and of the mother tissue did not make itself felt just in these sarcomas in so prominent a manner, that a particular name appears in fact justifiable. In order to characterize at once one of the most striking peculiarities of glioma, we might rather call the glioma a gliomatous degeneration of individual parts of the brain. If we have a glioma before us, we can at least quite accurately say, that this or that section of the brain, for example, the optic thalamus, the corpus striatum, the anterior part of the centre of Vieussens, or a larger portion of the cerebral cortex, has been converted into the glioma. The forms of these parts have been altogether and entirely maintained, although nothing of the histological peculiarities has been maintained, rather everything has been substituted by the glioma-tissue. Simple round, perhaps, knotted gliomas do not occur; moreover, it is often very difficult to establish the form of the glioma, because upon the one hand it can be distinguished by its consistence, and color, almost not at all from the consistence and color of the parts which it substituted, upon the other hand, because it passes over very gradually into the healthy neighborhood. The first of these two points is straightway enigmatical to me. I have a glioma, which occupies the left optic thalamus and corpus striatum, which consists throughout of genuine glioma-tissue (round cells arranged in bundles and fibre-lines), and which macroscopically still only makes the

impression of a genuine hypertrophy of the optic thalamus and corpus striatum. Gray and white substance recur in the usual alternation, and still I cannot find nerve-fibres either with, nor without the white substance of Schwann, nor ganglion-cells, &c. In a glioma, also of the cerebral cortex of the right anterior lobe, which exists in the collection at Zurich, the conformity of the color of the diseased and the healthy parts is striking, although the former consists entirely of small spindle and round cells. We have here only the one point of support, that the growth of the glioma depends essentially upon infiltration, and that consequently the normal structure gives the proportions also for the pathological. The vessels appear for the greater part to be maintained. Hence the tumor, if we examine it upon a section, gives quite the impression of a sarcoma. Only that the cells are in general very small, and similar to the common granules of the neuroglia, which would be a curiosity at least, for an ordinary round or spindle-celled sarcoma. Moreover, the glioma and the sarcoma are very nearly related; in certain gliomas we find places, which are larger celled than usual; by way of exception I have even met with spindle-cells of 0.4 mm. in length and of corresponding thickness (glioma sarcomatodes). The relationship, however, is expressed especially also in the varieties. Virchow has taught us of a glioma myxomatodes, which varies in all shades up to a pure myxoma. I have myself several times had the opportunity of investigating the hemorrhagic glioma. It is characterized by comparatively wide bloodvessels and the tendency to effusions of blood, which constantly occur into the centre of the tumor. The bulk of the effused blood may be so great, that the case, not only clinically, but at the first glance, also anatomically, presents itself as an apoplexia sanguinea. The tumor is often crushed, excepting a narrow border, which surrounds the pool of blood; still, this naturally suffices to betray to us the original nature of the affection.

The gliomas belong to the slowest growing tumors, therefore, occasionally attain a considerable size. That they, at least in part, may also decompose, is proven by the frequent occurrence of fatty metamorphosed portions in the interior of the tumor, though it would be more correct in these decompositions to think less of a possible cure than of the danger of an apoplexy, which threatens, when the resorption of the fatty detritus brings about a diminution of pressure and a disburdening of the vessels in the interior.

§ 744. The *myxoma* of the nerve-substance is to be judged of from almost the same points of view as the glioma. The myxoma just contrary to the glioma, occurs more frequently in the spinal marrow than in the brain, and more frequently upon the peripheral nerves than in the spinal marrow. Perhaps the different nature of the neuroglia, the slight modification of the mother soil therefore, explains this fact. The myxoma represents the glioma at the peripheral parts of the nervous

system. Origin and growth are the same. The myxoma proceeds from a hyperplasia of the nerve-connective substance, the perineurium, and uniformly extends by infiltration in all directions. The fibres of the spinal marrow, or of the peripheral nerves, are crowded asunder and partially perish. Upon the nerves, myxoma presents itself as a spindle-formed tumefaction, as a *neuroma* in the widest sense of the word.

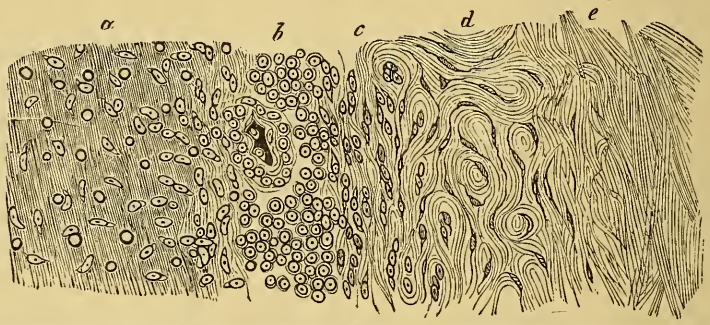
According to Virchow's precedent, we must make a strict distinction between genuine and false neuroma. Only the outer form is everywhere the same knotted spindle-formed swelling of the peripheral nervous trunks. The genuine neuroma, however, contains predominantly newly-formed nerve-fibres, while the false neuroma is produced by a local new formation from the interstitial connective tissue. This interstitial proliferation most frequently has the fibroid character, more rarely that of myxoma, or the softer forms of lipomatous sarcoma.

§ 745. Finally, the so-called *solitary tubercle* of the brain, must also be regarded as a production of the neuroglia cerebri. More frequent than all the previously named neuroglia-tumors, are these yellowish-white, exceedingly compact and dry caseous nodules, which are found in all parts of the brain and spinal cord, either actually single, and then usually in specimens which are characterized by considerable circumference, or in such wise, that several smaller nodules are distributed throughout the organ. In the cortex of the cerebrum and cerebellum, their favorite seat, the tumors develop close to the boundary of the gray and white substance; they are characterized by a very regular growth advancing with equal rapidity towards all sides, and hence, as long as no obstacles to growth are encountered from any one side, have a globular shape. Already, after they reach a very moderate size, the cheesy metamorphosis begins at their centre. As the smallest tubercles I have constantly found an aggregation of three to six nodules of the size of a pin's head, but already caseated. Whatever has once undergone the caseous metamorphosis, remains either entirely unchanged or there subsequently, although rarely, occurs a deposition of lime-salts, which, for its part, naturally excludes all further metamorphosis. This hardening of what has been formed, stands in abrupt contrast to the unwearied progress of the growth at the periphery. But few nodules have apparently completed their course. The nodule is usually surrounded by a soft, reddish-gray layer, permeated by bloodvessels, which contains the formative material of the tumor in the form of a germinal tissue, rich in nucleated round cells. The thickness of this layer stands in inverse proportion to the size of the tubercle. Upon tubercles of the size of a pea, it measures nearly a line; upon tubercles of the size of a pigeon's egg, scarcely half a line. Moreover, its tissue passes over continuously upon the one hand into the caseous tumor, upon the other, into the normal brain-substance. In order, therefore, to get an insight into the

more minute relations of the growth and the secondary metamorphoses of the tumor, we must prepare vertical sections, which side by side, contain the unchanged brain-substance, the layer of gray germinal tissue and the caseous substance. This we succeed in only after carefully hardening the material in Müller's fluid and alcohol. But what do these sections teach us? They teach us, that we are not justified in regarding without more ado, all solitary tubercles as being identical, that we are rather necessitated to concede two different tumors, which certainly present themselves under a surprisingly similar macroscopic picture, namely, an actually tuberculous and a non-tuberculous species of the caseous solitary nodule.

§ 746. Let us next consider a vertical section through the border of a non-tuberculous nodule from the cerebellum, of the size of a walnut (Fig. 202). At *b* is the layer of round-celled germinal tissue, at the

Fig. 202.



Solitary caseous nodule, so-called tubercle of the brain. *a* Normal white brain-substance. *b*. Proliferating layer of germinal tissue of the tubercle, inclosing a thickened vessel. *c, d, e*. Fibroid metamorphosis of the germinal tissue, at the same time the border zone of the caseous tumor. 1-300.

same time the matrix of the tumor (*c, d, e*), and the product of the cerebral substance (*a*). It contains the cross-section of a larger vascular branch; its lumen has collapsed, the walls, especially the adventitia richly infiltrated with cells. In other respects no sort of specific peculiarities, particularly nothing specifically tuberculous can be seen upon the germinal tissue. If we now turn our glance first to the left side, to follow up the origin of the germinal tissue, nothing further can be established here than that the number of cellular elements in the nervous substance always increases the nearer we approach the zone of proliferation. We see them in small groups, lying together by twos, by fours, and more, which would formerly have sufficed to explain it as a proliferation of the neuroglia-cells. This easy mode of explanation has, it is true, been taken from us by the migratory theory of Cohnheim, and we must ask, especially in the face of the walls of the vessel so richly infiltrated with round cells, whether a transmigration from the blood is not here the source of all the new formation?

Upon the other side, the relations are less doubtful. At *c* begins

the transformation of germinal tissue into the caseous tubercle. But how? May we, in the face of this picture, even but remotely think of retaining here our usual conception of the caseous metamorphosis (§ 33). We seek in vain after a fatty granular metamorphosis of the germinal tissue, in vain after the shrivelled cells, the tubercle-corpuscles of Lebert. We are reminded of fatty metamorphosis, principally by a tolerably dense, finely granular dust, which obscures the oldest parts of the tumor (*e*), without, however, leaving us in doubt for a moment, that the question here everywhere is not of cells, but only of fibres. The fibre-formation between the cells of the germinal tissue (*c*) is evidently that histological metamorphosis, which converts the soft germinal tissue into the firm tubercle. The fibre-formation and condensation, however, already immediately becomes so very predominant at the border of the tumor (*d*), over the cellular parts, that without hesitation, we may apply the term *fibroma* to this tissue. The intimate interweaving also of the fibres, which, where it occurs physiologically (cutis), we regard as the expression of intended greater durability, and which is so peculiar just to the fibroma, again recurs. What can we adduce in opposition to this, for the tuberculous nature of the tumor? That it is occasionally associated with miliary tuberculosis? This it has in common with all caseous masses. Or may we regard the formative material, the layer *b*, as a layer of miliary tubercles? Certainly not, without taking into consideration, that then these tubercles would have only apparently undergone a caseous, in reality a fibrous, degeneration.

According to all this it appears to me that there are solitary tubercles of the brain and spinal cord which rather deserve the name of fibroids. But if this is so there arises an agreeable uniformity of the neuroglia tumors with the sarcomas in general; we could recognize in them the known fibrous and cellular forms of sarcoma, modified by the place of development and the mother tissue.

§ 747. Upon the other hand there are caseous nodules, mostly multiple and smaller, which upon more accurate test, prove their more minute histological relations as in fact tuberculous. We can see in the gray proliferative layer of these nodules, even with the naked eye, that they are not homogeneous, but that they are composed of round portions which agree in form and size with miliary tubercles. If we pick out the central caseous nucleus here, this also shows upon its entire surface, round and roundish tuberosities. The caseous nodule consequently contains dead, the gray proliferating zone still living miliary tubercles; this explanation is confirmed throughout by the microscopic analysis. The process is a phthisis tuberculosa of the brain, and perfectly analogous to the destruction of the kidneys by localized miliary tuberculosis, &c.

The *disseminated tuberculosis* of the nervous system was treated of incidentally with leptomeningitis (§ 697).

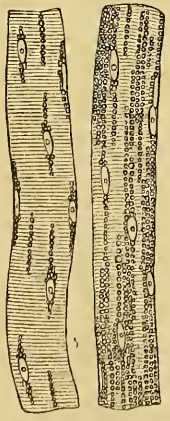
XVIII. ANOMALIES OF THE MUSCULAR SYSTEM.

§ 748. The two principal structural constituents of the voluntary muscles, the striated muscular fibres and the connective tissue, also divide between them the prerogative of being the starting-points of the various pathological changes which may affect the muscle. I say starting-point, because, in fact, they are often only the beginnings of the processes which exclusively affect the muscular fibres or exclusively the connective tissue, and the disturbances are wont very soon to pass over to the other structural parts. In individual cases it will even be impossible for us to say whether the process begins in the connective tissue or in the primitive fibres; hence I regard it as appropriate to form the division not according to this, but according to the usual clinical points of view.

1. Atrophy and Hypertrophy.

§ 749. The brown atrophy which we have learned to know in the heart-muscle as the effect of a decreasing nutrition *in toto* (senile and cachectic marasmus), does not occur in muscle subject to the will. The fatty degeneration also (Fig. 203) arises only exceptionally, otherwise than after preceding parenchymatous swelling (see § 36). The *progressive muscular atrophy* which gradually extends over a smaller or greater part of the muscular system of the body is traced back by Förster to fatty metamorphosis. A greater significance for the voluntary muscles has the *simple atrophy* complicated with the interstitial formation of fat, a disturbance which almost always develops in such muscles as have been sentenced to a long-continued, involuntary rest, as muscles which should flex and extend an immovable joint, paralyzed muscles, &c. Simple atrophy manifests itself in a decrease of volume of the muscular fibres. If we make a cross-section through the atrophic muscle we will, perhaps, observe not a single muscular fibre which yet fills out the space intended for it. The contractile substance

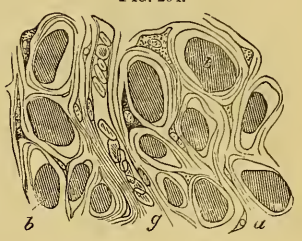
Fig. 203.



Fatty degeneration of muscular fibres. 1-500.

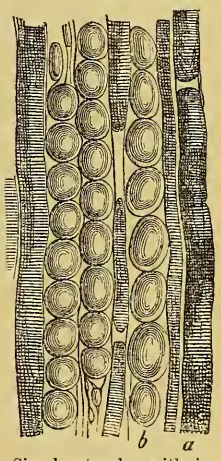
herewith loosens from the sarcolemma which remains in connection with the interstitial connective tissue. It forms a loosely fitting sac, that however, the longer the condition has endured, is so much the more difficult to present isolated, because the connective tissue completely incorporates it, and thereby itself experiences a certain thickening. The cells also of the interstitial connective tissue (Fig. 204), appear richer in protoplasm than usual, and may serve excellently for convincing, perhaps an unbeliever, of the existence and vitality of intermuscular connective tissue cells. In the great majority of cases these cells become the seat of a complementary fat-infiltration, they are converted into fat-cells. A very elegant histological picture arises by this combination of atrophy of the muscular fibre and fat-infiltration of the connective tissue. Fig. 205 again presents this in a longitudinal view. The fat-cells, on an average of the same size, lie in longitudinal rows, which, directed parallel to the yet existing muscular fibres, appear to have each replaced a vanished muscular fibre. That this is but apparent is self-evident. In our illustration we can also see a muscular fibre whose contractile substance has already been interrupted in places; at such places where therefore the contractile substance has entirely disappeared, we see how the sarcolemma extends as an empty tube from one fragment to the other; there is not a trace, however, to be seen of a formation of fat in the sarcolemma tube.

Fig. 204.



Simple atrophy of muscle. *a*. Interstitial connective tissue with large cells. *b*. Muscular fibres in various stages of decreasing volume. *g*. Filled capillary. 1–300.

Fig. 205.



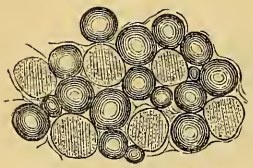
Simple atrophy with interstitial formation of fat. *a*. Atrophic muscular fibres. *b*. Rows of interstitial fat-cells running parallel to the muscular fibres. 1–300.

A quite analogous substitution of perishing muscular fibres by adipose tissue is found in the fattening of muscles, though here the formation of fat in the interstitial connective tissue is the primary, the disappearance of the muscle, although it may be founded upon insufficient movement, is secondary.

§ 750. From here, however, it is but one step to the recently several times observed *pseudo hypertrophy* of the muscles. Single muscles or entire groups of muscles swell up in the course of several months; but uniformly, so that the anatomical form, although in enlarged outlines, is preserved. This apparent hypertrophy, however, by no means conditions an exalted capacity of function; on the contrary, the muscles ever become weaker, finally as though paralyzed. Anatomically

we find a complete permeation of the muscles with fat, in which, however, the muscular fibres do not appear diminished, but only forced apart; none touches its neighbor, because it is separated from it by a row of interstitial fat-cells (Fig. 206).

Fig. 206.



Cross-section through a muscle in the state of pseudo hypertrophy. The well-preserved muscular fibres separated by the interstitial formation of fat-cells. 1-300.

§ 751. Genuine hypertrophy occurs in a marked manner only in the heart-muscle, and was spoken of more in detail at another place (§ 235). There is no doubt, whatever, that the voluntary muscles also of the trunk, and the extremities, may become larger and more vigorous by exercise, yet to demonstrate these hypertrophies anatomically can scarcely be possible at present.

2. Inflammation.

§ 752. The inflammation of muscle (myositis), may be acute or chronic. The acute begins with a parenchymatous swelling and proceeds to the formation of abscess; the chronic is a consequence of frequently recurring or long-continued hyperæmias (rheumatism, habitual mechanical irritations), and proceeds to hyperplasia of the interstitial connective tissue, the formation of indurations and bone. We find here a similar contrast as in the inflammations of the liver, and as, apparently (!), in all inflammations of parenchymatous organs.

§ 753. *Acute myositis* is most appropriately investigated in the first stage of its course in embolic, thrombotic, and apoplectic conditions of the larger muscular bellies. The parenchymatous swelling of the muscular fibres appears herewith as the first and most important factor. I have described this in § 240 of the heart-muscle, but find that the bounds there laid down are too narrow for the multiplicity of the phenomena in the voluntary muscles. In many cases the granular clouding is placed very much in the background over against a peculiar production of homogeneity and considerable tumefaction of the contractile substance. The nuclei are occasionally no longer to be seen; even the transverse striation disappears. All this, however, does not always happen uniformly in the entire length of the fibres, but in sections, so that places unstriated, tumefied even vitreously, alternate with those relatively normal. The dividing into fragments of the muscular fibre by transverse rents, so often seen and described, which is repeated at short distances, makes these differences peculiarly prominent. The whole phenomenon makes the impression as though the difference of the stronger and less refractive of the denser and less dense substance, were removed, as though the "sarcous elements" were swelled out, dissolved, fused with the connective substances to a homogeneous, shining mass.

In the typhous myositis, where the parenchymatous swelling of the muscular bundles likewise plays a part, we will have the opportunity of learning a further metamorphosis, designated by Zenker as "wax-like," as the synonymous continuation of this initiatory stage; in the ordinary acute inflammation the early occurring suppuration of the interstitial connective tissue makes the further tracing up of the changes difficult. I have most frequently seen fatty degeneration of the inflamed muscular bundles; occasionally, however, it appeared to me as though the rapid decrease of volume stood in relation to the production of the intrasarcolemmatous pus-corpuscles as if the material of the muscular fibres were consumed by the pus-corpuscles in their abundant formation. We cannot, indeed, directly see the like, but just as little can we, in view of this mutual relation of increasing pus-corpuscles and decreasing muscular substance, get rid of the instinctive conjecture which I indicate, and I do not conceive why we should not express it as such.

The pus-corpuscles, which soon collect in large quantity and form as an abscess, are derived, according to the assumption hitherto, from the cells of the interstitial connective tissue; they are partly the progeny of the so-called muscular corpuscles, *i. e.*, those few nucleated remains of the muscular formative cells situated at the inner surface of the sarcolemma (C. O. Weber). Entire muscular bellies, for example the psoas, may suppurate, more frequently the abscess-formation is limited to a place of the size of a pea to that of a walnut, according to the inducing cause. In embolic inflammations the depot will not essentially exceed the territory of the occluded artery. The sequestration of pus, the casting out and healing, likewise the resolution of the whole process, should such occur, ensue by the known means of second intention.

§ 754. *Chronic myositis* runs its course without suppuration, if this does not interfere as a casual accident. While in acute myositis a certain anæmia goes hand in hand, at least with the parenchymatous swelling, is perhaps entirely caused by it, in chronic myositis the hyperæmia demands exclusively for itself a longer prodromatous stage. The rheumatic muscular inflammations are wont to leave behind permanent traces only, after having through years always again attacked the same muscle; just so in the production of the so-called riding, and drill bones, it is always, only the traumatic hyperæmia excited anew, which finally leads to the formation of the ossifying blastema.

Chronic myositis, when it passes beyond the stage of hyperæmia, next manifests itself in the formation of an interstitial germinal tissue. Herein the muscular fibres are perfectly non-participative, and the question only is, whether we may yet hold to the connective tissue cells of the interstitial tissue as the cell-producers, or whether we must think of migration of colorless blood-corpuscles from the vessels. The fact that the bloodvessels have extraordinarily thickened sheaths,

and that this thickening depends upon an infiltration with round cells, can be established here as in so many other chronic inflammations. Touching this interstitial germinal tissue itself, the exudation of authors, this distinguishes itself in nothing from the ordinary type; it is reddish-gray, permeated by newly-formed capillaries, and in itself disposed to all kinds of further metamorphoses. The direct organization into a compact, dense connective tissue, is most common. The formation of a so-called "induration" is characteristic particularly of the rheumatic inflammation. The muscular fibres perish entirely in this induration, and there finally remains only a narrow, ribbon-like stripe, where there was originally a full muscular belly.

The same developments of form, as I will observe here by the way, serve for the reunion of the divided surfaces in wounds which have affected the muscle in its continuity. In vain have we sought for a regeneration of the muscular fibres in muscular cicatrices, and have been repeatedly deceived by the naturally intervening spindle-cells.

§ 755. The ossifying muscular inflammation is a peculiar variety of chronic myositis. This, upon the one hand, lies at the foundation of both the already mentioned curiosities, the drill-bone of the deltoid and the riding-bone of the adductors; upon the other hand, it occurs as a constitutional disease simultaneously in several muscles, in the first place, of the back, afterward of other regions. The germinal tissue here passes directly over into compact osseous tissue. The drill-bone is usually a three-cornered piece of bone, which arises in the left deltoid muscle near its tendinous insertion, and attains by concentric growth an average length of three to five inches, a breadth of one to two inches, and a circumference of four to five inches. In the former Prussian drill regulations, there was a very favorite position, in which the tube of the musket was struck with great force against the place in question. The same with the riding-bone of the adductors. We have recently had an interesting paper, by Münchmeyer, upon Myositis Ossificans Multiplex Progressiva, which in a histological relation establishes the fact, that the question here is about an actual ossification of the interstitial exudation.

There is also a simple deposition of lime into the primitive bundles of the voluntary muscles, which must not be mistaken for the myositis ossificans. The latter is an actual rarity, and plays only a very modest part, beside the frightful deformities of the muscular system, which are produced by the ossifying myositis.

3. Typhus.

§ 756. It has already been known for a long time, that in typhus abdominalis muscular abscesses occur; but that the typhus myositis, which also lies at the foundation of those abscesses, is an absolutely

frequent process we only know by the beautiful and, in this direction, pioneer researches of Zenker. The typhous myositis attacks by preference the groups of the adductors of the thigh. We there find, in the midst of the remaining healthy muscle, a circumscribed part of one to three inches diameter, which is characterized either only by a moderate swelling, and pale, wax-like constitution of the coarser muscular bundles, or by a pulpy softening, shading more into reddish, which latter imparts to the whole depot a superficial resemblance to a muscular abscess.

The histological changes which bring about these palpable anomalies belong among the most interesting that the entire pathological histology has to exhibit. We may distinguish three processes proceeding side by side, which each start from one of the various structural constituents of muscle, confine themselves to these, and complete themselves in it. Each of them forms a series exclusive in itself, but at the same time assumes thereby a part in the work of destruction and of building up, which here completes itself.

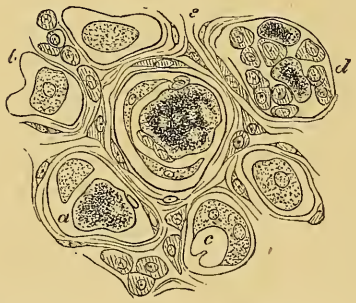
§ 757. Let us next touch upon the cause, which may soonest be, and in my opinion also, must be, regarded as specifically "typhous." This is the cellular infiltration of the interstitial connective tissue. In the consideration of typhus abdominalis (§ 112, *et seq.*) I could not avoid designating as the acme of the process the production of a cell-form, which, in individual formation, decidedly exceeds the common pus-corpuscles. The typhus-cells are, indeed, likewise relatively small, uninucleated elements, yet they are richer in protoplasm, and in so far also larger than the lymph- and pus-corpuscles, colorless blood-cells, &c. By the crowded juxtaposition in a limited space, they assume irregular, often directly polygonal forms, and commence to remind us of epithelial cells. Then, however, the retrogressive metamorphosis enters, and they break down mostly by fatty degeneration into a detritus capable of being resorbed. Now, the same cell again recurs also in the medullary infiltrations which typhus produces in organs not primarily participative; for example, upon the surface of the *pleura* it is also decidedly not wanting in the interstitial infiltration of muscles. Hence it is by no means to be conceived as an error of drawing if in the adjoining illustrations I have pictured the "pus-corpuscles" between the muscular fibres (Fig. 208, *c*) strikingly large and many formed. I rather hold the interstitial new formation, whether this proceed from the cells of the connective tissue, or whether the question is about accumulated migratory cells, as identical with the medullary infiltration, although the macroscopic effect is not the same, because of the concurrent parenchymatous parts.

§ 758. We cannot at present say with certainty in what relation the infiltration of the connective tissue stands to the processes in the muscular fibres. Waldeyer has directed our attention to such fibres as are

entirely covered with young cells, nay, even appear to be changed into them. According to this we ought to imagine either that these cells have migrated into the sarcolemma tube, or that the muscular corpuscles at the inner surface of the sarcolemma had partly entered upon a proliferation identical with that of the connective tissue process. I say partly, for just upon them devolves yet a principal part in the entire process, that of the regeneration of the muscular fibres, after these in their principal bulk, namely, the contractile substance, have been gradually but completely destroyed.

§ 759. We consequently come to the phenomena in the *muscular fibres* themselves. In what has been just said is implied that we must well distinguish upon them the behavior of the contractile substance from that of the muscular corpuscles. The contractile substance passes over directly from the condition of parenchymatous swelling into that of a wax-like metamorphosis (Zenker). In fact the single, parallelogrammatic fragments, into which the contractile substance breaks up, is characterized by a quite striking, therewith soft, wax-like lustre; and, what especially yet recommends the comparison, is the visible melting down of the same at the edges, this rounding off of the corners, this accommodation to the formed constituents, which, beside the fragments, demand an independent place (Fig. 207, *a*). A fatty, granular

Fig. 207.



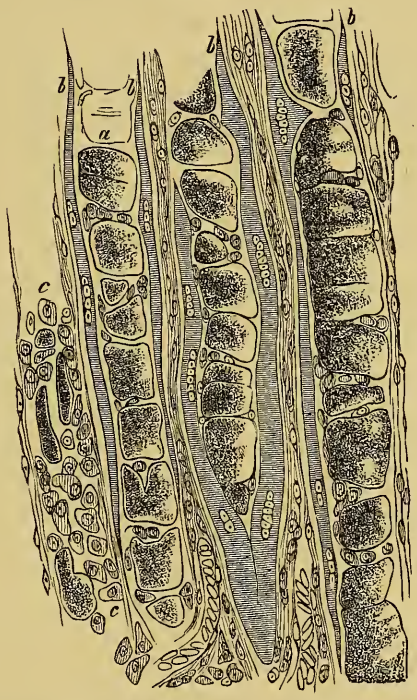
Myositis typhosa. Cross-section. 1–500. *a.* Wax-like degeneration of contractile substance. Beside it the cells with crescentic cross-section intended for its regeneration. *b.* A sarcolemma-tubule with a young muscular fibre which is round upon the cross-section. *c.* A similar one with a young muscular fibre which is yet crescentic in the cross-section, and incloses a gap in which the last remains of the degenerating substance may have lain. *d.* One of the same with numerous typhus-cells beside the remains of the old muscular fibre. *e.* Interstitial connective tissue infiltrated with typhus-cells. 1–500

clouding of the muscular substance, has hitherto usually not been seen; the mentioned fragments become rather smaller and smaller, they finally disappear, without having up to the last lost their lustre or wax-like constitution. An agreeable uniformity also prevails among observers upon this part of the process. Not so upon the third part, the regeneration.

I am conscious of not treating the subject in every sense, and especially not in the sense of the meritorious Zenker, when I ascribe the regeneration of the affected muscular fibres to the cells pre-existing in

the interior of the sarcolemma tubes. Meanwhile this is done with the firmest conviction. We can convince ourselves better upon cross-sections (Fig. 207) than upon longitudinal sections and teased-out preparations, that the young muscular fibres are formed in the interior of the sarcolemma tubes, not beside them. The young muscular fibres here present themselves, as also in the normal development, as elongated, spindle or ribbon-like elements, which possess a very finely granular protoplasm, and numerous small, vesicular nuclei, which latter are arranged in from two to twenty in elegant longitudinal rows (Fig. 208, *b*). The

Fig. 208.



Myositis typhosa. Longitudinal view, a section partly teased out. *a*. The wax-like, degenerating, contractile substance of the old muscular fibres. *b*. The young muscular fibres. (The transverse shading only represents the punctation for the sake of distinctness, and is not intended to denote striation.) *c*. Sarcolemma tube with very many typhus-cells, beside small remains of the contractile substance. The connective tissue richly infiltrated with cells. 1–500.

outer form of these cells adapts itself to the given relations of space; in the first place they form narrow ribbons, crescentic upon a cross-section (Fig. 207), which connect themselves most intimately to the, as yet little destroyed, cylinder of contractile substance; if, then, the muscular cylinder crumbles, and gaps occur between the melting fragments, the protoplasm of the growing muscular fibres also forces itself into these gaps, whereby the latter receive incurved conical serrations projecting inwards. The cross-section also shows how the decreasing old muscular fibres and the increasing young muscular fibres, divide in the existing

cylindrical inner-space of the sarcolemma tube. The former appear as roundish lumps, the latter as crescents, which embrace the lumps, and finally inclose them. We usually observe one, at times, however, also several, young muscle-cells in one sarcolemma tube. If there are several, upon further growth they run together just as well in the transverse direction as they enter into connection with each other in the longitudinal direction. Finally, the last remains of the old muscular tissue has been removed, and a single muscular fibre, produced by the confluence of many formative cells, occupies their space. This yet enlarges considerably, and assumes the transverse striation, the nuclei are uniformly distributed upon its surface, whereby then the new muscular fibre is completed.

Meanwhile, nay, yet ere the restitution of the muscular fibre is complete, the infiltrated round cells have also been decomposed by fatty metamorphosis. The myositis typhosa, like the medullary infiltration of all parts not superficial, heals without leaving behind a remainder.

4. Carcinoma.

§ 760. The primary occurrence of very soft medullary sarcomas (§ 761) in muscles, has probably been the occasion for mistaking it for soft carcinoma; in general, the metastatic carcinoma only occurs in muscular tissue as an independent tumor, and forms in it smaller and larger nodules. The muscular tissue is naturally, also, not spared by cancers, which extend in continuity. The epithelial cancer of the lip goes over to the muscles of the lip, the cancer of the tongue to the muscles of the tongue, cancers of the optic bulb also infiltrate the muscles of the orbit. In all these cases we have been convinced of the pre-eminently passive behavior of the muscular fibres. Muscular cancer is essentially an interstitial infiltration, by which the muscular fibres are forced asunder, thereupon ever becoming narrower, to disappear. This obtains without restriction of the contractile cylinder. The question only is, in how far the muscular corpuscles, or the sarcolemma-cells, participate in the new formation. That they are able to do this, and indeed in all forms of carcinoma, can scarcely be doubted after the illustration which C. O. Weber has given in Virchow's Archives, vol. xxxix, plate v. According to Weber, whole nests of cells form in the *interior of the muscular fibres*, where the question is about the advance of the epithelial cancer into the muscles of the lip, or about the advance of scirrhus mammæ into the pectoralis major. Upon the other hand, however, we must hold fast to this, that this participation is no constant appearance. In all the cases investigated by me of soft carcinoma of muscles, I could not surely convince myself of the inactivity of the muscular corpuscles in the disappearing muscular fibres. It

accordingly remains for us to leave to the future, for the time being, the correct limitation of the experience gained by Weber.

5. Sarcoma.

§ 761. The sarcoma of muscles, also, is an interstitial new formation. This was yet recently confirmed by C. O. Weber for a glio-sarcoma of the crural nerve, which had grown into the sartorius muscle. For the soft sarcomas, which occur primarily in muscles, I would furthermore yet call attention to the behavior of the sheaths of vessels; not that the tumor proceeds from these, but within them and in their nearest surroundings, it shows a certain tendency to variation. In an otherwise round-celled sarcoma of the deltoid, I saw around the vessels sharply contrasted areas, within which the sarcoma exhibited a large-celled nature, was even provided here and there with giant-cells. The sarcoma returned years after extirpation, and produced death by metastases.

That the cavernous tumor also occasionally visits the muscles, was discussed in § 129 *et seq.*, with all histological detail. All other histioid tumors, fibroids, lipomas, myxomas, enchondromas, are rare guests in muscles, and then also do not belong to the muscular tissue as such, but to the intra-fascicular strata of connective tissue.

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V. A. is synonymous with "Virchow's Archives."

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