Nothnagel's Encyclopedia of Practical Medicine

TYPHOID FEVER

AND

TYPHUS FEVER

BY

DR. H. CURSCHMANN

Professor of Medicine, Leipzig

EDITED, WITH ADDITIONS

BY

WILLIAM OSLER, M.D.

Professor of the Principles and Practice of Medicine, Johns Hopkins University, Baltimore, Md.

AUTHORIZED TRANSLATION FROM THE GERMAN, UNDER THE EDITORIAL SUPERVISION OF

ALFRED STENGEL, M.D.

Professor of Clinical Medicine in the University of Pennsylvania

---

PHILADELPHIA AND LONDON

W. B. SAUNDERS & COMPANY

1901

ELECTROTYPED BY
WESTCOTT & THOMSON, PHILADA.

PRESS OF
W. B. SAUNDERS & COMPANY.

PREFACE.

THE excellence of the series of monographs issued under the editorship of Professor Nothnagel has been recognized by all who are sufficiently familiar with German to read these works, and the series has found a not inconsiderable proportion of its distribution in this and other English-speaking countries. I have so often heard regret expressed by those whose lack of familiarity with German kept these works beyond their reach, that I was glad of the opportunity to assist in the bringing out of an English edition. It was especially gratifying to find that the prominent specialists who were invited to co-operate by editing separate volumes were as interested as myself in the matter of publication of an English edition. These editors have been requested to make such additions to the original articles as seem necessary to them to bring the articles fully up to date and at the same time to adapt them thoroughly to the American or English reader. The names of the editors alone suffice to assure the profession that in the additions there will be preserved the same high standard of excellence that has been so conspicuous a feature in the original German articles.

In all cases the German author has been consulted with regard to the publication of this edition of his work, and has given specific consent. In one case only it was unfortunately necessary to substitute for the translation of the German article an entirely new one by an American author, on account of a previous arrangement of the German author to issue a translation of his article separately from this series. With this exception the Nothnagel series will be presented intact.

ALFRED STENGEL.

EDITOR'S PREFACE.

It was with the greatest pleasure that I undertook, with the help of Dr. Cole, a member of my staff, the editing of a translation of Professor Curschmann's important work on Typhus and Typhoid Fevers.

The original edition is recognized by all special students of typhoid fever as the standard authority on the subject. Professor Curschmann has had exceptional opportunities to study the diseases considered in this monograph, which displays everywhere the thoroughness and fulness which we all recognize as characteristic of the literary work of the directors of the great medical clinics in Germany.

With the consent of Professor Curschmann, the additions have been made so as to run smoothly with the original text. The following are some of the more important changes, necessitated chiefly by the new work done since the issue of the German edition:

The chapter on the Bacteriology of Typhoid Fever has been thoroughly reviewed and new material added, particularly on the distribution of the typhoid bacilli, especially in the urine, in the rose-spots, and in the blood.

In the chapter on pathology many minor additions have been made, and the important work of Mallory has been incorporated. The literature on the localized lesions due to the bacillus, particularly of the bones, meninges, heart, pleura, bladder, etc., has been carefully revised and brought up to date. Thayer's exhaustive study of the state of the blood has been utilized. The surgical complications of the disease have been very fully revised with the aid of Keen's monograph.

The chapter on Perforation and Peritonitis has been practically rewritten, as has also the section on the Hepatic Complications of Typhoid Fever.

Many important additions have been made to the section on Diagnosis by Bacteriologic Methods, particularly with reference to the recent work on blood-cultures and on the detection of the bacilli in the urine.

In the chapter on Treatment I found little to change. The author's

methods in the application of hydrotherapy differ somewhat from those in use in this country, and the antipyretic drugs are not much in use here. Wright's method of antityphoid vaccination has been added.

I wish to express again my indebtedness to Dr. Cole, whose work has made him perfectly familiar with all the recent studies on the subject, and who has, moreover, utilized in the revision the articles in the "Studies in Typhoid Fever" from the Johns Hopkins Hospital, particularly those of Drs. Flexner, Finney, Thayer, Blumer, Parsons, Cushing, Camac, Hamburger, and Gwyn.

WILLIAM OSLER.

CONTENTS.

TYPHOID FEVER.

TYPHUS FEVER.

TYPHOID FEVER.

TYPHOID FEVER.

I. ETIOLOGY.

HISTORICAL.

THE recognition of the causative factors and of the nature of typhoid fever was long prevented by the inability clearly to separate it anatomically and clinically from other diseases bearing a superficial resemblance to it. Although the name typhus dates back to antiquity, it was not until within recent times applied to a clearly defined disease, but to a group of acute febrile conditions attended with stupor and obscuration of consciousness (τῦφος, breath, vapor). Typhoid fever is, without doubt, not a disease that has developed or appeared for the first time within the last few centuries. Certain statements and descriptions made even by early writers—as, for instance, Hippocrates—are applicable scarcely to any other disease than typhoid fever, as Wunderlich specially has shown.[1] With the increasing importance of anatomic investigation, Spigelius, Willis, and Morgagni as early as the seventeenth and eighteenth centuries made reports of post-mortem examinations that undoubtedly indicated typhoid fever. Clinical observation, however, could not yet be brought into perfect accord with the anatomic conditions at this time; the clinical and the pathologic descriptions often did not wholly coincide. The discrimination of the typhoid fevers from plague, malaria, and a number of septic processes was gradually learned; but until within quite a recent period typhoid fever continued to be confounded with typhus fever and relapsing fever. Less significance should be attached to relapsing fever in this connection, as it occurs less commonly and is confined to a more circumscribed area. Typhus fever constituted, however, a serious obstacle, especially in England and France, the countries from which, at the close of the eighteenth and the beginning of the nineteenth centuries, the most substantial impulses for the development of our knowledge of the disease emanated.

In France at the beginning of the nineteenth century the anatomic lesions of typhoid fever became gradually more clearly understood;

[1] *Geschichte der Medicin.*

but for a long time the idea was not abandoned that these lesions belonged as well to the disease that we know to-day as typhoid fever, as to all of those conditions known variously as war-typhus, starvation-typhus, camp-typhus, and similar designations, all of which were even at that time considered contagious. In England, on the other hand, where typhus fever had always been predominant, it could not for a long time be understood why post-mortem examination in the cases in question only exceptionally disclosed the lesions described with such detail by the French physicians.

In France, Prost[1] had as early as 1804 demonstrated that the typhoid fevers were constantly associated with definite intestinal lesions. His conclusion was based upon the unusually large amount of anatomic material furnished by 200 autopsies. His views were materially enlarged upon by Petit and Serres,[2] who called attention to the fact that under the conditions in question especially the lower portions of the small intestine were involved, and that the lesions should be considered specific, probably resulting from the action of a special poison. Although Bretonneau[3] further determined subsequently that the intestinal mucous membrane itself was not the seat of the morbid process in question, but the lymphatic apparatus of the intestine must be considered the basis of the disease; and after him Louis[4] established most clearly the relation between the intestinal lesion and the general condition; although, finally, Chomel[5] described the anatomic lesions more fully and the clinical manifestations with special clearness,—an absolute differentiation between the typhoid diseases, especially between typhoid and typhus fever, could not be made. Under the influence of those great French clinicians it was almost universally believed that, although typhoid fever was invariably associated with intestinal lesions, it could, however, be directly contagious, in the same way as small-pox and other acute exanthemata.

At the beginning of the nineteenth century, at a time when the French and the English were unable to reach a clear understanding, in spite of exact clinical and anatomic observations, remarkably definite views, approximating those of the present day, had been expressed in

[1] *Médecine éclairée par l'observation et l'ouverture des corps*, etc., Paris, 1804.

[2] *Traité de la fièvre entéro-mésentérique*, Paris, 1813.

[3] "De la dothiențérite," *Arch. gén. de méd.*, 1826. The name dothiențérite (ὁ δοθιήν, hemorrhagic ulcer, furuncle) was proposed by Bretonneau, and it was subsequently largely employed by the French, especially by Trousseau.

[4] *Recherches sur la maladie connue sous les noms de gastroentérite, fièvre putride, adynamique*, etc., Paris, 1829.

[5] *Leçons de clinique médic.* Tome i., *Fièvre typhoïde*, Paris, 1834.

Germany. Under the influence of Hildenbrand,[1] who published his important work in 1810, typhus and typhoid fever began to be differentiated. There were, as it appears, less exact anatomic and clinical data than intelligent empiric conceptions which pointed in the right direction.

It was not until the fourth and fifth decades of the nineteenth century that the differences of opinion were harmonized. At this time it became possible to secure general recognition of the individuality of the two diseases, and thereby to place the etiology upon a firm foundation. To two American physicians, Gerhard and Pennock,[2] belongs the credit for having finally established the differentiation. The clearness of their differential diagnostic statements is noteworthy for their time; as, for instance, their ability to distinguish the roseolous exanthem of each disease. Gerhard and Pennock's communication was supplemented and amplified by numerous papers from German, French, and English sources, among which those of Staberoh[3] and Stewart[4] may be mentioned, and, above all, the opinions expressed by the gifted Louis in the second edition of his famous work in 1841, in which he unconditionally accepts the new doctrine. The names of Jenner, Murchison, and Griesinger are associated with further great advances leading up to the views held at the present day.

Although it was difficult for physicians to renounce the doctrine of unity, they adhered, after its abandonment, to the conception of a close relation between typhus and typhoid fever. These views have not been entirely eliminated from some modern descriptions, and cannot be dislodged from the minds of some clinicians. In Germany the credit of having recognized fundamental distinctions between the two diseases belongs to Griesinger, and especially to Liebermeister in his classic description of typhoid fever; and the author of this article believes that he went a step further, in the third edition of *Ziemssen's Handbuch*, in giving expression outside of Germany to this important distinction by placing spotted fever among the acute exanthemata, and urgently demanding the abandonment of the designation typhus fever altogether.

Historic Considerations upon the Etiology of Typhoid Fever.—The discussion of the etiology of typhoid fever will be pre-

[1] *Ueber den ansteckenden Typhus*, Vienna, 1810.

[2] "On the Typhus Fever which occurred at Philadelphia in 1836, showing the Distinctions between It and Dothienteritis," *Amer. Jour. Med. Sci.*, vols. xix. and xx., 1837.

[3] *Dublin Jour. Med. Sci.*, vol. xiii., 1838.

[4] *Edinb. Med. and Surg. Jour.*, Oct., 1840.

ceded by some historic considerations. These will deal with one of the most interesting chapters in the history of the infectious diseases, and naturally will reflect all of the doubts and uncertainties that were encountered in the development of the knowledge of the nature of the disease and its differentiation from conditions superficially resembling it.

It need scarcely be emphasized that in the earliest times, before the clinical picture of typhoid fever had assumed definite shape, the most varied and vague factors were looked upon as etiologic. Especially apparent from the descriptions is the influence resulting from confounding other diseases with typhoid fever. With the formation of a better clinical conception of typhoid fever more definite etiologic views also arose, and these resulted in the doctrine of putrefaction and decomposition, which appeared next and lasted for a long time. At first, rather general and not specific processes were had in mind: putrid decomposition in the earth and contamination of the air, which were believed to be especially effective in small dwellings, lodging-houses, and other poorly ventilated apartments, and occasionally also decomposition of articles of food and drink. To all of these the indefinite conceptions of cold, overexertion, and emotional disturbances were added as of especial importance, and at times as even alone sufficient. With such factors in varying combination etiologic theories were formed. The names febris putrida, putrida nervosa, fièvre ataxique, etc. (Willisius, Wintringham, Tissot, Pinel), are the offspring of a period whose influence was appreciable until within recent times.

The putrefactive theory had distinguished adherents until beyond the middle of the nineteenth century. It received especial development at the hands of Murchison,[1] distinguished for his studies in connection with the infectious diseases, who gave the disease the name of pythogenic fever, and by reason of his great personal authority and apparently exact observations exerted a profound and lasting influence not only upon his countrymen, but also upon physicians in other countries. His views are reproduced in the subsequent air, soil, and water theories; and although they are replaced to-day by more accurate knowledge, they led at the time to the adoption in England of extensive practical measures, which may be considered as constituting the foundation of a large part of modern hygiene.

Murchison considered as especially dangerous the decomposition of organic substances, and particularly that of human fecal matter. These

[1] See his well-known work, *A Treatise on the Continued Fevers of Great Britain*, London, 1862. German edition by Zülzer, Braunschweig, 1867.

he believed to be of themselves capable of giving origin, independently of the patient and outside of his body, to the (naturally chemic) poisonous substances generating typhoid fever. In his large work and in many individual publications Murchison was able to fortify his teachings with numerous illustrations of endemics and isolated cases. At times the drinking-water or an article of food, at other times the air of dwelling-rooms and sleeping-rooms, was contaminated with putrid substances resulting from the decomposition of human fecal matter, and thus became the immediate cause for the development of the disease. His associates and successors followed the same line of thought, without the addition of anything new, so that their etiologic investigations and reports were quite uniform and even schematic. An advance appeared to be made with the experimental investigations of Stich, and subsequently of Panum, which aroused great interest. These observers believed themselves able to induce typhoid fever by the introduction of putrid substances into the bodies of animals, and thus to have established the entire subject upon a firm foundation. It will be seen later that their conclusions were based upon a fallacy.

Even before the time of Murchison, under the influence, it is true, of the imperfect differentiation of typhus and typhoid fever, a view wholly opposed to the decomposition-theory had arisen, namely, that of direct contagion. It was especially the great French clinicians, Leuret,[1] Bretonneau, and Gendron,[2] who maintained with great positiveness that typhoid fever was capable of immediate transmission through the surrounding air from the sick to predisposed individuals, and that this was by far the most common mode of origin. Trousseau subsequently also warmly defended this view, and undertook to support it with striking illustrations.

Thus two views prevailed contemporaneously for a time, the decomposition-theory and that of direct transmission, and frequently coming in direct antagonism with each other. Gradually an intermediate position was reached and held for a long time, which, while admitting the direct transmissibility of typhoid fever, at the same time accepted either as predominant or equal in importance or as subordinate the spontaneous "miasmatic" mode of development. Each of these two theories no doubt contained some objective truth. To Murchison and his disciples belongs the great credit of having called attention especially to the danger from the fecal discharges of the patient, although perhaps not in the sense of to-day; while those who believed in the contagiousness of

[1] "Mém. sur la dothientérite à Nancy," *Arch. gén. de méd.*, Ser. I., xviii.

[2] "Dothientérites observées aux environs de Chateau du Loir," *Ibid.*, Ser. I., xx.

the disease, which subsequently likewise proved justifiable, placed the personal influence of the patient, the view that the poison emanated from him, in the foreground.

Thus the way had been sufficiently prepared for Budd,[1] for whom was reserved the formulation of the views, in general correct, still held at the present day. His conclusions, remarkably acute for his time, were as follows: Typhoid fever cannot develop spontaneously; every case originates immediately from some antecedent case. The typhoid poison is generated by the patient himself; it adheres especially to the stools with which it is evacuated. It thus develops not outside, as Murchison and his disciples believed, but within the body of the typhoid patient; and it is not the product of indifferent general decomposition of fecal matter, but an agent of specific origin and specific activity. Budd even went so far as to consider the intestine as the immediate place of origin of the poison, in the same way as the skin performs a similar function with relation to the pustule of variola. Also the conception of the transmissibility and the capability of further development of the poison is contained in his distinctly enunciated view that a minimal amount thereof is sufficient for the conveyance of the disease and its further extension. With logical acumen Budd reached the fundamental conclusion that it would undoubtedly be possible to prevent the spread of the disease if methods could be devised capable of rendering the infectious stools innocuous; it might even be hoped that as a result of a rigid application of such measures in every individual case the disease could be wholly eradicated.

Budd's observation for all time must be considered as masterly. He is undoubtedly the founder of the prevailing views upon the etiology of typhoid fever. Nevertheless, the path by which our present conceptions have been reached followed a long and intricate course, in consequence of the misleading and obstructive influence of earlier theories.

Although the pythogenic theory of Murchison was gradually displaced by that of the specificity of the poison, the questions as to the mode of dissemination of the latter, the development of the typhoid fever in individual cases, in endemics and epidemics, the important questions further as to the influence of climate, of season, and of locality, interposed great difficulty to the progress of knowledge. Too frequently previous association of the patient with other cases of typhoid fever or their discharges could not be demonstrated. The probability or possi-

[1] "On Intestinal Fever: Its Mode of Propagation," *Lancet*, 1856. "Intestinal Fever Essentially Contagious; Its Mode of Propagation," etc., *Ibid.*, 1859. "On Intestinal Fever," *Ibid.*, 1860.

bility of contamination of articles of food, of drinking-water, and other substances with the poison appeared likewise not always adequate.

Instead of more carefully analyzing these conditions, they were minimized or wholly ignored, obviously to the great disadvantage of the subject. Study was directed rather toward more general conditions, toward circumstances amid which the poison generated by the patient and discharged from him could be further developed independently and retain its activity, in order subsequently to gain entrance under favorable conditions into the human body. In this way especially the earth came to be suspected as the repository and the place of generation of the poison of typhoid fever. The thought that the poison here underwent propagation, maturation, and multiplication was nourished until finally the idea was evolved that such an intermediate stage of the poison was the rule, and possibly indispensable, in the dissemination of typhoid fever.

Support for these views was thought to be found on retrospective observation in the endemic mode of dissemination of typhoid fever, its persistence in certain localities and circumscribed areas, and also in the apparently distinctive observation that in regions in which the disease prevailed the first cases appeared often where extensive excavations of earth were being made. This localization-theory has not been wholly abandoned even at the present day. In one or another form it still materially influences etiologic conceptions. This theory of localization attained its highest degree of development in the famous doctrine of Buhl and of Pettenkofer, of the relation between the ground-water and the development of typhoid fever. Buhl[1] claimed to have made the observation that the mortality from typhoid fever in Munich regularly exhibited fluctuations corresponding with the varying level of the ground-water, so that when this level was high the mortality was remarkably low, and *vice versa*. Pettenkofer,[2] upon the basis of elaborate statistical data and extensive local observations, further developed the theory of Buhl, so that at the end of the sixth and in the seventh decade of the nineteenth century the ground-water theory was considered in Germany, and probably also in other countries, as fully established for Munich, and, by reason of the adaptiveness of the statistical data, as applicable also to other localities and cities. Where this was not completely so, it

[1] "Ein Beitrag zur Aetiologie des Typhus in München," *Zeitschr. f. Biologie*, Bd. i., 1865.

[2] "Ueber die Schwankungen der Typhussterblichkeit in München von 1850 bis 1867," *Zeitschr. f. Biologie*, Bd. v., 1868. "Ueber die Aetiologie des Typhus," *Vorträge gehalten in der Sitzung des ärtzl. Vereins in München*, 1872.

was thought that at least an increase in the mortality from typhoid fever could be demonstrated in association with unusual dryness.

Although the supporters of the ground-water theory were unable to form any definite conception of the nature of the typhoid poison, and even permitted interest in this to lapse further in the background the more they became involved in the ground-water theory, they adhered to two views still valid at the present day, namely, the specificity of the poison and its capability of germination and multiplication. Truth and error were, however, mixed in the further belief that the poison after passing through a necessary "process of maturation" in the earth passed from this into the human body, being most frequently transmitted through the air, rarely through water or through other media. The escape of the poison from the earth, its "exhalation," was believed to be rendered difficult in damp weather and with a high level of the ground-water, for the reason that its breeding-point would be covered by this water, and thus be cut off from the surface of the earth; while when the level of the ground-water was low the deleterious layer of earth would be in direct communication with the atmospheric air through the ground-air, and there would thus be no obstruction to the emanation of the poison.

Apart from the fact that the theory of Pettenkofer ignored the nature of the typhoid poison and retarded its study, it was further attended with the not inconsiderable disadvantage that it brought strongly into the foreground, although as it now appears without sufficient ground, the dissemination of the poison through the ground-air and thence through the atmospheric air, and as a result greatly checked for a time the study of other etiologic possibilities.

It is especially interesting to consider the effective objections of Liebermeister[1] and subsequently of Biermer[2] to the ground-water theory and dissemination through the air, and to note their discriminating support of another mode of dissemination, namely, that through water-infection. Their views also gained numerous adherents. The ground-water theory, however, remained for a time so firm that in not a few places epidemiologic investigations were adapted to it, instead, conversely, of deducing etiologic views from the facts. As late as the years 1886 and 1887 the author of this article had such an unfortunate experience.[3] When he endeavored to trace the epidemic occurrence of typhoid fever in Hamburg at that time—more than 10,000 persons had been attacked—to specific infection of the water obtained from the river Elbe, and used for drinking and domestic purposes, it was found that certain circles did not consider it worth while to take this possibility into consideration. The ground-water theory was believed to be

[1] *Gesammte Abhandlungen.*

[2] *Volkmann's Samml. klin. Vortr.*, 1873, No. 53.

[3] Curschmann, "Statistisches und Klinisches über den Unterleibstyphus in Hamburg," *Deutsche med. Wochenschrift*, 1888.

wholly sufficient to explain the epidemic and to overcome the objections raised against the water of the Elbe.

As has been seen, one of the most valuable aspects of the doctrines of Buhl and Pettenkofer is the emphasis placed upon the vitality and the power of multiplication of the typhoid poison, to which Budd and his pupils had previously directed attention. We may recognize in this the forerunner of the present view of a living contagium. As early as the year 1871 this view began to assume more definite shape. Reference need be made only to the works of von Recklinghausen,[1] who called attention to the frequent occurrence of cocci in the organs of typhoid patients, especially in the kidneys, as well as to the less successful attempts of Klein,[2] Sokoloff,[3] Fischel,[4] and others to demonstrate an organized typhoid poison.

It was reserved for Eberth,[5] in the year 1880, to discover the bacillus at the present day definitely recognized as the cause of typhoid fever, and in the absence of confirmation by cultivation and inoculation, to establish its specificity with great probability. Almost identical observations were subsequently made by Robert Koch[6] and Wilhelm Meyer,[7] who worked under the incentive and direction of Friedländer, while the micro-organisms described by Klebs[8] are not at the present day considered identical by the majority of bacteriologists with those of Eberth. In England, Coates and Crooke confirmed the observations of Eberth, and also in other countries observers were soon industriously engaged in studying the new bacillus, without, however, materially adding anything to the knowledge of its biology. Neither Coze and Feltz nor Maragliano succeeded in cultivating and isolating the pathogenic germ.

Gaffky[9] was the first, as the result of a brilliant investigation, to bring the entire subject to its present firm foundation. He perfected in material points the morphology of the bacillus, and by means of numerous painstaking post-mortem examinations demonstrated its distribution and arrangement in the organs and tissues, and finally described the method for isolating it and growing it in pure culture. Although Gaffky was not successful in experimentally producing typhoid fever in

[1] *Würzb. Zeit.*, 1871. Compare also Eberth, *Zur Kenntniss der bakteriologischen Mykosen*, Leipzig, 1872.

[2] *Reports of the Medical Office of the Privy Council and Local Government Board*, No. 6, 1875.

[3] *Virchow's Archiv*, Bd. lxvi., 1876.

[4] *Prager med. Wochenschrift*, 1878.

[5] *Virchow's Archiv*, Bd. lxxxi. u. lxxxiii.

[6] *Mittheilungen aus dem kais. Gesundheitsamte*, Bd. i.

[7] *Inaugural Dissertation*, Berlin, 1881.

[8] *Archiv. f. exper. Pathol. u. Pharmak.*, Bd. xii. u. xiii.

[9] *Mittheilungen aus dem kais. Gesundheitsamte*, Bd. ii.

animals with these pure cultures, he was able, from the certainty and the extent of his other observations, especially from the undoubted constancy of its occurrence in cases of typhoid fever and its absence from healthy individuals, to formulate the definite conclusion that the organism is the specific cause of typhoid fever.

The studies of Gaffky were followed in all countries by an enormous amount of work with the typhoid-bacilli, so that Lösener a few years ago was able to make a collection of 689 papers on this subject. These confirm in general and amplify in some details the results obtained by Gaffky, at times proceeding skeptically, but still more frequently going beyond his views. At any rate, at the present day a clear conception has been formed of the morphology and the development of the bacillus, and considerable is known with regard to its behavior both within and outside of the body of the typhoid patient. Numerous strides have been made with regard to the presence and the behavior of the bacillus, not alone in the dead, but also in the living body. The organism has been obtained from the blood, the spleen, the skin, and the dejections, especially the feces and the urine. One result alone, which, as has been mentioned, Gaffky failed to secure, has not yet been attained, namely, the development of the disease experimentally in animals. Neither by means of the earlier crude methods of feeding typhoid stools to various experimental animals, as practised by Murchison, Klein, Klebs, Birch-Hirschfeld, and others, nor by inoculations with pure cultures, has success as yet been obtained in developing true typhoid fever in animals.

MORPHOLOGY AND BIOLOGY OF THE TYPHOID-BACILLUS.

The bacilli of Eberth, in their ordinary form, are comparatively short, thick rods, with rounded extremities, about thrice as long as they are wide, and in absolute length one-third the diameter of a red blood-corpuscle. In ulcerated Peyer's patches and in other parts at the height of the specific lesions the bacilli form, by longitudinal application to one another, filamentous structures, first described by Gaffky as "pseudo-filaments." Under various circumstances the bacilli undergo changes in form, size, and arrangement. Thus the pseudo-filaments already mentioned will be found in old bouillon-cultures or gelatin-cultures, as well as on potato of acid reaction, growing to remarkably long structures. The individual bacilli also appear to become plumper upon gelatin and potato than upon agar or bouillon. They yield up these

peculiarities, however, when transferred to other nutrient media, in accordance with the character of the latter.

Spore-formation was formerly incorrectly believed to take place in the bacilli, and the bright bodies that failed to take the stain lying at

FIG. 1.—Typhoid-bacilli; impress-preparation.

the extremities as well as in the middle of the bacilli were thought to be spores. These are at the present time considered as deficiencies, attributable either to a process of involution in the bacilli or as an artefact developed in heating and staining (H. Buchner [1]).

FIG. 2.—Typhoid-bacilli; pure culture with pseudo-filaments.

FIG. 3.—Typhoid-bacilli with flagella; stained by Löffler's method.

When cultivated in suitable fluid media (bouillon) and observed in hanging-drop, the bacilli exhibit active spontaneous movement, in which both the individual rods as well as the pseudo-filaments participate. This is dependent, as Löffler has demonstrated by special methods of

[1] *Centralblatt f. Bakteriologie u. Parasitenkunde*, Bd. iv.

staining, upon the presence of flagella, which arise in large numbers, up to 15 and even 20 and more, from all parts of the surface of the bacilli, and in suitable preparations can frequently be found detached and lying free. So far as is known, among bodies resembling the typhoid-bacillus, spontaneous movement, together with flagella causing it, occurs only in Bacillus coli and closely related forms. A difference appears, however, to reside in the fact that the number of flagella attached to Bacillus coli is much smaller, being stated to be never more than 10.

Typhoid-bacilli can be stained with anilin dyes, but with more difficulty than many other pathogenic micro-organisms. It is characteristic that staining by the method of Gram is never successful. At times, especially in old cultures upon feebly acid potato, the bacteria exhibit strongly refractive polar bodies, which stain more readily and more deeply than the remainder of the body of the bacteria (H. Buchner[1]). These also are undoubtedly not to be considered as spores, as is indicated by the fact that the organisms in which they are contained do not exhibit increased powers of resistance. Probably the appearance of the polar bodies likewise is rather to be referred to an involutional process.

Even though, as is unanimously agreed by the most experienced observers, the severity of an attack of typhoid fever is by no means always proportionate to the number of bacilli in the organs after death and during life, and as a matter of fact remarkably few bacilli are occasionally found in severe cases, it is generally easy, with a little skill, to obtain the pathogenic bacilli from the spleen, the mesenteric glands, and Peyer's patches, especially at the height of infiltration and with beginning ulceration. That they can be cultivated from the blood and the spleen during life, though with greater difficulty, and also from the dejections and the excretions, has already been mentioned.

In all of these connections it is important to know that the bacillus thrives best at the temperature of the body, about 37° C., although it develops rapidly and abundantly also at lower temperatures, as, for instance, at ordinary room-temperature. Like the majority of pathogenic micro-organisms, the typhoid-bacillus displays facultative anaërobiosis—that is, it lives and develops either with exclusion of oxygen (Liborius) or with access of oxygen—in the latter event, it is true, with greater energy and in greater abundance. The cultivation of the bacillus can be effected readily and upon various culture-media: upon gelatin, agar, blood-serum, and especially upon potato. An abundant growth takes place even when the last-named medium pos-

[1] *Loc. cit.*

sesses a slightly acid reaction. The bacillus exhibits active development and multiplication likewise in fluids, especially in bouillon and milk. The latter is rendered feebly acid, without undergoing coagulation, even after having been exposed for a considerable time to the action of the bacillus. The bouillon is rendered distinctly turbid in consequence of the development of the bacilli. A slight sediment that develops on standing separates on agitation into uniform minute particles. That the bacilli thrive luxuriantly, under favorable conditions, upon articles of food constituted of the substances named or of related substances need only be mentioned. We shall dwell more fully upon the importance of this matter in considering the special etiology.

When grown in a media containing glucose, lactose, or saccharose, there is no production of gas. When introduced into the peritoneal cavity of immunized guinea-pigs, or when introduced, together with serum from an immune animal, into the peritoneal cavity of normal guinea-pigs, the bacilli quickly lose their motility and break up into small granules—the so-called Pfeiffer's phenomenon (Pfeiffer and Kolle[1]). If a bouillon culture of the typhoid-bacillus is mixed with serum from an immune animal or from a person after an attack of the disease, the bacilli become immobile and collect into groups or clumps (Durham[2]). Finally, if such a culture is mixed with serum from a patient during an attack of the disease, a similar reaction takes place (Widal[3]).

The especial behavior of cultures of the bacillus of Eberth upon the solid and liquid nutrient media mentioned has been determined most minutely. With reference to the details, which would be out of place in a work of this kind, the special treatises should be consulted. Some statements may be made here with reference to the behavior of the bacillus on gelatin and agar.

Stab-cultures in gelatin appear as delicate, grayish-white, slightly granular filaments, becoming more attenuated toward the bottom of the test-tube. Upon the surface of the gelatin the bacillus exhibits active growth in the form of a thin, bluish-gray or greenish-gray, slightly iridescent deposit, proceeding from the point of puncture and soon reaching the border of the glass. On closer inspection it will be noted that the outer border is not regular, but slightly serrated. The bacillus forms a similar thin, iridescent, grayish-white or bluish-white deposit in gelatin plate-cultures. Here the superficial cultures, which exhibit no trace of liquefaction, appear at first as small, distinct, yellowish or grayish-yellow granules. After a short time larger circular spots appear, similar in color to the deposits in stab-culture and streak-culture, grayish white and likewise iridescent. Soon the center of such a spot appears grayish yellow and opaque, while toward the periphery the culture gradually becomes thinner and more translucent. These small areas also have an irregular, serrated margin, which, as microscopic examination shows, represents a delicate wrinkling of the culture, extending from center to the periphery.

Stab-cultures in agar also appear as delicate, slightly granular, grayish-white filaments. Here likewise the superficial growth about the point of puncture is active, so that it soon approaches the wall of the test-tube, but

[1] *Zeitschr. f. Hygiene*, Bd. xxi. [2] *Proc. of the Royal Soc.*, Bd. lix.
[3] *Bull. méd.*, 1896.

the margin is not serrated, but rather round and regular. Upon agar-plates also the large, usually round or oblong colonies are not serrated at the periphery as on gelatin. They appear opaque and yellowish white at the center, and more translucent, whitish, and not opalescent toward the periphery. Microscopically these cultures likewise are more or less coarsely punctate, with centrifugal linear formations similar to those upon gelatin.

Especially noteworthy is the behavior of the typhoid-bacillus upon potato, as first carefully studied by Gaffky, a feature that, according to existing knowledge, is not exhibited by any other pathogenic micro-organism. If a disk of boiled potato of feebly acid reaction is inoculated with a typhoid culture, scarcely any difference in the appearance of its surface will be appreciable to the untrained eye after the lapse of forty-eight hours, as compared with the surface of a sterile disk of potato similarly exposed but not so inoculated. On more careful scrutiny, however, the infected potato will appear somewhat less smooth and more moist for a greater or lesser distance from the point of inoculation. If a platinum loop be stroked over this area, a sense of increased resistance will be felt as compared with the uninoculated potato, and at times it is possible to detach small filaments or threads with the loop. In a word, one can convince himself that, starting from the point of inoculation, an extremely delicate, moist, glistening, colorless, transparent coating has formed upon the potato. On microscopic examination this membrane will be found to consist of a pure culture of typhoid-bacilli, which, transferred to various nutrient media, exhibit their characteristic peculiarities, especially the spontaneous movement in bouillon previously referred to. Since it was first described by Gaffky, this scarcely visible deposit has been recognized by all observers as an especially important characteristic. This opinion is naturally not influenced by the observation that upon potato of neutral or alkaline reaction or rendered artificially alkaline the membrane becomes visible as a greenish-white or yellowish-gray or even bluish coating, which not rarely is less extensive.

If after these few references to the morphology and the physiology of the Eberth bacillus we pass to a consideration of its *rôle* in the development and dissemination of typhoid fever, and to a description of the properties that confer this power upon it, the question arises:

Can typhoid fever be experimentally induced in animals by inoculation of the typhoid-bacillus?

The establishment of the etiology of typhoid fever has been in no small measure restrained by the circumstance that a disease wholly corresponding to typhoid fever in human beings apparently does not occur in any species of animal. It was, therefore, from the outset improbable that the disease could be developed experimentally, and as a matter of fact this has not yet been possible. Gaffky, in his well-known work,[1] was unable either after administration of pure cultures of the bacillus by the mouth or after intravenous injection to obtain decisive results; and also the experiments of Fränkel and Simmonds,[2] however valuable

[1] *Loc. cit.*

[2] *Centralblatt f. klin. Med.*, No. 44, 1885; No. 39, 1886. *Die ätiologische Bedeutung des Typhusbacillus*, Hamburg, 1886. *Zeitschr. f. Hygiene*, Bd. ii.

their results in other respects, have yielded no wholly conclusive results in this connection.

The investigators named were able by intravenous as well as by intraperitoneal injection of large amounts of pure cultures of typhoid-bacilli to cause rapidly fatal symptoms in mice, with peculiar anatomic lesions: swelling, even isolated ulceration of the follicles of the small and the large intestine, together with recent infiltration of the mesenteric glands, cloudy swelling of the liver and the kidneys, and considerable enlargement of the spleen. Microscopic examination disclosed also the presence of large numbers of typhoid-bacilli in the dead body and especial accumulation of them in the spleen. Fränkel and Simmonds, however, although they considered their experiments of great significance—forming the foundation for subsequent experiments in immunity and cure—were cautious enough not to identify completely the symptoms induced with typhoid fever. It was soon found[1] also that no noteworthy multiplication of the bacilli introduced into the animals took place in the living organism. In addition, it was noted that inoculation of small numbers of typhoid-bacilli did not—as in the case of other actively pathogenic micro-organisms, as, for instance, anthrax—give rise to noteworthy symptoms. Finally, the circumstance that the animals generally died before the end of the first day and earlier, but scarcely ever later than after three days, aroused suspicion that the condition was rather a direct intoxication than a true infectious disease resulting from the multiplication and continued development of the bacilli.

The certainty of the view that the condition is due to the action of toxins and not of the bacilli was established by the experiments of Sirotinin,[2] Brieger, Kitasato, and Wassermann.[3] By boiling the cultures or by eliminating the bacteria by filtration it was possible to introduce the toxins alone into the animals, and thereby to obtain the same results as Fränkel and Simmonds.

The statements of more recent observers,[4] that by systematic augmentation of the virulence of the bacilli they can be rendered actively pathogenic for animals—that is, their further development in the living body with the production of typical symptoms can be brought about—yet require confirmation. In such an event material advantage would be expected less for the etiology than for the solution of certain therapeutic problems.

In none of the previously quoted experiments do any of the observers claim to have produced in animals a disease with a course resembling that seen in human typhoid. A later observer, Remlinger,[5] found that by prolonged feeding of rats and rabbits on vegetables soaked in water containing typhoid bacilli he was able to induce a continued fever lasting from ten to twelve days, accompanied by diarrhea, loss of appetite, and wasting. Four of eight rabbits experimented upon became sick; one was killed on the

[1] See the articles of Baumgarten, *Centralblatt f. klin. Med.*, 1886. Wolfowicz (Baumgarten), *Inaugural Dissertation*, Königsberg, 1887. Sirotinin, *Zeitschr. f. Hygiene*, Bd. i., 1886. Beumer and Peiper, *Ibid.*, Bd. i. u. ii. R. Stern, *Volkmann's Samml. klin. Vortr.*, Neue Folge, No. 138.

[2] *Loc. cit.*

[3] *Zeitschr. f. Hygiene*, Bd. xii.

[4] Gilbert and Girode, *Comptes rendus de la Société de Biologie*, 1891, No. 16. Chantemesse and Widal, *Annales de l'Institut Pasteur*, 1892, T. vi., No. 11. Sanarelli, *Ibid.*, T. vi.; *Ibid.*, T. viii.

[5] *Ann. de l'Inst. Pasteur*, T. xi.

twelfth day, and one died on the twelfth day of fever. Three of the four gave a positive agglutination reaction. Autopsies on the two latter rabbits showed swelling of spleen, lymph-glands, and Peyer's patches, and there were a few ulcers in the lower part of the small bowel. Typhoid bacilli were obtained from the spleen. These very striking and unique observations have not yet been confirmed.

Taking up now the special questions as to the development of typhoid fever in human beings, one of the first and most important will be: How and by what route do the infectious agents leave the body of the patient? Then the question will naturally arise as to the further behavior of the bacilli, in accordance with the varying conditions under which they are evacuated and deposited. Especially will it have to be determined under what conditions and for how long a time they retain their vitality or are capable of multiplication independently of the patient.

BY WHAT ROUTE DO THE TYPHOID-BACILLI LEAVE THE BODY OF THE PATIENT?

In spite of numerous investigations, we are still in the first stage of knowledge with respect to this question. The secretions and excretions of the patient, as well as his blood, have naturally received especial attention. The blood is scarcely to be taken into consideration as a medium of infection. Also the sweat, the expectoration, and the expired air appear to be of slight significance as carriers of the germs of infection. Direct escape of the bacilli with the sweat is more than doubtful. Isolated results believed to be positive are probably to be considered as due to accidental contamination of the skin from the intestine. Although typhoid-bacilli have been demonstrated in the diseased lung in some cases of pneumonia, and, accordingly, elimination of bacilli in the sputum and the expired air cannot be denied, these media also probably act only exceptionally as carriers of the infection. The statement of Sicard[1] as to the almost constant presence of typhoid-bacilli in the expired air of typhoid patients is most remarkable, and requires confirmation.

Far more important than all of the sources hitherto considered are the fecal discharges and urine. Generally these are probably the exclusive media by which typhoid-bacilli leave the body. The history of typhoid fever teaches that even the older authors, naturally from different standpoints, considered the stools as the source and origin of the disease-virus. After the discovery of the typhoid-bacilli these views were con-

[1] *Semaine médicale*, 1892, No. 4.

siderably fortified by the demonstration of the constancy and the abundance of the micro-organisms in the medullary infiltration of the intestine, in consequence of which opportunity for admixture with intestinal contents is continuously afforded from the earliest stages of the disease to the period of exfoliation and the completion of the process of ulceration. If, in addition to the abundance of the bacilli in the portions of intestine the seat of the specific lesions, the relatively long duration of the latter and the number and copiousness of the daily fecal discharges are taken into consideration, there can be no doubt that the stools constitute a prolific source for the contagium of typhoid fever. The bacteriologic examination of typhoid stools has also demonstrated indubitably and frequently the presence of living typhoid-bacilli.[1] Recent observers have established this fact with certainty; as, for instance, Chantemesse,[2] who in examination of the stools of 16 typhoid patients failed to find the bacilli only thrice. They are found most constantly, in accordance with the nature of anatomic lesions, from the beginning of the second week to the end of the third week and later, or from the period of medullary infiltration of the lymphatic structures, their exfoliation and ulceration, until the complete cicatrization of the ulcers.

On account of the difficulty attending examination of the stools for typhoid-bacilli, a simple and reliable method for their isolation has long been wanting. That these difficulties are dependent especially upon the constant presence of numerous other micro-organisms is obvious. The most troublesome of these is the colon bacillus, which resembles the typhoid-bacillus in so many respects. The efforts to isolate the typhoid-bacillus from the stools, and especially to differentiate it from the colon bacillus, have resulted in the publication of several hundred papers.

Up to the time of the introduction by Elsner[3] of the medium now known by his name, the isolation of typhoid-bacilli from the stools presented almost insurmountable difficulties. By the use of this medium Elsner,[4] Brieger,[5] Richardson,[6] and others were able to isolate the typhoid-bacilli from the feces of typhoid patients during the febrile stage in a large proportion of cases. In these cultures, however, the possibility of contamination by urine was not guarded against. Capaldi,[7] Piorkowski,[8] Remy,[9] and others, by the use of special media, have also been able to demonstrate, with

[1] Fränkel and Simmonds, in their earliest publications. Pfeiffer, *Deutsche med. Wochenschrift*, 1885, No. 29. Merkel and Goldschmidt, *Centralblatt f. klin. Med.*, 1887, No. 22. Chantemesse and Widal, *Gaz. hebd.*, 1887, No. 9. Karlinski, *Centralblatt f. Bakteriologie u. Parasitenkunde*, Bd. vii. Vilchour, *Lancet*, 1886, vol. ii., No. 3.

[2] Soc. de Biol., Meeting Feb. 22, 1896.

[3] *Zeit. f. Hyg.*, Bd. xxi., 1895.

[4] *Loc. cit.*

[5] *Deutsch. med. Woch.*, 1895.

[6] *Boston Med. and Surg. Jour.*, vol. cxxxvii., No. 18.

[7] *Zeit. f. Hyg.*, Bd. xxiii.

[8] *Berlin. klin. Woch.*, 1899, No. 7.

[9] *Ann. de l'Inst. Pasteur*, T. xiv.; also T. xv.

more or less ease, the bacillus of typhoid in a large proportion of cases. Lately, Hiss[1] with a new method has isolated the typhoid-bacillus from the feces in 17 cases out of 21 studied. They occurred only rarely before the first day of the second week, and disappeared with the fall of the fever.

During the past few years various observers have demonstrated the great frequency with which typhoid-bacilli occur in the urine, and have called attention to the important *rôle* of this secretion in the spread of the disease. In 1890, Neumann[2] demonstrated typhoid-bacilli in the urine of 11 out of 48 cases examined. His results were received with some skepticism, however, and received no confirmation until Petruschky,[3] in 1898, published the results of cultures made from the urine in 50 cases, with isolation of B. typhosus from 3. Later, Richardson[4] obtained the bacilli from 23 out of 104 cases examined—22.1 per cent.; and Horton-Smith[5] obtained them from 11 of 39 cases—28 per cent.—the urine containing at times as many as 500,000,000 organisms in each cubic centimeter. During the past year, 1900–1901, from the urine of 55 typhoid fever patients in the Johns Hopkins Hospital the typhoid-bacilli were isolated in 19 cases. While the fact of the frequency of the bacilli in the urine is at times of importance in diagnosis, its greatest importance is in relation to the great danger of the spread and transmission of the disease. It shows the extreme care which should be observed in sterilization of the urine, to guard against any chance contamination of the water-supply or food.

THE VITALITY OF THE TYPHOID-BACILLI.

What are the conditions necessary for preserving the vitality of the typhoid-bacillus within and outside the human body, and what relationship do these conditions bear to infection of the individual and to the general dissemination of the disease? Are these conditions, and the relation of the typhoid-bacillus to them, sufficiently well understood that an explanation of the recognized methods of origin and spread of typhoid fever is possible? Numerous investigations in regard to the vitality of the typhoid-bacillus under various conditions have yielded important results. In general, the results of these investigations have made a positive answer to the latter question possible. Even the absence of spore formation, which is so important with relation to the resistance of bacteria, is not sufficient to throw doubt on the pathogenic significance of the typhoid-bacillus.

A large series of observations afford important evidence in favor of the persistence of the bacilli in the living human body. The typhoid-bacillus has been found in inflammatory exudates and in periostitic and muscular collections of pus caused by typhoid-bacilli, alive and capable of multiplication as long as a year and even longer after an attack of the disease (Sahli, Hintz). It is true that even should the bacilli be

[1] *Med. News*, vol. lxxviii., No. 19. [2] *Berlin. klin. Woch.*, 1890, S. 121.
[3] *Centralbl. f. Bak.*, 1898, No. 14. [4] *Jour. Exper. Med.*, vol. iii.; also vol. iv.
[5] *Lancet*, 1900, vol. i..

thrown off as a result of spontaneous rupture or of incision of such foci, typhoid infection will not, as a rule, be caused thereby. Nevertheless, in rare cases of obscure etiology such a possibility should not be left out of consideration.

The resistance of the bacilli appears to be rather limited in the human cadaver. Although multiplication has been observed to take place shortly after death (Fränkel and Simmonds,[1] Reher[2]), the occurrence of putrefaction soon exerts an injurious influence. That this action cannot always be depended upon, however, and that from the prophylactic point of view careful consideration must be given to the bodies of those dead of typhoid fever, appear demonstrated by the observations of Karlinski and of Petri, the former of whom found living bacilli in human cadavers after three months, while the latter found them in a living state in the bodies of dead animals as late as the seventeenth day. The persistence of the bacilli after they have left the human body is worthy of further investigation in various directions, physical as well as chemic.

With regard to the influence of various temperatures, it has already been mentioned that the physiologic body temperature is most favorable to growth and development; but also moderate external temperatures appear to exert no injurious influence. The typhoid-bacilli are extremely resistant to even considerable degrees of cold. They persist at temperatures as low as $-10°$ C. (14° F.), and even repeated freezing and thawing of fluid containing the bacilli do not appear to destroy them (Chantemesse and Widal, Janowsky[3]). The most extreme illustration in this connection is given by Prudden,[4] who observed that typhoid-bacilli kept in ice at a temperature between $-1°$ C. (30.2° F.) and $-11°$ C. (12.2° F.) retained their vitality for three months. The bacilli are far more sensitive to high temperatures, cultures dying in from ten to fifteen minutes at a temperature of 60° R. (167° F.). Heat is supplemented by light in the destruction of the bacilli, which, as Buchner[5] was the first to show, and then Janowsky[6] and Gaillard,[7] die in direct sunlight in the course of a few hours, while simple diffuse daylight appears to influence them far less unfavorably.

The bacilli are comparatively resistant to drying. Mixed with indifferent substances or dried upon inanimate objects—utensils, materials,

[1] *Loc. cit.* [2] *Archiv. f. Exper. Path. u. Pharmak.*, Bd. xix., S. 420.
[3] *Centralblatt f. Bakteriologie u. Parasitenkunde*, Bd. viii.
[4] *Medical Record*, vol. xxxi., 1887.
[5] *Centralblatt f. Bakteriologie u. Parasitenkunde*, Bd. xi., No. 25.
[6] *Loc. cit.* [7] *De l'influence de la lumière sur les micro-organismes*, Lyon, 1888.

etc.—they retain their vitality for many months. In dust and in sand, as well as in earth, the bacilli persist for several weeks (Uffelmann [1]). The same has been demonstrated by various observers for the soil, in which the bacilli have been found to retain their vitality for as long as five and a half months. It is, however, to be emphasized expressly that no competent observer has noticed multiplication of the bacilli in the soil, a fact that is directly opposed to the gratuitous assumption of the adherents of the ground-water theory that maturation, development, and reproduction of the typhoid virus take place in the soil, and therefore one which renders untenable an essential feature of this doctrine.

Among the drying experiments, those of Seitz,[2] Uffelmann,[3] Gaffky,[4] and Schiller[5] are especially instructive. While the last-named two observed the bacilli to retain their vitality for several months, and even for a year, on threads of silk, etc., under suitable conditions, the former observed the bacilli to persist from two to three months dried directly upon cloth.

Of decisive importance is the question with regard to the persistence of typhoid-bacilli in water, the answer to which is complicated and difficult. The simplest problem, from which many investigators started out, is the behavior in distilled water or in sterilized spring-water, well-water, or river-water. Under these conditions, in the absence of extremes of temperature and of other extraneous disturbing influences, it has been determined that the bacilli may persist for as long as three months. The interesting circumstance has developed—as it had previously been established also for other micro-organisms—that a difference in the vitality of the bacilli is exhibited as the water in question is at rest or in movement. In the latter event the bacilli are more quickly destroyed.[6] The conditions are far different in unsterilized drinking-water, river-water, or household-water, and therefore water under ordinary conditions. In this connection it may be stated at the outset that the possibility of preserving the bacilli varies widely in accordance with the different chemic and biologic peculiarities of the respective waters. From this point of view it is conceivable, and it has repeatedly been demonstrated practically, that in some waters the vitality of the bacteria is exceedingly slight, while in others it may be considerable. Of far greater importance than physical and chemic conditions in this connection are the presence and activity of water-bacteria. Nevertheless, the bacteria have

[1] *Centralblatt f. Bakteriologie u. Parasitenkunde*, Bd. xv.

[2] *Loc. cit.* [3] *Loc. cit.* [4] *Loc. cit.*

[5] *Arbeiten aus dem Reichs-Gesundheitsamt*, Bd. v.

[6] Di Matthäi ed. Stagnitta, *Annali dell' Instituto d'Igiene sperimentale di Roma.* 1889.

been found to retain their vitality for as long as eighty days in by no means ideal drinking-water (Chantemesse and Widal,[1] Strauss and Dubarry[2]). Even in greatly contaminated flowing water, as, for instance the Panke at Berlin, which was examined by Wolfhügel and Riedel,[3] the bacilli were found to retain their vitality and still to be capable of multiplication at high temperatures (16° C. and above). The germs were observed to retain their vitality for as long as three weeks in river-mud and in the sediment from wells.

That the conditions are more favorable in this connection in the usually well-protected general and house reservoirs is from the outset undoubted and especially to be noted in investigations into the mode of dissemination of the disease. We are indebted to Chantemesse for precise experimental evidence in this connection. The investigations have been extended also to artificially prepared and especially carbonated waters, which in times of epidemic may play an important *rôle* as presumably innocuous substitutes for ordinary drinking-water. Typhoid-bacilli have been found to retain their vitality in them for days and even for weeks.[4] Other ordinary fluids, and especially bouillon, have already been mentioned as good preserving and nutrient media for the bacilli. Not less important in this connection also is milk, and to this detailed reference will be made later. In this place it may be mentioned that the bacilli retain their vitality in boiled milk for as long as three months and more

Finally, a word may be said with regard to the persistence of the typhoid-bacilli in the intestinal discharges. This is in general and under ordinary conditions not inconsiderable. With a moderate external temperature and a feebly alkaline reaction of the stools the bacilli have persisted for more than three months (Karlinski[5]), while they die more rapidly when the external temperature is low, as well as when the stools are of highly acid reaction, or in the presence of ammoniacal decomposition, such as occurs especially when the stools are mixed with urine. In the dried stools the bacilli retain their vitality for a far longer period than under the conditions just named, and this naturally is of especial importance with regard to the dissemination of the disease.

All of the individual statements hitherto made indicate that the typhoid-bacillus, in spite of the absence of spore-formation and in spite of a certain sensitiveness to individual influences (high degrees of tempera-

[1] *Gazette hebd. de médecine et chirurgie*, 1887, No. 9.
[2] *Archives de médecine expérimentale*, Bd. i.
[3] *Arbeiten aus dem kais-Gesundheitsamt*, Bd. v., 1886.
[4] Hochstetter, *Arbeiten aus dem Reichs-Gesundheitsamt*, Bd. vi., 1887. [5] *Loc. cit.*

ture and direct sunlight), exhibits a tenacity within and without the body that wholly suffices to constitute the basis of the principal etiologic factors heretofore recognized. Under the most varied ordinary conditions (not induced experimentally) the bacillus is capable of surviving for days, weeks, and months, and even for more than a year, and under favorable conditions even throughout the winter. An additional conclusion is permissible—namely, that not alone the persistence of the germs, but also their dissemination through the media named, is certain. If in this connection the liquid media in general predominate, the dry media are not to be left out of consideration. It cannot be denied that the contagium attached to particles of dust may be disseminated through the air to a limited degree. We shall later have an opportunity to return to the more common and practically important methods of dissemination.

HOW DO THE TYPHOID-BACILLI GAIN ACCESS TO THE BODIES OF THE INDIVIDUALS INFECTED?

Almost all physicians are agreed at the present day that the digestive tract, as it appears especially to furnish the contagium, also is in turn by far the most frequent, even the almost exclusive, portal of entry for it. The conviction is held at the present day that typhoid fever is not transmissible in the sense of the "true contagious" diseases, as, for instance, typhus fever, scarlet fever, and measles. Mere presence in the vicinity of the patient is never sufficient for infection, as with the latter. The lungs and the skin, the most probable portals of entry for the acute exanthemata, are scarcely to be taken into consideration in connection with typhoid fever. If, in spite of this fact, infection through inhalation seems possible in rare cases, it will be found upon more careful investigation that here also the poison has gained entrance through the digestive tract. Under such circumstances the infection is conveyed through finely divided fluid containing bacteria or infectious particles of dust, which, although they have gained entrance into the mouth with inspired air, are then swallowed and have thus commenced their action in the intestine.

The principal manner in which the poison gains entrance into the body, and as compared with which all others are scarcely to be taken into consideration, consists in swallowing the infective agent, either in consequence of accidental, specific contamination of the buccal cavity and its surrounding structures, or through the introduction of food and drink containing the typhoid-bacillus. From the mouth the virus passes

through the esophagus and stomach into the intestine, in the feebly alkaline contents of which are furnished conditions favorable for its further development. The bacilli appear soon to pass from the lumen of the bowel into its wall, with especial preference for the lymphatic apparatus. From this point they migrate to the related lymphatic glands, and thence through the blood-stream to the tissues and organs that have been repeatedly pointed out as especially containing the bacilli.

For a comprehension of the processes of infection themselves, and in consideration of the experiences that have been had with other pathogenic organisms, particularly the cholera-bacillus, the question is important as to how the typhoid-bacilli behave with relation to the gastric juice. It is from the outset to be expected that the typhoid-bacilli, which thrive even upon feebly acid nutrient media, will more readily pass through the stomach uninjured than the cholera-bacilli, which are especially sensitive to the action of acids. As a matter of fact, both practical and experimental observations show that the bacilli of Eberth are relatively resistant to the secretion of the stomach, so that they may leave this viscus with their vitality preserved, especially if admixed with certain articles of food. The free hydrochloric acid need alone be taken into consideration as exerting a deleterious influence. Pepsin has proved to be absolutely harmless for the bacilli (Strauss and Wurtz [1]).

After Kitasato [2] had demonstrated the relative resistance of the typhoid-bacilli to acids, Seitz [3] showed that in a dilution of hydrochloric acid, 0.3 part to 1000, the micro-organisms retained their vitality for three days. In a dilution of 0.9 part to 1000 they were found destroyed by Strauss and Wurtz only after from two to three hours; and Chantemesse and Widal [4] showed that slight acidification with hydrochloric acid did not entirely inhibit development of the cultures. Stern [5] and Hamburger, [6] who took up the question anew, likewise came to the conclusion that the protection afforded by the hydrochloric acid of the gastric juice against the entrance of typhoid-bacilli is very doubtful.

On account of the quite rapidly increasing number of cases reported as typhoid without intestinal lesions, the question arises whether infection can occur through any other tract than the intestinal, or whether the bacilli may invade the body by passing through the normal intestine without causing any lesion in that tract. In regard to the first possibility, there is no proof at present that such a mode of infection can ever occur. The cases without intestinal lesions have lately been reviewed by Opie. [7] He concludes that the number of cases is too small to justify the assertion that typhoid-bacilli

[1] *Archives de médecine expérimentale*, 1889.
[2] *Zeitschr. f. Hygiene*, Bd. vii.
[3] *Loc. cit.*
[4] *Archives de Physiologie*, 1887.
[5] *Volkmann's Sammlung klin. Vortr.*, Neue Folge, No. 138.
[6] *Inaug. Dissertation*, Breslau, 1890, under the direction of Stern.
[7] *Bull. Johns Hopkins Hosp.*, vol. xii.

can ever enter through an absolutely intact intestinal wall, yet even in fatal cases the intestinal lesions may be so slight as not to be recognized at the time of autopsy.

THE MOST IMPORTANT CARRIERS AND MODES OF DISSEMINATION OF THE VIRUS.

Among the carriers of the virus, **water** is, according to the present state of knowledge, by far the most important. Even since the earliest times water has played an important *rôle* in the minds of both the laity and the medical profession in the development of most infectious diseases. Only for a time have theories now abandoned rendered doubtful its significance in regard to typhoid fever. Earlier authors, especially Dupré, Budd, Murchison, and Griesinger, emphasized the importance of water, however widely their etiologic views diverged in other respects. After them the dissemination of the disease through water was maintained by Gietl,[1] Biermer,[2] and Liebermeister,[3]—by the latter with a critical description of small and large epidemics. The fact that these views were held at that time, notwithstanding the deficient knowledge of the cause of the disease, will ever remain an example of scientific acumen.

The results of modern bacteriologic investigation, already fully considered, have permanently established the *rôle* of water, and have besides permitted a deeper insight into the innumerable and extremely variable conditions amid which it may serve as the carrier and disseminator of the typhoid virus. It is known that the water of streams, brooks, and springs, of conduits, of wells, of cisterns and reservoirs, of ponds, the bilge-water of ships, may contain the typhoid-bacillus in a living state, and under favorable conditions may even permit its further development. That this development is imperilled in flowing water, that the presence of a preponderant number of water-bacteria or putrefactive agents is capable of destroying the bacilli, is naturally not contradictory to the "water-theory," but rather furnishes important data for explaining the variability of the occurrence, the severity, and the distribution of the disease.

The forms in which water may serve as the means of conveying the noxious germ to human beings are in detail so extremely variable that they cannot all even be mentioned in this place. Every individual

[1] *Die Ursachen des Enterogenen Typhus in München*, Leipsic, 1865.
[2] *Volkmann's Sammlung klin. Vortr.*, No. 53.
[3] *Gesammelte Abhandlungen*, S. 27–65.

case, endemic or epidemic, carefully studied in this connection exhibits peculiar and in part new conditions, and the most varied relations with others long known. The simplest and certainly the most frequent occurrence consists in infection through drinking-water and liquid as well as solid articles of food that are prepared without adequate sterilization. Water used for cleansing and other domestic purposes can naturally not be separated from drinking-water. Under these circumstances also there is direct or indirect specific contamination of materials that gain entrance into the digestive tract.

The manner in which the water in question becomes contaminated by the dejections of typhoid patients naturally exhibits the greatest diversity. It may receive the germs directly from the patient or from privy-wells or cesspools, or through articles specifically contaminated accidentally, or it may be infected indirectly by previous saturation of the adjacent earth with fluids containing the germs. Even in the prebacteriologic period numerous careful observations bearing upon this point were made, among which a number could be directed with remarkable positiveness, in the sense of Budd and of Gietl, against the simple putrefactive theory of Murchison and his predecessors and successors. In this category are included, for instance, those cases in which wells that for a long time were demonstrably contaminated with the overflow from cesspools caused no or only general bad effects upon the consumers of the water, and only gave rise to the development of typhoid fever after the water had been specifically infected with the dejections from a case of typhoid fever.

In the nature of things, well-infections are confined to a few cases or to smaller or larger house-epidemics. Less commonly, when liquid articles of food used on a large scale (as, for instance, milk, or solid articles of food) are infected by means of water, will a larger number of cases arise directly from wells. Not rarely infection occurs indirectly if those directly infected convey the disease to other localities where new foci of infection develop. Endemics of considerable extent and even epidemic distribution are naturally more readily caused through the intermediation of larger and smaller rivers, streams, brooks, and springs. The relation of these to the development and dissemination of typhoid fever was established much later than that of wells. Many large epidemics which at the present day can be definitely traced to this mode of origin were for a long time used to support other theories, the pythogenic, the atmospheric, the earth-theory, or the ground-water theory. The inference was made that prior to the outbreak of the epidemic there was no typhoid patient throughout the community

or in its vicinity. How else, therefore, could the disease have arisen except through autochthonous, local development of infectious matters? Were not especially the conditions of the soil and their variations under the influence of the ground-water decisive as an etiologic factor? It was overlooked that the water-ways conveyed the specific poison from long distances; that brooks and streams might be infected through their tributaries; and that upon larger water-ways ships were capable of importing the infectious material from remote points.

Typhoid fever became most widely disseminated in large cities in which the water used for drinking and other domestic purposes, imperfectly or not at all filtered, was obtained from large streams that constantly served as receptacles for the contents of the sewers of these cities themselves or of those of neighboring cities.

All of these factors, it must be emphasized, to counteract the influence of the few remaining but persistent opponents of the theory of typhoid fever as a water-borne disease, are in no wise hypothetic. The demonstration of typhoid-bacilli in the water of wells and streams has often been made directly, and their persistence in these, as has been pointed out, is undoubted. That the bacilli have not been found in the suspected water-supply in every endemic or epidemic is not contradictory of this view. Thus, it has been repeatedly observed that in a given locality the typhoid-bacillus was evidently obtained from a certain source. Efforts were made further to obtain proof that a focus of typhoid fever had existed at a higher level; but when examination of the water was undertaken, the primary focus of infection had already been extinguished. It may also be readily conceded that it is by no means always possible to demonstrate the presence of typhoid-bacilli even in water that still contains them. Especially greatly contaminated water contains numerous other micro-organisms, which may render identification of the typhoid-bacillus difficult and even impossible even for an experienced observer. It should be noted especially that the distribution of the bacilli, particularly in connection with certain forms of pollution, is by no means uniform. They are often attached to isolated, irregularly distributed particles, so that only extremely time-consuming and painstaking investigation of large amounts of water will yield approximately trustworthy results.

The literature of all countries from the beginning of the nineteenth century until recent time contains a large number of reports of epidemics, some given with full detail, induced by infection of wells, springs, and streams. Limitations of space alone will not permit extended consideration of these. They have been collected in part by Murchison, Gietl, and Griesinger;

also Liebermeister[1] and Biermer[2] have given numerous bibliographic references in their works, which so brilliantly and definitely established the drinking-water theory. As an illustration of well-infection the following observation may suffice: In the early part of the seventies I treated a number of typhoid fever patients living in a suburb of Berlin upon a large estate which included almost 1000 inhabitants, who were crowded together in small, poorly ventilated rooms. My investigations disclosed that at the same time about 80 other patients were under treatment either at home or in hospitals. Further inquiry revealed that the water derived from the only well upon the place (the general water-supply had not yet been extended to this locality) was greatly polluted by organic material, was turbid, and offensive to the sense of smell. A year previously the water presented similar characters, and the cause was found to consist in a communication between a large cesspool and the well. My opinion that such contamination of the water by the contents of the cesspool still existed and must be the cause of the typhoid fever was met by the statement on the part of responsible individuals that in the previous year, when the water was similarly contaminated, there had been no typhoid fever in the community. Further investigation disclosed that this was correct, but also revealed a condition which explained the apparent difference and converted my suspicion into certainty—namely, that four weeks before the occurrence of the first cases of typhoid fever among the inhabitants of this section, a boy had arrived in the place, in whom symptoms of typhoid fever soon appeared, and from whom two children in the family with whom he lived were infected. There was thus no longer, as in the previous year, only general pollution of the well with fecal material, but an admixture with specific germs, the essential condition for the development of the disease.

A most instructive instance of dissemination of the poison through the water-supply is furnished by Liebermeister.[3] In the village of Lausen, in which for a long time only isolated cases of typhoid fever imported from Basle had occurred, and for seven years no case at all, in the year 1872, among 800 inhabitants, 130, almost 17 per cent., were attacked between the months of August and October. The epidemic set in so abruptly that almost 100 cases occurred within the first three weeks. A number of persons also who were only temporarily resident in Lausen were attacked. Careful investigation disclosed that all of the houses of the village that obtained their water from pump-wells were exempt from the disease, which invaded only those whose water-supply was obtained from running springs. With regard to these, it was determined that a small brook that constituted their source was contaminated by the overflow from a cesspool and a manure-pit attached to a house some distance above the village, and in which there had been four cases of typhoid fever during the months of June, July, and August.

[1] Cited by Liebermeister: Zuckschwert, *Die Typhus epidemie im Waisenhause zu Halle a. S. im Jahre 1871*, Halle, 1871. N. Bansen, *Ueber Aetiologie des Typhus abdominalis*, Züricher Dissertation, Winterthur, 1872 (Typhus in Winterthur). Compare also, concerning the same epidemic, Weinmann, *Correspondenzbl. f. Schw. Aerzte*, 1872, No. 23.

[2] Biermer, *Loc. cit.* Weissflog, "Ueber die Typhus Epidemie zu Elterlein von 1872," *Deutsch. Arch. f. klin. Med.*, 1873, Bd. xii., S. 320. Küchenmeister, "Der Reinhardtsdorfer Typhus, 1872–73," *Allg. Zeit. f. Epidem.*, Heft 1. A. Erismann, *Correspondenzbl. f. Schw. Aerzte*, 1873, No. 10. Quincke, *Ibid.*, 1875, No. 8.

[3] *Loc. cit.*, S. 64.

An instance of the development and epidemic distribution of typhoid fever on a large scale from a large stream is furnished by the conditions that prevailed in Hamburg in the eighties. In the years 1885, 1886, 1887, and 1888, 15,804 persons were attacked by typhoid fever, with 1214 deaths. As is known, Hamburg, until the great cholera-epidemic demanded even more urgently than typhoid the necessity of a change in its water-supply, derived all of its water for drinking and domestic purposes from the river Elbe, which was conveyed into the houses unfiltered and employed for all economic and commercial purposes without previous disinfection. Almost the only water filtered was that used for drinking and culinary purposes, but it was done with apparatus that, as is now known, was, by reason of its defective construction, calculated rather to exert an injurious effect than to subserve the purpose for which it was employed. Even at that time I contended that the development of the epidemic was attributable in greater degree to the obviously specifically infected water-supply than to all other influences.[1] I based my opinion especially upon the arrangement of the sewerage-system of Hamburg, the contents of which, poured into the Elbe, were capable of causing infection of the drinking-water, likewise obtained from the Elbe, because the point at which the sewage was emptied and that from which the water was obtained were not sufficiently separated. Especially was it in the highest degree probable, and even demonstrated by the experiments of Simmonds, that the reflux wave induced with the flood-tide of the Elbe carried the material emptied from the sewers up to and beyond the point from which the water-supply was obtained. From the uniform distribution of typhoid fever throughout the entire inner city also it was concluded that a uniformly distributed carrier of the poison was operative. This could scarcely be anything else than the water-supply. Even in the eyes of the most fanatic adherents of the localization-theory the conditions of the soil and the ground-water could not seriously be taken into consideration in a city that for a long time had been provided with a model, extensive, intricately ramifying, and excellently working system of sewerage. Additional positive evidence was found in the fact that in the neighboring city of Wandsbeck, immediately contiguous to Hamburg, and whose inhabitants live under identical external conditions, and the same conditions of soil, climate, and weather, there were only a few cases of typhoid fever during the same period. The only point of difference between the two cities was in the water-supply, Wandsbeck obtaining its water not from the Hamburg supply and not from the Elbe. Still more characteristic was the existence of an almost completely immune collection of buildings within a portion of the city of Hamburg, in which typhoid was as severe and as obstinate as in the remaining parts. The barracks in that section occupied by the Seventy-sixth Infantry Regiment, which contained in its young, vigorous members material in most marked degree predisposed to the disease, remained free from the epidemic, with the exception of a few obviously imported cases. It was not connected with the general water-supply, but received all of its drinking and other water from a well upon the premises. The soil and ground-water theories, however, at that time so thoroughly dominated the minds of those in authority that my opinions and recommendations[2] fell upon deaf ears. Subsequently the relations in question were investigated by Reinke, and my previously expressed views were fully confirmed and amplified by a large number of carefully established facts.

[1] *Deutsch. med. Woch.*, 1888.

[2] *Deutsch. Viertelj. f. öffentl. Gesundheitspflege*, Bd. xxviii., Heft 3.

The earlier inference that with every flood-tide the water of the Elbe between the point of discharge of the sewage and the source of supply for the water, and even far beyond, contained an increased number of germs, was removed beyond doubt by Dunbar.[1] Then Reinke demonstrated by tables the fact, to which I had already directed attention, that those portions of the city that received their water-supply from the common source were almost uniformly attacked by the epidemic, while the most peripheral districts (Winterhude, Eppendorf, and Horn), which at that time did not share equally in the blessings of the common supply, exhibited correspondingly and strikingly fewer cases. The clearest confirmation, however, is afforded by a consideration of the conditions in Hamburg since the time (May, 1893) when the source of water-supply was removed a considerable distance further up the stream and when the water itself was subjected to adequate filtration before it reached the city. For the years 1894 and 1895 the morbidity of typhoid fever was 462 and 597 respectively.

The following table of Reinke is more eloquent than words:

Year.	Number of cases.		Number of deaths.	
	Absolute number.	To 1000 of the population.	Absolute number.	To 1000 of the population.
1884	1053	2.35	108	0.24
1885	2172	4.65	160	0.34
1886	3890	8.09	333	0.69
1887	6543	13.26	446	0.90
1888	3199	6.23	275	0.54
1889	3172	5.89	222	0.41
1890	1539	2.73	147	0.26
1891	1197	2.06	128	0.22
1892	1941	3.30	203	0.35
1893	1094	1.84	106	0.18
Change in the source of supply and introduction of filtration.				
1894	462	0.76	37	0.06
1895	597	0.96	57	0.09

It is further interesting and distinctive that more than one-tenth of the cases of typhoid fever in Hamburg noted in the years 1894 and 1895 did not occur in the area supplied with good water, but were observed upon ships, on which it develops in consequence partly of infection of the bilge-water, partly of importation from elsewhere. Reinke properly emphasizes, besides, the danger of ships, to which typhoid fever is so indigenous, with relation to infection of the river-water, and also the water of other navigable streams. The Hamburg epidemic well illustrates the operation of a large vicious circle: Infection of sewage with typhoid-bacilli, conveyance of these by the flood-tide to the source of water-supply, distribution of the infected water throughout the entire city, as a result rapid multiplication of the typhoid-bacilli in the contents of the sewers, and through these a progressive increase in the number of bacteria in the water-supply. It was not until the year 1893 that the unfortunate circle was interrupted by changing the place for discharge of the sewage and the erection of suitable filtration-plants.

In addition to water, various liquid articles of food have already been designated as carriers of the typhoid contagium. Of these, **milk** is deserving of especial consideration. Milk is a source of infection naturally not in the same way as in the case of that from tuberculous

[1] Cited by Reinke.

animals, where it is infected directly by them, and so contributes to the dissemination of tuberculosis. Typhoid fever is not known with certainty to occur in animals. The *rôle* of milk as a carrier of infection rather resembles that of water, directly admixed with which or otherwise infected it exhibits its injurious activity. The experiences of the last twenty-five years have but too often shown that milk, like the water-supply, infected at its source or at its point of collection, may through its distribution lead to widespread dissemination of typhoid fever and give rise to small or even to more extensive epidemics.

Both in the unboiled and in the boiled state milk is an admirable preservative and nutrient medium for typhoid-bacilli, which persist in sterilized milk, according to the experimental observations of Heim,[1] for more than thirty days, and, what is especially dangerous, they do not cause coagulation, and do not change the milk in other respects (see previous observations) in appreciable degree. In all well-observed epidemics of typhoid fever due to milk the same series of events, modified in details, is repeated: Infection of the bulk of milk supplied by the producer for distribution, through well-water or spring-water to which, directly or indirectly, the dejections from typhoid patients have gained entrance. At times the cases of the disease have been found at a distance from the farm, far above the course of the supplying springs, and at other times in the dairy itself.

The special modes of infection of milk are various: Dilution with the infected water, preservation and transportation in vessels rinsed with such water, or direct infection through the hands of milkers, dealers, servants, and other persons who have come in contact with typhoid patients and their dejections, and who, having neglected suitable precautions, have conveyed the germs directly to the udder, the milk, or the vessels.

Naturally, other articles of food obtained from dairies and milk-depots may, similarly to milk, act as the carriers of infection. Butter especially, in which Heim[2] found the bacilli to persist for twenty-one days, and the different kinds of cheese, in which the bacilli may persist from one to three days in accordance with the method of manufacture, may act in this way.

As early as the seventies reports of milk-infection were made in England, following which an extensive literature developed. As an instance, a severe epidemic of typhoid fever in the year 1873, in the district of St. George's, Hanover Square, Marylebone, London, may be mentioned.[3] It soon devel-

[1] *Arbeit. a. d. kaiserl-Gesundheitsamte*, Bd. v. [2] *Loc. cit.*

[3] Gueneaud de Mussy, *Pub. de l'Acad. de Méd.*, 1881.

oped that servants and especially children, who were in the habit of drinking the milk from a certain well-known dairy, were attacked in large numbers. A commissioner, who was entrusted with the investigation of the dairy, found nothing suspicious; and a second, who reached a like result, endeavored further to establish the harmlessness of the milk by himself partaking thereof. He paid the penalty of his experiment with his life, inasmuch as he died shortly afterward from a severe attack of typhoid fever. The establishment was closed, and the epidemic soon subsided. Its mode of development was now shown to be as follows: The well with the water from which the dairy-man rinsed his vessels, and probably also diluted their contents, communicated with the soil contaminated by an adjacent dung-heap upon which had been thrown the dejections from a case of typhoid fever in the dairy.

Cameron[1] observed numerous cases of typhoid fever in Dublin in those houses in a given district that received their milk from a certain dairy, while the houses that derived their milk from other establishments remained exempt. It appeared that in the dairy first mentioned infection of the milk had resulted through 3 cases of typhoid fever. An epidemic observed by v. Mehring, and described by Schmidt,[2] is interesting, having occurred among the inmates of two prisons of Strassburg, as a result of the use of unboiled milk. This was obtained from a place in which cases of typhoid fever had occurred, and the disease subsided as soon as the supply of milk from this source was cut off. The etiologic interpretation of this epidemic is materially strengthened by the fact that the persons involved were almost, as in an experiment, cut off from general intercourse with others, and were exposed to identical, thoroughly controlled conditions. Further instructive instances of milk-infection are recorded also by Almquist,[3] Roth,[4] Reich,[5] Goyon, Bouchereau et Fourail,[6] Ali Cohen,[7] and others.

In contrast with milk, certain articles of drink are in repute among the laity as capable of diminishing the danger of infection. With this idea the suspected water is in times of epidemic mixed with tea, coffee, or alcohol, or the use of alcoholic beverages instead of water is recommended. With reference to tea and coffee, it may briefly be stated that so far as their chemic constitution is concerned they have no deleterious effect upon the typhoid-bacilli. With regard to spirituous liquors, the experiments of Pick[8] have shown that while they are capable of exerting a certain destructive effect upon the typhoid-bacilli, this is by no means so active as it is upon cholera-vibrios. The bacilli are generally not destroyed in ordinary white or red table-wine earlier than after half an hour, and at times even later. Addition of wine to water cannot, therefore, serve as a prophylactic. Lager beer and other light beers exerted no bactericidal effect within a reasonably practical time—

[1] See Brouardel et Thoinot, p. 54. [2] *Inaug. Diss.*, Halle, 1893.
[3] *Deutsch. Viertelj. f. öff. Gesundheit.*, Bd. xxi. [4] *Ibid.*, Bd. xxii.
[5] *Berlin. klin. Woch.*, 1894, No. 30. [6] *Rev. d'hyg. et de Pol. sanit.*, 1892.
[7] *Weckbl. v. h. Nederl. Tijdschr. voor Genesk.*, 1887, Bd. ii.
[8] *Arch. f. Hyg.*, Bd. xix.

nearly half an hour. The action of stronger alcoholic beverages naturally is comparatively more pronounced. Thus, Pick observed the bacilli to be destroyed in rye whiskey within five minutes. When, however, an equal amount of water was added, a half-hour elapsed before this result was brought about. The last experiment indicates that also the stronger beers and wines, especially the sweet wines, would be unreliable with reference to their destructive effect upon the typhoid-bacilli.

If the commercial relations with reference to other articles of food are subjected to close scrutiny, dangers similar to those that attend the use of milk will readily become apparent. They are, however, less under control, because the contamination is often accidental and difficult of demonstration, and not, as with milk, systematic and often repeated, and because, accordingly, rather isolated cases or, under certain circumstances, widely disseminated, small and therefore less conspicuous foci develop. It is quite clear and by no means sufficiently appreciated that typhoid fever may be disseminated from establishments from which vegetables and greens, especially, however, fruit, lettuce, and similar articles generally eaten in an uncooked state, are obtained, if these articles be rinsed or sprinkled with infected water. Not less important is direct infection of these articles of food by typhoid patients who live in these establishments or by those in attendance upon the patients. That bread and cake and many other articles eaten without being again cooked or heated may be a source of danger in a similar manner does not require further elaboration.

It need only be noted that vegetable-gardeners, before going to market, sprinkle their wares with water in order to keep them fresh; and consideration should be given to the especial danger if these are transported in large amounts by vessels upon large streams, which, as we have seen, are so frequently infected. Finally, attention should be directed to the conditions that prevail in the dwelling-rooms, the salesrooms, and the storage-rooms of dealers in vegetables and articles of food, and the manner in which these are crowded together in basements in large cities and communicate directly with one another. On account not alone of typhoid, but also of other infectious diseases, should sanitary supervision and regulation of these conditions be more thorough than has hitherto been customary.

Naturally, typhoid fever may develop in any private dwelling through direct or indirect infection of articles of food, and be conveyed elsewhere, the latter occurring especially if the members of the family or the servants take part in nursing the patient and also in domestic work, especially cooking. The conditions are most serious in this connection among the poorer classes, but also among those better situated almost incredible things will be done from want of knowledge and owing to

improper arrangements. Also in hospitals dissemination of typhoid fever occurs if the most scrupulous care be not given to the cleanliness of the patient and his vicinity, as well as to the disinfection of the discharges, and if in addition the attendants fail to observe the most rigid precautions. Most thorough disinfection of the hands and clothing, strict prevention of nurses engaged in the care of typhoid patients from aiding in the care, especially the feeding, of others, are especially important considerations in this connection.

Even among the better classes, not to speak of those less favorably situated, the physician cannot take for granted that thorough disinfection of the hands will be practised and appropriate precautions with regard to the care of the clothing of the attendants will be observed. The fewest of mothers or nurses, in going from the sick-bed to the dining-room, think of changing their clothing or washing their hands so thoroughly as to exclude the possibility of conveying disease-germs to articles of food and drink. Insufficient care in disinfection is certainly the most frequent means by which physicians and nurses acquire the disease. With regard to the latter, I have always been struck with the fact that especially new nurses, therefore those who from carelessness or lack of skill do not observe the necessary precautions, are more commonly attacked than older and better-trained nurses.

TRANSMISSION THROUGH THE AIR.

Reference has already been made to the relation of the air to the contagium of typhoid fever. It was pointed out that dissemination of the contagium through the air is possible, whether the carrier be in a moist condition or in a dry state in the form of dust. The first mode of infection requires little consideration. It would be operative almost exclusively in the event of a spraying of infected fluid and its accidental entrance into the mouth of a susceptible individual. Less commonly, indifferent fluids in the form of spray might carry the contagium attached to dust for a considerable distance, a possibility in favor of which Lassime[1] has presented evidence. Far more commonly in practice the possibility of dissemination of the contagium by particles of dust must be taken into consideration. Reference has already been made to the persistence of typhoid-bacilli in a dry state. The entrance of the contagium disseminated through the air will occur preferably through inhalation, the germs being deposited first in the mouth and the nose. Entrance into the body and the blood-stream, however, probably takes place only through the digestive tract. Whether entrance of the bacilli may take place also through the respiratory apparatus is still a debatable question. It is certain that entrance by this route would constitute the exception (pneumotyphoid?). Nevertheless, the observations of Buchner,

[1] *Thèse*, Paris, 1890.

which furnish experimental evidence in favor of this mode of infection, are worthy of consideration and confirmation.

No more can be said from the present point of view with regard to the dissemination of typhoid fever through the air. Its *rôle* has become a more subordinate one in comparison with that assigned to it in earlier times, when especially the imperfect differentiation of typhus and typhoid fever favored this view. Although clearness prevails in this connection at the present day, another earlier view has not been wholly eliminated from the minds of inaccurate individuals, which for a long time constituted the strongest support for the doctrine of the dissemination of typhoid fever through the air, namely, that air contaminated by putrid substances is capable of causing typhoid fever directly, or at least of acting as the carrier of the contagium. At the present day it is no longer held that putrid substances of themselves, especially the decomposition-products of feces, constitute the exciting agent of typhoid fever, and the opinion of Budd that the specific typhoid germ under these conditions finds, at least, its especial pabulum has also been abandoned. To-day we require the demonstration of other etiologic factors than formerly, when, with the appearance of typhoid fever, the discovery that foul air from an adjacent cesspool or other focus of putrefaction entered the dwelling was deemed fully sufficient to explain the cause of the outbreak.

It would naturally be going too far to ignore entirely the large number of cases reported by reliable early investigators in which it was believed that the contagium was disseminated by contaminated air. Some of these, it cannot be denied, are susceptible of scarcely any other interpretation. More recent histories of similar character would naturally be judged by an entirely different standard. At the present day it would be necessary to demonstrate that the air in question was laden with active typhoid contagium, and that the conditions for its movement and the entrance of the poison into the body were especially favorable. As an instance of the lack of precision in earlier observations, a personal experience and the history of two epidemics from the well-known work of Murchison will suffice.

At the beginning of the seventies, in a boarding-school in Berlin, in which 6 young persons occupied a large, well-situated bedroom, 1 of these was attacked with severe typhoid fever, and was sent by me, on account of his companions, all of whom remained well, to the hospital. Official examination of the case disclosed the presence upon one wall of the room of a moist, offensive-smelling spot, resulting from a leak in a broken discharge-pipe in the wall. Neither in the house in question nor in the adjoining house, as I was able to convince myself, had there been a case of typhoid fever within a long time. Nevertheless, the pipe and the spot upon the wall had to be considered as the source of the disease. My objection that the remaining 5 inmates, of about the same age and equal predisposition, had remained well, and that the disease of the sixth might have been acquired elsewhere from a third source, was received only with a sympathetic shrug of the shoulders.

Also, the well-known and much-quoted epidemic of typhoid fever in the school for boys attached to the Colchester Union in London[1] loses most

[1] See Murchison, *loc. cit.*

of its force on more careful scrutiny. In that instance many of the pupils in a schoolroom that communicated with a sewer by means of the chimney were attacked with a severe acute disease, which was most intense and appeared earliest in those seated nearest the chimney. Murchison had no doubt that the disease was typhoid fever, and that it resulted from the inhalation of injurious gases from the chimney in question. The inhalation as the cause of the disease is, from Murchison's description, most probable, and almost certain from the objective point of view; but how could Murchison know, without seeing any of the patients, that the disease was typhoid fever? Only from the fact that the school-inspector informed him that in the opinion of the attending physician the symptoms of the disease resembled those described by Jenner as the symptoms of typhoid fever.

Still less convincing is the well-known epidemic at the school of Clapham, likewise cited by Murchison.[1] In the summer of 1892, of 22 boys in that institution, 20 were seized within three hours with "ileotyphoid," with vomiting, diarrhea, and prostration. The disease was attributed to the fact that the boys had witnessed the reopening of a grave closed for many years, the greatly decomposed contents of which had been then spread upon the soil in the neighborhood of the playground of the school. Two of the affected boys died, one after an illness of twenty-three and the other after an illness of twenty-five hours. The autopsy disclosed acute swelling of Peyer's patches and the solitary follicles, with slight ulceration of one of these structures, together with enlargement of the mesenteric glands. The question at once arises in connection with this report: Is it not unusual that young, previously healthy individuals die from typhoid fever within from twenty-three to twenty-five hours? Can the anatomic conditions found develop in a case of typhoid fever within the time mentioned? Is the sudden, almost simultaneous, illness of the pupils suggestive of typhoid fever? Are vomiting, diarrhea, and prostration evidences of this disease? Do not, rather, all of these circumstances indicate simple intoxication with sewer-gas, which in fact was at first suspected by the observers? Such conditions have been recognized, and it is known from the experiments of Magendie, Leuret and Hammond, Barker, and others, that they can be induced experimentally in animals by the inhalation of putrid gases. It has been learned from the experiments of Stich[2] that animals poisoned by the intravenous injection of putrid substances exhibit intestinal lesions identical with those of the boys at Clapham, namely, intense catarrh of the lower portions of the intestine, especially the ileum, with acute swelling and even exfoliation of Peyer's patches and the solitary follicles, as well as consecutive hyperplasia of the related mesenteric glands.

SIGNIFICANCE OF EARTH IN THE ETIOLOGY.

Earth has played as important a *rôle* as air as a carrier and disseminator of the typhoid poison in the views of physicians and in the literature. It was considered as the essential medium for the storing up and the further development of the poison, which was believed to originate spontaneously in it from putrid substances, or, according to the view of Budd and his disciples, to be deposited as a specific contagium and there

[1] *Lancet*, 1829, vol. xvi.; *Med. Gaz.*, vol. iv. [2] *Charité Annalen*, 1853.

to undergo multiplication. It is characteristic of earlier epidemiologic views that this thought, which was evolved theoretically from certain general experiences, was utilized as a secure basis for all further conclusions. In this way were explained both the smallest as well as the most extensive epidemics. If typhoid fever occurred in a house, or on an estate, or in a larger area, only the infected subsoil was taken into consideration, provided that contaminated air was not operative. If in addition the swampy character of the earth or the proximity of dung-heaps and sewers was established, or if the earth had been strewn with refuse and manure a shorter or a longer time previously, all doubt was removed. As the nature of the contagium was unknown, and as this was considered rather as gaseous than corpuscular, it was possible to continue the construction of hypotheses without hindrance. The air was then especially considered as the vehicle for the poison in question, and it was believed that this escaped from the soil in consequence of a sort of evaporation, and was then further distributed. If it was possible to show further that the soil had been turned up in the neighborhood, and that shortly before excavations had been made, foundations dug, or drain-pipes laid, the transference of the infected ground-air to the workmen and others seemed demonstrated as in an experiment.

During the great typhoid fever epidemics of Hamburg, some, unfortunately influential, easily satisfied individuals explained the occurrence beyond doubt by the fact that large excavations and building operations were in progress about the harbor. That typhoid was distributed over the entire city, while the excavations in question were confined to a narrow section and that the adjoining streets were by no means especially affected, failed to affect the preconceived opinion.

The soil-theory received its scientific development through the well-known works of Buhl and Pettenkofer, and these dominated the theory of the origin of typhoid fever until within the most recent times. The ground-water theory of Buhl and Pettenkofer was based upon the statistical observation that the morbidity and mortality of typhoid fever in Munich rose when the ground-water was at a low level, while a corresponding reduction ensued with a rise in the ground-water. Pettenkofer believed that he was able to give a definite explanation for his observations, namely, that the specific typhoid poison develops and undergoes maturation in the deeper layers of the earth saturated with substances capable of undergoing putrefaction. When the ground-water is at a high level this dangerous layer of the soil is covered by the former, and is thus cut off from the surface of the earth, while when the ground-water occupies a low level this exclusion is wanting. In the latter event, with the aid of special local, seasonal, and personal

conditions, the contagium might not be prevented from escaping through the ground-air,[1] when it would be taken up into the body by inhalation, and in those predisposed would act as the excitant of the disease.

The theory of Pettenkofer aroused active opposition soon after its announcement, and this in part was based upon the experiences in other cities where the rise and the fall of the ground-water bore no relation to variations in the prevalence of typhoid fever, and in part was directed against the theoretical conclusions of that distinguished hygienist. Among the earliest attacks may be mentioned the papers of Liebermeister[2] and Biermer,[3] which are even to-day models of critical utilization of all that was known at the time. These impaired the stability of Pettenkofer's theory, which, in the light of present knowledge, has no longer the significance that was attached to it by its author and his pupils. With regard to the statistical observations, these are, it is true, applicable to the city of Munich; but it has been demonstrated that they are not applicable to a number of other cities, and they are certainly not susceptible of general application.

With relation to the behavior of the typhoid poison in the soil, according to the view of Pettenkofer, the knowledge confirmed experimentally that the bacilli of Eberth are capable of retaining their vitality in the earth for a long time—better in porous than in rocky or otherwise impervious soil—might be emphasized. Grocher and Dechamps observed them to persist for five and a half months at the depth of $\frac{1}{2}$ meter. This resistance is probably not greatly diminished by cold and dryness (see p. 35), so that the poison may under favorable circumstances survive in the earth both through the cold as well as the heated season. The conditions are different, however, with regard to the hypothetic maturation and propagation of the bacilli in the earth. The first, in accordance with existing knowledge, is not at all probable or is so in but limited degree. Any considerable multiplication of the bacilli in the earth or any increase in their virulence is wholly undemonstrated. In any event, these things do not occur, as a rule. Also, definite local or seasonal conditions exerting a favorable influence in this connection have not been clearly demonstrated.

Even if the other opinions of Pettenkofer were better supported, his hypothesis that the poison finds its way into the air from the earth and is disseminated in this way would be most difficult of demonstration. This would be conceivable of a gaseous poison. The known corpus-

[1] See Pettenkofer, *Ueber die Luft im Boden und Grundluft*, Braunschweig, 1873.

[2] *Ges. Abhandlungen u. Ziemssen's Handbuch*, 1 Aufl., Bd. i.

[3] *Volkmann's Sammlung klin. Vortr.*, 1873.

cular nature of the contagium is, however, directly opposed to such a view. Only in exceptional instances, attached to particles of dust acting as carriers, could it gain access to the body directly from the earth and cause infection. Thus, it is conceivable that in the course of excavations and other operations upon infected soil, germ-containing dust might gain direct entrance into the mouth and thence into the digestive tract of the workmen thus engaged and cause infection, and that the individuals thus infected might cause further dissemination of the disease. Even in these cases, however, the probability of infection through the soiled hands, clothing, articles of food, etc., is still greater than that through inhalation.

The principal mode of dissemination of typhoid fever from subsoil containing typhoid-bacilli will always remain that through water, a medium to which the believers in the localization-theory attached far too little importance from the outset. From all that is as yet known, water is by far best adapted to take up the bacillus from the earth and to effect its further dissemination. The germ may thus find its way into flowing water, or under favorable conditions gain entrance from the subsoil-water into wells, or be washed out of the upper layers of the earth by rain and melted snow.

INFECTION AND DISSEMINATION THROUGH HOUSEHOLD ARTICLES.

References to this subject have already been made.[1] In view of the practical importance thereof, it seems desirable, however, to return to it at greater length. Undoubtedly, the typhoid poison may remain attached in an active state for a considerable length of time to clothing, linen, bedding, and various household articles. Under such circumstances these articles are generally contaminated directly or indirectly through the dried dejections from typhoid patients. Naturally, under these circumstances the family of the patient, the attendants, laundresses, and other persons whose occupation requires that they come in contact with the articles in question are most exposed to danger. Infection is, however, frequently brought about indirectly through healthy intermediaries, who remain well, and who may convey the poison attached accidentally at the bedside to their clothing or their hands; and without doubt a number of cases of obscure etiology are attributable to such occurrences. Naturally, physicians should always bear in mind that

[1] See the statements on pp. 35 and 36 with regard to the persistence of the Eberth bacillus under varying conditions of desiccation.

they may themselves be the means of conveying typhoid fever, in the same way as some other infectious diseases, by failure to observe adequate precautions. There is no doubt that infection may take place at a distance by the transmission in infected utensils.

A number of years ago the following instructive experience occurred to me: A young merchant living in middle Germany, who was accustomed to send a portion of his clothing and linen to his home in Hamburg to be laundered, continued this practice when attacked with "gastric fever." Ten and twelve days respectively after the sister of the patient and a servant had washed the linen, they became ill, the one with a mild, the other with a severe attack of typhoid fever. That the brother had also suffered from the same disease was unfortunately demonstrated by autopsy, death occurring from copious intestinal hemorrhage in the course of an apparently mild attack. While the mode of infection just mentioned is by no means rare for the acute exanthemata, especially variola and typhus fever, and in the acute infectious diseases most closely allied to them, and must be taken into consideration in cases of obscure origin, little or no reference is made to it in the literature or in practice in connection with typhoid fever. The same thing happened with regard to this as occurred with a number of other circumstances of etiologic importance. They were all neglected or ignored for a long time from the custom of looking at all things from the point of view of the pythogenic or the subsoil-theory.

FACTORS THAT FAVOR INFECTION AND DISSEMINATION OF THE DISEASE.

Having thus far occupied ourselves with the direct causes of typhoid fever—that is, with the peculiarities of its specific contagium, especially its vital relations, the various possibilities of its multiplication, dissemination, and invasion in the human body—we shall now take up the contributory factors, namely, those that are of importance for the reception of the poison into the body, for its further development therein, and for its pathogenic activity.

Individual bodily conditions and acquired conditions favoring the development of the disease are especially to be taken into consideration in this connection. Perhaps with further advances in knowledge we shall learn to divide these influences into those that lower the resistance of the organism to the bacilli and those that directly favor their vitality and multiplication. At the present time but little is known concerning these matters. We have not advanced far beyond the theoretic guides to the lines for future investigation.

A second important group of contributory factors consists in the conditions existing outside of the body—locality, climate, season of the year, etc. Although these also to a certain degree act upon the individual, their principal significance, however, resides in the

influence that they exert upon the behavior of the poison deposited and preserved outside of the body, upon its persistence and its further development. Much that has been said with regard to the tenacity of the poison is applicable in this connection. On the whole, our present knowledge in this field is based rather upon empiric than theoretic, especially experimental, grounds.

FACTORS RELATING TO THE INDIVIDUAL.

Age and Sex.—The large number of statistical data with reference to these subjects, however exact they may appear, must be received with great caution. Many are obviously not at all in accordance with the facts, while others agree only on general lines. Most might be expected from extensive official statistical statements, covering all of the inhabitants of a country, both the well and the sick. Unfortunately, these suffer from variation in the reliability of the diagnosis and from the deficiency in anatomic data. In hospitals, on the other hand, where these conditions are the most favorable, other factors throw doubt upon the statistical results. Thus, there is often the smallness of the number of cases, and almost everywhere the class of patients admitted to the hospitals does not represent the average population of a community, and therefore the real average morbidity is not represented. In this connection it is especially to be taken into consideration that children and married persons are for obvious reasons less commonly sent to hospitals than unmarried adults, mechanics, laborers, servants, visiting strangers, etc. Of the married, experience has also shown that everywhere the women go to the hospitals less commonly and defer entrance longer than the men. In weighing the significance of statistical data these circumstances should receive appropriate consideration.

As to the influence of **age,** there is no doubt that youth especially predisposes to typhoid fever, and the period of life between the fifteenth and the thirty-fifth year is by far the most commonly attacked. In my experience fully four-fifths of all cases occur at this period, and in this connection it should be noted further that more than half (about 56 per cent.) occur between the fifteenth and the twenty-fifth year. Between the thirtieth and thirty-fifth years the number of cases diminishes somewhat, to fall considerably between the thirty-fifth and the fortieth year. After the fiftieth year the morbidity can be expressed in fractions of 1 per cent. In old age the disease can be considered as rare. Likewise in early childhood up to the first year of life typhoid fever is rare, as is known also of most other acute infectious diseases. From the first to the fifth year a gradual increase takes place. From the fifth to the

fifteenth year the predisposition becomes still greater, so that during this period more are affected than between the thirty-fifth and fortieth years.

The following figures, based upon observations made in the hospitals of Hamburg[1] and Leipsic,[2] may serve to illustrate what has been said:

Cases of Typhoid Fever in the Hamburg General Hospital, 1886–87.

	1886.				1887.			
AGE.	Male.	Female.	Total.	Percentage.	Male.	Female.	Total.	Percentage.
2	0	3	3	0.2	1	3	4	0.18
3	2	1	3	0.2	3	3	6	0.27
4	4	5	9	0.6	7	0	7	0.31
5	4	9	13	0.9	3	2	5	0.22
6	4	3	7	0.5	0	6	6	0.27
7	9	4	13	0.9	3	6	9	0.40
8	3	6	9	0.6	9	9	18	0.80
9	10	9	19	1.3	16	9	25	1.12
10	13	11	24	1.7	11	15	26	1.16
11	19	9	28	1.9	13	9	22	0.98
12	12	5	17	1.2	22	21	43	1.92
13	18	9	27	1.9	25	19	44	1.96
14	18	14	32	2.2	21	11	32	1.43
15–20	239	169	408	28.2	412	280	692	30.88
21–25	255	114	369	25.5	418	205	623	27.80
26–30	180	66	246	17.0	249	107	356	15.89
31–35	78	34	112	7.8	114	43	157	7.01
36–40	27	23	50	3.5	51	26	77	3.44
41–45	21	5	26	1.8	37	18	55	2.45
46–50	6	5	11	0.8	13	2	15	0.67
51–55	1	1	2	0.1	4	7	11	0.49
56–60	2	1	3	0.2	4	1	5	0.22
61–65	0	1	1	0.1	0	0	0	0.00
66–70 . . .	0	0	0	0.0	1	2	3	0.13
Age not specified.	6	7	13	0.9				
Total . . .	931	514	1445	100.0	1437	804	2241	100.00

[1] H. Schutz, "Beitrag zur Statistik des Abdominal-typhus," *Jahrb. d. Hamburger Staats-Krankenanstalten*, 1889, 1 Jahrg.

[2] C. Berg., *Inaug. Diss.*, Leipsic, 1893.

Both of these studies were made under my direction. The dissertation of Berg follows the work of Schutz with reference to the statistical questions considered and the arrangement of the material. From the year 1889 the results are based upon information obtained from answers to a series of questions that I have introduced into the Leipsic hospitals in the same form as used in the Hamburg hospitals.

An analysis of 1626 cases of typhoid fever in the Jacobsspital of Leipsic between 1880 and 1893 disclosed the following figures:

Age.	1880.	1881.	1882.	1883.	1884.	1885.	1886.	1887.	1888.	1889.	1890.	1891.	1892.	1893.
1	0	0	1	0	0	0	0	0	1	1	0	0	0	0
2	2	0	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	1	0	2	0	0	0	0	0	2	1	1
4	0	2	0	0	1	3	1	0	1	0	2	0	0	0
5–9	3	6	9	3	6	2	5	2	2	1	2	1	4	0
10–14	9	10	7	5	6	4	3	8	1	10	5	6	6	4
15–19	25	32	14	25	28	30	24	23	17	50	36	32	18	5
20–24	28	50	23	34	35	32	40	19	21	62	34	23	27	6
25–29	25	33	16	26	23	23	14	23	25	30	26	18	22	4
30–34	8	16	9	8	18	10	8	12	7	15	15	20	7	4
35–39	5	13	6	11	14	7	11	5	5	11	10	5	3	0
40–44	6	5	2	1	1	5	1	3	0	3	3	6	3	2
45–49	0	6	1	3	4	2	0	4	1	4	1	1	2	0
50–54	1	3	0	3	2	2	2	1	1	0	2	2	1	2
55–59	1	0	0	1						2	0	0	1	0
60–69	0	1	0	0	0	0	1	2	0	2	1	1	2	0
70–80	0	1	0	0	0	0	0	2	0	3	0	0	0	0
Total.	113	178	88	121	138	120	110	103	82	194	137	117	97	28

Arranged according to ages, these fourteen years showed the following relations:

Age.	Cases.	Percentage of all cases.	Age.	Cases.	Percentage of all cases.
1	3	0.19	30–34	167	10.40
2	2	0.13	35–39	106	6.61
3	7	0.44	40–44 . . .	41	2.50
4	10	0.63	45–49	29	1.80
5–9	46	2.80	50–59	20	1.25
10–14 . . .	86	5.40	60–69	10	0.63
15–19 . . .	359	22.40	70–80	5	0.32
20–24 . . .	434	27.00	Total . . .	1626	
25–29 . . .	315	19.50			

In view of the large number of children (451) treated at Hamburg in 1886–87, it may be profitable to consider these in tabular form:

Age.	Number.	Percentage of children attacked.	Age.	Number.	Percentage of children attacked.
2	7	1.60	9	44	9.90
3	9	1.85	10	50	11.15
4	16	3.70	11	50	11.30
5	18	4.20	12	60	13.30
6	13	3.30	13	71	15.50
7	22	5.05	14	64	14.30
8	27	6.30	Total . .	451	

The table shows, as has been indicated, that typhoid fever is not frequent in childhood until about the fifth year, when the frequency gradually increases until the ninth year, then to reach its height after the tenth year. A comparison with the statements of recognized authorities, as, for instance, Murchison,[1] Fiedler,[2] and Griessinger,[3] discloses agreement with the figures given.

[1] *Die typhoiden Krankheiten*, German by Zülzer, Braunschweig.

[2] *Arch. f. Heilk.*, 1862.

[3] *Virchow's Handbuch der speciellen Pathologie*, 1864, 2 Aufl., Bd. ii.

Thus, 52 per cent. of Murchison's patients were between fifteen and twenty-five years old. Fiedler[1] reports that 58.8 per cent. of his patients were between the twentieth and the thirtieth year of age, while 3.4 per cent. were above forty and only 0.7 per cent. were more than fifty. The statistics of Griesinger also, dealing with more than 510 cases observed in Zurich between 1860 and 1863, include 20.1 per cent. between the tenth and the nineteenth year, 46.6 per cent. between the twentieth and twenty-ninth year, and 16.8 per cent. from the thirtieth to the fortieth year. The statistics of Liebermeister[2] are particularly instructive, as this observer carefully endeavored to avoid the statistical errors attendant upon the inclusion of hospital-patients:

Age.	Number of cases of typhoid fever.	Percentage of the total number.	Percentage of this age in the total population.	Predisposition as compared with the average represented by 1.
From 16 to 20 years . . .	323	19	12	1.6
" 21 " 30 " . . .	987	58	29	2.0
" 31 " 40 " . . .	274	16	24	0.7
" 41 " 50 " . . .	88	5	16	0.3
" 51 " 60 " . . .	30	2	10	0.2
" 61 " 70 " . . .	11	0.6	6	0.1
Above 70 years	1	0.06	3	0.02

The frequency of typhoid fever at various ages has been estimated from the mortality-tables in a number of works characterized by the largeness of the figures. These collections fail to give a representation of the actual state of affairs, as the mortality is variable at different periods of life, and some periods, as, for instance, old age, exhibit unusually high figures. Liebermeister therefore reproduces the mortality-statistics of Hagenbach[3] with the same qualification. The following tabulation by Brouardel[4] of 16,036 cases is most instructive in this connection:

Deaths from Typhoid Fever in Paris from 1880 to 1889 considered according to Age.

Up to 1 year	36	From 30 to 35 years	1197
From 1 to 5 years	1041	" 35 " 40 "	771
" 5 " 10 "	1265	" 40 " 45 "	457
" 10 " 15 "	1386	" 45 " 50 "	380
" 15 " 20 "	2991	Above 50 years	535
" 20 " 25 "	3896		16,036
" 25 " 30 "	2081		

On comparing this with the preceding table, it will be seen that the marked differences in morbidity are obliterated; thus, for instance, the figures for children between the first and the tenth year equal those for persons between the tenth and the fifteenth year; and there is little difference between the ages from fifteen to thirty; while the figures for old age are comparatively high.

Sex causes, apparently, little difference with regard to infection with typhoid fever. On the whole, among adults men are attacked

[1] *Loc. cit.* [2] *Ziemssen's Handbuch*, 3 Aufl., Bd. ii., Heft 1, S. 124.

[3] *Jahrb. d. Kinderheilk.*, Neue Folge, 1875, Bd. ix.

[4] "Repartition de la fièvre typhoide en France," *Rec. d. trav. Comité consult. d'hyg.*, 1891.

rather more frequently than women. Whether this difference is due actually to the conditions of sex appears more than improbable. Of determining influence in the case of men is probably the greater opportunity for infection, in the presence of equal susceptibility, by reason of greater variations in residence, in nutrition, and in occupation. That these circumstances do not affect the statistics in greater degree is undoubtedly due to the fact that the predominant influence of water in the dissemination of the disease affects women in scarcely less degree than it does men. Mention of the fact further should not be omitted that in hospital-statistics males predominate somewhat because they enter hospitals more readily, and therefore with relatively greater frequency.

If in certain localities there is a marked majority of cases in males, this of itself indicates nothing, but rather requires investigation into the nature of the population. Thus, for instance, it can be understood that, in places that by reason of large establishments or factories attract young males in especial number, this fact would receive expression in the event of an epidemic of typhoid fever in the greater number of males attacked. Murchison believed the two sexes equally susceptible. Among 2432 cases treated in the London Fever Hospital between 1848 and 1861, there were 1211 males and 1221 females. Also, Bartlett[1] observed 1179 males and 1163 females among 2312 cases. Although Fiedler[2] observed 57.6 per cent. of males and 42.4 per cent. of females, this may agree with the usual proportions of the two sexes received into the hospital. Among 2235 cases of typhoid fever observed in Hamburg, I have found 2118 males (65.5 per cent.) and 1117 females (34.5 per cent.), but feel justified in stating definitely that this preponderance of males is not the expression of a difference in predisposition, but is the result of local conditions, leading to the admission of fewer women into the hospital.

Some writers on pediatrics (West, Barthez and Rilliet, Taupin) believe that the difference between the sexes with relation to predisposition to the disease extends into childhood. All observed that more boys than girls were attacked. Although it is not at all clear how such differences can arise prior to the period of sexual development, the following figures are striking: Barthez and Rilliet, 80 boys, 31 girls; Taupin, 86 boys, 35 girls.

I believe, however, that these figures are too small to exclude accidental influences, and that, therefore, they do not sustain the general statements based upon them. With a much larger field for observations, I have not been struck by the preponderance of boys. Among 451 children suffering from typhoid fever, I observed only a few more males than females, namely, 250 boys and 201 girls.

To what degree accidental influences may be operative, even with figures much larger than those previously given, was shown in considering sepa-

[1] Cited by Murchison.

[2] *Loc. cit.*

rately for each year the 451 cases observed in children during the years 1886 and 1887 in Hamburg. It then appeared that in 1886 there were attacked 116 boys and 88 girls; in 1887, 134 boys and 113 girls.

Certain physiologic conditions in women, as **pregnancy,** the **puerperal state,** and **lactation,** appear to diminish the predisposition to typhoid fever. With regard to the degree of immunity conferred by these states, not inconsiderable differences of opinion exist among various authorities. Griessinger considers typhoid fever exceedingly rare in the puerperium, and he believes nursing infants also to be particularly immune. In this respect he is in accord with Rokitansky. I have also observed typhoid infection but twice in the puerperium, and but rarely during lactation. With regard to pregnancy, in agreement with Liebermeister, I do not believe that the immunity is at all considerable.

In Hamburg, among 1117 women 38 were pregnant—3.4 per cent. In my experience at Leipsic 2 per cent. were pregnant. Even at those periods of life in which the predisposition to the disease and the chances of pregnancy are diminished, the figures are relatively high, as the following tabulation of the 38 Hamburg cases will show:

Sixteen were between the ages of fifteen and twenty years; 15 between twenty-one and twenty-five; 10, twenty-six and thirty; 4, thirty-one and thirty-five; 3, thirty-six and forty.

Brief reference may be made here to infection of the fetus with the typhoid-bacillus. Lynch,[1] who has reported 1 case, from the heart's blood, spleen, and kidney of which the typhoid-bacillus was isolated, and also 1 case with entirely negative findings, has carefully reviewed the literature and collected 16 undoubted cases in which the typhoid-bacillus was isolated from the organs of the fetus. In none of these cases were intestinal lesions found. Among the earlier cases may be mentioned those of Eberth,[2] Hildebrand,[3] and Ernst.[4] He has also collected 14 cases in which very careful examinations were made with entirely negative results. From the existing evidence it is probable that infection of the fetus is not the usual sequel of typhoid fever in the mother, but that favoring conditions must be additionally operative. Thus, in the case of Ernst the mother had fallen during pregnancy, and it can readily be conceived that in consequence of the traumatic laceration the placenta was rendered permeable to the bacilli. Probably the most favoring factor is to be found in the hemorrhagic infarcts of the placenta, which have been usually noted in the cases with positive findings. In Lynch's positive case there were found numerous microscopic hemorrhagic infarcts, while in the negative case none were found.

[1] *Johns Hopkins Hosp. Bull.*, vol. xii.
[2] *Fortschr. d. Med.*
[3] *Ibid.*, 1889, Bd. vii.
[4] *Ziegler's Beiträge*, Bd. viii., S. 188.

Constitution and Social Conditions.—With regard to **constitution,** all observers agree that typhoid fever is one of those diseases that occur with special readiness and frequency in well-nourished young persons situated amid favorable hygienic surroundings. In this respect typhoid fever stands in contrast with typhus fever and relapsing fever. While in large epidemics of the two latter diseases the poorer classes in the community, especially those laboring under physical distress and generally impaired nutrition, are attacked, typhoid fever demands its sacrifices alike from poor and rich, from high and low. Certain transitory mental and physical conditions appear to increase the predisposition, such as profound emotional disturbances, grief, care, and excessive physical and mental activity. Whether these influences operate by lowering the resistance to the invasion of the poison or by favoring directly the reception and development in the organs of the body, is as yet shrouded in doubt.

The **mode of living,** which plays so important a part with relation to the development of typhus fever, has by no means the influence upon the development of typhoid fever that was formerly attributed to it. While crowding in small rooms, deficiency of air, light, and ventilation increase directly the capability of infection and dissemination in the case of typhus fever, these influences appear to be operative only conditionally in typhoid fever. In connection with the latter, it is to be noted that defective household-conditions are usually associated also with imperfect drainage and provisions for cleansing, factors that favor the accidental transference of the poison to articles of food, to beverages, and to household-utensils. That typhoid fever, when once developed, may be materially and unfavorably influenced in its course by improper surroundings, as well as by defects in constitution and improper mode of life, is a matter of daily observation. Similar statements may be made in general with regard to social position and occupation. In this respect also a certain contrast to other infectious diseases is to be emphasized.

Typhoid fever is not confined to poverty and misery and the corresponding physical conditions. In densely populated cities—and these constitute the best field for observation in this connection—typhus fever and relapsing fever invade the homes of the poor, asylums and penal institutions, workhouses and jails, and avoid the dwellings of the rich; while typhoid fever fails to recognize these limitations, and occurs as frequently, if not more frequently, among the better classes of society up to the highest circles. The "misère physiologique" affords protection, instead, against the disease. The special relations of occupation to

typhoid fever are to be considered from this standpoint. Among the working-classes the vigorous, young individuals living under better conditions and engaged in more healthful pursuits are with preference attacked. A special predisposition is conferred only by those occupations that necessitate direct exposure to the invasion of the typhoid virus. In this class belong especially those employed about and upon the water, as laborers in harbors and seamen, as well as all whose occupation brings them in contact with patients and their dejections, namely, physicians, nurses, laundresses, disinfectors, and workmen on canals and in sewers. In addition, such occupations and conditions deserve especial mention that necessitate intimate association of individuals physically predisposed in marked degree, as, for instance, internes in hospitals, pupils in schools, soldiers in barracks, etc.

The question of **hospital-infection,** previously referred to, is worthy of more detailed consideration. Its frequency is extreme at different times and in different institutions. The modes of conveyance from typhoid patients to other patients or to healthy individuals can in general be only the same as those under other conditions. Unfortunate accidents, as a result of which the poison given off from the patient, and contained especially in the dejections, gains access directly or indirectly to the mouth and the digestive tract from the hands and the clothing of the nurses, or from infected articles, household-utensils, or from articles of food and drink, play the most important *rôle* in this connection. The frequency with which cases of typhoid fever originate in a hospital can therefore be taken as an index of its hygienic arrangements and the organization of the medical and nursing service. To what extent especial severity of the epidemic or especial personal susceptibility is operative in this connection is not yet clear, but they are not to be wholly ignored.

At times a hospital-epidemic that results from the mistake of a single inexperienced or careless assistant may upset the best hygienic regulations. We have recently had such an unfortunate experience in Leipsic in this connection. In Hamburg, where the hygienic conditions of the hospital are most admirable, I observed in the year 1887, the year of the most severe epidemic, only 21 cases among the inmates of the hospital—about 0.57 per cent. Among these there were only 11 who had previously been patients in the hospital, thus about 0.28 per cent. Among these 11 only 3 had occupied the same ward as other typhoid patients, while the remainder had acquired the disease in the surgical clinic and the skin-clinic, probably through the intermediation of some third person. Murchison's experience in the London Fever Hospital was also quite favorable, as among 10,048 cases of typhoid fever, but 2 were of hospital origin. The experiences of other hospitals have been somewhat less favorable. In the Jacobs-

spital of Leipsic 35 cases—2.15 per cent.—of nosocomial typhoid fever occurred in the course of fourteen years. Here the nurses and the assistants, among whom 28 cases occurred, were placed under far more unfavorable conditions than those under their care. Liebermeister had an almost similar experience, observing among 1900 cases (during the years from 1865 to 1871) 45—2.4 per cent. The experiences of Alexander at the Breslau Hospital were less favorable, 14 cases—3.6 per cent.—of nosocomial origin being observed among 393 patients. The experiences at Kiel were the most unfavorable (Goth[1]), namely, 5.5 per cent.

In the Johns Hopkins Hospital, Baltimore, 20 cases of typhoid fever have originated in the hospital since its opening, eleven years ago. During this time, 1100 cases of typhoid fever have been treated, making the percentage of cases of hospital origin 1.81. Of those infected, 8 were nurses, 3 physicians, 7 patients, 1 orderly, and 1 maid. Four of the 7 cases among patients occurred in one ward at the same time. Three cases of typhoid fever have occurred among doctors and students working in the pathologic laboratory of this hospital. In one case, that of a student, a possible source of infection could be traced to washing test-tubes containing cultures of typhoid-bacilli without previously sterilizing them.

On the whole, my experience shows that in well-conducted hospitals isolation of typhoid patients is not necessary. Only under special conditions, particularly when the administrative arrangements are insufficient, and the relations between the administrative and the medical officers is uncertain, would permanent, or at least temporary, segregation of typhoid patients from the remainder be required.

The action of **cold** and the transitory bodily disturbances referable to it are frequently mentioned as factors favoring the development of typhoid fever. For this there is, however, no positive evidence, and not even trustworthy support based upon experience, which, as will be seen, may be invoked in favor of other contributing conditions. I believe that the growth of the belief that cold favors the development of typhoid fever is the result of confusion with conditions that are themselves a part of the disease. I may mention in this connection the sense of cold and the sweating of the period of incubation, as well as the initial chilliness. Whether the influence of cold in those already infected—that is, in the period of incubation of typhoid fever—accelerates the outbreak of the disease, as appears demonstrated for a number of other infectious diseases, as, for instance, fibrinous pneumonia, is yet doubtful. The cases seem to have a positive significance in which the first symptoms of typhoid fever appeared after a cold bath, or a fall in water, or sleeping in the open air, etc. These cases are, however, by no means conclusive. It must always be borne in mind, for instance, that immersion in infectious water may be followed directly by entrance of the poison into the body and rapid development of the

[1] *Loc. cit.*

disease. In Hamburg I have more than once observed typhoid result from bathing in the infected water of the Elbe, and so far as my influence reached I have warned against all contact with this water.

Relations between Typhoid Fever and Still Existing or Antecedent Diseases.—In the first place, the acute infectious diseases are deserving of consideration in this connection. The existence of one of these, particularly at the febrile period of the disease, appears to protect with considerable certainty against infection with typhoid fever. I am unable to record an observation, either clinical or anatomic, opposed to this statement. I have exceptionally observed typhoid fever during convalescence from an acute infectious disease. Nevertheless, I have gained the impression that the patients under these conditions also are immune to a certain degree. At any rate, they appeared to me the more susceptible the further removed in time they were from the febrile stage of the antecedent disease.

In accordance with the view already mentioned, according to which well-nourished and robust individuals are more readily attacked than those in a reduced state, it is probable that when nosocomial typhoid fever occurs shortly after convalescence from antecedent infectious disease, the attack often assumes a milder or less profound character. In the latter connection mention may be made especially of angina simplex and rheumatic polyarthritis. Extensive observations on the part of others in this connection are not recorded. These would be very valuable, as only large statistics would be conclusive.

It has been asserted by some observers—assuredly not correctly—that epidemiologically small-pox and scarlet fever exhibit a certain antagonism to typhoid fever. This has been used as a weapon by the opponents of vaccination (Gressot,[1] Carnot[2]), who advanced the view, based upon superficial observation, that the repression of small-pox favors the development of typhoid fever. Also the opinion now and again expressed that malaria and typhoid fever are antagonistic to each other has not been confirmed. I have myself observed malaria and typhoid fever in the same place upon the Rhine.

Three cases of mixed infection with the malarial parasites and B. typhosus have occurred in the Johns Hopkins Hospital among about 1100 cases of typhoid fever treated, Lyon,[3] who has reported one of these cases, has collected 29 undoubted cases, besides numerous other cases in which the evidence was not so conclusive. He concludes that in tropical countries, where malarial fever is endemic and typhoid fever prevalent, it seems entirely probable that cases of combined infection are common.

[1] *Edinb. Med. Jour.*, July, 1855. [2] *Rev. de méd.*, 1856.
[3] *Johns Hopkins Hosp. Rep.*, vol. viii.

Among the chronic infectious diseases pulmonary tuberculosis has often been spoken of in this connection, tuberculous patients being on the whole looked upon as protected. Also, according to my experience, individuals in the middle and especially in the advanced stage of pulmonary tuberculosis are quite rarely attacked by typhoid fever, and this is the more noteworthy because such patients generally remain in the hospitals for a long time, and therefore are with relative frequency brought into contact with typhoid patients. It is my impression, however, that in this connection no specific condition of the body is to be taken into consideration, but that the emaciation of the patient is the important factor, for patients suffering from other chronic affections of various kinds, from malignant neoplasms, chronic constitutional diseases, and especially diabetes, are scarcely ever attacked with typhoid fever, in spite of frequent exposure to infection. In harmony with this view is the fact that well-nourished, afebrile tuberculous patients or individuals with latent tuberculosis are by no means immune to typhoid fever. Every experienced clinician will have had some gloomy experiences with reference to the development of tuberculosis or the rapid progress of previously recognized circumscribed infiltration of the lungs during the course of typhoid fever. Also the other chronic diseases of the lungs, emphysema and chronic bronchitis, as well as bronchiectasis, appear to behave, with relation to the liability of infection, in accordance with the age and general physical condition of the patient.

Chronic diseases of the nervous system, in so far as they occur in individuals within the predisposed period of life, and, as so often happens, for a long time do not injure the constitution, afford no immunity to typhoid fever. The statement that dietetic error with secondary gastro-intestinal catarrh gives rise to typhoid fever is no longer a matter for discussion at the present day. The view, conceivable from an earlier etiologic standpoint, is based upon an incorrect interpretation of various observations. Thus, it is certainly not uncommon for the first symptoms of typhoid fever to be confounded with those of simple gastro-intestinal catarrh. The danger is especially great with reference to cases of walking typhoid fever, whose true nature is often only first recognized when the patient is compelled to go to bed after a relapse attended with high fever. On the other hand, it can be readily understood that dietetic errors with their consequences may favor the lodgement and the development of the contagium, and it is not improbable that it may accelerate the outbreak of the disease in individuals already infected. Support for this view is afforded by the observation that

the occurrence of relapses and recrudescences is not rarely directly related to dietetic errors.

The predisposing influence of acute and chronic diseases of the stomach is probably dependent upon the alteration in hydrochloric acid secretion to which they give rise. According to observations made in other infectious diseases invading the body through the digestive tract, this was to have been anticipated. Although, as has been mentioned, the typhoid-bacilli are relatively more resistant than other pathogenic micro-organisms to the action of the gastric juice, it cannot be doubted that transitory or protracted absence or considerable diminution in the free hydrochloric acid materially favors their safe entrance into the intestinal tract. Theoretically, it may, on the other hand, be assumed, although practical evidence in favor of this view has not yet been presented, that gastric disorders attended with hyperacidity afford relative protection against the typhoid-bacillus. Certain observations that Bouchard and his pupil Le Gendre[1] emphasize may be in accord with the changes in the qualities of the gastric juice and in the character of the gastric contents. They believe the statement justified (Le Gendre) that about 60 per cent. of all typhoid patients have previously suffered from dilatation of the stomach. As patients with chronic dilatation of the stomach generally exhibit marked alterations in the gastric juice, particularly absence or deficiency in free hydrochloric acid, an explanation for the statements of those observers may be found in this circumstance. I feel compelled, however, on the basis of my own clinical and anatomic observations, to deny these statements emphatically. These have shown that the coincidence of dilatation of the stomach and typhoid fever is by no means especially common. I am unable to confirm also the further statement of Bouchard and Le Gendre that typhoid fever, on the other hand, not rarely causes dilatation of the stomach in previously healthy persons.

Repeated Attack; Immunity.—Whether there are individuals possessing congenital immunity to infection with the typhoid poison has not yet been determined. At all events, this is extremely rare, perhaps even less frequent than is known to be the case for other infectious diseases, particularly the acute exanthemata. On the other hand, it is a firmly established observation that recovery from one attack of typhoid fever confers relative protection from subsequent attacks of the disease. Even older observers (Bretonneau, Chomel, Louis, Budd, Jenner, Murchison, down to Griessinger) are in agreement as to this fact; but they as well as all more recent observers properly emphasize the fact that the immunity acquired by recovery from an attack of typhoid fever is not so protracted as has been shown to be the case for most acute exanthemata, including typhus fever. It is certain that in many persons it does not extend throughout the whole of life. Whether a severe attack of typhoid fever confers more marked or more protracted protection than mild cases is unknown. This would not be in accord with the experiences in other infectious diseases, and also with some recent experi-

[1] *Dilatation de l'estomac et fièvre typhoïde, etc.*, Thèse, Paris, 1886.

mental observations. According to my own experience, two attacks of typhoid fever in the same person are by no means rare. There are even individuals who have had three or four attacks during their lives. Such an occurrence naturally is a rare exception.

Among 1888 patients examined with great care in regard to this point during the epidemic in Hamburg in 1887, there were 54 in their second attack—2.4 per cent. One patient was with certainty in his third attack. Among these 54 patients there were 15 who, during the first attack of typhoid fever, also had been treated in the General Hospital, and the diagnosis could be verified from the preserved histories and temperature-charts. In the remaining 39 the statement was accepted only when the evidence was most positive.

Typhoid fever presents a noteworthy difference from the acute exanthemata in the fact that complete immunity does not exist, as in the latter, during the first period after the disease, and that progressive diminution does not subsequently take place in proportion to the time elapsing after the first attack. On the contrary, I have observed individuals attacked for a second time before the end of the first year or within a few years after recovery from typhoid fever.

I have reliable records upon this point in 46 cases in which a second attack occurred. These show that in 30 the second attack of typhoid fever occurred before the lapse of ten years. In the 15 cases in which both attacks were treated in the General Hospital, the intervals were as follows: nine months in 2 cases; one year in 4; two years in 2; three years in 1; four years in 3; five years in 2; thirty-nine years in 1.

In the case under observation in which 3 attacks occurred, the first 2 likewise had followed in quick succession. The patient was a man, forty-seven years old, who had lived in Hamburg from the year 1877, and was first seized with a severe attack of typhoid fever in the winter of 1877–78, and was attacked for the second time in the year 1879. The third and by far the mildest of the three attacks occurred in the year 1887. All of the attacks were treated in the General Hospital. Probably this patient had even had an additional attack of typhoid fever in the year 1856; at least he stated that he was at that time under treatment in Altona for three weeks for "gastric fever."

Observations of the repeated occurrence of typhoid fever in the same individual have been reported from various sources. The figures agree in general with my own. Thus, Goth in Kiel has noted two attacks in 2 per cent. of his cases, Beetz[1] in 1.8 per cent., and Freundlich[2] in 2.2 per cent. A high percentage is noted by Eichhorst,[3] who has given especially careful and exhaustive consideration to the subject. Among 666 cases of typhoid fever, he found 28—4.2 per cent.—in which two attacks had occurred. Also, he observed cases in which there had been

[1] *Deutsch. Arch. f. klin. Med.*, Bd. xvi. u. xvii. [2] *Ibid.*, Bd. xxxiii.
[3] *Virchow's Archiv*, Bd. cxi.

three and even four attacks, as also Quincke[1] and Goth[2] 1 case each in which there had been three attacks.

With regard to the intensity of the second and, in general, of any subsequent attack of typhoid fever, this need not, according to my experience, be less than that of the first attack. On the contrary, there have been among my cases some in which the first attack was mild, while the second was so severe as to terminate fatally. This is in accord, on the whole, with the every-day experience that relapses and recrudescences may be more severe and more protracted than the primary attack. In this respect also there is a certain contrast with the behavior of the acute exanthemata, as a type of which variola may again be mentioned. It is known that second attacks of this disease are almost invariably much less severe than the first attack.

All of the foregoing facts have been learned from and are based upon empiric observation. With increasing knowledge of the vital activities of the pathogenic micro-organisms, a better insight into the nature of immunity has been gradually obtained both theoretically and experimentally. Although certain definite and in some respects conclusive results have been reached with regard to a number of acute infectious diseases (tetanus, diphtheria), and which have even borne brilliant fruit from a practical point of view, this aspect of the question with regard to typhoid fever is still unsettled. It may be considered as demonstrated in this connection (R. Stern[3]) that the blood-serum of convalescents from typhoid fever continues to possess for some time the property of protecting experimental animals, especially mice, from the deleterious effects of typhoid cultures. It has also been possible to immunize animals to the action of the typhoid-bacillus by means of filtered or unfiltered typhoid bouillon-cultures; and it has also been found that the blood-serum of such immunized animals is in turn capable of immunizing other predisposed animals.

By means of an elaborate series of experiments, Pfeiffer and Kolle[4] have also shown that the blood-serum of typhoid convalescents contains substances which, when the serum in very small amounts, together with a culture of the typhoid-bacillus, is injected into the abdominal cavity of a guinea-pig, have marked bactericidal properties. These substances are the specific "anti-bodies," corresponding to those described by Pfeiffer in immune cholera-serum. They[5] later showed that similar "anti-bodies" could be produced in the serum of normal men by inject-

[1] *Deutsch. Arch. f. klin. Med.*, Bd. xxxix. [2] *Inaug. Diss.*, Kiel, 1886.
[3] *Deutsch. med. Woch.*, 1892, No. 37. [4] *Zeit. f. Hyg.*, Bd. xxi.
[5] *Deutsch. med. Woch.*, Nov. 12, 1896.

ing them with dead typhoid-bacilli of high virulence. A certain amount of reaction was caused by the injection, following which the serum showed marked bactericidal and agglutinative properties.

Similar results were obtained by Wright and Semple,[1] under whose direction this method of preventive inoculation has been practically employed to a very considerable extent in India and in the South African War. The results so far obtained appear very promising. All of these results have shown that immunity in typhoid is like that in cholera—it is due to the production of bactericidal substances in the blood, and not to the production of antitoxins. At present there is no evidence that antitoxic substances are ever formed.

EXTERNAL, NOT INDIVIDUAL, INFLUENCES.

Local Conditions; Geographic.—At a time when a spontaneous development of typhoid fever was still believed in, or, at least, when the opinion was held that the preservation, maturation, and dissemination of the specific contagium were dependent upon the earth and air, much greater and even decisive significance was attached to the local conditions. At that time it was believed that the poison was constantly present, undergoing a sort of storing up and constant reproduction in certain cities and entire regions. From this point of view, suspicious houses, streets, localities, and cities were spoken of. It was believed that here only general influences of season, temperature, water-level, especially of the ground-water, often in association with contemporaneous excavations of the soil and the construction of sewers, were necessary in order to render the stored-up poison active throughout the community. At the present day it is known, on the other hand, that the so-called local predisposition is scarcely dependent upon the constant preservation and reproduction of the poison in certain places, but upon the fact that certain conditions, temporarily or permanently peculiar to such places, are capable of rendering active temporarily, and of disseminating, the contagium arising locally from the typhoid patient or imported from without. To be taken into consideration especially are conditions that facilitate the dissemination of the poison and its conveyance to the human body through the digestive tract. It is obvious from previous considerations that here again the condition of the water-supply of a place is of utmost importance. In this matter the relations between the subsoil and the water-supply are naturally of importance, and from this point of view every physician should

[1] *Brit. Med. Jour.*, Jan. 30, 1897.

make himself familiar with the conditions of the soil and the ground-water of a place, especially in its relations to the wells and other sources of water-supply.

There have been made in this connection numerous valuable investigations bearing upon the differences in the permeability of the soil and upon the mode and the direction in which the specifically contaminated ground-water is conveyed. Not less numerous studies refer to the occurrence of the disease in places where the water used for drinking and for household purposes was derived not from wells, but from a distance through conduits, springs, and other waterways. Under such conditions the danger of contamination of the water with typhoid-bacilli during transmission is especially to be considered and investigated. It should particularly be established whether the water-supply is conveyed through conduits that are everywhere closed and protected in greater or lesser degree against the entrance of foreign bodies, or is derived from open water-courses. In the latter event the sanitary condition of the people dwelling in proximity to the stream, and the character of their industries, play a *rôle* that can be accurately estimated.

In addition to the local peculiarities just described, a number of general conditions are of great importance, especially the density and the character of the population, the food-supply, as well as other vital and special sanitary conditions. Also, the amount and the character of the commerce are of great importance with regard to the possibility of dissemination of the typhoid poison. In a word, there must be taken into consideration a large number of varied conditions, in part well known, in part still but little investigated and with difficulty estimated according to their importance, but which in all possible local and temporal combinations exert a marked influence. At the present day the etiology of typhoid fever in certain places and localities cannot be as easily and systematically laid down as appeared possible at the time when the ground-water-theory flourished.

How little bearing locality itself and its general atmospheric and climatic conditions have upon the etiology of typhoid fever is demonstrated by the general distribution of the disease over the entire world, and therefore including localities that exhibit the most violent contrast with regard to the conditions named: typhoid fever is present at a considerable elevation and at sea-level, in northern regions and in the tropics. It occurs wherever the reproduction and dissemination of the imported specific contagium are not prevented by local conditions; and although these are most variable in degree, with the aid of unfavorable accidents, they appear nowhere capable of preventing entirely the development and dissemination of the disease. Thus, it is always an unfortunate occurrence for the adherents of the localization-theory when the disease is suddenly imported into a place previously immune, and

when conditions favoring its dissemination, and previously, of course, not taken into consideration, make themselves actively manifest.

With regard to the special geographic distribution of typhoid fever, the works of Murchison, Hirsch,[1] and of Griessinger, who had very wide experience, give the best information. Typhoid fever prevails throughout Middle, Southern, and Northern Europe. The disease is encountered in Spain, in Turkey, in Italy and Greece, in Northern Russia, and in the Scandinavian cities. In England and in a number of countries of Eastern Europe it occurs endemically in the same places as typhus fever, a circumstance that, especially in England, prevented for a long time the clinical differentiation of the two diseases. Numerous reports have been made from North America, Central America and South America, from Mexico, Brazil and Peru, from Asia, especially from India and from the large islands of Java, Sumatra, Borneo, etc., as to the endemic occurrence and temporarily increased prevalence of typhoid fever. It has been observed also in Africa as far as communication has been established, particularly upon the east and the west coast, among the natives as well as among Europeans. Griessinger long ago proved, in a manner that must forever serve as a model for similar investigations, the endemic occurrence of typhoid fever in Egypt.

Apparently, the warm and tropical countries do not differ greatly from cold regions with reference to the occurrence and frequency of typhoid fever. Epidemics of typhoid fever have been observed even upon high mountains, in places more than 1000 meters high. The epidemic upon the great St. Bernard and in the valleys radiating from it, also cited by Griessinger, is well known. At that time one-third of all of the monks in the monastery at that place were attacked.

Apart from the ability of the typhoid-bacillus to become lodged and develop in any locality, and its not inconsiderable tenacity, the wide distribution of the disease depends further upon the apparently equal susceptibility of all races to it. In this regard also typhoid fever exhibits a contrast with other infectious diseases, since to these there are marked variations in racial susceptibility.

It should be mentioned that persons who have recently removed to a so-called typhoid locality or have resided in such a place but for a short time are, as numerous observations have shown, attacked with especial readiness. Such observations have been made in Paris and London by Louis, Chomel, Jenner, and Murchison. The physicians of Vienna, and especially those of Munich, have had a similar experience. An explanation for these undoubted facts is as yet wanting. Formerly,

[1] *Hist. geogr. Path.*

a sort of "acclimatization" was offhand considered as a prophylactic against the disease. As unsupported as this assumption has always been, it has become entirely untenable in the light of recent knowledge. Various conditions must be taken into consideration in the explanation. In the first place, the new, unusual mode of life for newcomers, often differing greatly from the previous mode of life, and so favoring the digestive diseases predisposing to typhoid infection, is of importance. In the next place, it must be borne in mind that the newcomer is in greater degree exposed to the danger of taking up the poison, because, unlike the natives, he has not been taught by experience against partaking of dangerous things. In this connection the drinking-water and articles of food eaten in the uncooked state are to be mentioned—in southern countries, for instance, raw fruit, oysters and other shell-fish. Too little importance should not be attached to the circumstance that among the newcomers there will be many with a marked personal predisposition. With regard to transitory residence or increase in population in a place, healthy, young, and adolescent persons, travellers, mechanics, laborers, servants, etc., are especially concerned.

"Acclimatization-diseases" are often spoken of, particularly diarrhea, by which newcomers in a typhoid place are attacked. It is not improbable that these are often dependent upon typhoid infection.

Cases of Typhoid Fever received into Jacobsspital, of Leipsic, from 1880 to 1892.

Year.	1880.	1881.	1882.	1883.	1884.	1885.	1886.	1887.	1888.	1889.	1890.	1891.	1892.	Total.
Jan.	9	10	12	6	12	21	9	3	2	10	10	9	9	122
Feb.	7	4	8	3	17	14	7	8	3	8	3	10	3	96
March	5	8	12	5	13	11	4	10	1	3	8	14	5	97
April	3	8	2	10	15	10	7	2	5	2	7	6	8	78
May	11	3	2	4	5	11	4	1	6	5	3	6	4	71
June	5	10	3	8	2	6	3	4	19	1	5	4	9	75
July	6	17	6	21	6	10	8	12	8	22	14	10	9	136
Aug.	13	37	10	16	21	16	14	18	8	46	25	15	8	252
Sept.	24	29	18	20	19	9	16	15	4	33	26	13	16	240
Oct.	17	21	5	11	10	5	23	16	9	30	18	12	7	193
Nov.	9	27	6	13	8	4	9	7	7	23	11	10	17	150
Dec.	4	4	4	4	10	3	6	7	10	11	7	7	2	88

Season and Meteorologic Conditions.—Typhoid fever exhibits a constant and for many countries a uniform relation to the seasons. Upon the continent of Europe, in England, and in countries presenting similar conditions, as, for instance, North America (Bartlett, Wood, Flint), there prevails, so far as reports go, remarkable unanimity in this regard. Everywhere the increased frequency occurs during the late summer and autumn months. In especially severe and widespread epidemics it persists or increases even into the winter, until November

and December. From this time there is almost always a slow or a more rapid decline. The period of least prevalence of typhoid fever is everywhere the spring and the beginning of summer, especially the months of March, April, and May.

In Leipsic, as the accompanying diagrammatic representation of the cases observed in the Jacobsspital between the years 1880 and 1892 shows, the months in which the largest number of cases occurred were invariably August, September, and October. November also exhibited on the average high figures. The lowest prevalence in Leipsic occurs in the months of April, May, and June. In July the increase, however, generally begins again, and it continues uninterruptedly to its acme during the autumn months (Fig. 4). A table showing the number of cases received during the different months and years is added. This is extremely interesting from the general uniformity in the conditions during the different years. Also in Dresden, according to the observations of Fielder,[1] extending over eleven years, the months of April and May exhibit the least frequency of typhoid fever, while August and September show the highest, while a greater number generally occur in the winter months than in June and July. A striking similarity to these observations is exhibited by the conditions in London as described by Murchison for the admissions to the London Fever Hospital between the years 1848 and 1862. I have prepared a diagram on the basis of his statements (Fig. 5). In its details the London

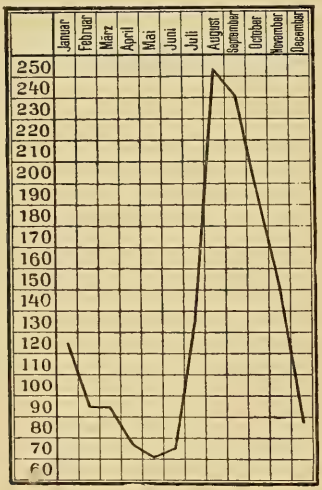

FIG. 4.

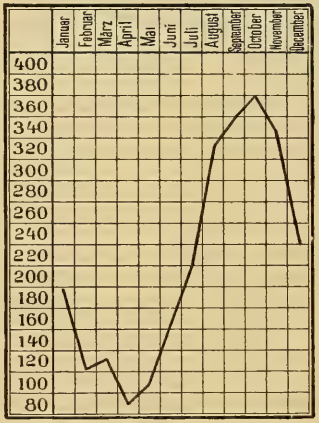

FIG. 5.

diagram as compared with that of Leipsic exhibits a reduction in frequency during the winter months from the maximum of the autumn months, although the number is still quite large during the month of December. This relation appears to exist especially in those places, and almost everywhere in those years, in which the ascent of the curve begins somewhat later and the maximum is reached correspondingly later (in London September and October, as compared with August in Leipsic). The epidemic of

[1] *Loc. cit.*

1886–87 in Hamburg is instructive in this connection, the rapid increase in the disease occurring during the months of September and October, and accordingly the months of November, December, and January exhibiting the maximum prevalence (Fig. 6).

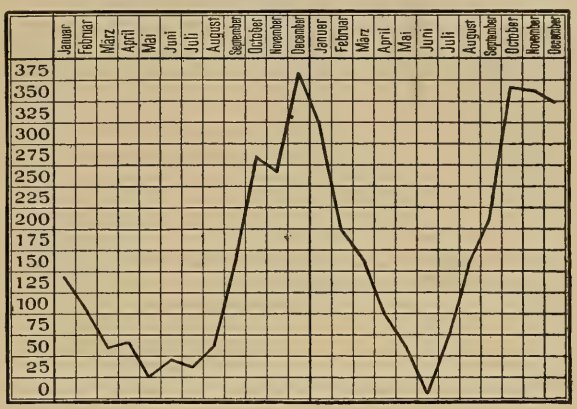

FIG. 6.

The causes for this remarkable uniformity in the relations of typhoid fever to season are as yet wholly unknown. The universality of the relation, its recurrence in all possible, remotely situated regions, indicate that it is dependent not upon local, but upon general conditions, possibly such as are responsible for the power of multiplication and the vital activity of the typhoid germ itself. Although much is known with regard to the details in this connection, an insight into the solution of general questions is wanting, particularly the relation of the poison to important cosmic conditions. It is, therefore, better for the present to leave a glaring deficiency rather than to bridge it over with unstable theories.

With relation to the influence of weather and temperature in the etiology of typhoid fever there is much diversity of opinion among writers, and there exists by no means unanimity with regard to season. In my opinion there are no fixed laws in this regard. Too much importance has certainly been attached to isolated impressions and observations in some endemics, and premature generalizations have been made. In general, it may be said that in most localities summer heat and dryness render probable an increase of typhoid fever in the autumn months—an observation that is in accord with the theory of Buhl and Pettenkofer and led up to the ground-water theory. Whether dampness and cold weather operate in an opposite direction is still doubtful. Careful observers, on the other hand, have attempted to attribute the development and the increase of the disease in some places to these

latter conditions. As a matter of fact, it is readily conceivable that the virus accidentally deposited upon the surface of the earth or in the upper layers of the soil may be carried off by rain-water or melting snow, and be disseminated by finding its way into water-conduits or wells.

Occurrence of the Disease in General.—Sporadic Cases; Endemics and Epidemics.—After having considered the etiologic relations in detail, and having presented an enormous mass of individual experiences and facts, a few words with regard to the general character of the disease and its general manifestations will be appropriate. In this connection also marked differences from other infectious diseases are apparent, especially from the acute exanthemata, particularly the true pestilences—small-pox, typhus fever, cholera, and plague. As has been mentioned, these are generally confined to definite portions of the earth and to certain countries in which, like a fire smouldering beneath the ashes, they occur constantly, but within narrow limits, and then, from time to time flaring up, they extend over great distances and areas. The pestilences included in the acute exanthemata—variola and typhus fever—are also little dependent upon the season of the year or upon the age. Typhoid fever, as has been seen, is, on the contrary, distributed over the entire world. Being rather dependent upon the individual and the activity of human intercourse, it almost never disappears in populous cities, while in the country it is generally absent or occurs but occasionally.

In further contrast with the exanthematous infectious diseases, typhoid fever generally occurs in sporadic cases or in groups of cases, occurring in dwellings as house-epidemics, or occasionally spreading throughout entire streets, if the conditions for conveying the infecting agent are accidentally thus uniformly distributed. By the juxtaposition of such disease-foci, or less commonly from the outset, owing to most favorable modes of dissemination—water-conduits, streams—actual epidemic distribution of the disease may result. In no instance, however, does rapid dissemination to neighboring countries or throughout the entire world take place from such a focus even though it is of considerable or of large size, as is the rule with typhus fever, cholera, and plague. Typhoid fever always maintains a tendency to local limitation, and this may be altered only by special conditions. This tendency can be readily explained; it is a necessary result of certain characteristics of the typhoid germ, which, as has been seen, is not easily transmitted, but only exceptionally is carried through the air, and then only for short distances, so that merely being near the patient, without contact, is

free from danger for even highly predisposed persons. Only by direct conveyance of the poison or conveyance through the intermediation of a third person, and then only by way of the digestive tract, is the disease transmitted. All of these facts were long ago given expression to in the circumstance that typhoid fever was not included among the "contagious" diseases, but received the designations "miasmatic" and "contagious miasmatic," which, according to existing views, are no longer permissible.

CONCLUSIONS.

The foregoing considerations have, it is hoped, shown that the etiology of typhoid fever appears at the present day in quite different light from that in which it was viewed in prebacteriologic times. It will be useful to summarize what has thus far been rendered certain or probable.

The development and the manifestations of typhoid fever are dependent upon the lesions in the human organism resulting from the invasion and the vital activity of the Eberth-Gaffky bacillus. The typhoid-bacillus is not identical with Bacillus coli. The relations that exist between the two micro-organisms, and their degree of relationship, must be established by further investigations. The growth and the development of the typhoid-bacillus take place exclusively in the body of the typhoid patient. The germs are thrown off especially with the intestinal discharges and urine of the sick, and give rise to new cases of the disease principally by gaining entrance in a viable condition through the mouth and the stomach into the intestinal tract of predisposed individuals. The entrance of the virus through the air-passages cannot be wholly excluded, but it is in general of subordinate importance. It is for this reason that mere presence in the vicinity of the patient, such as suffices for infection with the acute exanthemata, is not adequate for infection of even the most predisposed individual in the case of typhoid fever.

Typhoid fever does not belong to the "contagious" diseases in the older significance of the term. The typhoid virus is conveyed directly from the patient and his dejections or through household-articles and healthy third persons—nurses, attendants, etc.; or by reason of its marked tenacity it remains, under the most varied external conditions, attached to various media and for a long time, in a state of vitality, in order later to gain entrance into the human being, directly or indirectly. Typhoid fever may be conveyed for great distances by means of the sick themselves or by germ-laden media. The belief that the bacillus after leaving the body requires further development and maturation outside the body is untenable in the present state of knowledge.

The principal carrier and disseminator of the typhoid germ is water. Dissemination of the typhoid germ in the dry state, attached to particles of dust, through the air is possible but uncommon. The opinion formerly held that typhoid fever results from the swallowing or inhalation simply of putrid gases has been wholly abandoned. Deposited in the earth, the typhoid germ may remain capable of development for a time, to be spread from this point through various accidental conditions, among which entrance into subsoil-water, well-water, or flowing water plays the most important part. A local predisposition in the sense of constant impregnation of the earth in a given locality with the poison and maturation therein cannot be accepted, and still less the penetration of the poison into the ground-air and infection of the neighboring people by exhalations from the earth.

The susceptibility to typhoid fever is exceedingly widespread. No race is exempt or, so far as experience teaches, materially less predisposed. Typhoid fever has been observed in all civilized countries of the earth, in the most varied climates and altitudes. Young persons and adolescents principally are predisposed to the disease, and robust and well-developed individuals in general more so than the weak and those debilitated by disease. Children under the age of one year are attacked with extreme rarity. After the fortieth year of life the frequency declines rapidly. Sex in itself has no marked influence. Possibly men, in consequence of social and other conditions of life, are more greatly exposed to the possibility of infection, and therefore are more frequently attacked.

Recovery from one attack of the disease affords in the majority of cases protection from subsequent attacks throughout the remainder of life. A number of individuals are attacked a second time. The occurrence of three or four attacks in the same person is most exceptional. Almost everywhere, especially upon the continent of Europe and in England, the majority of cases of typhoid fever occur in the latter part of the year—in the late summer, the autumn, and the early winter months. In contrast with the true pestilences, typhoid fever has a tendency to confine itself locally, so that it commonly occurs in sporadic cases and groups of such cases—house-epidemics and street-epidemics —and under special conditions it may be distributed over an entire city or locality.

II. PATHOLOGY.

GENERAL SYMPTOMATOLOGY.

Few acute infectious diseases exhibit such great variations as typhoid fever in their manner of onset and their course. One may see the mildest attacks, lasting only a few days, scarcely compelling the patient to take to his bed, even scarcely attended with appreciable fever, as well as severe attacks, lasting many weeks or even months, with high fever, most profound general and local manifestations, and in certain cases long protracted convalescence; and if, together with this protracted type of disease, other cases are observed in which the disease, setting in with unusually severe manifestations from the outset, rapidly attains an alarming intensity and progresses uninterruptedly to death, the question will repeatedly arise in the face of such diversity of manifestations: Are they to be referred to a common cause? It cannot even be said that age, sex, or the general condition of the body exerts a definite influence upon the course of the disease. Both in general and in detail, factors of an uncertain character are here to be dealt with, among which possibly the intensity of the infection, certain peculiarities of the virus, and the predisposition of the infected individual play an important part. Accordingly it is not possible to give a general description of the course of typhoid fever. It will, however, be useful, in connection with the further discussion of the subject, to sketch in outline the picture of a moderately severe or severe case of typhoid fever terminating in recovery in a previously healthy adult. In connection with this description the pathologic anatomy and symptomatology of typhoid fever will be described, and then an attempt will be made to consider the various forms of course in so far as they have theoretic and practical significance.

Period of Incubation.—From the moment of entrance of the germ into the body to the beginning of the morbid manifestation to which it gives rise, a most variable period of time appears to elapse in a case of typhoid fever. It is, therefore, far more difficult to determine the period of incubation than in the case of some other acute infectious diseases, as, for instance, the acute exanthemata. Even the time when the contagium is received can but rarely be established, as this is not effected by mere presence in the neighborhood of the patient or simple contact with him, but by processes that are not susceptible of direct observation. Nor are the conditions more favorable with regard to a

precise determination of the end of the period of incubation and the beginning of the actual disease, the dividing-line between which is usually indistinct. Even the beginning of the fever, which in general is stated to be the most reliable sign of the beginning of the actual disease, is subjectively often so little marked that even intelligent patients make uncertain statements in connection therewith.

Taking all of this into consideration, the duration of the period of incubation can be stated, according to my experience, to be from one or two to three weeks. The cases are worthy of little credulity, and in any event are susceptible of varying interpretation, in which only a few hours elapse between infection and the beginning of the disease. The observation of a greatly prolonged period of incubation appears to me to be more probable. Every experienced physician has observed cases in which, many weeks before the outbreak of typhoid fever, general malaise existed that upon most careful examination could not be referred to local disease, and in which the patients dragged themselves about and felt as if something were wrong. Such ill-defined languor and indisposition in the presence of normal bodily temperature and absence of local manifestations are usual in the period of incubation of typhoid fever, in contrast with similar periods in other infectious diseases, as, for instance, the acute exanthemata already mentioned, which generally give rise to no manifestations during this stage.

An attempt has been made to divide the period of incubation of typhoid fever into a stage of complete latency and a true prodromal stage —that is, the period of indefinite bodily disturbances. This is pedantic and useless. It is best to say that the period of incubation is, as a rule, occupied wholly or in part by morbid manifestations, while a smaller number of individuals infected with typhoid germs may remain entirely free from symptoms during this period. An estimate of from 5 to 10 per cent. for the latter group will probably not be too high.

Among the principal manifestations of the period of incubation, languor, a sense of drawing in the extremities, headache, sacral pain, disturbed sleep, at times with night-sweats, may be mentioned. The appetite is generally impaired, nausea is present, the patients complain of a sense of pressure in the epigastrium, and often the bowels are constipated, although diarrhea also may be observed at this stage. Previously healthy, strong, and energetic persons continue wholly or in part in the pursuit of their work, and even women may continue in their activity. Observations of the bodily temperature at this time disclose no or but slight deviations from the normal, even in such patients as already exhibit increased susceptibility to temperature-

variations and are readily chilled on going into the open air or getting into a cold bed.

The actual commencement of the disease dates from the time when the patients exhibit the first marked febrile symptoms. Among all of the signs of the beginning of the disease these can be best determined objectively. Although some clinicians date the beginning from the time of going to bed or the appearance of diarrhea, this is indefinite and arbitrary. The duration of the morbid manifestations in well-developed cases is generally from three to six weeks. This period of the disease has been divided into various stages, namely, that of invasion and advance, that of acme, and that of subsidence of the symptoms of the disease. Often a classification is made according to weeks, based upon the clinical and the associated anatomic manifestations, but which therefore can be only grossly accurate because the latter appear at different times. Thus are placed the development of the typhoid lesions, with their symptoms, in the first week; the acme of the disease, with the completion of intestinal ulceration and exfoliation, is assumed to occur in the second and third weeks; while the fourth week is considered that of the healing of the anatomic lesions and of beginning convalescence.

In contradistinction to other infectious diseases, the beginning of the febrile stage of typhoid fever is generally marked by slight, often repeated chilliness. This is so much the rule that when a febrile disease begins with a single severe chill almost any other disease than typhoid fever is thought of. It is known that the absence of chill is to be referred to the gradual beginning and the slow ascent of the fever. Although not a few patients still hold out bravely, the majority generally take to their bed after the first chilliness.

The general sense of illness now increases pretty rapidly, and also the objectively demonstrable weakness of the patient. This usually corresponds with the increase in the fever, which at the end of the first week may give rise to elevation of the bodily temperature to 40° C. or over during the evening. The pulse is generally full, of good tension, and regular, but accelerated. In young, previously healthy men, and even in those in middle life, the increase in pulse-frequency is generally relatively not so great as the elevation of temperature, while in women and children the pulse-rate is greatly increased and appears proportional to the elevation of temperature. Toward the end of the first week the pulse is often already dicrotic. With the exception of children and the aged and previously debilitated individuals, the patients appear completely sensible during this period. They complain of headache, vertigo, roaring in the ears, with a sense of intense languor, and they are

often unable to secure a comfortable position in consequence of pain in the sacral region and the extremities. Food is often declined, while intense thirst is generally present. The tongue, at first still moist, heavily coated, yellowish white or brown, and also the mucous membrane of the lips and the mouth, exhibit a tendency to dryness toward the end of the first week. The not infrequent occurrence of epistaxis at this time is quite distinctive, and in some patients this may occur during the period of incubation. The facial expression of the patient is from the outset apathetic, the features relaxed, the cheeks reddened, and the skin feels hot and dry. Only during the first few days of the fever does slight sweating still exceptionally take place, especially during the night.

During the first week there are generally slight manifestations on the part of the respiratory organs. A number of patients will at this time exhibit a dry, short cough, while this is absent in others at first. Susceptible patients, it is true, complain now and again of increased difficulty in breathing. Objective examination of the lungs generally discloses nothing to account for this, although here and there dry râles may be audible.

In the majority of cases the abdomen is at first of normal form and not distended. Exceptionally, some meteorism becomes apparent toward the end of the first week. The epigastrium is not rarely tender on pressure, while palpation in the right iliac fossa does not elicit any expression of pain. In the majority of cases the bowels are normal or constipated. Less commonly there have been a few loose stools, while diarrhea alone in the first period appears to be less frequent. During the last days of the first week some patients complain spontaneously of pain and heaviness in the left side. In others increased sensibility is discovered only on palpation, and is dependent upon beginning enlargement of the spleen.

Toward the close of the first week the patient begins to approach the acme or fastigium of the disease. During the following week and beyond, the condition is comparatively severe. From the anatomic standpoint the stage is that of completed medullary swelling of Peyer's patches and the solitary follicles and the associated and progressive necrosis. The fever, after a step-like ascent during the first week, reaches its highest point at the beginning of the second week, or it rises to a slightly higher level up to the middle of this week. The temperature-curve for a period of a week or a week and a half pursues the course of a remittent continued fever, the variations between morning and evening temperature scarcely exceeding the normal. In milder cases, it is true,

the daily variation may now be more considerable, and give rise to an intermittent type of fever; while, on the other hand, in cases of especial severity, abnormally slight variations may result for days in an almost pure continued fever. With regard to the degree of temperature itself, this in cases of moderate severity will rarely be less than 39° C. in the morning. It may reach 40.5° C. at mid-day, and in the evening it may often rise still higher, up to 41° C. and even above.

With increase of the fever the complaints of the patient gradually cease. He lies in an apathetic, stuporous state, and, although at first, in so far as beginning impairment of hearing permits, he sluggishly responds to questions, it becomes increasingly difficult to maintain his attention. Fortunately, he now enters a state of narcosis. Should new complaints arise at this time, or should previous pains increase in intensity, complications should be looked for.

During the day the patients seldom sleep deeply. Generally, they lie with open or half-closed eyes, in a flaccid dorsal decubitus. The hours of greatest elevation of temperature are often occupied by delirium. The facial expression gradually becomes drawn, and the previous redness is replaced by pallor with slight cyanosis. The mouth is half-open; the upper lip retracted, so that the upper teeth, covered with a fuliginous deposit, are exposed. The lips are dry, covered with dark crusts, and readily bleeding from slight fissures. The tremulous tongue exhibits the same appearance, and toward the end of the second week it becomes small and thin from exfoliation of crusts and epithelium, with a smooth, red surface and persisting dryness. Viscid, brownish, sanguinolent, often desiccated mucus adheres to the reddened pharyngeal mucous membrane, the soft and the hard palate. The voice is likely to be weak, toneless, and at times possibly hoarse. In uncomplicated cases the pulse is still full and regular, though accelerated, and in the majority of cases markedly dicrotic. The bronchitic manifestations, which were but slight during the first week, now almost constantly undergo exacerbation. The dry cough not rarely annoys and disturbs the patient. Examination of the lungs discloses the signs of diffuse bronchitis, especially marked in the posterior inferior portions, which in severe cases may become the seat of hypostatic or other forms of inflammatory consolidation.

Upon the hot, dry skin the well-known roseolæ appear during the first days of the second week, not rarely even at the close of the first week, in the form of slightly raised hyperemic spots varying in size from that of a pinhead to that of a lentil. They appear earliest upon the abdomen, the back, and the lower half of the chest, extend, if present

in large number, to the upper arms and the thighs, while the forearms and the legs are rarely and the face is never occupied by them. Their development does not take place all at once, but regularly in successive crops throughout the entire second and into the third week, and in protracted cases still later.

The abdomen, which in the first week of the disease is normal or slightly distended, now generally becomes more markedly distended, but only in extremely severe cases or in those subjected to injudicious dietetic treatment does the abdominal distention attain a marked degree. In not a few cases the state of the bowels remains normal or constipation is present. In another large number diarrhea occurs, with from two to four, rarely more, thin, yellowish, "pea-soup-like" evacuations in the twenty-four hours. In severe cases the patient is slow to ask for the bed-pan, and in a number the stools and the urine are voided involuntarily. The enlargement of the spleen, which in some cases had been demonstrable during the middle or at the end of the first week, now often becomes distinct below the costal margin or makes itself apparent for the first time. At times, however, its demonstration is rendered difficult by the marked meteorism. The urine, which at first was abundant, becomes scanty and high-colored. Generally, it contains a moderate amount of albumin—so-called febrile albuminuria developing.

With a continuance and a partial exacerbation of the symptoms described the patient reaches the height of the attack. He is now often completely stuporous, mutters to himself, exhibits jerking of the tendons and floccillation, fails to ask for either food or drink, voids the stools and urine involuntarily, and presents a condition most alarming to the friends and the family—and not without reason. Progressive cardiac enfeeblement, paralysis of the nervous centers, complicating inflammatory affection of the lungs, intestinal hemorrhage, peritonitis, and other complications may induce a fatal termination, but fortunately not so frequently as the laity fears if appropriate nursing and treatment be instituted. The majority of patients enter upon the stage of recovery and convalescence from the middle or the end of the third week, or the beginning of the fourth week. Naturally, this period also is not free from danger. There may be recrudescences and relapses, or the life of the patient may be endangered by complications and exacerbations of such conditions as may have developed during the acme of the disease.

The transition from the fastigium to the stage of recovery is generally attended with a peculiar change in the course of the temperature. The curve, after at times marked fluctuations without apparent cause have preceded, becomes more or less markedly and often extremely

intermittent, with a declining tendency. This is designated the stage of steep curves. The pulse is now smaller, the lumen of the artery narrower, the dicrotism has disappeared, and the more nearly the temperature approximates the normal, the less becomes the frequency of the pulse, not rarely giving way to bradycardia.

Even during the stage of steep curves the skin is likely to be moist at times. The roseolæ gradually fade, and they are often replaced by another striking condition, namely, miliaria crystallina. The lips and the mucous membrane of the mouth also become clean and, together with the tongue, lose their dryness. The appetite and the sense of thirst return, and the patients now begin to ask for food—a demand that soon becomes more urgent and which often gives rise to annoying differences with the physician and the attendants. With the decline of the temperature the patients begin to make complaints. They become lacrimose or irritable—all manifestations of returning consciousness, and at the same time of an appreciation of their helplessness and weakness, which are shown also objectively in great emaciation and pallor. Fortunately for the patient, sleep returns, and with a disappearance of nocturnal restlessness and dreams the other annoying manifestations likewise subside gradually. Above all, the bronchitis disappears, and such pneumonic alterations as have developed subside. The enlargement of the spleen diminishes; the urine becomes more abundant and lighter in color, again free from albumin, and at times is even voided in unusually large amount. The diarrhea often persists into the afebrile period, the stools, however, gradually acquiring a darker color.

In favorable cases the patient now gradually becomes free from fever. Toward the end of the third or in the fourth week the previous physiologic body-temperature is generally resumed, with the normal daily fluctuations, and in all severe cases the temperature usually falls still further below the normal, so that morning temperatures of 36° C. and less, and evening temperature of rarely more than 36.5° C., may be the rule for days or even weeks. The pulse, which is especially small, often infrequent and slow, is, like the body-temperature, unstable and readily variable. Slight mental or physical disturbances give rise to slight elevation of temperature, and cause considerable transitory increased frequency of pulse. In other respects also the extremely debilitated convalescents are readily excited without feeling especially ill. At this time, provided there be no complication on the part of the digestive organs, the patient exhibits great hunger. All of his thoughts and reflections revolve about the ingestion of food, and the large, covetous

eyes with which he follows every movement of the nurse or the physician, from whom he hopes for fulfilment of his desires, are characteristic.

It has already been indicated that during the period of involution and that of convalescence the patient is exposed to the danger of recrudescences and relapses, and even at this time life may be threatened by hemorrhage and intestinal perforation. Among the remaining dangers, bed-sores, erysipelas, and abscesses, the sequelæ of pneumonia, especially pleurisy and empyema, as well as parotitis, typhoid laryngitis with ulceration and necrosis of cartilages, may be mentioned. Changes in the myocardium also may at this time assume an alarming *rôle*. Meningitis and other severe disturbances on the part of the central nervous system are fortunately less common. All of these and still other disturbances subsequently to be described in detail may quickly cause a fatal issue in the course of a few hours or days, or after long-continued suffering may terminate either in recovery or in death. How frequent are weeks of hope and fear, and finally everything to have been in vain! When recovery finally takes place after complicated, long-protracted convalescence, it is, fortunately, more frequently complete than in the case of many other infectious diseases. The patients generally recover with remarkable rapidity after subsidence of the local manifestations, and their nutrition improves, so that they present the well-known picture of the contented, fattened typhoid convalescent.

SUMMARY OF THE POST-MORTEM CONDITIONS.

The following section will be comparatively less comprehensive than some others in this work, as a part of the facts that might be considered here will be treated of in other sections. Thus, for convenience in descriptions, detailed statements as to the morphology and the biology of the typhoid-bacillus have already been made in the section on Etiology and will be made in the section on Diagnosis, while in the section devoted to an analysis of the individual symptoms it was impossible in many places to avoid a full description of the anatomic alterations. I believe that this apparent irregularity has rather contributed to comprehensiveness, and that it is the best means of eliminating otherwise unavoidable repetition.

EXTERNAL APPEARANCES.

Accordingly as death has taken place during the first stage of the disease, whether as a result of the severity of the infection or of intestinal hemorrhage, or of other sudden accident, or in the second stage after protracted suffering or in consequence of severe complications, the

external appearances of the body may be diametrically opposite. In the first event the body is generally well nourished, the skin smooth and tense, the layer of fat often well developed. Frequently the remains of miliaria crystallina are present, while roseolæ or traces thereof are never appreciable. The muscles are dry, tough, and dark red. The blood exhibits a diminished tendency to coagulation and is exceedingly dark. The large veins are generally filled with dark, loose clots, and the tissues are generally the seat of considerable imbibition of blood.

The bodies of those dead after a protracted attack of the disease often exhibit, in contrast to the conditions just described, extraordinary emaciation, with a pale, desquamating skin, occasionally abscesses, furuncles, and secondary ulcers of considerable size. Not rarely bed-sores also are present. At times there is edema about the ankles. The muscles in such cases are wasted, pale, and infiltrated with serum. The blood also appears lighter and diffluent, with a tendency to the formation of pale or wholly colorless clots. Unless profound cardiac or pulmonary complications are present, the bodies of typhoid patients exhibit lividity of the face seldom or in but slight degree. Post-mortem suggillation also is comparatively little marked. The tendency to putrefaction does not occur so early, and is not so marked as in other infectious diseases, as, for instance, typhus fever and small-pox. Rigor mortis persists for a relatively long time—at any rate, longer than in typhus fever.

MUSCLES, BONES, AND JOINTS.

The appearance of the **muscles** in general has been referred to in the description of the general appearance. Their condition is, however, when considered in detail, often striking, particularly when death has occurred at the height of the disease. The dry, brownish-red muscles, resembling smoked meat and presenting a dull luster on section, are friable, although they appear firm to the touch. In places they present a striate or punctate, grayish-yellow or pale-yellow discoloration. At times entire groups of muscles acquire this appearance, especially in cases in which death occurs from the middle of the third to the fourth week of the disease, or even later. These alterations may actually involve all of the voluntary muscles of the body. They are most frequently evident in the large thoracic muscles, the abdominal recti, and the muscles of the thighs, especially the adductors. Not rarely the muscles of the tongue and of the diaphragm appear to be involved.

The muscles, when most affected, frequently exhibit ruptures, together with extravasations of blood—an indication that they are not

of post-mortem origin, but have developed during life. Although these muscular lacerations, to which Rokitansky first and Virchow subsequently called attention, occur also in the course of other acute infectious diseases, as, for instance, typhus fever, they appear to be especially frequent and extensive in cases of typhoid fever.

The microscopic appearance of the muscles affected in the manner described was studied with especial care by Zenker, who distinguished, in addition to simple, non-degenerative atrophy, two other varieties of degeneration, the granular and fatty, and the waxy, which he found generally associated or combined. The portions of muscle undergoing waxy degeneration, especially between the second and the fourth week of the disease, exhibit the firm consistency already mentioned, and an appearance at first striate and punctate, then grayish red, and subsequently waxy gray or fish-meat-like; while the granular and fatty degeneration becomes manifest by change in color, marked pallor or yellowish discoloration, only after it has existed for a long time and has attained a high grade of intensity. The appearance of the degenerated muscles may further become especially conspicuous from the fact that the hemorrhages previously mentioned may be associated with the degeneration. At times the extravasations of blood appear as striate and punctate figures, while at other times, as has been mentioned, they form extensive hemorrhagic collections with destruction of the muscular tissue. The distribution of these lacerations and hemorrhages throughout the muscular system is quite irregular, in contrast with the distribution of waxy degeneration, which often is symmetrical. Naturally, they will be found most frequently in those situations that are involved in the degenerative process in greatest degree and earliest. Accordingly, their principal seat is the abdominal rectus, more often the lower than the upper half, the greater and lesser pectoral, and the iliopsoas. I have observed them in a number of instances in the biceps and triceps of the arm, and remarkably seldom in the adductors of the thigh, considering their frequent involvement in the waxy form of degeneration. The further disintegration of such foci, with the peculiar changes in their contents, has often given rise to the opinion that muscle-hematomata may undergo suppuration. Although, from existing bacteriologic knowledge, this possibility cannot be wholly excluded, yet it must be exceedingly uncommon. True muscle-abscesses in the course of typhoid fever appear to be rare. I have observed them in a number of instances as part manifestation of secondary septic processes. Recently, attention has been repeatedly called to muscle-abscesses due to the pyogenic activity of the typhoid-bacillus.

Thus, Cahradnicky[1] has observed during life an abscess as large as an egg in the greater pectoral muscle which contained only typhoid-bacilli. This case is especially interesting further on account of the demonstration of the great persistence of the Eberth bacillus in the living body. The individual, who was subjected to operation in December, 1894, had had an attack of typhoid fever in September, 1893.

The **bones** and the **joints** are involved much less commonly, though in a more varied manner. Attention has been directed to these lesions, especially through the work of Keen.[2] In his later work he collected 237 cases of ostitis and periostitis, and since then numerous other cases have been reported. So far as bacteriologic investigations at present go, not a small number of cases of periostitis and osteomyelitis in the course of typhoid fever are due to the bacillus of Eberth (Cornil and Peau[3]). This organism was isolated in pure culture from 4 out of 5 cases reported by Parsons.[4] From the fifth case Staphylococcus pyogenes was isolated as well as Bacillus typhosus. Typhoid periostitis and the generally associated inflammation of the contiguous superficial portions of bone usually occur during the latter course of the disease, at the earliest during the period of steep curves, but generally during the first part of convalescence, but may occur late in convalescence, and even months or years after the attack of fever. Bruin[5] has reported one case, from which the typhoid-bacillus was isolated, occurring six years after the primary attack; and Bruschke[6] has reported one occurring seven years afterward. Quincke[7] has found the bacilli in the bone-marrow during the disease, and in some cases as long as four months after convalescence. It is probable that they may remain quiescent in the bone-marrow for very long periods of time, and only give rise to inflammatory conditions when a condition of localized lowered resistance, possibly due to injury, occurs. Young persons, and generally those at about the age of puberty, are preferably attacked. I have, however, observed the condition also in young children and isolated instances in elderly individuals; once, for instance, in a woman, forty-seven years old. The long, hollow bones, and among these the femur and the tibia, are attacked most frequently; also the sternum and the ribs (Helferich) have been involved in isolated instances. In young persons the process in the long bones begins preferably in the region of the epiphysis.

[1] *Wien. klin. Rundschau*, 1895, No. 43.

[2] "Toner Lectures," 1876, *Smithsonian Miscellaneous Collections*, No. 300. Also, *The Surgical Complications and Sequels of Typhoid Fever*, Philadelphia, 1898.

[3] *Bull. de l'Acad. de Méd.*, 1891.

[4] *Johns Hopkins Hospital Reports*, vol. v.

[5] *Ann. de l'Inst. Pasteur*, 1896.

[6] *Fortschr. der Med.*, 1894.

[7] *Berlin. klin. Woch.*, 1894.

The disease of the bone may occur in one or in several parts of the skeleton at the same time. Occasionally, it is confined to a small area, and may undergo involution without injury to the bone; while in other instances periostitic abscesses may develop, with extensive necrosis of the bone, and even rupture into the joint, with all of the concomitant dangers. Termination in the formation of exostoses, which has been mentioned especially by French clinicians, appears to be exceedingly rare.

Typhoid affections of the joints, which may appear as monarticular or polyarticular, and as suppurative or simple inflammatory serous processes (Keen, Stromeyer, Volkmann), have hitherto received little thorough anatomic study. The suppurative lesions appear almost always to be the result of complicating septicemia.[1] Ponfick[2] has, however, made a thorough study of the changes in the bone-marrow, and has discovered conditions suggesting those present in the spleen and the lymphatic glands. He describes peculiar large cells, containing as many as 20 red blood-corpuscles and more, in the bone-marrow of those dead at the height of the disease. During convalescence these structures, previously mentioned by Neumann and Bizzozero, evidently undergo such transformation that the red blood-corpuscles are transformed into large clumps of pigment or masses of fine, dark granules. When these cells are present in large number they impart a brownish-red color to the bone-marrow, which persists for some time after complete recovery has taken place.

DIGESTIVE ORGANS.

Reference to the condition of the tongue and the mucous membrane of the mouth and pharynx has already been made in the description of the general symptomatology. Further consideration of this, especially to the interesting typhoid lesions of the fauces and the pharynx, referred to by Louis and Jenner, will be given under the symptomatology. In the dead body they are represented by rounded ulcers of varying size, at times confluent, rarely, however, of great extent, but exceedingly shallow, and covered by a thin, grayish-yellow, readily detached deposit. Louis claims to have observed similar changes down into the esophagus. It should be mentioned additionally that, according to Hoffmann, the muscular structure of the tongue is not rarely involved in waxy degeneration. Further details with regard to the salivary glands will be given in connection with the analysis of the individual

[1] Ebermayer, *Deutsch. Arch. f. klin. Med.*, 1889, Bd. xliv.
[2] *Virchow's Archiv*, 1872, Bd. lvi.

symptoms. At this place it will only be mentioned that they are often found enlarged when death has taken place at an early stage of the disease. They then appear firmer than normal, darker, discolored brownish yellow or yellowish red, and on microscopic examination they exhibit, in addition to evidences of hyperemia, cloudy swelling of the glandular cells.

The stomach and the upper part of the intestine occupy a subordinate place in relation to the remainder of the small intestine, the large intestine, and the rectum, with regard to their anatomic lesions. Even the earlier observers and all of those who followed them mention the occurrence of detachment and punctate redness of the gastric mucous membrane, particularly in the vicinity of the pylorus, at times with numerous superficial erosions, or a marked mammillated appearance. Louis had already shown that these lesions represent nothing at all specific. Ulceration of the esophagus and stomach occasionally occurs. Mitchell[1] has reported such a case and reviewed several others. From none of these have typhoid-bacilli been isolated, and they are probably due to a secondary process. Stricture of the esophagus following typhoid fever rarely occurs. Such cases have been reported by Packard,[2] Mitchell,[3] and others. Probably this condition is due to a cicatrization of the secondary ulcers. The attempts of Cornil[4] and Chauffard[5] to establish a peculiar typhoid affection of the stomach in the form of focal accumulation of lymphatic elements in the mucous membrane yet requires corroboration. In the duodenum also at times, in my experience less commonly than in the stomach, swelling and redness of the mucous membrane are present. In one instance I observed superficial erosions. Specific lesions of this portion of the intestine have likewise not as yet been demonstrated with certainty.

Of enormous importance and dominating the entire picture of the anatomy of typhoid fever, however, are the lesions present in the middle and lower portions of the intestine, from the lower third of the jejunum downward. Before entering upon a detailed consideration of these, some general statements as to the anatomic and topographic conditions may be made. In accordance with the conditions present toward the close of life, the bodies of those dead of typhoid fever frequently exhibit meteorism. This is likely to be especially marked and uniform in distribution in all parts of the digestive tube only when extensive peritonitis is present. When this is absent, the distention involves preferably the

[1] *Johns Hopkins Hosp. Rep.*, vol. viii. [2] *Phila. Med. Jour.*, 1898.
[3] *Loc. cit.* [4] *Gaz. hebdom. des Sci. méd.*, 1880.
[5] *Thèse de Paris*, 1882.

large intestine, and generally the small intestine in less degree. When the colon is unusually long or occupies an abnormal situation, or exhibits atypical arrangement of its convolutions, the small intestine may be entirely covered by it. The lower portion of the ileum is often of normal caliber, or even contracted. The upper portions of the small intestine often exhibit moderate or even marked meteorism. Generally, on external inspection of the ileum, especially its lower portions, dark linear spots can be seen opposite the attachment of the mesentery. On palpation these exhibit a denser consistency than the remainder of the intestinal wall, and, as will be disclosed on opening the intestine, they correspond to the specific typhoid intestinal lesions. This condition is dependent upon a peculiar inflammatory hyperplasia of the lymphoid structures, which, in accordance with its seat in the small or the large intestine, occurs as hyperplasia of Peyer's patches or of the solitary follicles.

Bretonneau was probably the first who directed attention emphatically and intelligently to the typhoid lesion of the intestine. He considered it specific, although he compared it with the variolous lesion of the external integument. Similar opinions have been expressed by other observers of the same and of a later period. In the celebrated book of Louis, however, especially in the second edition, the intestinal lesion is clearly recognized and in the main thoroughly described.

In the detailed description of the typhoid intestinal lesion several stages are appropriately recognized: 1, the stage of hyperemia; 2, that of medullary infiltration; 3, that of necrotic destruction and ulceration; and 4, that of cicatrization. In general these anatomic stages correspond with certain portions of the clinical course. It should, however, be borne in mind that the intestinal lesion does not develop and extend simultaneously and uniformly, but rather in stages, often distributed over a considerable period of time, and it likewise undergoes involution in a corresponding manner. The lower portion of the ileum and the neighborhood of the ileocecal valve are generally attacked earliest. Often the impression is created as if the process extended gradually or in stages from this point. But if it be taken into consideration that relapses and recrudescences of typhoid fever are attended with renewed involvement of the intestinal mucous membrane, it can be understood that by no means rarely the various stages of the specific lesion, namely, infiltration, sloughing, ulceration, and even complete cicatrization, can be studied in the same portion of the intestine.

The first stage, that of hyperemia of the intestinal mucous membrane, which probably occupies the beginning of the first week, in

isolated instances even the entire week, is not understood in detail, on account of the exceeding rarity with which opportunity for anatomic investigation is afforded. Rokitansky and Trousseau believed that at this time hyperemia of Peyer's patches and the solitary follicles occurs as the forerunner of medullary infiltration; Cornil and Ranvier also claim to have made similar observations. In a case of suicide I have observed in the middle of the first week detachment and marked hyperemia of the mucous membrane of the cecum, the adjacent portions of the ileum, and the colon, with slight swelling of the agminate and solitary follicles. The frequency, the extent, and the depth of these alterations in the individual case, whether they may be wanting, whether in cases of so-called abortive typhoid fever they do not give rise to further lesions, whether in certain varieties of the disease the diffuse catarrhal swelling of the intestine reaches especially high grades of intensity, are all questions that await answers based upon more extensive experience.

With the beginning of the second week, in severe cases probably at the end of the first, medullary infiltration takes place, probably with a lessening of the diffuse hyperemia and swelling of the intestinal mucous membrane. In general, Peyer's patches appear to be somewhat in advance of the solitary follicles with regard to the evolution of the process. Not rarely entire changes are observed uniformly in both, while infiltration of the solitary follicles preceding that of Peyer's patches does not appear to be frequent.

In their form and situation, the typhoid lesions naturally correspond in general to their anatomic substratum. They are oval, with their longitudinal axis corresponding to that of the intestine, are situated principally in that portion of the intestinal canal opposite the mesenteric attachment, and generally appear as sharply circumscribed, disk-shaped, even fungus-shaped formations with overhanging margins. At first greatly reddened, they subsequently acquire a grayish-red or, at the beginning of exfoliation, a grayish-yellow color. The surface of the patches, which may project from 3 to 5 or even up to 8 mm. above the intestinal mucous membrane, is at times smooth, at other times slightly granular or even somewhat nodular. These irregularities are doubtless due to the fact that some follicles entering into the formation of the patch have not yet become completely confluent or, at least, are not swollen to the level of the surrounding tissues. The consistency, the degree of infiltration, and the depth to which they extend are extremely variable in different cases. Even at the present time, French clinicians are in the habit of making certain distinctions in this

respect. According to them, the soft patches and the hard patches of Louis play an important *rôle* that is not quite comprehensible from our present point of view.

The medullary swelling is by no means always confined to the limits of the patches. At times the infiltration extends beyond them to the adjacent mucous membrane. Under such circumstances several infiltrated patches may coalesce, and, in consequence, peculiarly shaped elongated formations in the direction of the axis of the bowel may often result. In other cases, on the other hand, the patches are only partly involved in infiltration. Generally, the coalescence of the infiltrated portions occurs preferably and most extensively in the lowermost portions of the ileum just above the ileocecal valve and in the adjacent portions of the cecum.

The infiltration of the solitary follicles commonly present in addition to the swelling of the patches, and exhibiting in different cases the most varied distribution throughout the large intestine, and at times extending into the sigmoid flexure and even into the rectum, gives rise to the formation of roundish, grayish-red or greatly reddened elevations, frequently surrounded by a garland of vessels. They project above the mucous membrane to the size of a pea and larger, and, like the patches, not rarely exhibit an extension of the infiltration beyond the original limits of the follicles. They may then develop into large fungus-shaped formations up to three-quarters of an inch in diameter. With the commencement of involution they generally assume a yellowish color, and then, especially if of moderate size, acquire a pustular appearance. The continuance of medullary swelling, in both the agminate and the solitary follicles, is brief. Already in the second week, often at its beginning, involution sets in. Cases of commencing exfoliation as early as the fifth and the sixth day of the disease have been recorded. In contrast with these, it is true, observations also have been made in which the infiltrations exhibited no sign of commencing disintegration at the end of the second week. It may be objected to these statements that the determination of the exact day of the disease is difficult, but, as a result of unequivocal personal observation, I believe that they are well founded.

Involution of the medullary swelling may in general be brought about in one of two ways: either in the form of actual absorption of the pathologic products, or, as is by far the more common method, in the form of necrosis, with subsequent exfoliation and the formation of corresponding ulcers. Both of these varieties of involution are frequently observed in the same intestine; even in the same patch, simple absorp-

tion quite commonly occurs in association with ulcerative processes. If it be remembered, as has been indicated, that the various stages of the lesions in the same body generally exhibit various grades of evolution and involution according to the portion of the bowel involved, it can be comprehended that occasionally almost all of the anatomic processes described may be observed at the same time in the same bowel. Just as in respect to infiltration, with regard to regressive alterations, so the Peyer's patches are generally somewhat in advance of the solitary follicles. With reference to the regressive changes in detail, the infiltrations that disappear by absorption generally at first present a grayish-yellow discoloration, and then progressively collapse, at first at the center and from this point toward the periphery. In the parts involved in necrosis, the first indication of this process consists in a certain sponginess and swelling of the tissue, frequently with reactive redness and tumefaction of the surrounding mucous membrane. The patches and follicles then acquire a grayish-yellow, next a pale-yellow or dirty grayish-yellow color, and soon become from dirty brownish green to dark olive green from imbibition of the contents of the intestines, especially bile, so that the intestine in consequence presents to the inexperienced observer a most remarkable appearance.

As to the immediate cause of the necrosis, Virchow was of the opinion that it is a form of caseation much like that occurring in tuberculosis; while Orth thinks that it is an anemic necrosis due to pressure exerted on the blood-vessels in consequence of the great hyperplasia of the cells. In this connection the work of Mallory[1] on the histologic changes in typhoid fever should be mentioned. He concludes that, due to the action of a toxin produced by the typhoid-bacillus, there is a proliferation of endothelial cells. These cells are phagocytic in character, and the swelling of the intestinal lymphoid tissue is due almost entirely to their formation. The necrosis, he thinks, is due to occlusion of the veins and capillaries by fibrinous thrombi which owe their origin to degeneration of phagocytic cells beneath the lining endothelium of the vessels. He describes a similar process occurring in the mesenteric glands and the spleen.

The process of exfoliation is rarely equally advanced and equally deep at all parts of one patch of Peyer, so that eschars are generally not thrown off in one piece. This takes place, as a rule, in larger or smaller particles, in one situation more superficially and in another more deeply. Patches, in which between still sloughing portions ulcerated areas, in consequence of exfoliation, are already present, generally acquire

[1] *Jour. Exp. Med.*, vol. iii.

a peculiar irregular appearance. These have been designated plaques gaufrées by Louis. The more rare exfoliation of the sloughs as a whole takes place preferably in the extremely dense areas and in those presenting deep infiltration (plaques dures).

The ulcers left after exfoliation of the sloughs attain a variable depth in accordance with the extent of the antecedent infiltration. At times they scarcely penetrate the mucous membrane; at other times they extend down to the muscular coat or even destroy a layer thereof; and at still other times the entire muscular coat is destroyed, so that the ulcer extends to the serous layer. Even this is often greatly thinned, even down to a delicate membrane. The margins of the ulcers are sharp, and, particularly at the beginning, are steep in consequence of still-existing infiltration in the neighborhood; the latter, however, soon disappears. The edges are generally little, if at all, detached. The base of the ulcer presents a more or less dark-red appearance shortly after exfoliation has been completed, and it is often still covered in various places with small remains of sloughs. The older portions soon exhibit a slaty discoloration. The intestinal ulcers assume the form of the previous areas of infiltration only in so far as these have not undergone involution by simple absorption. It is worthy of mention that large confluent ulcers may form in place of the confluent patches, and that these are most frequently situated in the neighborhood of the ileocecal valve and the lowermost portion of the ileum.

The ulcers resulting from the solitary follicles generally attain a size from that of a lentil or a pea up to three-quarters of an inch in diameter. The longitudinal axes of the larger ulcers are not rarely directly transverse to the axis of the intestine. In the rare cases in which a number of ulcers lie close together, even annular ulcers with subsequent stenosis of the large intestine may occur. Further extension of the typhoid ulcers after exfoliation of the sloughs I believe, with other observers, to be uncommon. On the other hand, gradual deepening of the ulceration is probably not at all rare, so that ulcers may occasionally give rise to perforation at a time when completion of the process of cicatrization might be expected. In the majority of cases, however, perforation does not result from such secondary extension of the ulcer in depth, but from the circumstance that the infiltration from the outset extends down to, even involves, the serosa, and that, after exfoliation of the slough, such a thin, unresisting membrane is left that it is not able to withstand the pressure of the intestinal contents. There is accordingly a good anatomic basis for the most frequent occurrence of perforative peritonitis at a time when exfoliation of the sloughs takes place, while the secondary

ulceration mentioned explains in part the occurrence of perforation at a much later period of the disease.

In cases in which death has resulted from intestinal hemorrhage, the anatomist is sometimes confronted with the most difficult and the simplest technical problems side by side. The excessive, rapidly fatal hemorrhages may take place either from large intestinal vessels opened in the process of exfoliation, and whose stumps are readily demonstrable, or mainly from capillary vessels, so that even on post-mortem examination it may be difficult to demonstrate the source of the massive hemorrhage. The hemorrhages from large vessels are observed especially when the so-called indurated patches are exfoliated as a whole or in large masses. The bleeding taking place from capillaries or from numerous minute vessels is not rarely encountered in the earlier stages of necrosis before exfoliation of the slough. Under such circumstances a few, or many, or almost all, of the sloughs are found to be spongy, friable, irregularly villous, suffused with blood, and blackish red or dark in color. These cases fully explain the frequent occurrence of copious intestinal hemorrhage in the early stages of typhoid fever before the close of the second week.

Cicatrization of the typhoid ulcers occupies as long a time, and often a longer time, than the preceding stages of intestinal alteration. That the most extensive ulcers with relation to size and depth also require the longest time for healing is a matter of course. No doubt, under the influence of general physical debility, the process of healing may be abnormally protracted even in the presence of less profound ulceration. In this category the condition described by earlier writers as atonic ulceration is in part to be included.

After cicatrization has taken place the affected areas are still somewhat depressed, thinner than normal, smooth, and at first lighter in color than the surrounding tissues. Subsequently they become more or less markedly pigmented, either diffusely or preferably at the margins. On account of this change in the cicatrices, as well as their shape and location, the previous occurrence of an attack of typhoid fever can often be recognized in the dead body after the lapse of months or even years. It is a matter of course that the lymphoid structures at the sites of previous infiltration and ulceration are permanently destroyed. It is a matter of discussion whether intestinal villi are regenerated over the cicatrices; Rokitansky, Klebs, and Birch-Hirschfeld support this view, and as the result of a considerable anatomic observation I can agree with them as to its occurrence. In general, examination of a considerable number of bodies dead of typhoid fever will disclose the widest

variations with regard to the number, size, depth, and distribution of the typhoid ulcers in the different portions of the intestines. To what extent individual conditions, or the severity or mildness of the infection operate, cannot readily be stated, as no explanation has as yet been forthcoming for the fact that the intensity of the intestinal lesions varies much during different epidemics. Age and sex appear clearly to determine differences. In children the extent of the medullary swelling, both of Peyer's patches and of the solitary follicles, is on the whole not so great as in adults. The sloughing also is generally not so marked as in the latter, and this circumstance explains the greater rarity of intestinal hemorrhages and perforative peritonitis in childhood. Undoubtedly, also, involution of the medullary swelling by absorption is more conspicuous in children.

With regard to the number of infiltrated Peyer's patches in the individual case, some intestines are observed in which not more than 3 to 5 altogether are affected. In contrast with these cases are others in which scarcely a single patch in the lower two-thirds of the ileum escapes; in which the neighborhood of the ileocecal valve is almost continuously infiltrated and is thereby converted into one large ulcerative surface. Not rarely the vermiform appendix, with its follicular apparatus, is greatly involved in the morbid process, and it may occasionally be the seat of perforation. I have observed as many as 36 diseased patches in a single body, and I know that other writers have spoken of a still larger number. A moderate number of intestinal ulcers is far more common, however, than a very large number. In a study of 304 autopsies that I made in Hamburg from the end of 1885 to 1887 with relation to the number of ulcers, in 208 cases the specific intestinal lesions were discrete and in greater or less number. With reference to the localization of the ulcers, the notes of 577 autopsies at the Hamburg and Leipsic hospitals are available. There was involved: the cecum in 510 cases, 88.39 per cent.; the cecum (often together with the vermiform appendix) in 247 cases, 42.81 per cent.; the colon in 184 cases, 31.89 per cent.; the jejunum in 41 cases, 7.10 per cent.; the rectum in 12 cases, 2.08 per cent.

Just as variations occur in the number and the intensity of the intestinal ulcers in different localities and epidemics, so are variations in localization to be observed also. It is interesting, for instance, that Hoffmann, in the epidemic at Basle, observed involvement of the large intestine in 40.3 per cent. of cases, Griessinger at Zurich in 40 per cent., while in Tübingen this localization was observed in 24 per cent. The most common combination in the seat of the intestinal lesion is apparently the ileum, the ileocecal valve, and the cecum; with this is frequently associated involvement of the first portion of the colon. Less common than this combination is involvement of the ileum alone, or of this and the lower half of the jejunum; and still less common is involvement of the cecum and the colon alone, or of the lowermost portion of the large intestine alone; while exclusive involvement of the descending colon down into the rectum is probably least common. In the uppermost portions of the jejunum, and especially in the duodenum, I have, together with most observers, never found any specific ulceration. It should, however, be mentioned that Hamernyk observed such a condition.

In the same number of 577 autopsies I found the frequency of intestinal

perforation and consecutive peritonitis to be 13 per cent. These figures are almost identical with those obtained by Murchison from a collection of 435 autopsies from various English and French hospitals, namely, 13.8 per cent. The statistics of Murchison, as well as my own, are compiled from a long series of years, and are thereby free from accidents due to the character of individual epidemics. How great variations may occur in individual epidemics is shown by the observations of Hoffmann at Basle, who found perforation in only 20 of 250 autopsies—8 per cent. The seat of the perforation of the bowel corresponds with regard to its frequency in general with that of the localization of the ulcers. Of 64 perforations that I have studied in this connection, there was involved: the upper portion of the ileum in 5 cases; the lower portion of the ileum in 39; the neighborhood of the ileocecal valve in 7; the vermiform appendix in 1; the colon in 11; the rectum in 1.

Having considered the specific alterations in the mucous membrane, the condition of those portions of the large and the small intestine that are not involved in the processes of infiltration and ulceration may now be discussed. Upon this point the anatomic observations are not so systematic and extensive as would be desirable from the clinical point of view. Generally, references are found only to the character of the mucous membrane in the immediate vicinity of the intestinal infiltration and ulceration, and especially those alterations are mentioned that are most intimately related to those processes. As, however, the "intestinal symptoms" in cases of typhoid fever—that is, diarrhea, meteorism, etc.—undoubtedly do not at any stage of the disease stand in direct relation to the intensity and extent of the specific lesions, they must be, at least in part, explicable from the condition of the remainder of the intestinal mucous membrane. Doubtless, it would be found upon further investigation that extensive catarrhal alterations, particularly in the first weeks, exert a determining influence.

Still another question obtrudes itself, not alone from the theoretic, but also from the practical standpoint, namely, Can typhoid fever—that is, the specific infectious disease induced by the bacillus of Eberth—exist also in the absence of specific intestinal lesions? Even the pathologic anatomist, who from the rigidly objective standpoint of the results of post-mortem examination might be disposed to answer this question in the negative, may hesitate, with a knowledge of cases presenting such slight ulcers in such small number as have been mentioned. In the same way that diphtheria may be unattended with the formation of membrane, and acute exanthemata without characteristic cutaneous eruption, so the follicular apparatus of the intestine may certainly, though with extreme rarity, be involved in minimal degree in cases of typhoid fever. Almost every experienced clinician will recall cases in this connection, in which, after most careful consideration of all of the circum-

stances, typhoid fever had been diagnosed, but upon post-mortem examination only the general appearances of a profound infectious disease without specific localization were found. Unfortunately, such cases were formerly not examined bacteriologically. Proof still seems to be wanting that typhoid fever can occur with no lesion whatever in the gastro-intestinal tract during any stage of the disease. This possibility, however, must always be borne in mind, and several authentic cases have been reported where lesions could not be found at autopsy.

The **changes in the mesenteric glands** stand in most intimate relation to those of the intestine. They are as constantly enlarged as the lymphatic structures of the intestine, and like them exhibit the characters of medullary infiltration. In general also the localization of the process in the glands corresponds with that customary for the intestinal lesion, so that the glands in the lower part of the ileum, the cecum, and the adjacent parts of the colon are, on the whole, involved most frequently and in greatest degree; while those in the uppermost part of the small intestine and the lowermost part of the large intestine more frequently remain wholly free or are but slightly involved. This correspondence will naturally not be found complete if large numbers of cases are studied. Under exceptional circumstances profoundly involved portions of intestine may exhibit slight glandular involvement, while, on the other hand, a slightly developed intestinal lesion is sometimes associated with disproportionate glandular hyperplasia.

The enlargement of the glands almost always extends far beyond the narrow zone of those most clearly related to the intestine. Generally, those of the stomach and the portal fissure, as well as the retroperitoneal and the bronchial glands, are involved. The changes may extend even still further to the lymph-glands in the vicinity of the mouth, the larynx, and the deeper structures of the fauces, as well as to those of the neck and the inguinal glands.

The enlargement of the mesenteric glands does not begin much later than the infiltration of the lymphatic structures of the intestine. The glands become prominent as early as the commencement of the second week, and attain their greatest size at the height of the disease. They are then generally from the size of a pea to that of a walnut, or even as large as an egg, tensely elastic, from grayish red to bluish red in color, globular, and with a smooth or somewhat nodular surface. On section the projecting glandular structure is more markedly reddened in the cortical than in the medullary portions, the latter at times presenting a grayish red, and in the center even a yellowish red, appearance. On

microscopic examination the process is found to be similar to that seen in Peyer's patches and the intestinal follicles.

The involution of the glands keeps pace with that of the intestinal lesion. The swelling grows progressively less, the color becomes paler from the center toward the periphery, and the glands may thus, simply through absorption, return to their normal size. This mode of involution is, no doubt, the more common and prevalent one. Not rarely, however, it is preceded by a process of softening in the glands. This may be present in small single or multiple areas in various parts of the gland. The softened mass may then undergo absorption directly. Less commonly larger portions of the gland or even the entire gland undergoes softening, and involution will then be much more difficult. Under the most favorable circumstances there may be gradual inspissation, terminating in calcification; occasionally, however, perforation and partial or even general peritonitis may result.

Liver and Biliary Passages.—It is remarkable that the best observers make directly contradictory statements with regard to the condition of the liver in the typhoid cadaver. While some describe the organ as intact or but little changed, others describe quite constant alterations in its structure, discernible even macroscopically. These contradictions are dependent principally upon the fact that the structure of the liver exhibits alterations of varying distinctness at different stages of the disease, but that these are at no time likely to give rise to considerable, constantly recurring changes in volume or shape. While the liver appears hyperemic, firm, and somewhat enlarged during the early febrile period, it becomes flabbier and lighter in color at the height of the disease. The condition represents the commencement of parenchymatous changes, the progress of which keeps pace with those of the disease in general.

In the middle and toward the end of the second week the flabby, somewhat friable structure of the liver presents upon section a peculiar pale, grayish-brown appearance. The outline of the lobules, which previously could be seen distinctly from the surface, now appears blurred upon section, and at times, and especially in some parts, entirely obliterated. In not a few cases the liver on section presents a variable appearance: in some areas of greater or less extent marked discoloration with a yellowish tint, in others better preservation of outline and of color, which more nearly approaches the normal. This appearance shows that the parenchymatous degeneration is not rarely developed in different degree in different parts of the same organ.

Microscopic examination of the tissue of the liver discloses, in correspondence with the results of macroscopic examination almost unexceptionally in the febrile stage, more or less advanced alterations in the liver-cells. These appear at first albuminous and fatty, granular and turbid; and they then become swollen and filled progressively with large and small granules and fat-drops, and finally break up into detritus. The degenerative process generally begins at the periphery of the liver-lobule, and rarely attains the same degree at the center even in its further progress. At first the granular and turbid cells can be cleared up by addition of acetic acid; but subsequently, if progressive fat-infiltration takes the place of albuminous granulation, this will be possible in but slight degree, if at all. In cases of especially severe onset and long duration the parenchymatous degeneration and the disintegration of the liver-tissue attain so marked a degree that the organ becomes diminished in size, flabby, and pale grayish-yellow in color, and is thus suggestive of the condition observed in acute yellow atrophy of the liver.

Wagner[1] described as a specific feature of typhoid fever the presence of small, generally interacinous, grayish-white nodules in the liver-tissue, which he described as accumulations of lymphoid cells, and considered analogous to the lymphoid hyperplasia of the intestinal follicles and the similarly constituted nodules of the peritoneum. Hoffmann observed these formations in 38 of 250 cases, but he believed them to be actually still more common. Later examinations, however, have not shown them to be peculiar to typhoid fever, as they have been observed in other infectious diseases also. Reed,[2] from a study of these so-called lymphoid nodules, concluded that they are not composed of lymphoid cells, but that in the earlier stages the abundant nuclei present arise in lesser part from the disintegration of nuclei of the liver-cells, and in greater part are those of polymorphonuclear leukocytes which have wandered into the necrotic area. He thought the necrosis was probably not due to the immediate presence of the typhoid-bacillus, but probably due to the action of a circulating toxin. Mallory[3] thinks there are two varieties of the focal lesions: one consists in the formation of phagocytic cells in the lymph-spaces and vessels around the portal vessels, and is due to the action of the toxin; the other is due to the obstruction of liver-capillaries by phagocytic cells, derived chiefly by embolism through the portal circulation of cells originating from the endothelium of the blood-vessels of the intestine and spleen.

[1] *Arch. d. Heilk.*, 1860.

[2] *Johns Hopkins Hosp. Rep.*, vol. v.

[3] *Loc. cit.*

The liver-cells lying between the occluded capillaries then undergo necrosis and disappear. Reed was able to show no intimate relation between the typhoid-bacillus and these areas. The character of the bile corresponds with the extensive changes in the parenchyma of the liver; and this secretion, in contradistinction from that in other acute infectious diseases, is generally light in color and limpid. Its specific gravity is between 1010 and 1016, as compared with from 1026 to 1030 under ordinary conditions (Brouardel). Much less commonly, as is the rule, for instance, in typhus fever, it is viscid and dark.

Great interest has recently been attracted to the anatomic alterations in the large biliary passages. Ulcerative and even diphtheric processes in the wall of the gall-bladder and the large biliary passages, with secondary destruction and abscesses in the liver or perforative peritonitis, had previously been described as rare occurrences (Andral, Louis, Jenner, Leudet, Rokitansky, and others). After Gilbert and Girode[1] had first demonstrated typhoid-bacilli in the gall-bladder, Chiari[2] showed that the necrotic processes in the biliary passages were in general due principally to these organisms, and that they could be regularly found in the gall-bladder. He was able to demonstrate the bacilli in 20 of 22 autopsies. Similar observations were made by Birch-Hirschfeld,[3] who, in agreement with Chiari, concludes that the gall-bladder probably constitutes a common and important source for reinfection.

In addition to direct extension of the ulcerative process in the large biliary passages to the surrounding hepatic parenchyma, abscess of the liver may occur in cases of typhoid fever under other conditions also, as part manifestation of general pyemia and as a result of septic thrombosis of branches of the portal vein, which is usually dependent upon ulcerative and suppurative conditions of the intestine, especially perityphlitis and paratyphlitis. For a more detailed description of these conditions reference may be made to the clinical part of this work, in which my own clinical experiences and those of other observers are recorded together with the anatomic.

Changes in the pancreas are mentioned by few writers on account of their relatively slight importance. Among older writers, Röderer and Wagler,[4] Louis, and Murchison refer to the occasional occurrence of induration, enlargement, and hyperemia of the organ in

[1] *Sem. méd.*, No. 58, 1890, and *Compt-rend. de la soc. biol.*, 1891, No. 11.
[2] *Prag. med. Woch.*, 1893, No. 22.
[3] *Lehrbuch d. path. Anat.*, 4 Aufl., Bd. ii., S. 694.
[4] *De Morbo mucoso*, Göttingen, 1762.

the bodies of those dead of typhoid fever. Hoffmann[1] was the first to devote attention particularly to the pancreas, and he observed changes similar to those in the salivary glands recurring with considerable regularity. In the first period of typhoid fever the gland is generally enlarged, hard, grayish red, and even more deeply red in color. On microscopic examination there will be found dilatation and overfilling of the smaller and smallest vessels, with serous infiltration of the adjacent, still-intact parenchyma. In the later stages the pancreas, which at first was enlarged, becomes discolored and presents a grayish-yellow or even grayish-brown appearance. Toward the end of the attack the pancreas again becomes diminished in size, and upon complete recovery acquires its normal consistence and color. In the second stage the increase in the size of the gland appears to be dependent upon enlargement, multiplication, and active division of the cells, and the discoloration upon albuminous-fatty degeneration.

HEART AND VASCULAR SYSTEM.

Little is known concerning the anatomic condition of the myocardium in the initial and the first febrile stage on account of the rarity of death at this period. Generally, the size, consistency, and color of the myocardium are described as normal, although, even in early stages, increased friability, flabbiness, dilatation, especially of the right half of the heart, and discoloration of the heart-muscle have often been mentioned. These conditions almost constantly occur in the height of the disease and the subsequent course of the febrile stage. This was known already to earlier observers. Laennec[2] speaks of "softening" of the heart, with violet or brownish-yellow discoloration. Subsequently, Louis, Stokes, and Rokitansky gave descriptions of the macroscopic changes in the heart-muscle at the height of the attack of typhoid fever that at the present day are still considered models. Naturally, these observers were unable to advance materially the clinical comprehension of these conditions. It is only within recent times that a clear insight into the nature of the functional disturbances of the heart in cases of typhoid fever has been obtained as the result of a large number of valuable studies of the histologic changes in the myocardium. At first, under the leadership of Virchow,[3] a number of parenchymatous changes and consecutive regenerative processes were established by

[1] *Loc. cit.*, p. 191 *et seq.*

[2] *Traité de l'auscultation médiate*, second edition, 1826.

[3] See the famous article upon parenchymatous inflammation in *Virchow's Archiv*, Bd. iv.

Böttcher,[1] Zenker,[2] Waldeyer,[3] Hoffmann,[4] Hayem,[5] and others, to which was subsequently added a knowledge of interstitial inflammatory processes, first indicated by Hayem,[6] and recently materially advanced by Romberg.[7]

Among the parenchymatous alterations, consideration should be given especially to albuminoid granulation. Less common, especially as compared with other infectious diseases, as, for instance, diphtheria (Romberg), fatty, and in isolated cases hyaline, waxy degeneration have been observed. In addition, there is remarkable enlargement of the nuclei in the form of elongation or distention almost constantly, at least in adults, with abundant deposition of pigment in their vicinity (Romberg). The muscle-fibers themselves often exhibit a sort of vacuolation and a peculiar change in the form of numerous transverse tears—myocardite segmentaire (Renault)—which, however, von Recklinghausen, Zenker, and recently also Romberg are disposed to consider as agonal products.

The parenchymatous alterations have been found in hearts presenting macroscopically little change, as well as in those that from their external appearances had to be designated as friable, brittle, discolored, and dilated. They involve both the left and the right side of the heart, and appear to be more extensive and more constant in the outer and inner layers of the myocardium than in the middle layers, which, however, also present considerable alteration at times (Romberg). Not much of a definite nature has as yet been determined with regard to the relations between the parenchymatous changes and the clinical symptoms.

Fuller knowledge exists with regard to interstitial myocarditis, which exhibits microscopically the characters of true interstitial inflammation: round-cell infiltration between the larger muscle-bundles, which extend from this point between the finer bundles; capillary ectasis, the vessels often being greatly distended with white blood-corpuscles. In addition, a peculiar affection of the smaller and smallest arteries of the myocardium has been described by French observers (Hayem, Martin) as important and frequent, and been designated obliterating endarteritis. Hayem claims to have observed this especially in a number of cases in which sudden death occurred in collapse. He describes the

[1] See the famous article upon parenchymatous inflammation in *Virchow's Archiv*, Bd. xiii.

[2] *Ueber die Veränderungen der willkürlichen Muskeln in Typhus abdominalis*, Leipsic, 1864.

[3] *Virchow's Archiv*, Bd. xxxiv.

[4] *Loc. cit.*

[5] *Arch. de phys. norm. et pathol.*, 1870.

[6] *Ibid.*, 1869.

[7] *Arbeit. a. d. med. Klin. z. Leipsic*, 1893.

affection as an inflammatory hyperplasia of the cellular elements of the intima of the smaller arteries, which as a result suffer considerable thickening of their walls and narrowing of their lumen. Romberg has been able to verify these observations only in isolated instances, and therefore with good reason expresses doubt as to their frequency and general significance. So far as is known, the inflammatory process extends in such a way that both the right and the left sides of the heart are involved, the latter generally in greater degree and preferably at the apex and the base. Romberg was able to demonstrate that the myocarditis frequently originated from similar inflammatory processes of the (visceral) pericardium and the endocardium. As clinical experience also shows, the interstitial myocarditis appears in a majority of cases to undergo complete involution, without leaving functional or anatomic disturbances in the myocardium. In rare instances (von Leyden, Romberg) permanent fibroid changes can probably be demonstrated. Whether abscess of the heart may be a result has not been demonstrated.

In contradistinction from other infectious diseases, **endocarditis,** especially that involving the valves and terminating in valvular lesions of the heart, is extremely rare. Vegetative or ulcerative endocarditis also only exceptionally comes under observation (Griessinger, Liebermeister, Bouchut). Several cases have been reported in which the typhoid-bacillus in pure culture was isolated from the affected valve. Probably the lesion is usually due to secondary infection with the pyogenic cocci. Romberg has called attention to focal, generally mural, endocarditis beyond the limits of the valves, and demonstrable only on microscopic examination. It appears rarely to acquire considerable extent in cases of typhoid fever, and to acquire clinical significance only under special conditions.[1] With a certain degree of preference it extends deeply by way of the vessels or the interstices between the muscles, thus giving rise to a direct transition into myocarditis. According to Romberg, more or less extensive round-cell infiltration, the source for which consists in a dense network of small veins and capillaries in this situation, is present more frequently in the depth of the visceral layer of the pericardium, at the junction between it and the superficial layers of the myocardium. This inflammatory process also extends preferably deeply into the myocardium and rarely toward the surface of the pericardium. Gross forms of **pericarditis,** with fibrinous deposits or fluid inflammatory effusion, appreciable macroscopically and giving rise to clinical manifestations, is, accordingly, quite exceptional. In

[1] See the appropriate section in the clinical part.

isolated instances, it is true, I have found fibrinous deposits upon the pericardium, in association with complicating croupous pneumonia, and in a few instances purulent pericarditis as a part manifestation of complicating sepsis.

The changes in the large vessels, although responsible for a number of not uncommon clinical manifestations, have as yet not been thoroughly studied. The veins are more frequently affected than the arteries. Typhoid phlebitis appears to be the usual cause for phlegmasia alba dolens during convalescence from typhoid fever, while a special variety of arteritis is probably responsible for spontaneous gangrene of the extremities, which, fortunately, is rare. The anatomic alterations that take place are considered in detail in a later section, together with the clinical manifestations.[1] In the same section will be found a complete description of the state of the blood in cases of typhoid fever.

THE SPLEEN.

In its behavior the spleen is comparable essentially to Peyer's patches and the follicles of the intestine and the mesenteric glands. Like these it is almost always swollen at the commencement and at the height of the disease. In any event, absence of enlargement of the spleen at this period in youthful and older individuals under the age of forty-five years is most exceptional. Apart from a few cases inexplicable in this connection, it appears to be wanting only after antecedent disease of the organ, giving rise to considerable and universal thickening of its capsule or firm hyperplasia of its stroma (Hoffmann), and thereby permanently destroying its distensibility.[2] In elderly persons senile atrophy of the spleen at times prevents the occurrence of tumefaction. The enlargement of the spleen is most marked at the height of the febrile stage, while at the commencement of this stage and in individuals dying in the stage of defervescence its volume is not markedly increased. The enlargement of the spleen in typhoid fever is in general not very considerable. When the swelling is at its greatest, the organ may be twice or thrice its usual size. A greater degree of enlargement is extremely rare, and even enlargement to thrice the normal is disproportionately much less common than to one and a half times or twice the normal, as will be seen from the following table of Hoffmann, giving the measurements of the spleen in 118 fatal cases of typhoid fever:

[1] See the clinical section.

[2] Consult particulars as to cause, nature, and temporal relations of enlargement of the spleen in the section on Analysis of the Individual Symptoms.

Duration of the Disease.	One-half the normal.	Normal.	One and one-half times the normal.	Twice the normal.	Two and one-half times the normal.	Three times the normal.	More than three times the normal.
2 weeks	1	5	12	7	4	3	
3 "	. .	11	15	12	4	6	
4 "	. .	6	8	17	4	3	
5 "	. .	11	3	4	5	1	
6 "	. .	2	3	. .	3		
7 "	. .	5	3				
8 "	. .	2	2	1	. .	1	
9 "	. .	2	. .	. .	1		
10 "	. .	2	1				
11 "	. .	1	2				
13 "	1	. .	. .	. .	. .	. .	1
14 "	1	. .	. .	1			
16 "	. .	. .	. .	1			
23 "	. .	1					
27 "	. .	. .	1				
28 "	. .	. .	1				
31 "	1						
Total	4	48	51	43	21	14	1

The cause of the enlargement of the spleen is to be attributed to two main factors—distention with blood and hyperplasia of the tissue. If opportunity be afforded to examine the spleen from the middle of the first to the middle of the second week, the organ appears smooth and tense, upon section dark red in color, extremely bloody, with an indefinite outline. Toward the end of the second and in the third week the organ, which has become still larger, is softer, at times dark brownish red, even brownish black in color, and, while previously the knife-blade drawn over the cut surface removed little, it now readily takes with it in considerable amount the mushy, diffluent splenic pulp. With the advent of defervescence the spleen undergoes relatively rapid diminution in size. The previously distended capsule becomes relaxed and wrinkled, and the hyperemia subsides, while the hyperplasia, especially that of the stroma, persists. These changes result in a lighter color, the transverse section presenting a yellowish-red appearance, at times yellowish-brown from the presence of pigment, while the outline of the stroma becomes again more distinct and the knife removes scarcely anything from the cut surface. The entire organ now acquires a peculiar tough consistence.

Among other alterations in the spleen, infarcts, which are rare and are dependent upon thrombosis or embolism of the splenic arteries, and abscesses, which are still rarer, may be mentioned. Not all of the conditions that have been described by earlier observers as abscesses are to be considered as such. Doubtless, old discolored and softened infarcts

have been included in this description. The true abscesses of the spleen also appear in part to result from infarction (Jenner, Hoffmann, Leudet). Others are a part manifestation of general sepsis. Both infarcts and abscesses may rupture into the abdominal cavity and give rise to general, in more favorable cases circumscribed, peritonitis. Some cases of "spontaneous" rupture of the excessively distended spleen, filled with blood, at the height of an exceedingly severe attack of typhoid fever are also referred to in the literature (Loebl, Leudet). Although such cases are among the rare exceptions, and each instance is to be accepted with great reservation, they certainly cannot be entirely ignored in view of the extreme tension, softness, and attenuation of the capsule, such as occur in that organ in severe and protracted cases.

The finer alterations in the spleen, which have been already described by numerous observers, especially Billroth[1] and Birch-Hirschfeld,[2] are related, as is known at the present day, most intimately to the invasion of the organ by the typhoid-bacilli, which during the febrile stage of the disease are quite constantly present in this organ in abundance and in peculiar arrangement. They are distributed throughout the organ in the form of innumerable irregularly arranged groups, in which the bacilli lie so close together that in stained sections they appear as dark, opaque spots, at the periphery of which individual bacilli may be recognizable (Fig. 7).

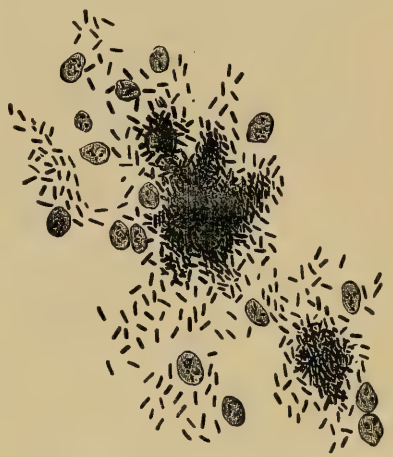

FIG. 7.—Section of the spleen, showing groups of typhoid-bacilli.

In other respects the histologic alterations are in general scarcely different from those of the acute infectious splenic tumor: In the early stage, especially hyperemia, particularly with overdistention of the cavernous veins of the pulp, and with further advance in the morbid process, most active hyperplasia of the cellular elements of the spleen and of the stroma, together with the appearance of those large cells (phagocytes) containing red blood-corpuscles, which recently have acquired such great theoretic importance. The significance of inflammatory changes in the smaller

[1] *Virchow's Archiv*, Bd. xxiii.

[2] *Arch. d. Heilk.*, Bd. xiii.; and *Tagebl. der 47 Versammlung deutscher Naturforscher u. Aerzte.*

arteries of the spleen, to which French investigators especially have directed attention (Siredey), has not as yet been sufficiently established.

ALTERATIONS IN THE URINARY ORGANS.

Apart from the rare cases in which death takes place in the early stages of typhoid fever, the kidneys generally exhibit more or less marked alterations appreciable to the naked eye, which are comparable to those in other parenchymatous organs, especially the liver. At the beginning or the middle of the second week the kidneys are usually still of normal size or but slightly enlarged, usually greatly reddened upon their external aspect, upon section markedly hyperemic, so that the medullary structure often is dark bluish red in color, the cortex somewhat lighter, from red to grayish red. With the progress of the disease the organ generally undergoes further enlargement. It becomes firmer, its color lighter, and the capsule removable with difficulty. The cortex now appears enlarged, pale grayish red, often with a yellowish tint, while the pyramids for a time retain their dark-red color, with the exception of the papillæ, which soon acquire a yellowish appearance. After a long and severe attack of fever, especially in protracted cases, the kidneys subsequently become smaller, flabbier, and often lighter in color, in the same way as has been mentioned with regard to the liver. The diminution in size generally takes place at the expense of the cortex, which now appears smaller, and pale grayish yellow in color, while the medullary substance also frequently becomes somewhat paler.

The alterations described are the macroscopic expression of the beginning progressive parenchymatous degeneration, eventually attaining a high grade. Microscopically this is manifested by albuminous-fatty turbidity of the epithelial cells of the uriniferous tubules, which soon undergo vitreous swelling, become filled with smaller and larger fat-globules, finally disintegrate, and thus, together with innumerable hyaline and granular tube-casts, often occlude the uriniferous tubules for a considerable distance. The cells are then present constantly also in the cloudy fluid that can at this time be expressed from the apices of the papillæ. The parenchymatous degeneration almost always begins, as can be distinguished with the naked eye, in the cortical structure, and only later, and often not in equal degree, is the medullary structure also involved.

The alterations described have been recognized for a considerable time, at least macroscopically, as part manifestations in cases of typhoid fever of moderate and of severe course. Gregory[1] and Rayer[2] have

[1] *Edinb. Med. Jour.*, 1831.

[2] *Maladies des reins*, 1840.

referred to this condition in connection with febrile albuminuria, and Hoffmann [1] and E. Wagner,[2] upon the basis of extensive statistics, have discussed it in an exhaustive manner. In rare cases the changes mentioned do not proceed beyond this stage; but, on the other hand, clinically well-defined conditions of acute nephritis also occur. These may appear early, in the middle of the second, even at the end of the first week, and they may dominate the clinical picture to such a degree that French observers especially have felt justified in applying to such cases the designation nephrotyphoid.[3] The anatomic picture of typhoid nephritis is generally that of acute parenchymatous hemorrhagic inflammation, usually with subordinate involvement of the interstitial tissue.

Wagner [4] and von Recklinghausen [5] have called attention to a peculiar variety of nephritis attended with numerous miliary, interstitial, purulent foci, which in rare cases, as I have myself observed in one instance, may coalesce into abscesses varying in size from that of a bean to that of a walnut. Von Recklinghausen had already attributed this affection to emboli of micrococci. At the present day there is scarcely any doubt that the condition is generally of septic origin. However, cases of multiple abscesses in the kidney, due to the action of the typhoid-bacillus, may occur, as in the case reported by Flexner,[6] in which there was a typhoid septicemia with focal abscesses in the kidney, from which the typhoid-bacillus was isolated in pure culture.

In one case I had the opportunity of examining the kidneys from a man dead after symptoms of pure hemoglobinuria. The organs were of normal size, dark sepia-brown in color, and unusually hard. On section the cortex was dirty brownish gray, the pyramidal tissue dark brownish red, almost black. The renal epithelium, both in the cortex and in the medullary tissue, was in a state of albuminous-fatty clouding and disintegrated, and the convoluted and straight uriniferous tubules were filled with masses of brownish-red, glistening hemoglobin tube-casts and flakes.

As in the liver, Wagner has occasionally demonstrated in the kidney also the presence of small gray lymphomatous nodules, which develop almost exclusively in the cortical tissue in the immediate vicinity of minute vessels. Hoffmann has observed them half as frequently as in the liver.

[1] *Loc. cit.*

[2] Ziemssen's *Handbuch der speciellen Pathologie*, Bd. ix., 3 Aufl., 1 Th.

[3] Compare the literature in the clinical portion, Disturbances on the Part of the Urinary Organs.

[4] *Loc. cit.* [5] *Verhandl. d. physik.-med. Gesellsch. z. Würzburg*, 1871.

[6] *Jour. of Path. and Bact.*, 1895, vol. iii.

Infarcts of the kidney are observed rarely, Hoffmann having found them 10 times in 250 autopsies.

The alterations in the remainder of the urinary tract are extremely uncommon as compared with those in the kidneys. I have in a number of instances observed continuous hemorrhages of considerable amount or numerous smaller extravasations of blood in the mucous membrane of the pelvis of the kidney, as they have been described by Louis and Rayer. Purulent pyelitis, which also is mentioned in the literature, I have never encountered. The mucous membrane of the ureters is rarely altered, here and there small hemorrhages are occasionally seen. The urinary bladder likewise exhibits more or less extensive hemorrhage into the mucous membrane only in rare cases. At times these are associated with catarrhal states, or even "diphtheric" destruction of the mucous membrane. Quite exceptionally the latter gives rise to phlegmonous inflammation of the wall of the bladder, with perforation and peritonitis.

The urine of typhoid patients may contain very large numbers of typhoid-bacilli without giving rise to symptoms or signs of an associated cystitis. Frequently, such urine contains a larger or smaller number of pus-cells, but it is not uncommon for typhoid urines not so infected to contain a few pus-cells. To the condition of typhoid-bacilli in the urine without associated cystitis the term "bacilluria" has been given. This occurs in 25 to 35 per cent. of all cases of typhoid fever. It is difficult, however, to draw a sharp line between the cases of bacilluria and those of true cystitis. The presence of a cystitis at autopsy is a rare occurrence. It is probable, as Horton Smith[1] suggests, that a bacilluria only gives rise to a cystitis when there occurs marked retention, or if the bladder-walls should be damaged in any way. Young[2] has reported a most interesting case of chronic cystitis, due to the typhoid-bacillus, persisting seven years after the attack of fever. He has collected from the literature two other similar cases, having, however, a shorter duration.

The possibility of infection of the bladder from without by introduction of the typhoid-bacillus on a sound or a catheter has recently been suggested by a case reported by Brown,[3] the bladder of which showed an acute inflammation. Cultures showed only Bacillus typhosus, and the only apparent possible mode of infection was by means of a catheter. This case is apparently unique.

[1] *The Typhoid-bacillus and Typhoid Fever*, London, 1900.

[2] *Johns Hopkins Hosp. Rep.*, vol. viii.

[3] *Med. Record*, March 10, 1900.

ALTERATIONS IN THE RESPIRATORY ORGANS.

The nasal cavity generally exhibits the appearances of catarrh with scanty secretion. At times, especially when obstinate epistaxis has taken place during life, superficial erosions and bloody suffusion of the mucous membrane of the turbinates and the septum are present in places. Croupous and diphtheric deposits in the nares are rare, and almost always only in association with like processes upon the soft palate and the tonsils.

Larynx.—Upon the mucous membrane of the larynx mild catarrhal manifestations are among the most frequent occurrences; less commonly they attain a considerable degree of severity. Even laryngeal ulceration in milder grades occurs in a fairly large proportion of the severe cases. Griessinger found such ulcers in 26 per cent. of the fatal cases. The more severe typhoid alterations in the larynx are interesting and important. Keen[1] has collected and reviewed 221 cases, obtained from the literature up to 1898. These lesions generally arise from superficial erosions, which may rapidly penetrate deeply and give rise to extensive ulceration, with perichondritis and destruction of the cartilage. The usual seat of typhoid ulcers of the larynx is the posterior internal wall of this organ, whence they may extend to the posterior portion of the vocal bands, generally in the form of superficial erosions. On the posterior walls, however, the ulceration is often deep, at first attended with extensive edema of the adjacent parts, the mucous membrane of the arytenoid cartilages, and the interior of the larynx, especially the false vocal cords. Not rarely the process extends down to the cartilage. In correspondence with the seat of the ulcer, perichondritis develops most frequently, with more or less extensive necrosis of the cricoid cartilage and the arytenoid cartilages, which destroys the former throughout a large extent and may involve the latter in necrosis, with total exfoliation. The process may even extend into the mediastinum, leading to emphysema and infiltration of the mediastinum with pus, as occurred in several cases cited by Keen.[2]

Not much less common are ulcerative lesions of the epiglottis. Generally, these remain superficial, surrounding the margin of the epiglottis individually or in groups. At times they extend down to the cartilage and cause exfoliation of small portions of its border. Extensive destruction of the epiglottis is rare, and when it occurs it may involve more than half of this structure. Perichondritis and necrosis of the thyroid cartilage appears to be by far the least common.

[1] *Surgical Complications and Sequels of Typhoid Fever*, Philadelphia, 1898.

[2] *Loc. cit.*

With regard to the mode of origin of typhoid ulceration of the larynx and its sequels the last word has not yet been said. To consider them as "decubital," in the strict sense of the word, as older writers did, is as little justified as the assumption that the more extensive lesions are due to true diphtheria. A portion of the ulcers, especially those of the posterior wall of the larynx, undoubtedly arise from superficial erosions and fissures of the mucous membrane, which then probably increase in extent through secondary infection. In another group of cases the condition is certainly dependent upon a peculiar affection of the mucous membrane in the form of an infiltration of its lymph-follicles, which in its nature is comparable with that constantly present in the intestine and other organs. These swollen lymph-follicles occur especially at the base of the epiglottis, on the posterior wall between the arytenoid cartilages and at the posterior attachment of the vocal cords, and they appear, like the other lymphoid infiltrations, to undergo disintegration, and thus to afford the first impulse to the process of ulceration. Further careful microscopic and bacteriologic examinations are still needed to establish the specific character of these lesions. Luscatello[1] has reported the cultivation of the typhoid-bacillus from the inflamed mucosa of the epiglottis in one case, but his report is very incomplete. More satisfactory is the report of Schulz,[2] as to finding that organism both in sections and in cultures from the swollen lymphoid nodules.

The opinion is held by some that perichondritis, with abscess-formation, may develop independently, without antecedent ulceration of the mucous membrane. Conditions of this kind would be comparable with the typhoid periostitis of the long bones and the ribs, and examination of the pus for typhoid-bacilli would be especially desirable.

The **trachea** and the large **bronchi** are rarely the seat of profound alterations. Generally, at the height of the disease their mucous membrane is markedly reddened, covered with scanty, viscid secretion, and the seat here and there of small erosions. Only exceptionally do these become deepened into actual ulcers, and but rarely do they give rise to perichondritis, necrosis of cartilage, and peribronchial suppuration. A number of observers, particularly Griessinger, report the occurrence of pseudomembranous diphtheric deposits. These are in any event extremely rare, and they have not yet been subjected to thorough study by modern methods. The occurrence of extensive fibrinous tracheobronchitis (Eisenlohr) is noteworthy, and it is to be distinguished clearly by its clinical course from true diphtheric lesions.

[1] *Berl. klin. Woch.*, 1894, Bd. xxxi., No. 16. [2] *Ibid.*, Bd. xxxv., No. 34.

In not a few cases there is considerable recent hyperplasia of the bronchial glands. This is not a condition associated with the local alterations in the air-passages, but is a part manifestation of the general typholymphoid hyperplasia. The smaller and the smallest bronchi, like the larger, present generally, at the height of the disease and throughout the entire febrile stage, only slight swelling of the reddened mucous membrane and scanty secretion from it. With the majority of recent observers, I consider this catarrh as specific and peculiar to typhoid fever. The atelectasis and lobular pneumonia, which occur so frequently, are intimately associated with the typhoid bronchiolitis. These processes have by no means been sufficiently studied bacteriologically. In a large proportion of cases the condition belongs, so far as streptococci and staphylococci act as the cause of the inflammatory process, among the true complications; while, according to the examinations of Polynère,[1] Finkler,[2] and others, in another proportion it is due directly to the activity of the typhoid-bacillus.

Lungs.—After death following severe, long-continued attacks of typhoid fever, not rarely also after death at the height of the febrile stage, hypostatic condensation is found in the posterior and inferior portions of the lungs. This condition is due to the bronchitis, with swelling of the mucous membrane and atelectasis, involving first and preferably the portions of the lungs above mentioned, and also to the cardiac weakness and the influence which the position of the body has upon the distribution of the blood, the latter factor exhibiting twofold intensity under the conditions present. The generally short duration of typhoid fever in children, and the much less common occurrence of cardiac weakness, are undoubtedly responsible for the fact that hypostatic splenization is much less common in them than in adults.

Among the lobar inflammatory processes in the lungs in the course of typhoid fever true fibrinous pneumonia plays an important *rôle*. Horton-Smith[3] says: "It occurred in nearly 5 per cent. of our fatal cases." It was present in over 8 per cent. of 2000 autopsies at the Munich Pathologic Institute.[4] Clinically, it occurred 6 times in 500 cases reported by Fränkel,[5] and it has been present 15 times in 829 cases at the Johns Hopkins Hospital. The disorder is almost always dependent upon the Fränkel-Weichselbaum diplococcus, while the bacillus of Friedländer acts as the cause only in isolated instances. Undoubtedly, mixed infections occur, especially of Diplococcus pneu-

[1] *Thèse*, Paris, 1889. [2] *Die acuten Lungenentzündungen*, Wiesbaden, 1891.
[3] *Loc. cit.* [4] *Münch. med. Woch.*, 1891, Nos. 3 and 4.
[5] *Deutsch. med. Woch.*, 1899, Bd. xxv., No. 16.

moniæ with streptococci and staphylococci. They have, however, not yet been so thoroughly studied anatomically that any definite statement can be made with regard to their frequency. Not rarely macroscopic inspection of the cut surface of the lung will raise a suspicion that an instance of this complicated variety may be present.

In rare instances streptococcic pneumonia,[1] which, as has been mentioned, generally occurs in lobular form, is found in lobar form. Still less frequently staphylococcic pneumonia appears to occur as a mono-infection in cases of typhoid fever.

Mixed infections of streptococci and staphylococci with Bacillus typhosus have also been described. The question as to whether cases of true pneumotyphoid occur has lately been considered by A. Fränkel,[2] who says: "One can say definitely that the occurrence of a pneumotyphoid in the old sense—that is, a pneumonia occurring as the expression and result of the primary localization of the typhoid-bacillus in the lungs—must be regarded as not yet demonstrated." Whether a secondary lobar pneumonia occurring during the course of typhoid fever may be caused by the typhoid-bacillus alone is also open to some question, notwithstanding the fact that several cases reported as such are contained in the literature. In some of these cases cultures were made so late in the disease that, even though the pneumococcus had been present earlier, it might have died out. Such are the cases reported by Bensaude[3] (Observation IX.) and by Foà and Bordoni-Uffreduzzi.[4]

The second case reported by Bensaude[5] (Observation LXIX.) is more convincing, but the bacteriologic report is incomplete. Other reports of cases of lobar pneumonia due to the typhoid-bacillus have been made by Chantemesse, Finkler, Bruneau,[6] and others.

Gangrenous portions of lung,[7] or those in a state of hypostatic splenization, or even lobar pneumonia[8] due to the pneumococcus, may undoubtedly be invaded by typhoid-bacilli. Although, in view of the great variety of inflammatory conditions which may be induced by the typhoid-bacillus, it is possible that it may cause a true lobar pneumonia, yet this form of lung involvement, if it ever occurs, must do so very

[1] See the case of Koch from my clinic, *Inaug. Diss.*, Leipsic, 1896; also Neumann, *Berlin. klin. Woch.*, 1886, No. 6; Finkler, *Congress-verhandlungen f. innere Medicin*, 1888 u. 1889.

[2] *Deutsch. med. Woch.*, 1899, Bd. xxv., No. 16.

[3] *Thèse*, Paris, 1897.

[4] *Riforma med.*, 1887, No. 1.

[5] *Loc. cit.*

[6] *Thèse*, Paris, 1893.

[7] Flexner and Harris, *Johns Hopkins Hosp. Bull.*, 1897.

[8] A. Fränkel, *Zeit. f. klin. Med.*, Bd. x., S. 439.

rarely. Accurate histologic and bacteriologic reports are much needed to clear up this most interesting and important point. All of the varieties of pneumonia mentioned as occurring in the course of typhoid fever appear, though rarely, to be capable of giving rise to the development of abscess of the lungs. Metastatic abscesses, as local manifestations of a complicating pyemia, have also been observed. Pulmonary gangrene appears to occur somewhat more frequently, sometimes as the sequel of lobar, especially fibrinous, pneumonia, in severe protracted cases, and in previously debilitated individuals, and also as the result of putrid-purulent embolism, and, finally—and this is of especial importance—as the result of aspiration-pneumonia of most varied origin. The last-named condition may be due to putrid, infectious materials, derived from the food if the mouth is not well cared for, or may arise from purulent, putrid affections of the mouth and of the commencement of the respiratory passages, dental caries with gingival abscess, purulent, gangrenous tonsillitis, or from laryngeal ulcers with perichondritic abscess and necrosis of cartilage. Spontaneous gangrene of the lungs, as was observed by Liebermeister, has not occurred in my experience.

Hemorrhagic infarction of the lung, as well as the same condition in the spleen and the kidneys, is not rarely found in the bodies of those dead of typhoid fever. The infarct may undergo involution by absorption and contraction, eventually with cicatrization; or it may undergo purulent or even gangrenous disintegration, generally then with the development of exudative pleurisy, especially empyema. The peripheral situation and the wedge-shape of the majority of these infarcts are at once indicative of their embolic origin. As a matter of fact, mural, softened thrombi are under such conditions frequently found in the right side of the heart, particularly in the auricle and in the auricular appendix. Such emboli may be derived also from the large branches of the pulmonary artery itself, which not rarely exhibits acute alterations of the intima in cases of typhoid fever. In connection with infarction, sudden death is to be borne in mind, the cause of which is to be looked for in embolism of a main branch of the pulmonary artery. The source of this embolus also may be found in the heart or in the large peripheral vein of the body.

Pleurisy in the form of a more or less extensive fibrinous deposit is not rare as a condition associated with the various forms of pneumonia complicating typhoid fever, and under such circumstances, in so far as previous investigation has disclosed, is to be attributed to the micro-organisms responsible for the pulmonary disorder. Fibrinous and septic pneumonia also lead at times to empyema. Serous or serofibrinous

pleuritic effusions of considerable amount are remarkably rare in the course of typhoid fever. Pneumothorax occurs only exceptionally, and generally as the sequel of purulent or gangrenous focal disease of the lungs.

The *rôle* of Bacillus typhosus in the serous pleurisies and empyemas complicating typhoid fever has recently been discussed by Fränkel,[1] Remlinger,[2] and others. Fränkel observed 4 cases of empyema among 500 cases of typhoid fever. Cultures from the purulent effusions showed in 2 cases B. typhosus; in the third, streptococcus; and in the fourth, pneumococcus. Among 829 cases of typhoid fever in the Johns Hopkins Hospital, but 1 case of empyema occurred. The pus in this case contained the typhoid-bacillus in very large numbers. Remlinger has reported 8 cases of empyema and of pleurisy with effusion from the exudate, in 7 of which the typhoid-bacillus was isolated. He has also collected 19 similar cases. Still several other cases are contained in the literature. While the bacteriologic examination in some of the earlier cases may be open to doubt, there can be no question that in a number of cases the typhoid-bacillus has occurred alone, and its primary etiologic significance seems fairly well established.

Tuberculosis is an important complication of typhoid fever, especially tuberculous disease of the lungs. It occurs in various forms, namely, as part manifestation of a complicating general miliary tuberculosis; as acute cheesy, lobular, rarely lobar, pneumonia; in the form of acute tuberculous peribronchitis; or as a direct exacerbation and acute dissemination of a pre-existing apical tuberculosis, hitherto pursuing a sluggish course. Also in the other forms, tuberculous affections of some standing of the lungs and the bronchial glands or of more remote organs may always be found after death as the source of the recent tuberculosis. Also the occurrence of tuberculosis as a mixed infection is interesting, and has been carefully studied in a few cases. Especially in cases of typhoid pneumonia the tubercle-bacillus has been found repeatedly together with the pneumococcus of Fränkel and Weichselbaum, then naturally in conjunction with correspondingly complicated histologic conditions.

ALTERATIONS IN THE NERVOUS SYSTEM.

In contrast to the marked predominance of clinical manifestations with reference to the central nervous system in cases of typhoid fever pursuing a severe course, the anatomic findings are extremely slight. Doubtlessly, this is due to the fact that the profound nervous

[1] *Loc. cit.*

[2] *Rev. de Méd.*, 1900, No. 12.

disturbances are attributable especially to a specific intoxication dependent upon the typhoid-bacilli, and which generally gives rise to a transitory impression wholly disproportionate histologically to the intensity of its symptoms.

Cerebral Meninges.—The **dura** not rarely presents hyperemia and more or less marked recent adhesion to the inner surface of the skull, which in turn is then generally the seat of osteophytic deposits. The large veins and the sinuses are often distended with dark fluid blood, while the formation of thrombi appears to occur only exceptionally, and then at a late stage in cases of protracted course.

The **pia-arachnoid** is usually the seat of edematous infiltration, slight cloudiness, injection, and adhesions, and there is usually an increase in the clear or slightly turbid ventricular fluid. Quite noteworthy are the observations of Fr. Schulze,[1] who noted, on microscopic examination of the brain and meninges of cases that during life had exhibited more or less pronounced symptoms of meningitis, in addition to the macroscopic appearances mentioned, a small-cell infiltration of the meninges and a continuance of this process along the vessels into the cerebral tissue.

Subarachnoid meningeal hemorrhages were early described by Chomel as a rare condition, and later by Hoffmann and Griessinger. It appears that they may occur at an early stage, as demonstrated by the 2 cases of Griessinger, who observed them as early as the second week of the disease.

Purulent cerebral and cerebrospinal meningitis are mentioned exceptionally in the earlier literature, but have only recently been specially pointed out on account of their clinical significance (Duchek, Griessinger, Buhl, Leyden, Erb, Curschmann). These affections may, as I have emphasized,[2] occur as early as the first week of the disease. They rarely terminate fatally. The varieties that occur later, toward the end of the febrile period or even shortly after defervescence, are far more severe, and they more frequently come to autopsy. Under these conditions extensive and profound evidences of inflammation often appear in the form of fibrinopurulent infiltration of the cerebral and spinal pia-arachnoid. Whether these processes are identical etiologically or are of varied origin is involved in doubt, as thorough histologic and bacteriologic studies are yet wanting. It is not improbable that in a portion of the cases the bacillus of Eberth is the sole or, at least, the predomi-

[1] *Verhandl. d. Cong. f. inn. Med.*, Wiesbaden, Bd. v., S. 469 and following.

[2] *Ibid.*, Bd. v., S. 469 and following. See also Wolff, *Arch. f. klin. Med.*, Bd. xliii. (Reports from my service at Hamburg.)

nant exciting agent of suppuration. In late years at least 10 genuine cases have been reported in which the typhoid-bacillus was isolated in pure culture. These have been collected up to July, 1900, by Hofmann.[1] An additional case has lately occurred in the Johns Hopkins Hospital. In other cases, particularly in those with associated fibrinous pneumonia, there is good ground to consider the Fränkel-Weichselbaum diplococcus as the causative factor. Still other cases are to be attributed, in all probability, to the exciting agent of true (epidemic) cerebrospinal meningitis. Apart from isolated bacteriologic observations, the fact that meningitic symptoms are encountered with remarkable frequency in cases of typhoid fever occurring in places and at times where both diseases—cerebrospinal meningitis and typhoid fever—prevail together is also in favor of this view.[2] It is undoubted finally that also streptococci or staphylococci alone, or in the form of a mixed infection with other micro-organisms, may give rise to purulent meningitis. This is the case especially as a part manifestation of complicating septicemia, but it must be emphasized that only a small minority of all cases of typhoid fever complicated by pyemia exhibit this localization.

Another important variety of secondary purulent meningitis is that following purulent inflammation of the middle ear, with meningophlebitis, sinus-thrombosis, and caries of the petrous bone. It is the more noteworthy from the fact that the affection of the ear is not rarely overlooked during life in the profoundly stupid or completely comatose patient.

With regard to the condition of the **cerebral tissue,** it may be said that in cases of typhoid fever it presents no constantly recurring lesions or changes intimately associated with it. Buhl[3] endeavored to establish cerebral edema with consecutive softening of varying degree as an alteration generally present. There is no doubt that this, associated even with moderate dilatation of the lateral ventricles, is demonstrable in many cases. Focal softening is quite rare, and, when it occurs, is the result of thrombosis of the cerebral arteries that have undergone the degeneration previously mentioned (obliterating endarteritis) or of coagulation in one or more cerebral sinuses or large veins.

Meynert has called attention to a yellowish-brown discoloration of the cerebral cortex, the surface of the corpora striata, the optic thalami, and the corpora quadrigemina, which he was able to trace microscopi-

[1] *Deutsch. med. Woch.*, July 12, 1900.

[2] I was struck by this particularly during the epidemic at Hamburg in 1886–87. See also Wolff (*loc. cit.*).

[3] Buhl, "Ueber den Wassergehalt des Gehirns bei Typhus," *Zeit. f. ration. Med.*, 1858.

cally to a diffuse yellowish discoloration and accumulation of brownish pigment-granules in the nervous elements, especially in the ganglion-cells. The outlines of the cells become obliterated, as Hoffmann also observed, so that finally the cell-body is shown indistinctly and principally from its pigment-content.

Peculiar round-cell accumulations, especially in the perivascular lymph-spaces, have been observed by von Recklinghausen and Popoff. These are believed to be capable of penetrating the nerve-cells and causing them to undergo degeneration. These observations, which are at present difficult of interpretation, have been confirmed from various sources (Duke Carl, of Bavaria, Blaschko, and others). Hemorrhage into the substance of the brain appears to be extremely rare. I have observed only 2 cases of the kind. Abscess of the brain occurs occasionally as a sequel of purulent inflammation of the middle ear, or as a result of metastasis. In one instance I have observed such a condition in connection with general pyemia in the sequence of a putrid bed-sore, and in another instance in connection with abscess of the lung.

Anatomic alterations in the **medulla oblongata** and the **spinal cord** are almost unknown. Kümmell has observed 2 cases of bulbar hemorrhage. One case has occurred in my experience, having symptoms of acute bulbar paralysis and terminating fatally, in which the autopsy disclosed softening and capillary hemorrhages into the tissue of the medulla oblongata. Microscopic examination was, unfortunately, not made.

With regard to the spinal cord, the statement is encountered that it often exhibits hyperemia and also a hyperemic state of its meninges. In isolated instances foci of myelitis and especially the occurrence of circumscribed anterior poliomyelitis (Shore) have been mentioned. In one case,[1] in which the course of an attack of typhoid fever was dominated exclusively by spinal symptoms, and presented the clinical picture of an acute ascending (Landry's) paralysis, numerous typhoid-bacilli could be demonstrated microscopically in transverse sections of the spinal cord, and could be cultivated also from its tissue. In structure, the cord presented insignificant alterations only. The case sheds light upon quite a similar one of Leudet's,[2] presenting symptoms of acute Landry's paralysis during convalescence from a mild attack of typhoid fever, which terminated fatally, and which upon post-mortem examination exhibited no material changes in the spinal cord. In another case,[3] also showing the clinical course of an acute ascending

[1] Curschmann, *Verhandl. d. Cong. f. inn. Med.*, 1886.

[2] *Gaz. méd. de Paris*, 1861, No. 19.

[3] Curschmann, *loc cit.*

paralysis, capillary hemorrhages and areas of softening were found in the medulla. The bacteriologic examination in this case gave negative results. Kümmell[1] has reported a similar case.

Finally, Schiff[2] has reported a case with a very similar clinical course, but which was very acute, death occurring in eighteen hours. The examination of the cord in this case showed an acute hemorrhagic transverse myelitis at the level of the fourth and fifth cervical segments. Cultures in this case were also negative. All of these anatomic conditions must be considered as extremely rare as compared with the presence, not uncommonly, of marked spinal symptoms. In this connection there exists a great deficiency in the study of typhoid fever at the autopsy-table.

The **peripheral nervous system** likewise has been but rarely studied in cases of typhoid fever. In association with certain clinical manifestations the anatomic lesions of parenchymatous neuritis have here and there been found, at times throughout a wide distribution (Pitres and Vaillard).

Alterations in the Organs of Special Sense.—Little has hitherto been learned anatomically with regard to the eyes, which clinically exhibit various disturbances. Ulceration of the cornea, iritis, and iridochoroiditis, and, in isolated instances, optic neuritis have been observed. The changes in the ears have been more frequently and more thoroughly studied. Although by no means all, at least most of the disturbances of this organ are attributable to extension of catarrhal and more profound disturbances from the nasopharyngeal cavity, the tonsils, and adjacent structures. Thus, catarrhal conditions of the mucous membrane of the Eustachian tube and the tympanic cavity are among the more common complications. At times purulent catarrh of the middle ear occurs, with perforation of the tympanic membrane, and, further, purulent affections of adjacent structures, especially of the cells of the mastoid process, the related veins, and the adjacent sinuses. Diphtheric affections of the Eustachian tube and of the middle ear have also been observed repeatedly as the immediate extension of similar processes in the nasopharyngeal structures.

ANALYSIS OF THE INDIVIDUAL SYMPTOMS; COMPLICATIONS.

The clinical picture of typhoid fever, so extraordinarily variable with regard to severity, duration, grouping, and development of the individual symptoms, as well as to sequels and terminations, can, on the whole, be

[1] *Zeit. f. klin. Med.*, 1881, Bd. ii. [2] *Deut. Arch. f. klin. Med.*, Bd. lxvii., 1900.

attributed to two principal factors, namely, the vital activity of the typhoid virus and its effects upon the body, and the individual reaction of the patient. While our views with regard to the second factor—a result of constant change and gradual evolution of clinical knowledge—are at the present day extended and deepened in all directions, the first, the relations of the typhoid-bacillus to the complete picture of the disease and its individual symptoms, is still in its incipiency in spite of a large number of isolated facts. At present it may be definitely stated that the effects of the typhoid-bacillus, viewed collectively, consist in its local and its general manifestations. The latter is attributable essentially to the toxins generated by the bacillus, the earliest knowledge of which we owe to Brieger and Fränkel. In addition to the effects of the bacillus of Eberth, those of other pathogenic micro-organisms are daily becoming more important, being exhibited alone or in combination with the former in certain organs or groups of organs. Considered strictly, only the first group of symptoms should at the present day be included in the actual typhoid disease, while the conditions dependent partially or exclusively upon other infectious agents are to be considered as complications.

Also, in the prebacteriologic period, complications and sequels were considered apart from the actual symptoms of the disease, although from other points of view. At the present day the previous division appears quite arbitrary, but we are unable to replace it with anything better. If an attempt were made to insist upon such a division from the modern standpoint, the objection would at once arise that the present state of bacteriologic investigation of typhoid fever is by no means such as to justify a separation of the actual symptoms of the disease from the complications. In detail much that is new and surprising may be brought forward. A whole series of alterations that until recently were considered as complicating and independent of the typhoid germ are now recognized as mixed infections of typhoid-bacilli and other pathogenic micro-organisms, or even dependent upon the typhoid-bacillus alone. It may suffice in this connection to refer only to the purulent processes, to affections of the bones and joints, to certain forms of pneumonia and pleuritic effusions, as well as to some manifestations on the part of the nervous system and the heart. Under existing conditions, however, it will be better in the following description to abstain from a rigid separation of the complications from the actual symptoms of the disease, and to treat of both together. In so far as this may be possible, an effort will be made to present the various processes as specific, as pure complications, or as mixed infections, as this differentiation is of

decisive importance for the comprehension of the disease generally and for its further study.

ALTERATIONS IN THE EXTERNAL INTEGUMENT.

Some statements with regard to the condition of the external integument in cases of typhoid fever have been made in the description of the general clinical picture and the anatomic alterations. The skin in all stages of typhoid fever exhibits various manifestations, important from a diagnostic standpoint as well as in their bearing upon the course and the termination of the disease. One of the most frequent and most important is the roseola. This has been specifically designated as the typhoid roseola, and with what propriety will be shown in the following statements.

The **roseola** (tâche rosée lenticulaire, Louis) appears in the form of small, roundish, well-circumscribed red spots, varying in size from that of the head of a pin to that of a lentil, and always slightly elevated, which fade completely on pressure (best made with a glass pleximeter) at every stage, and thus are shown to be purely hyperemic. Pale red and punctate when they first appear, the roseolæ rapidly become larger and darker in color. They are almost always discrete; here and there two, rarely several, coalesce. They appear first in the second half of the first week or in the beginning of the second week of the disease. Cases in which the exanthem appears later, not before the middle or at the end of the second week, are rare. Exceptionally, roseolæ appear early, from the second to the fourth day of the disease. I have observed this especially in women and children.

The roseolæ appear first upon the chest, the abdomen, and the back. Upon the back they often appear twelve, even twenty-four, hours earlier than upon the abdomen and the chest, and in the situation first named they are not rarely somewhat larger than in the others. From the trunk the roseolous eruption generally does not extend further, although in exceptional instances it may invade the arms and the thighs, and quite exceptionally the forearms, the dorsa of the hands, the legs, and the feet. Such extensive distribution upon the extremities almost always presupposes a relatively dense involvement of the trunk. It may be accepted as a rule that this part of the body is preferably and most densely the seat of the roseolæ, and their number diminishes progressively the further from the trunk the affected part of the body is situated. In a case in which a roseolous exanthem was more dense upon the distal portions of the extremities than upon the proximal portions, and even upon the trunk, I would from this alone have some

hesitancy in making a diagnosis of typhoid fever. Roseolæ very rarely appear upon the face. Only exceptionally have I found them upon the neck, and even at the lower border of the inferior maxillary bone.

In general and in comparison with the efflorescences of other infectious diseases the roseolous exanthem of typhoid fever is not abundant. When it develops simultaneously in large number and in great density the appearance created is striking, and great care in diagnosis will be required, as confusion with other infectious diseases is readily possible. Thus, I have now and then observed syphilitic roseola with eruptive fever and enlargement of the spleen to give rise to unpleasant confusion.

In the large majority of cases the roseolæ are present at one time singly or in small number, from 5 to 10 or 30. In young children they are, in my experience, generally still fewer than in adults. In the latter the number is again diminished in advanced age. With regard to sex, the exanthem appears in general to develop somewhat more abundantly in women than in men. As opposed to some observers, as, for instance, Murchison, I would distinctly emphasize the fact that the roseola may be entirely wanting throughout the entire course of the disease.

Thus, of 1261 cases observed at the Leipsic clinic, persistent absence of the roseolæ was observed in 260. Undoubtedly, the profusion and the development of the exanthem vary at different times and in different epidemics. In the year 1887 I observed in Hamburg a relatively much larger number of cases in which the exanthem was scanty than in other years. Of 1601 cases, which at that time were carefully examined from this point of view, no roseolæ or but isolated ones were found in 325. As opposed to this there were periods in which the roseolæ were but rarely absent, and in which their average profusion was especially striking. Perhaps the opinion of some observers, that the roseola is to be considered as an indispensable feature of typhoid fever, may have been formed during such periods.

There is no definite relation between the severity of the disease and the density of the roseolous eruption, although I think I have observed complete absence more frequently in milder or abortive cases than in severe and long protracted cases. The eruption is therefore of diagnostic and not of prognostic significance. The duration of the individual rose-spot is evidently not long, on the average from three to five days. I believe the longest period may be placed at from seven to ten days. A duration of fourteen days, as stated by Trousseau, has not occurred in my experience. It is, however, a characteristic feature of the roseola of typhoid fever that, while the old spots disappear, new ones are constantly developing, so that consequently the total duration of the eruption is comparatively long. I should place the average total duration

of the exanthem as between twelve and fourteen days. I have rarely encountered a longer duration than three weeks. In general it may be stated that the roseolæ rarely persist beyond the febrile stage of the disease. Although it cannot be denied that now and again isolated roseolæ appear during the afebrile stage, one should be extremely critical in regard to them.

During recrudescences and relapses the roseolæ generally reappear, often in equal profusion and even in greater density than in the primary attack, and they continue so long as the fever persists. Under such circumstances roseolæ may be found in the fourth and the fifth week of the disease, and even later.

Do roseolæ occur also in the course of other diseases? I believe efflorescences like the typhoid roseolæ do but rarely. The more skilled and the more experienced the observer, the less commonly will he report instances of this character. Only in a few instances of acute miliary tuberculosis and of cerebrospinal meningitis, which were shown on post-mortem examination not to be complicated by typhoid fever, have I observed upon the skin eruptions indistinguishable from the typhoid roseolæ. While in cases of the acute exanthemata, as, for instance, small-pox and typhus fever, the appearance of the specific eruption is generally preceded for a longer or short time by certain evanescent exanthems, I have but rarely observed these as forerunners of the typhoid roseola. Only in a few instances in women and children, or in delicately built, blonde, blue-eyed young persons have I observed evanescent, diffuse or punctate erythemas upon the trunk and the extremities.

It is noteworthy that the roseolæ, after they have faded, generally leave no trace; nor can they be demonstrated upon the dead body. As the sole trace remaining during life, there are occasionally observed light-brownish or yellowish spots of but short duration, or, more frequently, slight branny desquamation at the site of the roseolæ and in their immediate vicinity, a condition that appears to occur especially when the roseolæ have been profuse and have persisted for a considerable time. I have now and then observed in children and young adults that the lenticular efflorescence, instead of simply subsiding and fading, is converted at its center into a minute conical vesicle, whose contents soon become turbid and undergo desiccation. This process takes place in the superficial layers of the epidermis, so that a scar is never left.

It is a noteworthy fact that the roseolæ themselves, representing, as we have seen, a purely hyperemic exanthem, practically never become hemorrhagic even throughout the course of their further existence. I believe that I have observed this in but a few cases among thousands. Only in

the extremely rare cases of hemorrhagic typhoid fever, such as have been described especially by Murchison and Liebermeister, do some of the roseolæ become hemorrhagic, together with extensive bloody suffusion of other portions of the skin free from roseolæ. From this condition must be sharply differentiated the insignificant hemorrhages into the hair-follicles of the legs, which are not at all rarely observed during convalescence from severe attacks of typhoid fever, in association with the development of edema about the ankles.

Recently, attention has been directed to a study of the blood obtained from the rose-spots, not alone because of the theoretic significance, but also because of the possible diagnostic value. Neuhaus[1] claims to have found the Eberth bacillus in more than half of the cases examined by him, and also Rütimyer[2] was equally successful in 1 case. In a large number of observations directed to this point I have obtained only negative results, as have also other observers, as, for instance, Fränkel and Simmonds, Seitz, Janowski, Chantemesse, and Widal.

Since the above was written, typhoid-bacilli have been obtained from the rose-spots by Thiemich[3] in 3 out of 7 cases examined; by Neufeld,[4] 13 out of 14 cases; Curschmann,[5] 14 out of 20 cases; Richardson,[6] 5 out of 6 cases; Scholz and Krause,[7] 14 out of 16 cases. The method used in most of these cases consisted in incising the spot, collecting a drop of the exuding blood, and inoculating this, together with some of the tissue-scrapings, into fluid media.

E. Fränkel,[8] by excising the spots, placing them in bouillon, and so allowing the bacteria to multiply in the tissue, has been able to demonstrate the bacteria in sections. From all of this work it seems probable that a collection of the bacteria in the blood of the rose-spots always occurs.

The roseolæ of typhoid fever are absolutely distinct from the exanthem of typhus fever. The latter is made up of true macules, and not papules. At most they may be slightly raised for a short time immediately after their appearance. In form they are not so regular as the roseolæ, and their borders are diffuse and indistinct. Purely hyperemic and pale red at first, they soon become hemorrhagic from the center outward, so that in contradistinction from the typhoid roseolæ they can only in part be made to disappear on pressure. Their color then becomes coppery red or dull bluish red and even dirty livid. They leave traces, in the form of greenish-yellow or brownish spots (blood-pigment), far into convalescence. The exanthem of typhus fever, in addition, appears, on the average, somewhat earlier than the typhoid roseolæ, namely, from the third to the fifth day of the disease. It never appears in crops, but all at the same time, so that in from

[1] *Berlin. klin. Woch.*, 1886, Nos. 6 and 44.
[2] *Centralbl. f. klin. Med.*, 1887, No. 9.
[3] *Deutsch. med. Woch.*, 1895.
[4] *Zeit. f. Hyg.*, Bd. xxx.
[5] *Münch. med. Woch.*, 1899, No. 48.
[6] *Phila. Med. Jour.*, 1900, vol. v.
[7] *Zeit. f. klin. Med.*, Bd. lxi.
[8] *Zeit. f. Hyg.*, Bd. xxxiv.

twenty-four to forty-eight hours, on the average, the eruption is likely to have attained its definite development and distribution. I have never observed in connection with the exanthem of typhus fever the recrudescences that constitute the rule in cases of typhoid fever. The distribution of the exanthem of typhus fever also differs in a most distinctive manner from that of typhoid fever. Although in both the trunk is involved first and preferably, the eruption of typhus fever extends not rarely to the face, and especially to the extremities. In fact, it is often not less dense upon these than upon the trunk, and it is a characteristic feature, besides, that the exanthem, in marked contrast to the distribution of the typhoid roseolæ, is likely to be especially marked upon the forearms and the dorsa of the hands, while those parts of the extremities nearest the trunk are not involved in greater, but often even in less, degree.

Urticaria and papular exanthems (Griessinger) may be mentioned as rarities in the course of typhoid fever. I have noted urticaria only in exceptional instances at Hamburg, and in 0.3 per cent. of the cases at Leipsic. Jenner, Raymond, LeMaigre, and others report the presence of scarlatiniform eruptions, and also of measly eruptions, which appeared during the second and also the third week, and were by no means evanescent. Apart from the initial varieties of rash previously mentioned, I have observed nothing of the kind, and am inclined to the view that at least a portion of these eruptions are to be considered as drug-exanthems, and this seems the more probable, as for a long time it was customary to treat typhoid fever with large doses of antipyretic drugs, capable often of inducing varied exanthems. Peculiar bluish, livid spots, varying in size from that of a lentil to a half-inch in diameter, have been described by the older French observers—a most complete description has been given, for instance, by Trousseau—as a frequent lesion of the skin. They have been designated tâches bleuâtres or as typhoid peliomata, and were considered by Murchison and Trousseau as almost specific and prognostically favorable signs of the disease. The famous typhoid peliomata came to an ignominious end: they were found to be due to pediculi.

The eruption designated **miliaria crystallina** is worthy of more careful consideration. It occurs much more frequently in cases of typhoid fever than in those of other infectious diseases.

Although I cannot agree with Louis, who was inclined to attach specific significance to the eruption, I should not fail to mention that of 150 successive cases of typhoid fever examined for the presence of sudamina, these were found in more or less marked degree in 98. With regard

to the other infectious diseases, I may state that I have observed crystalline miliaria rarely in cases of measles and scarlet fever, and more frequently in cases of acute septicemia and typhus fever.

The eruption of miliaria generally appears, on the average, later in the course of typhoid fever than the roseolæ—from the middle or the end of the second to the end of the third or the beginning of the fourth week. It appears in the well-known form of roundish, distinct vesicles, varying in size from that of the head of a pin to that of a lentil, and of which, if the eruption be well developed, two or more generally coalesce to form larger efflorescences of irregular contour. Filled with contents of water-like clearness, they cover the skin like drops of dew. The imaginative Trousseau and Louis compared them with tears. On account of the colorless contents and the exceedingly thin covering of the vesicles, they may readily be overlooked with imperfect illumination. Not rarely they are first appreciated on palpation, if the palm of the hand is passed over the parts occupied by them. They can be seen especially well if viewed with oblique light. The content of the sudamina I have always found feebly acid or neutral, and never alkaline. It never becomes purulent, and disappears by absorption or rupture of the vesicles, after which, if they were numerous, branny desquamation of the skin persists for a few days. Miliaria appear earliest and in greatest profusion upon the lower portion of the abdomen, extending from this situation to the chest and the lateral portions of the neck, as well as to the thighs. The exanthem is usually scanty upon the forearms and the legs. I have observed it but rarely upon the hands and the dorsa of the feet, and never upon the face.

Herpetic eruptions are so rare in cases of typhoid fever that I consider this circumstance of diagnostic importance in the differentiation from other infectious diseases. Every experienced physician is aware of the frequent association of this variety of eruption with pneumonia, malaria, cerebrospinal meningitis, influenza, and typhus fever. During the epidemic of typhus fever at Berlin in 1879 I observed, for instance, herpes in 5 per cent. of all cases. When present at all, I have found herpes in cases of typhoid fever especially upon the face, and here in the usual situations. It then appeared principally in the first week, at times even before the appearance of the roseolous eruption, and far less commonly at a later period. In cases of convalescence from typhoid fever I have noted it in a few instances upon the trunk and the extremities, in the form of intercostal and femoral herpes. The observation of Gerhardt and Seidel, that herpes is more frequent in children than in adults, is not in accord with my own experience.

The occurrence of **furuncles, abscesses, phlegmons,** and **erysipelas** in the course of typhoid fever is quite serious. While phlegmons and erysipelas are less common and to be considered rather as accidental conditions, often in connection with slight injuries, bed-sores, etc., furuncles and small cutaneous abscesses are more common and of unpleasant significance, especially during the period of defervescence and of convalescence. After severe attacks of typhoid fever, convalescence may be greatly protracted by them. I have even observed life threatened directly in debilitated individuals. I have encountered cases in which from 60 to 80 larger or smaller furuncles and abscesses developed successively upon the skin and had to be incised. The most frequent seat of furunculosis is the dorsal aspect of the trunk, especially the gluteal region. Then the chest and the abdomen, the thighs, and the arms are preferably attacked. Furunculosis of the skin appears to occur with especial frequency at times when typhoid fever is vigorously treated with frequently repeated and exceedingly cold baths. Since I have abandoned this method of treatment furunculosis has become less common among my patients. To be separated from this condition are the abscesses of the skin that have been observed as associated manifestations of a complicating pyemia, with suppuration of joints and purulent metastases in internal viscera. Fortunately, these occurrences are rare.

Bed-sores, which formerly were one of the most dreaded sequels of typhoid fever, have become an uncommon manifestation with the development of a rational mode of treatment and of nursing of the patient. Even in severe cases of long duration they can generally be avoided or aborted in their early stages. Apart from exceptional conditions, the occurrence of a bed-sore in private practice, as well as in the hospital, is a reproach to the physician and the attendants.

In the epidemic of typhoid fever at Hamburg in 1886–87 I observed bed-sores in 1.9 per cent., and in Leipsic in only 1 per cent. of the cases. In connection with these small figures it must additionally be taken into consideration that disproportionately many severe cases, often in a neglected state, are sent to the hospitals.

The seat of predilection for bed-sores is, as is well known, the lower sacral and the gluteal region; less commonly the heels, the scapular region, that of the spinous processes of the vertebræ, as well as the occipital region, are involved. Apart from exceedingly severe cases complicated by septic or other equally grave conditions, in which bed-sores may appear as early as from the eighth to the fourteenth day, the affection is always a late manifestation of the disease. It persists from

the latter portion of the febrile stage into the period of convalescence, which it often aggravates, complicates, and protracts extremely.

Various forms of bed-sores can be distinguished—a fact that, it may be parenthetically remarked, is not sufficiently appreciated by some observers. The simplest and most common is that induced by pressure of the usually soiled body upon the bed. It generally begins in the sacral region and on the most prominent points of the nates, with diffuse circumscribed redness, with or without ecchymoses. Then exfoliation of the epidermis occurs, with exposure of the corium, which bleeds readily and is already somewhat discolored. Meanwhile there develops a red line of demarcation, followed by yellowish discoloration and desiccation of the affected part, with the formation of a parchment-like slough, which, after a varying time, is thrown off as a whole or is detached in threads or is removed artificially. Even with the first slough, which also may be discolored, soft, and smeary, the skin and subcutaneous connective tissue down to the muscle may be exfoliated. In especially severe and particularly long-neglected cases the destruction advances more and more deeply down to the bone. This also may undergo necrosis and subsequently be exfoliated, and I have in several instances observed the sacral canal to be opened.

Another variety of bed-sore, which, by reason of its mode of origin, may appear simultaneously in several, even in numerous places, develops in connection with ecthyma and eczematous and furunculous eruptions in the gluteal and sacral regions. It gives rise to small superficial ulcers of irregular outline, confluent at various points, and it is especially the result of want of cleanliness in the care of the patient.

A third variety I would designate the subcutaneous bed-sore. It does not always develop in places that are most subjected to pressure in the recumbent posture, but it occurs rather below the gluteal region, preferably over the lowermost portion of the sacrum and the coccyx, in the depth of the anal fold. Developing almost exclusively in cases of especial severity, this variety of bed-sore is indicative of a profound constitutional disturbance of nutrition. It is that variety that may be unavoidable even with the most scrupulous care. In the generally profoundly stuporous patients, who exhibit no manifestation of pain, it occasionally acquires considerable extent without the attention of the attendants being attracted to it, this occurring especially because at the beginning, in spite of considerable progressive deep-seated destruction, the skin exhibits slight or no alteration. When I have been able to follow the process more closely, a dense, at times remarkably insensitive, infiltration appeared beneath the unaltered or somewhat reddened,

edematous skin. The skin generally then became gradually discolored bluish red or even greenish yellow from imbibition of hemoglobin. Meanwhile the indurated area has undergone softening to the degree of distinctly demonstrable fluctuation, and now discharge of diffluent, putrid, dirty pus takes place from a number of small irregularly distributed openings, unless an incision has been previously made. It is most characteristic of this variety of bed-sore that the destruction is far more extensive deeply than would be suspected from the extent of the palpable infiltration or the thinning or discoloration of the skin. If extensive incisions have been made, or if the thinned skin has been permitted to exfoliate spontaneously, the necrotic cellular tissue may be removed with the pus in large, friable, discolored shreds. It is distinctive of this variety further that the destructive process, however extensive it may be, rarely extends beyond the subcutaneous connective tissue into the depth. Its main characteristic is subcutaneous necrosis and suppurative softening of the cellular tissue.

Naturally, a distinction is not possible in practice between the several varieties of bed-sores described such as has been made for purposes of completeness in presentation. Often the different varieties are merged into one another or appear simultaneously or successively in the same individual. Circumscribed gangrene of the skin in other situations than those threatened by bed-sores occurs with extreme rarity and only in greatly reduced individuals, and it is then of ominous significance. Occurring here and there entirely without obvious cause, it appears at other times on parts of the skin that have been subjected to accidental traumatism or to the effects of measures employed for therapeutic purposes. Thus, I have observed in situations where previously a mustard-plaster, a dry cup, or some other so-called resuscitating agent had been applied circumscribed gangrene of the skin in an area of corresponding form and extent. Also, in situations that had been exposed for an excessively long time to the action of a poultice or an ice-bag, I have exceptionally observed the development of cutaneous gangrene—naturally not including acute burns or freezing. The occurrence of true noma as a sequel of typhoid fever is so frequently mentioned by earlier writers that I am inclined to doubt whether the diagnosis of that condition was always correct. Among the large number of cases that have come under my observation I have only once seen an affection in a child under the most wretched conditions that could be considered as noma.

A word may be added with regard to changes in the **hair** and the **nails.** Falling out of the hair is well known and so common that scarcely any typhoid patient is wholly exempt therefrom. It occurs

almost exclusively upon the scalp, less commonly the beard, scarcely ever upon the pubes or in the axillæ. Two cases of complete alopecia, with loss absolutely of all the hair of the body, that I have observed during convalescence from typhoid fever were perhaps unique, and the lesion was scarcely related to the original disease. The loss of hair usually begins during the last week of the disease, and continues far into convalescence or even up to the time when the patients resume their usual occupations. The patients can be assured with comparative certainty that they will gradually regain their hair without artificial aid. Generally, the hair begins to be replaced in certain parts while it is still falling out in other situations. The new hair is generally thicker, tougher, and is lusterless. Upon transverse section it is often for some distance, rarely throughout its entire length, not round, but elliptic—a circumstance that is probably associated with the curliness almost constantly present.

After protracted severe attacks of typhoid fever the nails are not rarely thin, lusterless, and friable. Only in one instance have I observed them to be completely thrown off from the fingers, and in part also from the toes, and this occurred in one of the cases of total alopecia previously mentioned. Further, slight changes in the finger-nails, far less commonly in the toe-nails, are frequently observed even after cases of typhoid fever of moderate severity in young persons, and to which A. Vogel[1] called attention many years ago. These consist in transverse gutter-like depressions and grooves in the body of the nail, which occur in the stage of most profound depression of the bodily nutrition, of which it is the local expression. It is interesting to note that behind this depression or groove there frequently occurs a more or less wide, wall-like thickening and elevation of the nail, which evidently is due to the improved, often unusually increased, nutritive conditions during convalescence.

COURSE OF THE FEVER; ESPECIAL CONDITION OF THE BODY-TEMPERATURE.

The alterations in body-temperature constitute one of the best-studied chapters of typhoid fever. Since the determination by Wunderlich of the typical course of the temperature-curve, its observation has become one of the most important diagnostic and prognostic aids. Wunderlich's conclusions are, on the whole, still applicable. They constituted the starting-point of further extensive investigations on the part of his pupils and successors, and will undoubtedly constitute the

[1] *Deutsch. Arch. f. klin. Med.*, Bd. vii., S. 333 and following.

basis for subsequent studies of the febrile course of typhoid fever. Without doubt, the temperature-variations in the course of typhoid fever are to be considered as the expression of bacterial intoxication and the resulting general changes in the body and the viscera, in connection with which, naturally, individual conditions, and especially the physical state of the patient before the attacks, are co-operative in the fullest degree. With the conception of the fever as the expression of the specific morbid conditions taking place within the body, the observation made by Wunderlich and his pupils, that the various anatomic stages of the typhoid disease-process are reproduced in approximately typical cases in the form of the curve, is in accord. Wunderlich even added, with perfect justice, that, even in cases pursuing a less regular or a complicated course, certain distinctive features of the typical curve passed through the febrile course like a red line. The statement of Wunderlich, that far-reaching diagnostic conclusions can be formed from the curve and from certain parts of it, is based upon these facts.

The scientific study of the fever-curve occupied a large number of clinicians during Wunderlich's [1] time and for many years afterward. Among Wunderlich's pupils who deserve especial credit in this connection, Thierfelder,[2] Uhle,[3] Fiedler,[4] Wachsmuth,[5] and Thomas [6] should be mentioned.

An excellent summary, based upon personal experience, has been made by Griessinger.[7] The publications of Bäumler,[8] Liebermeister,[9] Jürgensen,[10] Ziemssen,[11] and Immermann [12] constituted further a mine of important observations bearing upon the fever of typhoid.

The average duration of the febrile period in a moderately severe or severe case of typhoid fever is, as has been mentioned, from three to four weeks. Generally, the schematic representation of the temperature-curve is based upon a duration of four weeks, the character of the curve being established for each individual week. It appears better to me to divide the disease into three or four parts, and appreciate from the outset

[1] Wunderlich, *Arch. f. physiol. Heilk.*, Bd. xvi., 1857, and Bd. xvii., 1858. *Arch. d. Heilk.*, Bd. iii., 1861. *Die Thermometrie am Krankenbette*, 2d ed., Leipsic.

[2] *Arch. f. physiol. Heilk.*, Bd. xiv.

[3] *Ibid.*, Bd. xviii.

[4] *Arch. d. Heilk.*, Bd. iii.

[5] *Ibid.*, Bd. iv.

[6] *Ibid.*, Bd. v., S. 331 u. 527.

[7] *Loc. cit.*

[8] *Deutsch. Arch. f. klin. Med.*, Bd. iii.

[9] *Collected Works.* "Typhoid Fever" in *Ziemssen's Handbuch.* Liebermeister and Hagenbach, *Beobachtungen und Versuche über die Anwendung des kalten Wassers bei fieberhaften Krankheiten*, Basle, 1868.

[10] *Klinische studien über die Behandlung des Abdominaltyphus mit kalten Wasser*, 1886. "Die leichteren Formen des Typhus," *Volkmann's Sammlung klin. Vortr.*

[11] In a number of smaller personal publications and similar publications by his pupils.

[12] Ziemssen and Immermann, *Die Kaltwasserbehandlung des Typhus abdominalis*, 1870.

that these are by no means equally long and in the individual case alike, but that each may be shorter or longer, extended or abbreviated.

We shall now describe, somewhat schematically, as is unavoidable in a systematic presentation, the form of the **temperature-curve** for a moderately severe or severe case of typhoid fever of typical course. Then the variations in the course of the curve under special individual and temporal conditions will be considered, and finally, it will have to be pointed out how varied its separate parts may be under varying circumstances. Before describing the curve of the actual febrile stage, a few remarks may be made concerning the state of the body-temperature during the period of incubation, namely, the time when the typhoid process is unattended with either objective or subjective symptoms, or

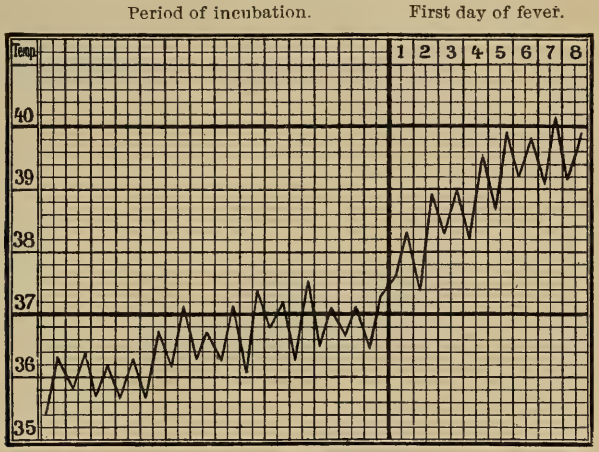

FIG. 8.—Temperature-curve from a case of typhoid fever in a man, twenty-one years old. Nosocomial infection during convalescence from a severe febrile attack of rheumatic polyarthritis. Even before the beginning of the characteristic curve of the first week of typhoid fever, the subnormal temperature following recovery from polyarthritis rises to the average normal level and exhibits a number of fluctuations more than usually marked.

before transitory, ill-defined, and varying disturbances and complaints are present. In general, this stage is free from true febrile manifestations. If, however, careful observation be made in times of epidemics, particularly if the temperature of apparently still healthy predisposed relatives of the patient be taken regularly, if cases are observed that are admitted into the hospital during the period of incubation with an indefinite diagnosis, or if nosocomial attacks are thoroughly studied from the outset, the course of the temperature-curve in the period of incubation will show in not a few that something is taking place within the body. In a certain proportion of the individuals in question it will be found that, without actual febrile elevation of temperature, a more marked variation in the daily curve takes place than under physiologic condi-

tions; the temperature may be somewhat lower in the morning, and a few tenths of a degree higher in the evening, than was observed in the patient while in a state of health. In other patients a temperature of 38° C. or somewhat higher is occasionally attained toward midday or evening, either spontaneously or more frequently after physical and mental exertion. In those convalescent from other febrile diseases who exhibit subnormal temperature in consequence of exhaustion, the body-temperature rises somewhat, to the normal of the individual, as they enter upon the stage of incubation of the attack of typhoid fever, and under such conditions it exhibits at times unusual fluctuations between morning and evening (Fig. 8).

This instability of the temperature-curve during the period of incubation is quite generally associated with considerable variability in the pulse, which on slight provocation increases suddenly in frequency, and particularly in the evening is often much more rapid than it is during health.

I believe that greater importance than is commonly given should be attached to the pulse-temperature ratio during the period of incubation. Careful observation of this ratio at this time may occasionally lead the trained observer in the right direction. Invariably, and almost in a typical manner, it occurs repeatedly that dwellers in a hospital, for instance, servants, laborers, mechanics, who exhibit only general symptoms and apparently are free from fever, are sent to the hospital with an indefinite diagnosis, and sometimes with a suspicion of simulation. Under such circumstances no especial organic alteration will in fact be found, and only on careful observation of the abnormally marked fluctuation in the daily curve and the instability of the pulse will attention be awakened to the fact that important processes are taking place in the body. The experienced clinician will then, among other things, think of the incubation-stage of typhoid fever, and recommend rest in bed with a restricted diet. Often the occurrence of repeated chilliness at the beginning of the febrile stage and the subsequent characteristic elevation of temperature will show how justified was the caution observed (Fig. 9).

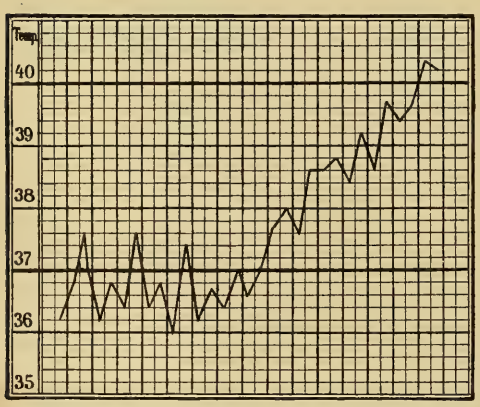

FIG. 9.—Temperature-curve from a case of typhoid fever in a waiter, twenty-six years old, admitted with a suspicion of simulation. During the first nine days there was no febrile elevation of temperature, but only abnormally wide daily fluctuations. On the tenth day the febrile period of a moderately severe attack of typhoid fever pursuing a regular course set in.

In the first week of fever the elevation of temperature attains the definitive height of the febrile period in general, or it may rise even higher. The mode of ascent of the temperature-curve, in contradistinction from that of many other infectious diseases, as, for instance, typhus fever, pneumonia, and variola, is generally, in the case of typhoid fever, more gradual. Usually, the ascending movement of the curve continues for from three to five days; less commonly the entire first week is occupied by it. This mode of protracted ascent is in itself of importance in differential diagnosis. In addition, the remarkably uniform, characteristic course of this portion of the curve in detail is characteristic. The temperature rises in such a manner that it is regularly from 0.6° to 1.0° C. higher in the evening than on the preceding evening, while it exhibits each morning a reduction of from 0.4° to 0.6° C., so that it does not become as low as it was on the previous day. The form of the ascent is, in other words, step-like. If, in this way, on the evening of the third to the fifth day, or in markedly protracted cases as late as the sixth or the seventh day, the definitive height of the temperature is reached at 40° C. and above, even 41° C, the fever then remains continued for a week or even longer, not rarely for a week and a half or two weeks; 40° C. and above in the evening, and toward morning a reduction not exceeding the physiologic variation.

In isolated instances slighter daily variations than the normal may take place either for a few days or throughout the entire febrile stage, so that the course of the temperature closely approximates that of a continued fever in the true sense. This feature is observed almost always in severe cases. Stated in detail, variations only of from 0.3° to 0.5° C. occur, or even less, between the highest evening and the morning temperature, and at times no variation at all is observed for several days. In cases of such especial severity the average temperature also is generally higher. It is in such cases that the temperature reaches 41° C. and above, and in which, if the patient does not previously succumb to the disease, the stage of continued fever may be extended to two whole weeks and even more. Cases setting in with such severity sometimes acquire a more favorable aspect after the first week of the continued fever in so far that the temperature-curve during the second week declines to a somewhat lower level, although the slight degree of variation persists (Fig. 10).

That period in which the continued fever or the remittent continued fever becomes more markedly remittent or even intermittent is generally designated the third febrile period. This first manifests itself by the circumstance that the evening temperature still remains at its usual height,

or approximately so, while the morning reduction becomes much more marked, from 1.5° to 2° C. and more. If the disease pursue a mild course, such remissions may make their appearance as early as the middle or the end of the second week, while in more marked and in severe cases the beginning is deferred to the third or even the commencement of the fourth week. The duration of this portion of the curve is variable: from three to five days, rarely longer. It is especially this portion of the curve that is most frequently shortened, ill defined, or modified. It may even remain wholly undeveloped, so that the stage of descending curve follows directly that of continued fever or remittent continued fever.

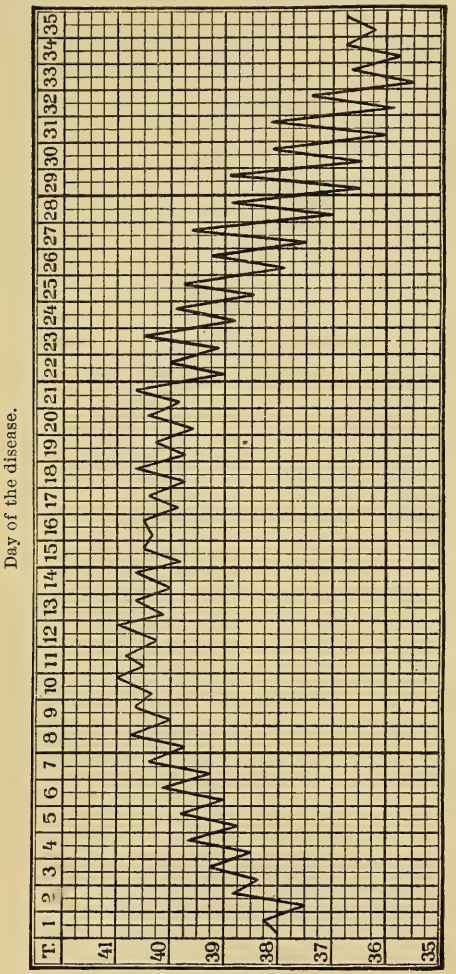

FIG. 10.—Temperature-curve from a case of typhoid fever in a man twenty-eight years old Severe attack of some-what protracted course, without complication. Typical temperature-curve.

The stage of the descending febrile curve, which, together with the preceding, corresponds to the anatomic process of clearing up of the last intestinal ulcers and of progressive cicatrization, is generally placed between the end of the third and the middle of the fourth week. From five to ten and even fourteen days then elapse before the normal is reached. In this stage, which is often appropriately designated that of steep curves, the variations in temperature are often more marked than in the previous stage, so that persistently or for days variations between the morning and evening temperatures may be observed, such as are customarily observed in the course of diseases presenting a true intermittent type of fever. Temperature-variations of from 2° to 2.5° or even 3° C. are under such circumstances not

uncommon. Traube has with propriety pointed out the similarity between such curves and those of certain forms of pulmonary tuberculosis, and has accordingly spoken of a hectic stage.

In special cases the descent of the curve takes place in such a manner that the morning and evening temperatures of the following day are lower than those of the preceding day. At the same time the decline in the morning temperature at the beginning of the steep curves is generally more marked than the height of the evening rise. In milder cases pursuing a regular course it may be mentioned that the entire course of the febrile stage may not rarely be compressed into a period of three weeks, with the characteristic development of the four stages of the curve as just described for the severe cases. The initial stage under such circumstances lasts about four days; the succeeding period of continued fever continues until the end of the second week, thus scarcely more than a week; while the stage of intermittent and declining curve occupies the last days of the second and the third week. Such a course may be illustrated by the diagrammatic chart of Wunderlich (Fig. 11).

We are indebted to the extremely careful and painstaking observations of Thomas,[1] Jürgensen,[2] Ziemssen and Immermann,[3] and others for such complete knowledge of the course of the temperature in cases of typhoid fever that this has become familiar to us both for day and night and from hour to hour. There is usually an uninterrupted ascending tendency of the curve in the course of the day, so that in the late hours of the afternoon, generally between five and seven o'clock, the maximum temperature is likely to be reached. From this point on, into the night and until morning, there is a gradual decline, so that the temperature usually reaches its lowest point between six and nine o'clock in the morning.

The temperature-curve often exhibits a noteworthy deviation in persons who by reason of their occupation transform night into day. Thus, I have observed, especially in bakers, the height of the temperature to occur in the middle of the night or even at an early hour of morning, and the decline in the curve toward the evening. The aged and children also occasionally exhibit this inverted type of temperature.

It is noteworthy also that for days and even for weeks more than one elevation of temperature may take place in the course of twenty-four hours. Not at all rarely there are two such elevations, one of which

[1] *Arch. d. Heilk.*, 1864.

[2] *Klin. Studien über die Behandlung des Abdominaltyphus mit kaltem Wasser*, Leipsic, 1866.

[3] *Die Behandlung des Abdominaltyphus*, Leipsic, 1870.

generally occurs in the middle of the day, far less commonly at a late hour of the evening or during the night. More than two elevations of temperature in the twenty-four hours are less frequent. Curves with two or more such elevations in the course of the day may sometimes persist throughout the entire fastigium. They are not especially rare in cases in which the curve in general exhibits a tendency to marked remissions and intermissions (Fig. 15). Concerning the causes of the multiple

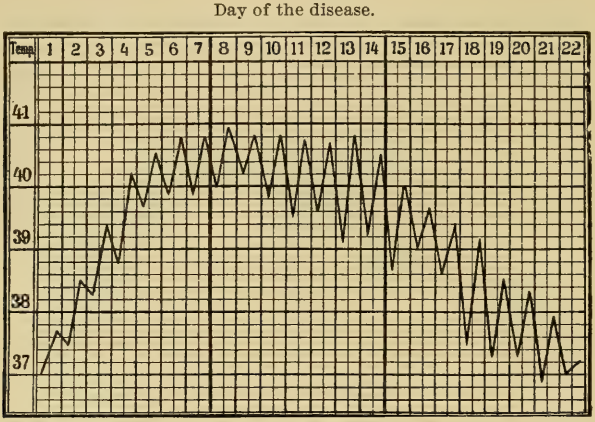

FIG. 11.—Temperature-curve from a mild case of typhoid fever of regular course (after Wunderlich).

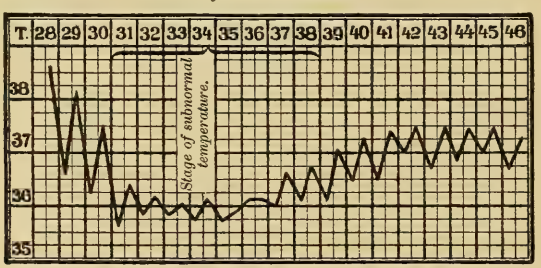

FIG. 12.—Temperature-curve from a case of typhoid fever in a previously healthy, robust man, twenty-three years old. Severe case of typhoid fever of regular course. Stage of convalescence.

elevations of temperature nothing is known, especially with regard to those that persist regularly for a considerable time. As a transitory phenomenon the manifestation is not at all rarely caused by external disturbances, in part by mental or physical exertion, and in part also by complications.

The stage of convalescence, like that of incubation, has by no means been sufficiently studied with relation to the state of the body-temperature. At this time also the curve exhibits a typical character in far

greater degree than in the case of the other acute infectious diseases. This is doubtless due to the more protracted duration of the preceding febrile stage, which naturally must exert a corresponding influence upon the form of the curve in the afebrile stage, and in all severe and particularly long-protracted cases may cause the stage of convalescence to be characterized by emaciation.

The first period after defervescence may be most appropriately designated as the stage of subnormal temperature. In detail, the curve pursues such a course that, on the morning following the last febrile day, less commonly on the next succeeding day, the body-temperature declines to 36° C. or lower.[1] From this time on, after a febrile stage of rather severe or long-protracted course, it remains about 36° C. or considerably below, continuing at times up to one and a half or even two weeks, and rarely even longer. If the patient is kept at rest physically and mentally and in bed, the daily fluctuations at this time generally remain unusually slight—slighter than the physiologic. They are then scarcely more than half a degree, generally less, so that in the evening the body-temperature rises little above 36°, at most to 36.5° C. With the progress of convalescence, the daily fluctuations in the temperature become somewhat greater, approximating the physiologic, and then the temperature begins to rise again, until, at the beginning or the end of the second week of the afebrile stage, rarely at the beginning of the third week, it has reached the level normal to the individual (Fig. 12).

Both during the stage of subnormal temperature, as well as during the succeeding period, the course of the temperature in convalescents, however uniform it appears to be during rest, may exhibit marked instability. All possible external and internal influences—slight mental excitement, visits, news, hopes and disappointments, slight dietetic errors or transitory constipation—now generally give rise to sudden, often not inconsiderable, elevations of temperature. Even though the temperature do not rise from the subnormal much above the normal, the elevation is nevertheless attended with symptoms common to actual febrile states. Individuals presenting persistent subnormal temperature for a considerable time exhibit febrile symptoms, even at temperatures that during health fall within the limits of the normal.

The stage of subnormal temperature in severe protracted cases terminating favorably is as sharply and constantly marked as all the other stages of the febrile period. When it does not immediately follow the stage of steep curves, the possibility of irregularities must be thought of,

[1] I have observed cases in which the temperature-curve remained subnormal for as long as three weeks and even longer after defervescence.

and suspicion should especially arise that the morbid process has not entirely subsided. As a rule, recrudescences or relapses then occur. These are, furthermore, to be expected if enlargement of the spleen does not disappear with reduction in the body-temperature. It will be instructive at the conclusion of this section to reproduce half-diagrammatically the entire temperature-curve, not alone that of the initial and the febrile stages, but also that of the period of incubation and that of convalescence (Fig. 13).

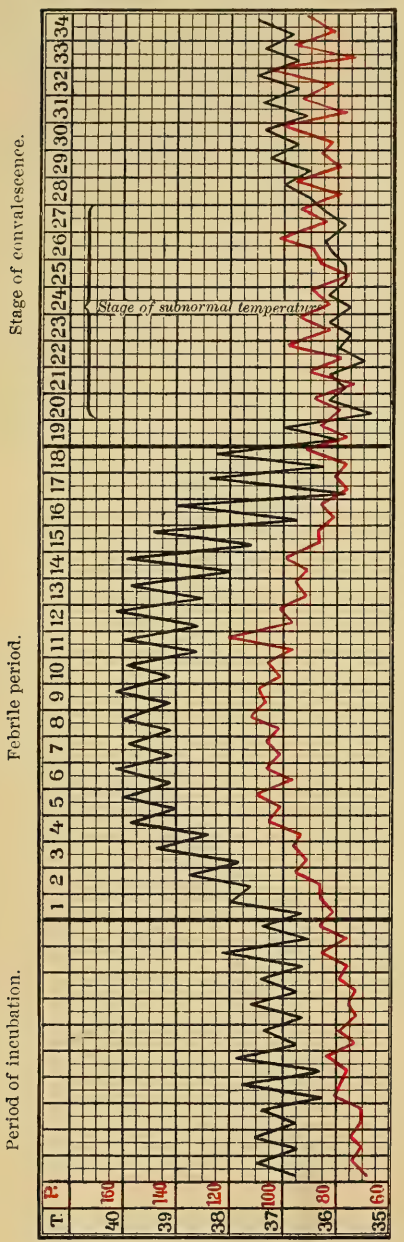

FIG. 13.

Duration and Form of the Individual Sections of the Curve.—The time of the first **ascent of the temperature-curve** usually occupies, as has been previously mentioned, from three to five days, and then especially, less commonly in adults, it may take longer. There also occur, however, cases in which the period of ascent is shorter; thus the temperature, rising by steps, may reach its height in forty-eight hours, or may even in still shorter time rise at a single jump to the beginning of the level of the continued fever. In the latter event the febrile period often sets in with a chill, which is a rare occurrence in cases attended with a slow, step-like ascent.

The old rule of Wunderlich, that in a case of typhoid fever the temperature after the commencement of the ascent does not return to the normal even during the morning hours, still holds good for the overwhelming majority of all cases. But rarely, and

then mostly in mild or abortive cases, the step-like ascent of the temperature is modified by a transitory decline to the normal or below in the morning.

Exceedingly rapid ascent of the initial temperature is encountered far more frequently in children than in adults, and in the former the fastigium and the stage of defervescence also are often greatly abridged. In general—and this refers to children and adults alike—a rapid ascent of the temperature is peculiar rather to the milder, and therefore to the shorter or even abortive, cases.

Far greater variability with relation to the duration and the form of the curve is exhibited by **the period of febrile elevation** than by the initial stage. If the curves of a few cases, mild and severe, are placed side by side, nothing of a typical character would be noted. If, however, large series of charts are studied, some regularity will, on the whole, be observed. Wunderlich has distinguished two large groups of cases depending upon the duration of the height of the disease. In the first he includes short cases of three weeks' duration or not much longer, with a fastigium of from a week to a week and a half; and in the second he includes protracted cases, in which the fastigium lasts from three to six weeks and even longer. Between these there are naturally all possible gradations and variations, approximating more or less to one or the other variety. Finally, there is a group of atypical cases to be considered, to which Wunderlich attached far too little importance, in which the temperature-curve exhibits absolutely nothing characteristic. The first of Wunderlich's groups includes almost solely mild cases that regularly terminate in recovery, or those that pursue an unfavorable course only in consequence of accidental unfavorable conditions and complications, such as intestinal hemorrhage, perforation, etc. The second group, as such, has little relation to the course and the mode of termination. Although this group includes the majority of the severest cases, it comprises also many of moderate severity, even down to the mildest.

The total duration of the febrile stage, concerning which a few statistical statements may be made before we pass to special consideration of variations in its course, is considerably longer than in most other acute infectious diseases. For adults up to the age of fifty-five years it was in more than half of my cases (50.5 per cent.) not more than twenty-one days. In not a few cases it was, however, from twenty-two to thirty-three days (29.3 per cent.), while only in 14 per cent. was the febrile stage longer than this. The last event was observed especially in the aged and in previously debilitated persons. The course of the fever is then likely to be oscillating and irregular. In children the febrile stage is, on the whole, shorter. Among 443 children up to the age of fourteen years, in whom I made

observations upon this point, I found a duration of twenty-one days or less in 88.5 per cent.; of between twenty-two and thirty-three days in 16 per cent.; of more than thirty-three days in 7.5 per cent.

If the older children are separated from the younger, it will be seen distinctly that the former rather approximate the type of adults. The duration of the fever was:

	In children between eleven and fourteen years old inclusive.	In children up to the age of ten years.
Twenty-one days or less	60.0 per cent.	81.9 per cent.
Between twenty-two and thirty-three days .	25.7 "	11.3 "
More than thirty-three days	11.8 "	4.8 "

With regard to the peculiarities in the course of the fever, let us now consider the severe and the severest cases. Both those of short duration and those of more protracted course in adults up to the thirty-fifth or the fortieth year of life generally exhibit a considerable degree of elevation and noteworthy regularity of the temperature. The difference between morning and evening temperature is generally not more than one degree, often less; while the average morning level is from 39° to 40° C., and the evening level up to 40.5° C. and above. Of itself it is of grave omen if with a high temperature but slight morning remissions take place, especially if the temperature remains uninfluenced in spite of the employment of cold baths or other antipyretic treatment (Fig. 14). If the temperature be especially high, possible complications should be carefully looked for. Septic conditions, pneumonia, and secondary meningitis are especially to be kept in mind.

Day of the disease.

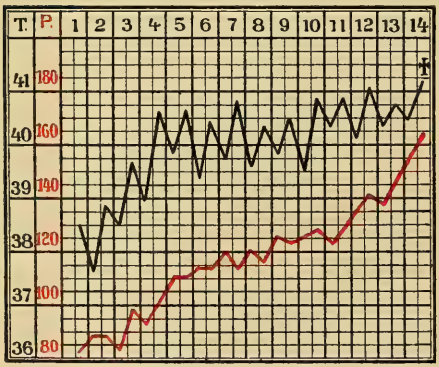

FIG. 14.—Temperature-curve from a case of typhoid fever in a man, twenty-two years old. Unusually severe course without special complications. Death on the fourteenth day of the disease.

At times the severe continued fever is interrupted by one or more marked intermissions. The temperature then declines suddenly, more frequently during the day than during the night, often falling several degrees, and not rarely falling far below the normal. Marked simultaneous diminution in the size of the pulse, with considerable increase in its frequency, stamps this occurrence as true collapse (Fig. 23). Less commonly, and then especially in individuals between the ages of twenty-five and

thirty years, not less marked variations in the curves occur temporarily without obvious cause, but unattended with corresponding diminution in tension and size of the pulse and without increase in its frequency. Such interruptions of the high continued fever, in other respects also not attended with alarming symptoms, and which are designated pseudocollapse, I have observed in several cases in which there were two or three elevations daily (Fig. 15).

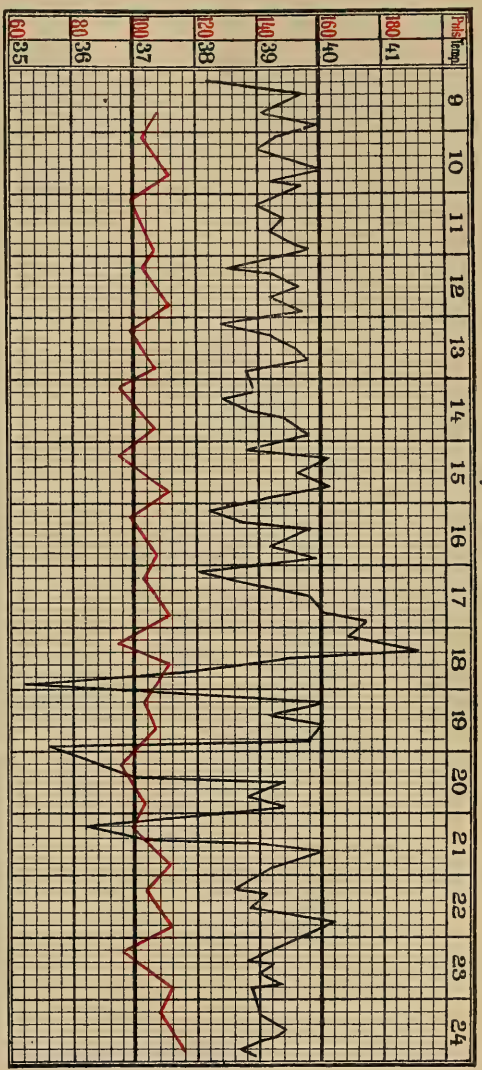

Fig. 15.—Temperature-curve from a case of typhoid fever of severe course in a girl, sixteen years old. Unusually marked intermissions in the temperature-curve without actual manifestations of collapse (pseudocollapse).

The explanation of this remarkable, and from the prognostic standpoint generally indifferent, occurrence will long remain obscure.

In the presence of such pseudocollapse, however, the prognosis should be guarded if the stage of steep curves does not soon thereafter begin or the intermissions do not actually make their appearance. Should, on the contrary, the body-temperature rise again to its previous level, so to continue in the form of the earlier continued or remittent continued form, the further course of the case may be expected to be severe. I have then subsequently observed true collapse, during which death occurred. If severe cases of long duration begin to pursue a more favorable course, the high continued fever is, at the end of the second or the commencement of the third week, generally converted into

a remittent or even an intermittent fever with differences of from 1.5° to 3° C. and more between morning and evening temperatures (Fig. 16). The curve may then continue for eight days and more, either with regularly repeated remissions, or—and this applies especially to severe cases—days of high continued fever alternating with others of remittent continued fever. Less commonly, in my experience, beginning improvement is characterized by the circumstance that the high average temperature gradually subsides without increase in the remissions or with only isolated considerable daily fluctuations.

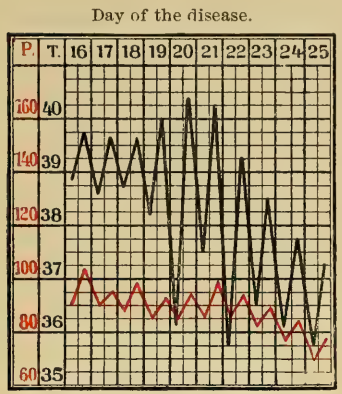

FIG. 16.—Temperature-chart from a case of typhoid fever of moderate severity in a man, thirty-four years old. Marked fluctuations in the temperature-curve without corresponding alterations in pulse frequency.

The less common cases of severe protracted course in childhood exhibit with especial frequency a form of temperature-curve with marked remissions and intermissions. Even when in the severest cases the fastigium exhibited at the beginning the characteristics of a continued fever, this period is likely to be much shorter and soon to be replaced by a period of marked fluctuations. These markedly intermittent curves are most constant in children up to the eleventh year, while older children up to the fourteenth year more frequently exhibit the conditions observed in adults.

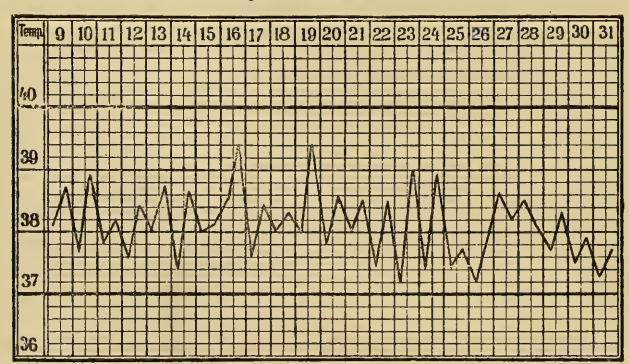

FIG. 17.—Temperature-curve from an exceedingly severe protracted case of typhoid fever in a man, fifty-six years old. The temperature-curve exhibits a senile form.

The form of the temperature-curve is quite remarkable in severe cases in persons of the age of forty-five years and above, as it is

often also in younger adults who have become old prematurely or debilitated by a dissipated mode of life, alcoholism, or exhausting chronic disease. Under such circumstances the temperature, in spite of the most severe course of the disease and the most alarming general condition, remains not rarely, even at the height of the attack, remarkably low, so that during the morning hours the temperature scarcely rises above the normal or remains below, and at night does not exceed 39° C. The form of the curve in such cases is remarkably irregular: marked remissions alternate with wide, collapse-like fluctuations, and, while death is likely to occur almost always in young patients while having exceedingly high temperature, under the circumstances in question marked preagonal decline of body-temperature may take place. Inexperienced observers may readily be deceived by the low temperature-level during the course and by the fall at the most serious period, and thus be tempted to give a favorable prognosis (Fig. 17).

The mild and the mildest cases of typhoid fever pursue their course at times speedily, in a week or only a few days, and accordingly with a scarcely appreciable fastigium; but, on the other hand, they may be unduly prolonged. We shall later return to the separate consideration of abortive and the mildest afebrile cases. Here only the mild cases, lasting up to three weeks, and the protracted mild cases, will be discussed fully. The mild cases, lasting three weeks, most frequently resemble of all the forms the typical. With a relatively short duration the individual stages are characteristically marked in the curve (Fig. 11, p. 126). After the height of the fever has been reached within two and half, at the latest four, days, the duration of the true continued fever is likely to be from four or five days to a week. Then there occur more marked fluctuations of temperature of 1.5° C., and frequently much more, at first still with rise of the evening temperature to that of the preceding day, after which, at the end of the second and the beginning of the third week, the decline begins in the form of a true steep curve.

Another exceedingly common variety of mild course is that which from the beginning exhibits great daily fluctuations in the temperature-curve, with complete absence of true continued fever, or with an indication of this for two or three days at most. In some cases the intermissions exhibit such regularity and uniformity as to time as are observed in cases of true intermittent fever. If, under such circumstances, the remaining symptoms of typhoid fever are not sufficiently well marked, difficulty and error in diagnosis may readily arise (Fig. 18).

Especially the markedly intermittent and remittent cases, particularly

those with considerable irregularity in the form of the curve and, on the whole, moderate elevation of temperature, are at times of unusually long duration, without the appearance of any alarming symptoms throughout the entire course. In not a few cases with an intermittent curve the initial stage also exhibits this character, and recrudescences and relapses are also likely to be attended with equally marked fluctuations in the curve. Also, certain cases of ambulatory typhoid fever are, in my experience, attended with considerable remissions in the temperature-curve, at times even with such marked intermissions that in the morning or late in the evening or during the night the temperature is scarcely above the normal level, while considerable elevations take place only during the midday or for a short time late in the afternoon. I

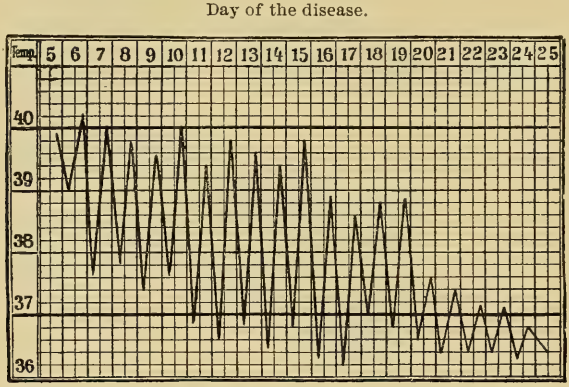

FIG. 18.—Temperature-chart from a mild case of typhoid fever in a girl, eighteen years old. From the twentieth day of the disease the course of the attack was afebrile. The curve was markedly intermittent from as early as the sixth day. The fever was almost purely of quotidian type.

have in a number of instances observed that in such cases the diagnosis of malaria was made, and with all the greater certainty when the elevation of temperature was initiated with a chill. Only when the patients went to bed and roseolæ, splenic enlargement, and characteristic stools appeared was the diagnosis corrected.

In cases of mild typhoid fever in children the remittent and intermittent form of the curve is usual. Under such circumstances the temperature-curve is very rarely regular, like that of intermittent fever. On the contrary, the most marked irregularity is the rule. Unusually marked fluctuations in the curve, alternating with periods of lower level or with periods of causeless low temperature, the inverted type with low evening and higher morning temperature, often combine with a number of other irregularities to make a quite remarkable curve. At the same

time, the course of such cases is often protracted, so that the febrile period may continue for as many as six or even eight weeks, and the patience of the friends and the physician may be sorely tried.

Too much attention cannot be paid to the intermittent and remittent febrile courses described and to the great irregularities of such curves. One who is unfamiliar with and incapable of interpreting them is exposed to the liability of great error in diagnosis and prognosis. It is especially in such cases that cryptogenetic septicemia, miliary tuberculosis, and other diseases far more feared than typhoid fever are often incorrectly diagnosed. It has already been noted that not much is known in general with regard to the causes of the marked fluctuations in temperature. The conditions are different with regard to influences that temporarily exert such an effect. Especially intestinal hemorrhage and extensive peritonitis are to be mentioned in this connection. Persistent diarrhea also is often responsible for marked remissions and irregularities in the curve. Transient marked elevations of temperature without grave significance may often be attributed to extraneous exciting influences, mental as well as physical. The high temperatures observed in the first hours after entrance of the patient into the hospital are familiar, and these are often not again attained throughout the entire attack. They are undoubtedly referable to the disturbances associated with separation from one's family and to the transportation. Not less familiar are the febrile elevations in cases of typhoid fever after the presence of visitors, as well as those that are caused by protracted conversation, exciting news, dietetic error, or getting out of bed contrary to instructions. Naturally, all of these occurrences are permissible in explanation of sudden elevation of temperature only when, after most thorough examination, this cannot be attributed to some local complication or to sudden exacerbation of the general process.

Variations in the Curve in the Stage of Defervescence.—In the large majority of all cases of typhoid fever, the severe and the moderately severe, as well also the milder, if they have in the preceding stages approached the typical form of the curve, the transition of the temperature to normal is likely to take place in the form of the so-called steep curve. This period lasts for from three to eight days in cases of moderate and not too protracted course. Quite generally, after severe as well as after mild cases, the curve passes far below the normal with the last marked decline, so that on the morning following the first afebrile evening the temperature will be between 35° and 36° C. The temperature then varies in different cases: it may—as is not uncommon

and has been described—remain subnormal for a week and longer, the stage of emaciation thus following immediately. In other cases, after the normal has been reached, there follow more or less marked, irregular fluctuations in the curve, through which the physiologic evening temperature is reached and probably also is exceeded. After this has continued for a few days and the disease tends toward definitive termination, the characteristic stage of emaciation begins. Only in the mildest cases can recovery and return of the temperature-curve to the preceding physiologic form and level follow immediately, without the occurrence of the stage of emaciation.

The cases are not rare in which the decline of temperature takes place not with great fluctuations, but gradually. This uniform decline is

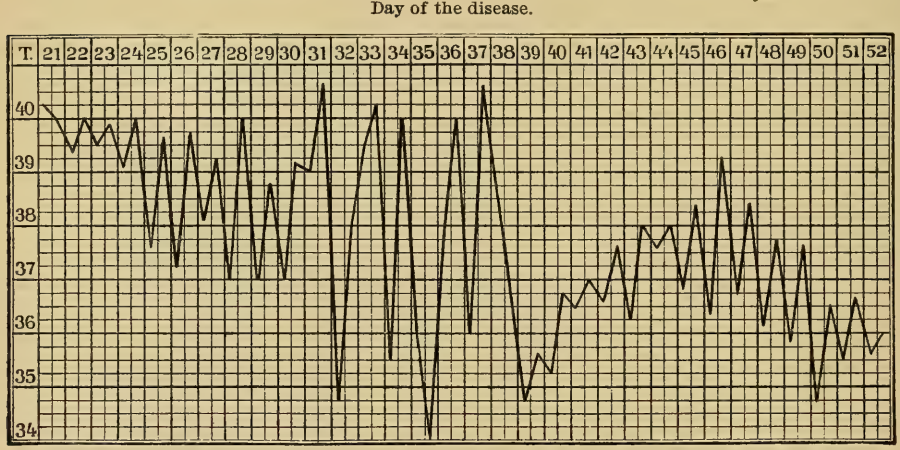

FIG. 19.—Temperature-chart, with unusually marked fluctuations in the temperature-curve before the primary defervescence, from a case of severe typhoid fever, of greatly protracted course, in a workman, seventeen years old. A slight recrudescence began on the forty-first day of the disease.

likely to be completed, on the average, in two or three, rarely more, days. Still another variety of defervescence is that in which, after unusually marked fluctuations in the curve persisting for days, the difference between morning and evening temperature being at times 4 or 5 degrees, definite reduction in temperature takes place within from twelve to eighteen hours, occasionally within a still shorter time, in a single stroke. In such cases I have observed recrudescences and relapses with remarkable frequency (Fig. 19). At times this variety of sudden decline of temperature is preceded by one or two such marked fluctuations, after the curve has previously preserved the characteristics of a remittent continued fever. Under such circumstances the temperature-fluctuations are more often initiated and accompanied by chills,

and this may at times cause great embarrassment in diagnosis. This may be transformed into satisfaction if it soon appears that this is only

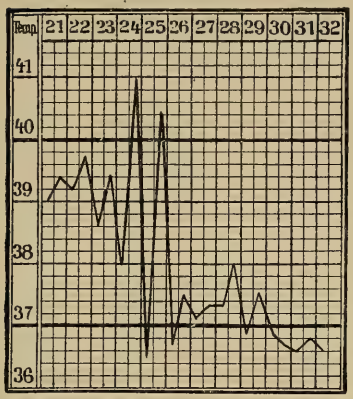

FIG. 20.—Temperature-chart from a severe case of typhoid fever in a woman, thirty-six years old. Defervescence with two marked fluctuations in the curve, with chills.

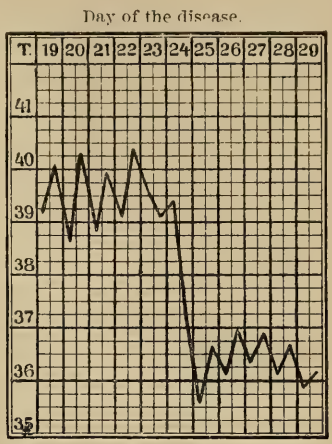

FIG. 21.—Temperature-chart from a severe case of typhoid fever in a woman, thirty-one years old. From the twenty-fourth to the twenty-fifth day of the disease there occurred a critical decline, without antecedent marked fluctuation in the curve.

a peculiar form of reduction in the curve, and not an indication of a complication (Fig. 20).

It is probably least frequent for the remittent continued fever of the fastigium to terminate suddenly, with a critical decline, at a single stroke, or for the crises to be preceded only by a precritical elevation on the preceding evening. I have observed this variety of defervescence more frequently in young persons, and especially in children, but it occurs also now and then in adults (Figs. 21 and 22).

Finally, in the less common cases of typhoid fever that pursue an irregular and protracted course or are attended with relatively low temperature in the presence of severe general manifestations, often no marked transitional stage in the curve can be noted. This stage then pursues an irregular course, with more or less marked fluctuations, the morning and evening temperatures becoming grad-

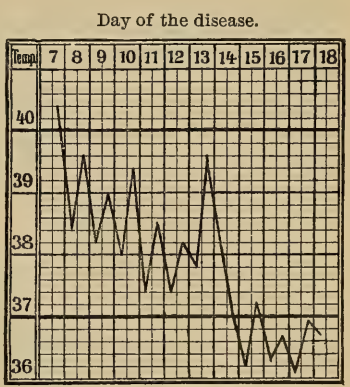

FIG. 22.—Temperature-chart from a mild attack of typhoid fever in a man, twenty-five years old. Critical decline of the temperature with defervescence after precritical elevation.

ually lower, and the normal temperature is slowly reached. Viewed anatomically, these are perhaps cases with slowly healing ulcers, with recrudescences and sluggish lesions. These are the cases also in which for a long time doubt exists, and certainty may be wanting at times even after the end of the disease, as to what parts of the curve belong to the actual typhoid process and what to possible complications and sequels. The alterations in the form of the curve in connection with definite modes of course of the typhoid attack, and with important sequels and complications, will be more appropriately discussed in the respective chapters.

CHANGES IN THE CIRCULATORY ORGANS.

The discussion of these will be taken up here on account of the intimate relation of the heart and the pulse to the fever, and especially to the state of the body-temperature. It is well, for reasons that will later be more fully detailed, to separate in the description cases without especial cardiac disorders and those with severe heart-affections.

We shall begin with a consideration of the character of the **pulse** in cases pursuing an uncomplicated course. In all stages of such cases a close correspondence exists between the form of the pulse-curve and the state of the temperature.

In the initial stage it will be observed in the majority of cases that the increase in the frequency of the pulse takes place in the same step-like manner as the ascent of the temperature-curve. In some cases the form of the pulse-curve imitates exactly that of the temperature-curve. In other instances the pulse-frequency rises relatively more slowly; while in irritable individuals, on the contrary, it reaches its highest average level more quickly than the temperature-curve, persisting also during the first period of the continued fever. Likewise, during the period of fever-height, both curves often exhibit a striking parallelism. In the amphibolic stage the pulse-frequency then generally declines, still more so in the period of steep curves, so that, if the temperature has again reached the normal or has fallen below this, the pulse-frequency will be again approximately normal, at times somewhat below, at other times above.

In general it may be stated that in the first days of the afebrile period the number of pulse-beats more frequently is relatively high than low, the former especially if the body-temperature at this period does not become subnormal, but remains steadily at about 37° C. or above. This parallelism between the pulse-curve and the temperature is, according to the present state of knowledge, not referable to the action of the

latter upon the heart and the cardiovascular system, as earlier writers believed. Both are due rather to a common cause, namely, the action of toxins, which, in accordance with the intensity of the infection and the reactive susceptibility of the individual, reaches a definite expression in each individual case.

Quite remarkable and not emphasized in deserved degree by even some recent writers is the relative degree of infrequency of the pulse often observable during the ascent of the temperature-curve and throughout the entire stage of continued fever. In other words, the pulse in many, even moderately severe and severe, cases does not attain the frequency that we are accustomed to encounter in other infectious diseases with like elevation of temperature. This is observed especially in young, robust individuals, up to about the fortieth year of life, and more frequently in men than in women. It is quite generally found under such circumstances that, with an average temperature of 39° or 40° C., and even more, the pulse ranges about 80 in the morning and between 90 and 100 in the evening, rarely rising higher. Even in the presence of severe manifestations—marked diarrhea, meteorism, and slight stupor—this character of the pulse need not be absent. As a matter of fact, well-marked cases of moderate severity are not rarely encountered in which the pulse-frequency in the morning scarcely exceeds the normal, and throughout the entire course of the disease does not reach 100 in the evening. This peculiar relation between pulse and temperature is responsible for the familiar characteristic appearance of the charts upon which both are recorded simultaneously with the remarkably wide separation of the two curve-lines. Of all febrile diseases, this relation occurs by far most frequently in cases of typhoid fever, and it may therefore be of itself an excellent diagnostic aid.

As has appeared in several connections, the course of the disease in older children approximates that in adults; so also the relative infrequency of pulse occurs not rarely in older children, although this is almost always wanting in younger children. I can wholly confirm this observation, first made by Roger.[1] While, however, the statements of this writer apply to children after the sixth year, I have observed the phenomenon almost only in those between the tenth and the fourteenth year. In younger children, on the contrary, I have observed, almost without exception, rather high pulse-frequency.

For adults Liebermeister,[2] among recent writers, emphasizes the infrequency of the pulse, and he mentions Sauvages, Hufeland, and Berndt as earlier witnesses of the manifestation. The explanation suggested by Liebermeister, that the typhoid poison induces directly, through an irritative

[1] *Rech. clin. sur les mal. de l'infance*, T. i., Paris, 1872. [2] *Loc. cit.*, p. 91.

effect upon the central nervous system, especially the medulla oblongata, diminution in pulse-frequency, appears to me noteworthy and probable. Other poisonous substances, as the biliary acids which circulate in the blood, at times are known to have the same effect. Naturally, the interesting question is by no means wholly disposed of by the hypothesis mentioned. Further, possibly experimental, observations are urgently necessary.

It is noteworthy that among the well-known earlier observers of typhoid fever, Griessinger, Louis, and Murchison considered infrequency of the pulse only as an exceptional condition.

With regard to the quality of the pulse in previously healthy, robust individuals in the initial stage and at the height of the disease, it appears full and, particularly in the first period, notably tense. If special circumstances do not arise during the course of the disease, the pulse is likely to remain equal and regular until the end of the febrile period. At the end of the second and in the third week, in severe cases earlier, the pulse quite generally is noted to become softer without corresponding diminution in its fulness. The cause of this manifestation—the reduction in the tension of the arterial wall—is responsible for another quite usual simultaneous change in the pulse: the pulse becomes dicrotic, even tricrotic, and in extremely rare cases polycrotic. Also, this character of the pulse again is undoubtedly much more frequent in cases of typhoid fever than in those of most other febrile diseases, so that, with many other writers, I attach diagnostic significance to it. If it is additionally associated with the relative infrequency of the pulse already mentioned, the probability of the existence of typhoid fever is thereby increased.

The dicrotic pulse is observed most frequently and most distinctly in adults, even in elderly persons, unless the existence of atheroma prevents the conditions necessary for its occurrence. In children the dicrotic pulse is, in my experience, observed less commonly and least commonly in young children, obviously on account of the natural smallness of the pulse, due to the physiologic narrowness of the arterial lumen. In older children, near the age of puberty, I have observed dicrotism now and again. In very severe, and especially in fatal, cases the dicrotism generally diminishes and soon disappears entirely at the height of the fever, owing to the diminution in the fulness of the arterial tube and in pulse-tension. Toward the end of the febrile stage in almost all severe and moderately severe cases, and also in mild cases that pursue a protracted course, the pulse becomes smaller, while its softness persists, and the dicrotism disappears.

The time of the day causes no material difference with relation to the fulness and the tension of the pulse, but all the greater difference with regard to the frequency. It may be stated in general that the daily

variations of the pulse in cases of typhoid fever are comparatively marked. The differences in pulse-frequency at the hours when the temperature is highest and at those when the temperature is lowest is likely to be from 10 to 20 and even 30 beats. In general, the high and the low number of pulse-beats and the high and low degrees of temperature of the daily curve correspond in time. If, however, more frequent pulse-observations are made, quite marked differences can be made out, especially on different days and at different times of the day. Undoubtedly, the variations in pulse-frequency are slightest in those patients who are kept especially quiet and undisturbed mentally or physically. In this respect—that is, in so far as they take little notice of what goes on about them—soporose patients resemble them. These patients also exhibit comparatively slight daily variations, even when the frequency is considerable and the tension of the pulse is increased. All of these facts indicate that external conditions exert an important influence upon the pulse-frequency. In entire accord with this statement is the fact that in conscious patients, at all stages of the disease, excitement of the most varied kind makes its influence apparent in the pulse-curve. Every hospital physician is familiar with the increased frequency of the pulse on visiting days. Not rarely the physician, with his finger on the pulse, is able to anticipate the wish that the patient is about to express, since the frequency of the pulse then suddenly becomes increased. This tendency to transitory increase of the pulse should always be borne in mind, especially from the prognostic standpoint: it is one of the peculiarities of the typhoid curve, and in the absence of complications is almost never of serious significance.

The cases are to be interpreted quite differently and more seriously in which, from the outset, the pulse-frequency constantly is especially high or in which the pulse-curve reaches a rather high level even at the commencement of the period of febrile elevation. Under such circumstances the disease may be expected to pursue a severe course. Apart from this fact, persistent acceleration of pulse-frequency is often indicative of complications of most diverse kind. In this connection attention should be directed especially to inflammatory affections of the lungs and the heart, not less than to the possibility of complicating peritonitis and intestinal hemorrhage. With reference to the latter two conditions, the pulse is all the more noteworthy, since with the onset of peritonitis the temperature exhibits a most inconstant character, particularly often showing no elevation whatever, and also that considerable intestinal hemorrhage may exhibit its influence upon the pulse before the discharge has taken place externally. With reference to

intestinal hemorrhages, it is especially to be borne in mind further that, if at all considerable, they give rise to rapid fall of the temperature. This fall of temperature and the increase in pulse-frequency give rise to those intersections in the curve (Fig. 24, p. 222, Digestion) familiar to the experienced clinician as most ominous. . That an entirely similar relation between pulse and temperature may also attend states of collapse of other origin need only be mentioned at this place (Fig. 23).

In especially severe cases, particularly those in which death results from the intensity of the infection, the pulse-curve loses all its characteristic features in the last days, and even for a longer time previous to death : fulness and tension diminish appreciably after the dicrotism has already disappeared; the frequency becomes constantly higher, with

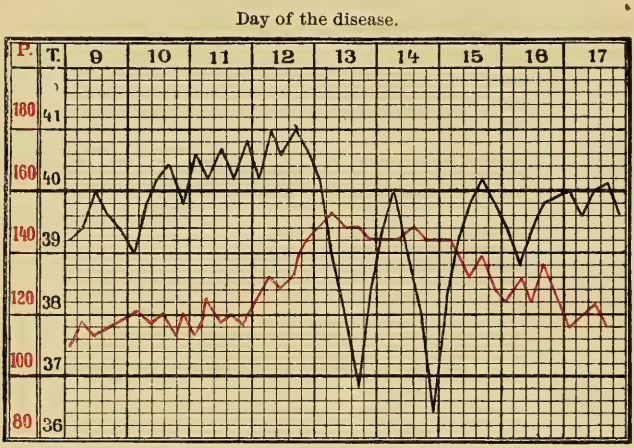

FIG. 23.—Temperature-chart from a severe case of typhoid fever in a man, twenty-seven years old, with collapse without directly demonstrable cause.

progressively diminishing daily fluctuations; finally, the pulse is wholly irregular, scarcely palpable, and not to be counted (Fig. 14).

The stage of defervescence and of afebrile convalescence is likewise deserving of especial consideration with reference to the pulse, such as has been given with reference to the course of the temperature. Already in the stage of steep curves the pulse frequently becomes smaller and harder, with indistinctness or disappearance of the dicrotism. With the marked fluctuations in temperature, there occur not rarely in irritable individuals correspondingly wide fluctuations in the pulse-curve. More frequently, however, the latter do not exhibit a corresponding extent of range, but they may be conspicuously smaller than the temperature-fluctuations, so that no more than the physiologic daily variations appear.

While thus, at the period of steep curves, in patients kept perfectly at rest in bed, the pulse by no means so constantly as the temperature exhibits the remittent and intermitted type, it is characterized by unusual and far more marked variability with every deviation of the patient from the typical course than in the earlier stages. Especially in greatly reduced patients, in irritable men, in women and children, extrinsic and intrinsic influences, themselves inconsiderable, induce quite remarkable variations in the pulse-curve. If the patient sits up or turns over in bed, or with the approach of the physician or of strangers, accelerations up to from 100 to 120 or 130 are quite frequent.

In the first stage of convalescence, which we have designated that of subnormal temperature, the pulse in the majority of cases does not become subnormal. It may, moreover, be accepted as a rule that it now ranges somewhat above the physiologic (individual) normal, at about 80 in the morning up to 100 in the evening. The transitory wide fluctuations due to mental and physical disturbances are also now just as common as in the stage of steep curves.

The cases are infrequent and unexplained in which in the stage of subnormal temperature the pulse-frequency also is subnormal. I have observed the pulse to decline to 50, even to 40, in the evening, and to 36 and even 28 in the morning. Under such circumstances it is always conspicuously small and slow, and at the same time exhibits all of the characteristics peculiar to states of emaciation. Possibly in most cases the explanation is to be looked for in this direction. The subnormal pulse-rate may be observed to persist at times for only a few days, at other times for a week and longer, or into the period in which the temperature-curve rises to the physiologic level. I have observed this infrequency of the pulse also in association with the clinical manifestations of infectious myocarditis, without the discovery in the cases in question of any explanatory peculiarity. Also, during the second period of convalescence, in which the abnormally low temperature again rises to the individual level, the pulse-frequency is likely on the average to remain relatively high, although always with a special tendency to transitory marked fluctuations. This at times becomes especially alarming to young physicians and the friends when the patients begin to be more lively in bed, or after eating, or straining at stool. Even for the first few days after getting out of bed considerable acceleration and instability of the pulse are quite usual. In some patients fourteen days elapse before the previous frequency and uniformity are again attained. In long-protracted, especially severe cases this period may be more extended.

It need scarcely be mentioned specially that, on the whole, previously normal pulse-conditions are restored far more rapidly in healthy young men than in irritable, previously sick individuals or women and children.

The characteristics of the pulse described occur much more frequently during convalescence from typhoid fever than during that from other acute infectious diseases, especially small-pox, which is often cited, typhus fever, and relapsing fever, as well as pneumonia. It will thus be seen that, like the state of the body-temperature, that of the pulse is also of important diagnostic and prognostic significance.

From the diagnostic point of view, the relative infrequency of the pulse in the febrile stage and the dicrotism, so frequent in no other infectious disease, may finally again be emphasized. In addition, the diagnostic significance of the sudden acceleration of pulse-frequency attending conditions of collapse and varied complications may be recalled. From a prognostic point of view it may be said that relative infrequency of the pulse, with good volume and tension at the height of the disease, is of good significance, while dicrotism and polycrotism are without special significance in prognosis. It becomes a matter for concern if tension and volume of the pulse fail early. Also, marked pulse-frequency at an early period in the disease, in the initial stage, or at the beginning of the fastigium, indicates, if at all persistent, a severe course. This is especially true in the case of men and elderly individuals, while women and children in general may exhibit considerable acceleration of pulse without serious significance. Frequently repeated acceleration of the pulse to 130 or 140, apart from children, is ominous under any circumstances. Isolated, quickly subsiding, marked and extreme fluctuations do not indicate much, at least in the terminal stage or during convalescence. Rapid elevation of temperature and acceleration of pulse occurring simultaneously and not quickly disappearing are of grave significance. Intersection of the two curves in such a manner that the pulse is greatly accelerated while the temperature declines rapidly is even more serious.

Irregularity and inequality of the pulse must be considered as grave signs at all stages, but most so naturally in the earlier. They are indicative of cardiac weakness and other profound functional and anatomic disorders of the circulatory organs. Of the two, the inequality is of the far greater significance. Irregularity, especially transitory intermission, may occur in the febrile stage as well as during convalescence —more frequently in women and children than in men—without further consequences. I have observed such intermission of the pulse, together

with retardation and abnormal slowness, especially in the stage of subnormal temperature.

Changes in the Heart-muscle.—It is a matter of course that the state of the pulse in no small degree reflects the condition and the functional activity of the heart—the part taken by the remainder of the circulatory apparatus is not yet sufficiently known—and it would therefore be advisable to discuss both together. Separate consideration has already been given the pulse only for extraneous reasons. In the first place, its character is so closely related to that of the temperature-curve that for this reason alone a certain community in the description of both seemed necessary; and, in the next place, in spite of marked recent advances in anatomic knowledge of the profound changes in the heart in connection with typhoid fever, so little is known concerning the anatomic conditions of the organ in mild, moderately severe, and even severe "uncomplicated" cases that, when the disease pursues its ordinary course, any comprehension of the relations between the heart and the pulse and the arterial system is entirely wanting.

With regard to the condition of the heart in the initial stage of typhoid fever and throughout the entire course of mild and moderately severe cases, a sufficient number of thorough anatomic studies, particularly such as will meet the requirements of modern methods, have not as yet been made, on account of the relative rarity of death at this period. From the clinical and the physical diagnostic point of view nothing especial is appreciable in the heart in such cases, and, as will be shown directly, nothing is made out also in many cases pursuing a severe uncomplicated course. That, nevertheless, simple "functional" disorders of the heart and the vasomotor system are not responsible for such characteristic changes in the pulse, but that under these conditions at least slight transitory tissue-changes take place, cannot be doubted. Of severe and fatal cases of typhoid fever, however, it has long been known that they exhibit profound anatomic lesions corresponding with the clinical manifestations. For the present, however, they cannot be included in the description of the ordinary anatomic and clinical condition of the heart, and are considered as severe specific localizations or complications. Perhaps their relations are comparable to those of febrile albuminuria to true typhoid nephritis.

Laennec early mentioned that "heart-softening" occurs in severe febrile, especially typhoid, states. Louis and Stokes also recognized anatomically and clinically the occurrence of profound changes in the heart in cases of typhoid fever. Friedreich[1] was the first to call

[1] *Verhandl. d. physik.-med. Gesellsch.*, Würzburg, 1855.

attention to the occurrence of acute dilatation of the heart in connection with fever, and his observations were verified by many observers, and were incorporated into the text-books in relation also to typhoid fever. It is known at the present day (see also Anatomy) that the profound typhoid disorders of the heart are dependent upon parenchymatous degeneration of the myocardium as well as upon true myocarditis. The significance of these changes in detail has not as yet been fully cleared up. E. Romberg,[1] in his admirable work, has properly called attention to the fact that the various parenchymatous alterations in the myocardium, the frequent albuminous degeneration of Virchow, the less common waxy degeneration, the segmentation of the fibers, the diverse nuclear changes, and the fatty degeneration of the myocardium can be recognized with difficulty from their clinical manifestations. Probably the last two conditions are more frequently responsible than the others for morbid manifestations observed during life. The overwhelmingly preponderant *rôle* is played undoubtedly by the interstitial inflammatory processes first described by Hayem;[2] a limited *rôle* possibly also by his specific obliterating endarteritis[3] of the smallest arterial branches of the myocardium and the pericardium.

Clinical Symptoms of Typhoid Myocarditis.—Cardiac symptoms of considerable degree, resulting from inflammatory processes in the myocardium, are likely to begin at the end of the second or the beginning of the third week, and to last into the fourth week or even longer. As Stokes early emphasized, the condition is principally one of cardiac weakness of rapid onset, often of considerable degree, which does not always accord with the severity of the general course and the manifestations on the part of other organs. The pulse especially becomes unusually frequent, without corresponding rise in temperature, and this is particularly striking in young, robust individuals who previously had had moderate pulse-frequency. Still more significant are the irregularity and inequality of the pulse, which often soon appear, and to which first Griessinger and subsequently Hayem especially called attention in this connection. Occurring at the height of the febrile period, if the heart was healthy before the onset of the typhoid disease, they constitute almost certain signs of important changes in the circulatory apparatus. To the acceleration and irregularity of the pulse there

[1] *Arbeit. a. d. med. Klin. z. Leipsic*, Vogel, Leipsic, 1893.

[2] *Arch. de phys. norm. et path.*, T. ii., 1869; T. iii., 1870.

[3] This has been described also by later French observers—H. Martin (*Rev. de Méd.*, 1881 and 1882), Landouzy and Siredey (*Ibid.*, 1885 and 1887), while Romberg was scarcely able to demonstrate it in spite of most careful investigation.

is soon added a diminution in volume and intensity; the dicrotism disappears; the pulse becomes small, soft, and readily compressible.

Soon after the appearance of the changes in the pulse, occasionally even at the same time, symptoms of dilatation of the heart begin to make their appearance. Their development and their extension rarely take place rapidly; much more frequently they progress gradually. The dilatation is likely at first to involve the left side of the heart. Far less commonly the right side of the heart also is dilated, and then almost never in considerable degree. The apex-beat is at times slightly enfeebled, at other times indistinct and diffuse, and in the most severe cases not at all demonstrable. If visible and palpable, it will be present in the fifth interspace in the mammillary line, rarely more than two finger-breadths beyond this. The dislocation of the apex-beat corresponds with an increase in the area of cardiac dulness to the left, while the dulness rarely extends beyond the right border of the sternum. To the left of the sternum and over the sternum the upper limit of cardiac dulness is not rarely displaced upward.

In severe cases auscultation discloses exceedingly faint heart-sounds, almost to the point of complete disappearance of the systolic sound. The second aortic sound is quite generally enfeebled, while the second pulmonic sound at times exhibits distinct accentuation. This may occur without a heart-murmur, particularly without a mitral murmur, which is, as Romberg appropriately states, the expression of an increase in pressure in the lesser circulation in consequence of deficient activity on the part of the left ventricle. Under other circumstances, in association with the accentuation of the second pulmonic sound, there is heard, most distinctly at the apex of the heart or with almost equal frequency over the point for auscultation of the pulmonary artery, a systolic murmur, which is generally dependent upon relative mitral insufficiency. It is either a direct result of dilatation of the left side of the heart and of its auriculoventricular orifice, or of the impaired activity of the papillary muscles, or of both.

However alarming these disturbances may at times appear, they seem in general to be attended with little danger in cases of typhoid fever, especially when compared with the anatomically similar myocarditis of diphtheria. In the vast majority of cases, according to observations made in my clinic, complete subsidence of the symptoms takes place, and this is generally accomplished at the end of the febrile period, at times even somewhat earlier. The dilatation also appears usually not to continue beyond this period. Slight disturbances persist occasionally for a longer time without serious injury, entirely dis-

appearing eventually. In some cases which terminated fatally from other complications, some remains of the anatomic alterations were still demonstrable.

Chronic myocarditis dependent upon typhoid fever, with or without permanent dilatation, I have as yet never observed with certainty. I know, however, that isolated instances have been reported by others (Landouzy and Siredey, Sommer-Henoch), and I believe that on further observation still others will be added.

Besides occurring at the height of the disease, severe cardiac symptoms may also make their appearance during the stage of convalescence from typhoid fever without distinctive symptoms having been detected during the febrile stage even in carefully observed cases. Attention has already been called, in the discussion of the state of the pulse, to the frequency of relative acceleration, instability, and irregularity of the action of the heart during convalescence without objectively demonstrable lesions of the heart.

Cases do, however, occur, although but rarely,[1] in which, after attacks of both severe and mild course, without external provocation, without any demand upon bodily activity, with the patient kept most strictly at rest in bed, from one to three weeks after defervescence of the fever there may appear and persist serious disturbances of the pulse, which occur otherwise during convalescence only after certain injurious influences, and then are but transient. The marked acceleration and the irregularity of the pulse under these conditions obtrude themselves —far more than during the febrile period—distressingly upon the consciousness of the patient as palpitation of the heart, often associated with abnormal sensations underneath the sternum, in the left lower mammary region and in the epigastrium. Not a few patients are conscious, without feeling the pulse, of every intermission in the action of the heart, and are disturbed thereby as if by heart-pains. There now soon develop the symptoms of dilatation of the heart, in the same way as in association with the myocarditis of the febrile period; here also the left rather than the right side of the heart is involved, and likewise not rarely with symptoms of relative mitral insufficiency.

The symptoms of this myocarditis of convalescence may persist for a relatively long time—up to two months and more. It is, however, important and comforting to know that the condition is almost invariably attended with a favorable prognosis. Even in those cases in

[1] Romberg properly emphasizes this rarity in comparison with the occurrence of myocarditis during the febrile stage of diphtheria.

which severe general circulatory disturbances develop,[1] with cyanosis and edema of the ankles, at times reaching half-way up the calves, recovery is likely to take place. A fatal termination is certainly exceptional (see the case of Liebermeister,[2] and that of Zaubzer,[3] which possibly also belongs in this category). Although sufficient post-mortem data bearing upon this myocarditis of late occurrence are as yet wanting, it is nevertheless undoubted that the condition here is likewise one of severe parenchymatous or interstitial change in the myocardium; and, if a conclusion by analogy is permitted, interstitial inflammatory lesions will, as in cases of diphtheria and scarlet fever, play the most conspicuous *rôle*. Whether the myocarditic symptoms of the period of convalescence develop only at this time, or represent a manifestation of anatomic alterations in the heart-muscle developing insidiously at an earlier period, cannot at present be decided with certainty. For the majority of cases the latter appears the more probable.

The history of typhoid alterations of the myocardium is comprehended in that of myocarditis attending infectious diseases generally. While previously (Laennec, Louis) only indefinite conceptions of the anatomic basis of the cardiac disturbances in question were held, and weakness, softening, etc., were spoken of, the fundamental work of Virchow[4] upon parenchymatous inflammations first brought clearness into this field. Subsequently, Böttcher, Waldeyer, and Zenker[5] continued the investigations into parenchymatous alterations in the heart in cases of infectious disease, including among others also the typhoid heart. They demonstrated the relative frequency and occasional intensity of the parenchymatous alterations, and attributed the greater portion of the clinical symptoms to fatty degeneration. A new fruitful agitation was inaugurated by Hayem[6] with the demonstration of interstitial myocarditis. While French investigators soon verified and amplified his statements, these received the appreciation they deserve among Germans at first only at the hands of Leyden.[7]

It is to the credit of Romberg in Germany to have emphasized with especial vigor the matters in question in his publications from my clinic,[8] to have analyzed them critically, and to have supplemented them with anatomic and clinical facts. Especially he was the first to point out the peculiarity of the cardiac affection during convalescence, and to attempt to give a clinical description of it.

Pericarditis and endocarditis are of far less importance in cases of typhoid fever. Although in the majority of cases examined anatomically by Romberg[9] small-cell infiltration of the capillary walls and of the

[1] The case of general edema mentioned by Strümpell (*Lehrbuch*, Bd. i.) is probably, from the extent, as well as the localization, not attributable alone to stasis due to cardiac weakness.

[2] *Ziemssen's Pathologie*, 3d ed.

[3] *Bayrisch. ärztl. Intelligenzbl.*, 1870.

[4] *Virchow's Archiv*, Bd. iv.

[5] See the literature cited by Romberg, *loc. cit.*

[6] *Loc. cit.*

[7] *Zeit. f. klin. Med.*, Bd. iv., 1882.

[8] *Loc. cit.*

[9] *Loc. cit.*

smallest vessels of the deeper layers of the pericardium were present in addition to myocarditis, it may still be maintained that these processes rarely attain such an intensity and extent as to give rise to the clinical symptoms of pericarditis. Anatomically, it also happens occasionally that rather extensive fibrinous deposits take place, at most a slight membrane, especially surrounding the large vessels. I have observed fluid pericarditic effusions only with extreme rarity in cases of typhoid fever. In cases in which I have observed the development of distinct, extensive, long-continued friction or severe exudative pericarditis, the conditions present were such that, from other symptoms as well, they had to be referred to mixed infection. In cases of typhoid fever complicated by true septic processes, I have in isolated instances observed even empyema of the pericardium.

Scarcely more frequent, at least clinically demonstrable, is endocarditis. According to Romberg's anatomic investigations, this is one of the less common accompanying manifestations of myocarditis, and is generally recognizable only microscopically. Occurring in small foci that occasionally coalesce, generally mural, beyond the range of the valves, it is situated at various points of the endocardium, with especial frequency in the neighborhood of the cardiac apex. The rare occurrence of valvular lesions of the heart in the sequence of typhoid fever appears to be dependent upon the rare anatomic involvement of the valves. Contradictory reports, especially on the part of earlier observers, are in part probably attributable to the fact that formerly relative insufficiency as a sequel of myocarditis was not known, and it was confused with mitral endocarditis. True valvular endocarditis I have now and then observed in the form of so-called ulcerative endocarditis, with verrucose deposits upon the valves, and ulcerative loss of tissue, either on the aortic or the mitral valve, or on both together. These were always associated with other septic symptoms, especially multiple emboli of the skin, and thereby proved themselves to be part manifestations of this symptom-complex. Non-septic endocarditis, terminating in chronic valvular disease of the heart, occurred, as has been stated, but exceptionally in my experience. Whether such a condition is to be attributed to the direct action of the typhoid poison must be reserved for future decision. In my cases only the left side of the heart was affected, and, with a single exception, in which the aortic valves were involved, the mitral valve alone was affected. Endocarditis of the right side of the heart has been reported in 1 case by Bouchut. These cases of possibly specific typhoid endocarditis develop, in my experience, at the height of the febrile stage—in the second and at the beginning of the third week.

They cannot easily be distinguished from myocarditis with relative mitral insufficiency. Only the persistence of the symptoms, especially the systolic murmur at the apex, and the accentuation of the second pulmonary sound, are indicative of this endocarditic character, and the latter will be decisively confirmed by the persistence of a valvular lesion. In one case I believed myself justified in assuming the associated presence of endocarditis and extensive myocarditis in a young man who, together with endocarditis followed by mitral insufficiency and stenosis, exhibited also symptoms resembling those of severe angina pectoris, with pains radiating to the epigastrium, the back, and the left arm. Quite exceptionally—so far as I can recall in but 2 cases, in one a year and in another a year and a half after an attack of typhoid fever—I have observed the appearance of the first distinct clinical symptoms of mitral insufficiency, which had not manifested themselves during the attack in the form of valvular endocarditis, but for whose development no other cause could be elicited. I suspect that in these cases a rather extensive mural endocarditis was present, which developed during the febrile period of the attack of typhoid fever, and extended close to but not upon the valves. The progressive cicatricial contraction that gradually took place in the process of healing probably then involved portions of the papillary muscles also, as well as the points of attachment of the valves and the tendinous cords, and in this way gave rise to secondary insufficiency. Such occurrences seem to me to be probable also in other acute infectious diseases; especially do I believe that valvular lesions of the heart developing after apparently uncomplicated attacks of scarlet fever are in part to be explained in this way.

In connection with the changes in the myocardium, a few words may be appropriate here with regard to states of collapse in the course of typhoid fever, especially since it is still customary to attribute them mainly to profound changes in the heart, with the exception of a few cases due to embolism, especially of the pulmonary artery. Sudden alarming attacks of weakness in cases of typhoid fever, unfortunately not rarely terminating fatally, were known to earlier writers and were given careful consideration decades ago, especially by Griessinger[1] and Ackermann.[2] I have observed them as early as the second week, at the height of the febrile stage, but still more frequently toward the end of the febrile period and during the period of convalescence. They may occur once or several times at irregular intervals in the same patient, at times without, at other times after, direct external influences. Among these exciting factors belong emotional disturbances and

[1] *Arch. d. Heilk.*, 1861.

[2] *Virchow's Archiv*, Bd. xxv.

excessive physical activity, sitting up contrary to instructions, expulsive efforts and straining at stool, etc. Those cases are generally especially severe in which, without demonstrable cause, collapse appears even early, at times during the second week, and is repeated while body and mind are kept absolutely at rest. They frequently terminate fatally.

The clinical symptoms of collapse are those usual in so-called acute cardiac failure: pallor and lividity, especially of the face and the extremities, drawing of the features, cold sweats, derangement of consciousness, thready, small, frequent, irregular pulse. The anatomic investigations thus far made have either yielded a negative result, or, when they have yielded any result at all, have disclosed parenchymatous degeneration of the heart, fatty degeneration, and dilatation. A thorough study of such cases by modern methods (Krehl-Romberg) is at yet wanting.

I would expressly emphasize the fact that I have repeatedly observed death in collapse without any explanatory alteration in the body after death, and particularly without change in the form, size, color, and consistency of the myocardium. If such cases are not lightly dismissed from consideration, but are grouped with other threatening transitory circulatory disturbances without clinically demonstrable changes in the heart, the question naturally arises: Are all of these "cardiac" disturbances, from the milder and transitory to those causing fatal collapse, necessarily referable to the heart alone? This question cannot be answered unconditionally in the affirmative. Every unprejudiced observer will recognize here a deficiency in our knowledge, which, further, is applicable not alone to typhoid fever, but likewise to similar conditions associated with other acute infectious diseases. A number of more recent studies appear to shed light upon this subject, and among them especially that carried out at my clinic by Romberg[1] in association with Bruhns and Pässler. They have shown that the action of toxins of the exciting agents of the infectious diseases, especially of the pneumococcus, the diphtheria-bacillus, and the Bacillus pyocyaneus, is exerted, not alone upon the heart, but also especially upon the vasomotor system, so that in explanation of the symptom-complex of "profound cardiac weakness" paralysis of the vasomotors is often to be invoked.

The especial difficulties that attend experiments with the poison of the typhoid-bacillus have hitherto prevented a special experimental

[1] Address before the Congress of Naturalists at Lübeck, 1895; minutes of the meeting. Also, *Berlin. klin. Woch.*, 1895, Nos. 51 and 52. Pässler and Romberg, *Verhandl. d. Congr. f. inn. Med.*, Wiesbaden, 1896 (address by Pässler).

study of them. Nevertheless, it is scarcely to be doubted that in cases of typhoid fever a number of circulatory disturbances are in whole or in part to be attributed to vasomotor disturbances. To what extent this is operative, to what degree especially the ordinary typical circulatory disturbances in the febrile stage of typhoid fever are referable to such conditions, cannot as yet be stated absolutely. Future investigation must determine what part is attributable to the heart itself, and what to the vasomotors, and finally what to the combined injurious influence of both.

Changes in the Blood-vessels, and their Clinical Manifestations.—Little is known with regard to the arteries from either an anatomic or a clinical point of view. A probably specific disease of the arteries—typhoid arteritis of French investigators—is especially deserving of mention. This is possibly the principal cause of that remarkable condition, fortunately observed but rarely, the so-called spontaneous gangrene of the extremities in the course of typhoid fever.

The tendency at present is to consider the thrombosis as due to an infective arteritis; and several investigators have claimed to have cultivated the typhoid-bacilli from the walls of the occluded arteries. More numerous and exact observations are still needed in relation to this important point.

Typhoid gangrene is observed particularly in the lower extremities, and almost always of one extremity only. Large portions of the member may become gangrenous: all the toes, the entire foot up to the knee, even up to the middle of the thigh. Under such circumstances thrombosis will be found in the distribution of the iliac or femoral artery, or only in certain large branches of the latter, among which the posterior tibial artery plays an especial *rôle*.

This peculiar variety of gangrene was, so far as I know, first described by Bourgeois,[1] then by Gigon[2] and Patry.[3] An interesting case of bilateral gangrene of the legs was shortly afterward described by Bachmayr.[4] Also, Trousseau, in his lectures at the famous clinic at the Hôtel Dieu, has devoted a short chapter to this manifestation. Among more recent writers Potin,[5] Mercier,[6] and Le Reboulliet[7] may be mentioned.

Keen,[8] in his admirable monograph, has collected 115 cases of gangrene in typhoid fever due to arterial thrombosis or embolism. The earliest appearance of the gangrene was on the fourteenth day, the latest in the seventh week. In gangrene of the lower extremities it occurred as frequently on the right as on the left side. Keen advises amputation in gan-

[1] *Arch. gén. de Méd.*, Aug., 1857.
[2] *Union méd.*, Sept., 1861.
[3] *Arch. gén. de Méd.*, Feb. and May, 1863.
[4] *Verhandl. d. Würzburg. med. Gesellsch.*, 1868.
[5] *Loc. cit.*
[6] *Arch. de méd. expér.*, 1878.
[7] *Union méd.*, 1878.
[8] *Loc. cit.*

grene of the extremities, but says that as a general rule it is best to wait for a line of demarcation; but operation should not be deferred long after its appearance.

I have personally observed typhoid gangrene of the lower extremity in 2 instances. In one case gangrene of the foot and the lower third of the thigh developed in a previously healthy man, forty-one years old, in consequence of thrombosis of the popliteal and posterior tibial arteries occurring in the stage of the amphibolic curve. In another case,[1] which occurred in a young girl, and terminated fatally, the gangrene resulted from thrombosis of the iliac and femoral arteries, which was associated with thrombophlebitis of the corresponding veins, and involved the foot and the entire leg to the lower third of the thigh. The complication appears to be extremely rare in the upper extremities. I have personally observed gangrene of 4 fingers of one hand and the cutaneous covering of the back of the hand in a patient who escaped with his life. Gangrene has been noted in isolated instances in the distribution of other arteries; thus, in that of the external carotid, in which case the auricle, the parotid gland, and the integument covering them and the adjacent soft parts became gangrenous and were exfoliated (Patry[2]).

Possibly certain cases of circumscribed cerebromalacia occurring during the terminal stage of typhoid fever are to be attributed to inflammatory thrombosis of the related cerebral arteries. Thus, in a woman, thirty-seven years old, I observed the gradual development of right hemiparesis with aphasia during convalescence from typhoid fever without antecedent apoplectiform attack. The case, which came under my observation in consultation at a distance, terminated fatally. The report of the autopsy by the attending physician mentioned as the cause of the condition extensive softening of the middle portion of the left cerebral hemisphere in consequence of adhesive thrombosis of the artery of the fossa of Sylvius, the walls of which were, besides, considerably thickened.

Welch[3] mentions 4 other fatal cases of thrombosis of the middle cerebral artery or its branches during typhoid fever. In the case reported by Osler, severe convulsions suddenly occurred on the ninth day of a mild case of typhoid fever. Death occurred in ten hours after the onset of the cerebral symptoms. At autopsy there was found thrombosis of branches of the middle cerebral artery, the adjacent brain-substance being studded with hemorrhages, but not much softened.

In the aorta and the large arterial trunks I have repeatedly observed extensive reticular turbidity of the intima and plaques of fresh sclerosis, here and there even dilatation occurring. In one case, occurring in a man, thirty-five years old, perfectly healthy before the onset of the attack of typhoid fever, the arch of the aorta, which presented extensive reticular thickening and turbidity of the intima, was dilated to almost double the normal. Neither in this case nor in the others under my observation were symptoms present during life.

[1] The case, which was under my care when I was assistant at the St. Rochus-spitale in Mainz, has been reported by Masserell (*Deutsch. Arch. f. klin. Med.*, Bd. v., S. 445 ff.). I do not, however, agree with some of the opinions expressed in this paper.

[2] *Loc. cit.*

[3] "Thrombosis and Embolism," *Allbutt's System of Medicine*, vol. vii., London, 1899.

The obliterating visceral arteritis previously mentioned, described by Landouzy and Siredey,[1] and given undue prominence in France, is of little significance clinically or diagnostically. I would emphasize expressly that in a large number of post-mortem examinations in cases of typhoid fever in which I noted the condition of the coronary arteries, I never found them diseased. In accordance with this observation, I have also never encountered angina pectoris (apart from the single case already mentioned), either during the course of an attack of typhoid fever or among its sequels.

Embolism of arteries of moderate or smaller size, of which marantic (?) thrombosis of the left side of the heart, especially the auricle, is usually the source, is quite rare. Emboli in the kidneys and the spleen are relatively the most common, although they are generally unattended with distinctive symptoms. In one case I observed sudden death during convalescence from typhoid fever, in consequence of embolism of the basilar artery. Embolism of the pulmonary artery, which, according to Hoffmann, quite commonly exhibits whitish turbidity of the intima, following thrombosis of the right side of the heart or the peripheral venous trunks, has already been mentioned as a cause of sudden fatal collapse.

The veins are more frequently than the arteries the seat of disease in cases of typhoid fever. Thrombosis of the large veins of the leg, with the familiar symptoms of phlegmasia alba dolens, is not an especially rare manifestation in the later stages of typhoid fever, especially during convalescence. Even at the present day the condition is often considered the expression of marantic thrombosis, and this explanation is probably correct for a portion of the cases. On the other hand, the disorder is frequently observed to develop in previously healthy, robust individuals after a relatively mild attack, and in the absence of particularly marked emaciation. If, in addition, its onset is attended with febrile symptoms, and often with considerable tenderness in the course of the crural and iliac veins, even with distinct symptoms of periphlebitis, the possibility that the condition is dependent not upon a simple thrombosis, but upon an inflammatory state of the wall of the vein, must be taken into consideration. Whether such typhoid phlebitis is specific and is attributable to the direct activity of the bacillus of Eberth is not yet certain, but it is not improbable from the observations that have been made in so many other organs. That other micro-organisms also, especially pyogenic cocci, may participate in this process, that therefore

[1] See the section on Anatomic Alterations in the Circulatory Organs.

a complicating phlebitis in the strict sense may occur, can scarcely be doubted after the observations of Dunin.[1]

Like typhoid arteritis, phlegmasia alba dolens generally appears upon one side. In only 2 instances have I observed the second extremity become after a time equally edematous, obviously in consequence of extension of the thrombosis to the lower portion of the inferior vena cava, and thence to the other iliac vein.

The venous obstructions in the course of typhoid fever are under all circumstances most undesirable complications. It is true that recovery usually follows, but the duration of the disease is considerably protracted; not rarely for as much as two or three months, and even more. I have not observed gangrene develop as a sequel, but now and again, fortunately rarely, detachment of fragments of the thrombus occurs with fatal embolism.

Next to thrombosis of the femoral vein, phlebitis and occlusion of the saphenous vein alone, or of the popliteal vein and the deep veins of the muscles of the calf, with edema of the foot up to the calf, and especially with firm infiltration and considerable tenderness of the muscles, appear to be not rare. In isolated instances I have observed also phlebitis and periphlebitis in old varicose dilatations of the veins of the leg in men and women suffering from typhoid fever. In my experience, venous thrombosis in the course of typhoid fever has occurred with exceeding rarity in other portions of the body than the lower extremities. In one instance the axillary vein and in another the right subclavian vein was involved. Besides, like many other writers, I have noticed cases in which phlebitis and thrombosis were part manifestations of, or actually the source for, general septicemia complicating typhoid fever.

Changes in the Condition of the Blood.—Numerous statements with regard to the condition of the blood in cases of typhoid fever are contained in the writings of earlier observers. They refer, however, only to the external appearances of blood obtained on venesection or from the dead body or that escaping accidentally. These observations disclosed so little that for a long time the study of the blood was altogether neglected. With the adoption of improved methods, such investigations have recently been resumed with more success. The morphology of the blood and certain chemical changes in it, particularly the behavior of the hemoglobin, have been studied, and special consideration has been given to bacteriologic investigation.

Changes in the Formed Elements of the Blood.—With regard

[1] *Deutsch. Arch. f. klin. Med.*, Bd. xxxix., Hefte 3 u. 4.

to the red blood-corpuscles, these but rarely exhibit marked changes in form, size, and color, but their enumeration has yielded not uninteresting results. While earlier writers, especially Malassez and Hayem, were unable to demonstrate a reduction in their number, most recent writers have found that in the majority of cases the number of red corpuscles undergoes slowly progressive reduction during the febrile period. Evidence in support of this statement is contained in the articles of Zäslein,[1] Tumas,[2] Halla,[3] and Leichtenstern,[4] and as a result of observations made in my clinic I am in accord with them. We also observed[5] reduction in the number of red cells, even from the beginning of the febrile period. This reduction is generally slight in young, robust men, so that the number still equalled 4,000,000 or somewhat more, while in women and debilitated individuals a reduction to 3,000,000 or even somewhat less occurred. Thayer,[6] from an analysis of all blood-counts on typhoid patients in the Johns Hopkins Hospital during the past eleven years, states that the average loss is about 1,000,000 per c.mm. The reduction continues to increase until toward the end of the febrile period, and even into the afebrile period. In cases of long duration, however, regeneration may begin well before the end of defervescence. During convalescence, usually from two to three weeks after defervescence, the number is likely to return to the normal. It appears, however, that the number of red blood-corpuscles physiologically normal to the individual is but slowly attained. We have failed to find the normal number in patients who had been free from fever for even seven weeks. With the onset of relapses, the number of red blood-corpuscles will often be found smaller than during the first febrile period of the disease. This is obviously due to the cumulative effects of the two periods.

An interesting circumstance mentioned by various observers consists in occasional variations in the number of red blood-corpuscles in the same individual during the course of the fever. We have observed a transitory increase in the number to the extent of 500,000, and even of 1,000,000. Probably under such circumstances there is not a real, but only a relative increase, in consequence of variations in density—that is, in the amount of water contained in the blood. Thus, we have noticed such an apparent increase in the number of red blood-

[1] *Inaug. Diss.*, Basel, 1881.
[2] *Deutsch. Arch. f. klin. Med.*, Bd. xli.
[3] *Zeit. f. Heilk.*, Bd. iv.
[4] *Untersuchungen über d. Hämoglobingehalt des Blutes im gesunden u. kranken Zustande*, Leipsic, 1871.
[5] Kölner, *Inaug. Diss.*, Leipsic, 1896.
[6] *Johns Hopkins Hosp. Rep.*, vol. viii.

corpuscles after profuse sweating. Grawitz[1] has observed the specific gravity of the blood, and therefore its density, increase after cold baths, owing, as he correctly believes, to the effect which stimulation of the vasomotor nervous system exerts upon the water-content of the blood. Possibly statements as to the relative increase in the number of red blood-corpuscles at the beginning of the febrile period are attributable to influences that at times give rise to a reduction in the fluids of the blood.

The reduction in the percentage of hemoglobin in the blood during the febrile period appears to correspond with, but in no event to exceed, that in the number of red blood-corpuscles (Quincke). That this reduction, however, is not constant, and by no means considerable, is shown by the negative observations of Leichtenstern. In my clinic, average reductions to from 80 to 75 per cent. have been observed, rarely lower figures. In the afebrile period, especially during the first weeks of this period, all observers, including Leichtenstern, observed a lower percentage of hemoglobin than during the febrile period, this again corresponding with the greatest reduction in the number of red blood-corpuscles which usually occurs at this stage. Laache[2] states—and in this we can agree with him upon the basis of personal experience—that during convalescence, while the number of red blood-corpuscles is again in process of increase, a further reduction in the percentage of hemoglobin may take place. It probably usually happens that where the anemia has been appreciable the return of the hemoglobin to the normal is, as in most secondary anemias, more gradual than that of the red blood-corpuscles.

In comparison with what is known concerning the leukocytes in other infectious diseases, the state of the white blood-corpuscles during typhoid fever is striking. While in the majority of acute infectious diseases the white blood-corpuscles are found increased at the height of the attack, this increase is wanting with great constancy in cases of typhoid fever; a diminution, which may even be very considerable, is often present (Halla,[3] Tumas,[4] von Limbeck,[5] Rieder,[6] Grawitz,[7] Naegeli,[8] Thayer[9]). It even happens, as Rieder showed, that, with increase in the symptoms of the disease, with marked elevation of the temperature, and with the onset of recrudescences, the number of white blood-corpuscles undergoes still further reduction. We have arrived at the same

[1] *Klin. Pathol. d. Blutes.* [2] *Path. d. Blutes.*

[3] *Loc. cit.* [4] *Loc. cit.* [5] *Zeit. f. Heilk.*, Bd. x.

[6] *Beiträge zur Kenntniss der Leukocytose und vercoandter Zustände des Blutes*, Leipsic, 1892.

[7] *Loc. cit.* [8] *Deutsch. Arch. f. klin. Med.*, Bd. lxvii. [9] *Loc. cit.*

conclusions as the observers named, and can confirm especially the occurrence of increased reduction in the number of the leukocytes with exacerbations of the disease.

In uncomplicated cases during the febrile stage we have found from 9000 down to 2000 white blood-corpuscles in the cubic millimeter. Exacerbations of the disease not rarely gave rise to a further reduction of 1000. Counts above 10,000 are rare, and usually indicate the onset of some complication or the effect of some foreign influence. Thayer has shown that cold baths cause an immediate transient increase in the number of leukocytes in the peripheral circulation. Complications with such conditions that ordinarily give rise to leukocytosis are attended with an increase in the number of white corpuscles to the normal and above. Thus, in a case of intercurrent pneumonia 11,600 were counted, and with the development of an abscess over the sacrum 4500, as compared with 2400 previously.

As to the effect of other complications upon the leukocytes, it may be said that hemorrhage may exercise little or no influence, though often there is a tendency toward a leukocytosis reaching its maximum twelve to twenty-four hours after the hemorrhage has occurred. Thrombosis and phlebitis are associated with a leukocytosis. The behavior of the white corpuscles in perforation is of great importance, especially in relation to early diagnosis. Thayer concludes from quite frequent and accurate counts on 8 cases that perforation of the bowel is usually followed by an increase in the number of leukocytes in the peripheral circulation. This may be considerable or only slight, and appreciable only in comparison with previous counts. Not infrequently, however, there is an absence of increase; even a diminution in the number of leukocytes may occur, the latter being generally an indication of the malignity of the infection or the prostration of the patient.

No distinct difference in the reduction in the number of the white corpuscles in accordance with the severity of the attack appears to occur, at least not in such a degree that prognostic conclusions can be drawn. In my clinic recovery ensued, for instance, in a case in which a reduction to 1400 occurred. While, therefore, no special prognostic significance can be attached to enumeration of the white blood-corpuscles, the procedure is, nevertheless, not without significance in differential diagnosis, particularly with regard to diseases that are constantly attended with marked increase in the number of white blood-corpuscles, and that occasion difficulties clinically. Pneumonia, septic processes, and cerebrospinal meningitis may be mentioned in this connection.

It is surprising that an observer like Virchow reports an increase in the leukocytes in typhoid fever, and the question arises whether his observations are referable to the initial stage. French investigators, as, for instance, Bonne,[1] have found considerable increase during the first week, and only subsequently a rapid decrease in the number of white blood-corpuscles.

During the period of convalescence the number of leukocytes appears again to increase slowly; and in debilitated persons, according to our observations, more slowly than in robust individuals, in whom often a return to the normal may be noted during defervescence or during the first afebrile days. In isolated instances, Kölner[2] relates having observed during convalescence, without especial apparent cause, transitory increase in the number of white blood-corpuscles above the physiologic, up to 12,000, in one instance even up to 17,500. This observation is supported in a remarkable manner by a similar observation of Laache.

As to the variations which occur in the relative number of the different varieties of leukocytes, Thayer[3] says there are three main changes, and other authorities agree with him in the general statements (see Naegeli[4]).

(1) There is a progressive diminution in the percentage of polymorphonuclears.

(2) There is a progressive increase in the percentage of mononuclear forms, the increase being mainly in the large mononuclear varieties.

(3) A constantly small percentage of eosinophilic cells occurs.

Naegeli thinks that the eosinophiles usually entirely disappear during the height of the fever, and that their persistence is a very favorable prognostic sign.

Bacteriology of the Blood.—Since the time of Gaffky, numerous observers have devoted themselves to the investigation of the blood for micro-organisms, particularly typhoid-bacilli. Gaffky himself, as is known, obtained negative results in his own investigations in this direction. Later investigators have directed their studies in part to the examination of the blood obtained from some convenient part of the body, generally the tip of the finger, and in part to an investigation of that obtained from certain parts of the body the seat of specific lesions, especially the roseolæ. The results are widely divergent, and in part are markedly contradictory. While, for instance, Meissel[5] found typhoid-bacilli in the blood constantly in 9 cases examined for this purpose, others, as, for instance, Almquist[6] and Silvestrini,[7] have been able to demonstrate them only in isolated instances. Observers of

[1] *Thèse de Paris*, 1876.
[2] *Loc. cit.*
[3] *Loc. cit.*
[4] *Loc. cit.*
[5] *Wien. med. Woch.*, 1886, Nos. 21 and 23.
[6] Göteborg, 1885.
[7] *Riv. gen. di clin. med.*, 1892.

especial skill, such as Fränkel and Simmonds,[1] also Lugatello[2] and Seitz, have, however, just as did Gaffky, invariably obtained negative results.

Newer work with better methods has, however, shown that, instead of typhoid-bacilli occurring only exceptionally in the blood, they probably are present in every case during some stage of the disease, and can be demonstrated in a majority of all the cases if proper methods in making cultures are employed. Cole,[4] by using considerable amounts of blood and diluting very largely in liquid media, was able to demonstrate the bacilli in 11 out of 15 cases examined. In 6 of these cases the bacilli were cultivated from the blood before the Widal test was positive, so that the method has considerable diagnostic importance. These results have since been confirmed on numerous other cases at the Johns Hopkins Hospital.

Schottmüller[5] has lately obtained the bacilli from the circulating blood of 40 out of 50 cases examined by him. Aeurbach and Unger[6] report positive results in 7 out of 10 cases, and Castellani[7] has cultivated the bacilli from the blood of 12 out of 14 cases.

In the same way as with regard to examinations of the blood generally, observers differ also with reference to the presence of bacilli in the typhoid roseolæ. It was hoped at first that the study of these structures might yield important results. It would undoubtedly be of great diagnostic significance to be able to demonstrate the specific bacteria in the frequent characteristic alterations in the skin. These hopes have, however, not been fully realized. It is true Neuhaus[8] believed that he had demonstrated them in more than half of the cases examined by him (in 9 of 15 patients) in blood from the roseolæ. Opposed to him, however, are the entirely negative results of the observers previously mentioned, Fränkel and Simmonds, Seitz, Lugatello, Gaffky and Janowski.[9]

However, within the past few years the frequent, probably constant, presence of typhoid-bacilli in the rose-spots has been demonstrated by Neufeld, Curschmann, and Richardson in 32 out of 40 cases from which cultures were made by these observers. E. Fränkel has also demonstrated their presence in sections of the rose-spots (see section on Discussion of the Individual Features—Roseola).

[1] *Loc. cit.* [2] *Boll. d. Roy. Acad. di Genova*, 1886. [3] *Loc. cit.*
[4] *Bull. Johns Hopkins Hosp.*, vol. xii., No. 124.
[5] *Deutsch. med. Woch.*, Aug. 9, 1900.
[6] *Ibid.*, Dec. 6, 1900. [7] *Rif. med.*, vol. i., Nos. 6 and 7.
[8] *Berlin. klin. Woch.*, 1886, Nos. 6 and 24. [9] *Loc. cit.*

In addition to examination of the circulating blood and the roseolæ, attention has been directed also to the blood of the spleen. Positive results could most reasonably be expected from this, as it is well known that examination of the splenic pulp after death for bacilli almost always yields positive results. Among the first who obtained positive results from the examination of the blood of the spleen during life are Chantemesse and Widal,[1] Redenbacher,[2] Philipowicz,[3] and E. Neisser.[4] Attempts were made to utilize these findings—and Neisser had this especially in view—for purposes of early diagnosis. I believe that there are serious objections to this practice. In the first place, the results in question are by no means constant, as the observations of Stagnitta,[5] for example, show; and even if this were not the case, the danger of the procedure would stand in the way of its employment. One need but think of the tensely distended spleen often observed after death, with the stretched and thinned-out capsule, and also of the tendency, which is by no means slight, to spontaneous rupture, and one will not escape the fear that puncture of the spleen during life may readily result in rupture and dangerous hemorrhage. I have never been able to make up my mind to perform the operation.[6]

SPLEEN AND THYROID GLAND.

Enlargement of the Spleen.—Although recent enlargement of the spleen, obviously a manifestation of the infectious process, is observed in all infectious diseases, nevertheless, apart from malarial fevers and septic diseases, splenic tumor is in no disease of as great diagnostic significance as in typhoid fever. This fact has even given rise to exaggeration of the value of the symptom. Some physicians will not venture a diagnosis of typhoid fever at all without the demonstration of enlargement of the spleen. In addition to the frequency of enlargement of the spleen, its early occurrence, its relatively long duration, and its constant reappearance in recrudescences and relapses are especially indicative of typhoid fever.

The frequency of typhoid enlargement of the spleen in general

[1] *Loc. cit.*
[2] *Zeit. f. klin. Med.*, Bd. xix.
[3] *Wien. med. Blätter*, 1886, Nos. 6 and 7.
[4] *Zeit. f. klin. Med.*, Bd. xxiii.
[5] *Rif. med.*, 1890.
[6] Also, Neisser (Haedke, "Die Diagnose des Abdominaltyphus und Widal's Serumdiagnostisches Verfahren," *Deutsch. med. Woch.*, 1897, No. 2) has recently reported that at present he performs puncture of the spleen for diagnostic purposes only in the rarest cases, since he had found on post-mortem examination of one patient on whom the operation had been performed a fine tear, 0.5 cm. long, in the capsule of the spleen, and 100 grams of blood in the abdominal cavity.

cannot be estimated with certainty from the results of clinical examination. As will be more fully discussed later, its demonstration at the bedside is attended with various difficulties, so that, if a trustworthy conclusion is desired, the aid of anatomic observation must be invoked. In young, robust individuals, when death occurs at the height or toward the end of the disease, even a short time after the onset of defervescence, more or less recent hyperemia of the spleen is rarely wanting. In conformity with clinical experience, however, and to this extent also available in examination and diagnosis, is the fact that in cases of typhoid fever moderate sized splenic tumors are far more frequent than especially large ones. Enlargement of the organ to double the normal or to two and a half times the normal is the rule, three times the normal volume being somewhat less common. The maximum size has probably been reported by Rokitansky as six times the physiologic.

The enlargement of the spleen is likely to be greatest at the height of the disease, while at the commencement and in the period of steep curves or on the first afebrile days its volume is less. In the later stages of convalescence enlargement of the spleen is present only exceptionally.

Undoubtedly, the mean size of the splenic enlargement varies, like many other symptoms of typhoid fever, in different epidemics. I have noted periods in which, anatomically and clinically, the enlargement of the spleen was slight; and others, for instance the Hamburg epidemic of 1886–1887, in which an unusual number of large splenic tumors were observed. Of 300 successive autopsies of which I have notes, there were found exceedingly large tumors in 127, and tumors of moderate and considerable size in 173. In no case was enlargement of the spleen wanting. In Leipsic, on the other hand, among 211 autopsies on cases of typhoid fever, there were observed exceedingly large tumors in 45, tumors of moderate size in 115, small tumors in 21, and absence of splenic enlargement in 30. The table of Hoffmann should also be consulted.

When enlargement of the spleen is wanting during the febrile period, this is dependent in the majority of cases upon special conditions. Thus, in advanced life, or in young or middle-aged individuals when the attack of typhoid fever has been preceded by diseases attended with marked emaciation, enlargement of the spleen is frequently wanting throughout the entire course of the disease and upon post-mortem examination. The conditions last named give rise rather to atrophy of the spleen, and if then infectious enlargement of the organ takes place at all, this will be just sufficient to restore it to its physiologic size.

At times, antecedent disease of the spleen itself may prevent

enlargement of the organ in typhoid fever. Thus, the splenic tissue may be the seat of cicatricial change, in consequence of previous large or multiple infarction; or its elasticity may be impaired by chronic diffuse connective-tissue hyperplasia or by widespread inflammatory thickening of its capsule. Perhaps in the conditions last named may reside the explanation of my observation that when typhoid fever occurs for the second or the third time in the same patient enlargement of the spleen is absent with remarkable frequency. Finally, it should be mentioned that profuse acute hemorrhage may cause rapid diminution in the size of an enlarged spleen. Especially when death results from profuse intestinal hemorrhage is the spleen found not rarely of normal size, but remarkably pale, flabby, and wrinkled.

The absence of splenic tumor without demonstrable cause is, during the febrile stage of the disease, an extremely rare anatomic condition. I have myself, it is true, exceptionally made this observation in young persons, but then the parenchyma of the spleen was usually at least abnormally hyperemic, soft, and bulging, thus, in a condition of acute transition; in 2 cases, in fact, recent considerable extravasations of blood were found in the spleen.

Among 577 autopsies (Hamburg, Leipsic), I found absence of splenic enlargement noted in 49. If from these cases are deducted those in which one of the factors named explained the condition, there remain but 9—1.6 per cent. of all cases—in which enlargement of the spleen was wanting during the febrile stage without demonstrable cause.

The ultimate cause of typhoid enlargement of the spleen and the special conditions for its occurrence are, as yet, unknown. The earlier assumption that the pyrexia alone was the responsible factor must certainly be rejected. Undoubtedly, the development of the typhoid enlargement of the spleen stands in most intimate relation with the bacillus of Eberth and its toxins. In favor of this view, perhaps, is the almost constant presence of bacilli in the spleen after death, and also the successful demonstration of them by puncture of the spleen during life, to which reference has already been made.

The splenic tumor, as has been said, is a manifestation of the febrile stage of the disease. Neither the time nor the degree of its development appears to bear any relation to the severity or the character of the febrile course. Marked enlargement of the spleen is observed even early in the mildest cases of typhoid fever with a short remittent or intermittent febrile course, and also in the protracted cases with high fever. I have generally observed enlargement of the spleen even in cases of typhoid fever almost unattended with fever. With the onset of con-

valescence—that is, with reduction in the fever—involution of the splenic tumor usually begins. At the close of the third or during the fourth week it is then no longer, demonstrable in cases that pursue an ordinary course. The greatest degree of splenic enlargement is exhibited generally in the second up to the beginning of the third week; only in especially protracted cases is it likely to be deferred to a later period. The time for the commencement of the splenic swelling is, from anatomic and clinical knowledge, on the average the middle or the second half of the first week. In the last days of the first week its clinical demonstration is quite frequently possible.

Premature reduction in the size of the enlarged spleen during the febrile stage is exceptional. This generally occurs only under special conditions, as has been mentioned; in connection with profuse hemorrhage, now and again also after especially profuse diarrhea. During the stage of steep curves involution of the splenic tumor is more frequent, as occasionally can be confirmed anatomically. It should be noted, however, that softening of the spleen with preservation of its size, as is peculiar to the stage mentioned, may clinically be readily mistaken for actual diminution in size.

Abnormally protracted persistence of the splenic tumor occurs almost exclusively in cases that otherwise also pursue a protracted course. In any event, it should be borne in mind that so long as the typhoid splenic tumor is demonstrable, the disease cannot be considered as having terminated. This is true even for patients in whom the fever has already disappeared. They are still under the influence of the infection, and are threatened especially by the danger of relapse. Also, when the splenic tumor has already undergone involution, renewed increase in its size is indicative of the advent of a recrudescence or a relapse, often occurring even before elevation of temperature has taken place. Mention of the occurrence of splenic tumor at an abnormally early period should not be omitted here. I have observed several cases in which enlargement of the spleen was with certainty demonstrable clinically even before the fourth day of the disease. Splenic tumors are probably not so rare even in the period of incubation as is generally assumed; there is not often reason for examination at this time, for examination is undertaken only when complaint of local symptoms is made.

I have been able in 2 cases to determine the presence of enlargement of the spleen during the period of incubation. The first occurred in a woman, twenty-five years old, who complained one morning of pain in the left side on fastening her clothing, which had developed during the night, and a cause for which was found in a recent splenic tumor, to which the commencement of

the febrile symptoms was added three days later. The other patient, an apparently healthy lad, fourteen years old, complained suddenly in walking and running of a sharp pain in the left side. On examination he was found free from fever, and without roseolæ and diarrhea. At the same time, however, a distinctly palpable, tender splenic tumor was present. In the course of two days chilliness appeared for the first time, with the commencement in the elevation of temperature. The case pursued a severe, tedious course, with two relapses, between which the swelling of the spleen disappeared. Similar observations have been reported also by others. I need refer only to the case of Friedrich mentioned in his famous treatise upon acute splenic tumor.[1]

In spite of the anatomic constancy of enlargement of the spleen, its demonstration clinically, as has been mentioned, can frequently not be made either for a short or longer time, if exact landmarks only are observed. This is dependent in part upon the fact that during various periods and epidemics the average size of the splenic tumor varies considerably, and in part upon the fact especially that examination for splenic enlargement in the individual case is attended with not a few general and individual difficulties. A general idea of the statistics in this connection may be obtained from the following estimates made at Hamburg and Leipsic. In the year 1887, among 2205 cases in the Hamburg Hospital, splenic tumor was demonstrated in 1859—84.3 per cent.; was palpable in 34.2 per cent.; and uncertain or wanting in 346—15.7 per cent. This epidemic was characterized, as the anatomic observations showed, by the frequency of large splenic tumors.

In Leipsic, among 1626 cases, splenic tumor was demonstrable in 1051—69.4 per cent.; was uncertain or not demonstrable in 575—30.6 per cent. These data are obtained from statistics covering a period of more than thirteen years, and collected by different observers. The number of cases in which enlargement of the spleen was uncertain or not demonstrable appears remarkably large in comparison with the corresponding Hamburg figures. According to my general experience, I would believe that throughout the entire course of the disease enlargement of the spleen is not demonstrable in from 20 to 25 per cent. of the cases.

With regard especially to the difficulties attending examination of the spleen in cases of typhoid fever, these are due in part to the size of the organ and to the manner in which it reacts at different times to the infectious process, and in part to topographic, often individual, factors, or to antecedent or associated lesions in adjacent organs.

Above all, it should be mentioned again at this place that the typhoid splenic tumor in general does not attain any considerable degree

[1] *Volkmann's Sammlung klin. Vortr.*

of size. In the middle or toward the end of the first week, even at the beginning of the second week, it is often demonstrable only on percussion or is palpable by those expert in palpation on deep inspiration just below the costal arch, either as a distinct round or rather sharp border, or as a sense of inspiratory increase in resistance in the region in question. Also, at the height of the disease, with which, as anatomic observation has shown, most marked enlargement of the spleen coincides, it is possible in not a few cases to detect only an increase in the intensity and the extent of the dulness without trustworthy findings on palpation.

In the minority of cases, at the beginning or in the middle of the second week, at times even somewhat later, the splenic tumor appears distinctly two or three finger-breadths below the costal arch even during the respiratory mid-position. The anterior inferior border of the spleen rarely extends much further downward; then probably only when the tumors are abnormally large or when the spleen has an unusual shape (considerable longitudinal diameter—tongue-shaped), or, finally, if the spleen is displaced downward and forward, as a result of congenital or pathologic conditions or due to relaxation of the ligaments or abnormal adhesions of the displaced organ. In such cases, in which the splenic tumor can be palpated throughout a considerable extent, one can convince himself that in the beginning and at the height of the disease the spleen is of tense elastic consistency, while after the height of the disease has been passed it becomes distinctly softer, at times to such a degree that it is less readily demonstrable. From the differential diagnostic point of view it is probably true that old malarial splenic tumors or splenic enlargements due to leukemia and pseudoleukemia appear firmer and less elastic, while enlargements of the spleen induced by septic processes frequently are likely to be softer from the beginning and throughout their entire duration.

Palpation of the enlarged spleen in the course of typhoid fever is attended with little or no tenderness. At times, however, on palpation as well as on percussion, complaint is made of a certain degree of pain. Still more rarely patients complain spontaneously, without pressure or movement, of dull pain beneath the left costal arch. More marked tenderness on palpation, or in rotation, on flexion, and in breathing, is indicative of special disease of the spleen or its immediate vicinity, including first of all perisplenitis, which may even be associated with pleuritis, less commonly infarcts and abscesses.

With regard to special anatomic, topographic, and individual influences that may render difficult and prevent the demonstration of a

splenic tumor, accidental conditions play no small *rôle* in this connection. Among the factors that must frequently be taken into consideration, meteorism especially is to be mentioned. As meteorism in cases of typhoid fever generally involves the large intestine, and especially the neighborhood of the greater curvature and the flexures in most marked degree, while the distention of the small intestine may be slight or absent, the increased difficulty in demonstrating the splenic tumor need by no means always be dependent upon marked overdistention of the entire abdomen. In addition to the gaseous distention of the intestine, abnormal size and position of adjacent portions of bowel, especially the frequent formation of a loop of colon,[1] may constitute an obstacle to the recognition of the enlargement of the spleen. Not rarely there are associated with these conditions the displacements of the spleen already mentioned, either congenital or acquired, occasionally with fixation in abnormal situations. Exceptionally also the organ is divided into several individual parts, a spleen with so-called supernumerary spleens, thus interfering with palpation. That technical skill is also a factor in the examination in question may finally be worthy of mention.

In the latter connection it should be especially pointed out that if the diagnosis of splenic tumor be based upon the results of percussion alone, the examination should be made frequently throughout a certain period of the disease, and it should always yield approximately the same result. Dependence should by no means be placed upon the results of a single percussion.[2] It is noteworthy that to the skilled clinician, in cases in which, on account of meteorism or other local conditions, increased limits of the area of splenic dulness cannot be demonstrated, special intensity of the dulness will indicate that the organ is abnormally large. The greatest significance, however, should be attached to the results of palpation of the spleen, which is always to be practised bimanually with the patient in the right lateral decubitus, in such a manner that the left hand from the lumbar region endeavors to push the posterior abdominal wall and the organ to be palpated against the right hand, applied anteriorly just below the costal margin.

Little is to be said clinically concerning other affections of the spleen in the course of typhoid fever. Infarcts and profuse hemorrhage in the splenic tissue almost always elude diagnosis, as do abscess and rupture of the spleen, which occur with exceeding rarity. The last-named conditions are indicated almost solely by symptoms of acute peritonitis, which are of such varied etiologic significance that those complications will at most be thought of only by way of exclusion. They might

[1] "Topographisch-klinische Studien," *Deutsch. Archiv*, Bd. liii.

[2] See also von Ziemssen, "Klinische Beobachtungen über die Milz," *Münch. med. Woch.*, 1896, No. 47, a communication that contains a number of valuable technical and diagnostic suggestions.

most readily be suspected if—as has now and again been observed—the onset of the peritonitic symptoms were immediately preceded by sudden severe pain below the left costal arch.

Even on post-mortem examination special anatomic lesions of the splenic tissue are quite rare. Among 577 autopsies at Hamburg and Leipsic I observed infarcts and hemorrhage in 25, abscesses in 4, rupture in 2, and extensive recent perisplenitis in 16. The last-named figure, judging from my other experiences, is rather small. The statistics of Griessinger bearing upon anatomic changes in the spleen quite agree with my own. Among 118 autopsies he noted considerable disease of the spleen in 9.

Changes in the Thyroid Gland.—Although little has been reported anatomically with regard to the condition of the thyroid gland during the ordinary course of typhoid fever, even less has been observed clinically in this connection. Only in exceptional cases are changes found in this organ, and these may be of an inflammatory nature of varying intensity, up to termination in abscess-formation. Nevertheless, they play a more prominent *rôle* as a complication of typhoid fever than of the remaining infectious diseases.

Walther,[1] who reported several cases of typhoid thyroiditis from my clinic, was able to show that among 73 cases of acute strumitis and thyroiditis collected by him, 40 were traceable to typhoid fever—an interesting illustration of an observation previously made.

The symptoms of **typhoid strumitis** consist in acute painful enlargement of the thyroid gland, and almost always of only one-half or of a still smaller portion. Inflammation of the entire gland appears to be extremely rare in the course of typhoid fever.

Just as we were able to demonstrate with regard to inflammation of the parotid gland, so also in the case of the thyroid gland, the morbid process is generally observed to terminate either in suppuration or in involution of the inflammatory process without the development of an abscess. The disorder appears almost always to pursue a favorable course, as Liebermeister has shown, and I have been able to determine from personal experience. Alarming symptoms, among which dyspnea from compression and displacement of the trachea may be mentioned, are among the rarest exceptions. Griessinger, it is true, mentions a case of death from suffocation, and Forgue lost a patient by rupture of an abscess of the thyroid gland into the trachea.

With reference to the etiology of typhoid strumitis, it is especially to be pointed out that it occurs more frequently in previously hyperplastic organs, and it is therefore more often seen in regions where goiter prevails, for instance, Switzerland.

[1] *Inaug. Diss.*, Leipsic, 1896.

The relatively frequent occurrence of thyroiditis in Switzerland has been demonstrated by the statistics of Griessinger and Liebermeister. The former observed the condition 4 times in 118 autopsies, the latter in 15 of 1700 patients, in 6 with abscess-formation. In other countries thyroiditis is far less common in accordance with the greater rarity of goiter. Among 349 autopsies in Hamburg I failed to observe a single case. Further, during the great typhoid epidemic in that city I observed the condition but twice during life. In Leipsic also it is a great rarity. Topfer[1] has reported 3 cases of abscess of the thyroid gland among 927 autopsies at Munich.

It is interesting to note that Lichtheim-Tavel,[2] Jeanselme,[3] Schudmark and Vlachos,[4] and several others have demonstrated the bacillus of Eberth as the exciting agent of the inflammatory process. In other instances the ordinary pyogenic micro-organisms, streptococci and staphylococci, have been found. Under these conditions the course was often more unfavorable, in so far as the condition was a part manifestation of a general septicemia. With regard to the period when typhoid strumitis occurs, it appears to coincide especially with the beginning of convalescence or the last week of the fever. There are but few reports of its occurrence at an earlier period in the course of typhoid fever.

GENITO-URINARY ORGANS.

The Urinary Apparatus.—From the practical standpoint, it appears desirable to describe now the changes in the state of the urine, in so far as they relate to the constitutional disturbance underlying the attack of typhoid fever, especially to the febrile state, and to follow this with a description of the conditions that are attributable to direct, more profound, and more independent disease of the urinary apparatus. During the febrile stage the urine resembles in many respects that excreted in other acute infectious diseases. Its amount is generally diminished, especially during the first three weeks of the disease—that is, during the ordinary duration of the fever. In spite of abundant administration of fluid, this diminution in the amount of urine almost always occurs, naturally with variations in accordance with the severity of the attack, and especially in accordance with the intensity and the duration of the fever.

In the stage of steep curves the amount of urine is generally again increased, returning to the physiologic even as early as the beginning afebrile period. An unusual increase in the secretion of urine

[1] "Die Complicationen des Abdominaltyphus," *Münch. med. Woch.*, 1892.

[2] *Ueber die Aetiologie der Strumitis*, etc., Basle, 1892, Sellmann.

[3] "Contrib. à l'étude des thyroidites infect.," *Arch. gén.*, July, 1893.

[4] *Wien. klin. Woch.*, 1900, No. 29.

during the progress of convalescence is by no means a rare manifestation, so that the amount may reach 10,000 c.cm. and more in twenty-four hours. The urine is then remarkably light, as clear as water, and of exceedingly low specific gravity—down to 1002. Rarely, and then especially in nervous persons, women as well as men, this polyuria may be apparent as early as the later portion of the febrile period.

With the reduction in the amount of urine during the febrile stage, the remaining manifestations of concentration are present: abnormally dark color, generally clear, or with a sediment, which then consists principally of urates and uric acid. Not rarely the dark color does not correspond entirely with the specific gravity. The color may be intensified by the presence in the urine in considerable amount of urinary pigments other than the ordinary ones. These will be discussed briefly later. The specific gravity is almost always considerably increased—up to 1030 and above; rarely it declines to 1020. The reaction of the urine from the beginning of the disease and at the height of the fever is invariably strongly acid, unless especial conditions are present. At a later stage the acidity diminishes, while during convalescence the urine frequently presents a neutral or even an alkaline reaction.

Among the solid constituents of the urine, the urea should be mentioned first. The almost invariable and marked increase in the amount of urea eliminated in twenty-four hours throughout the entire febrile period has already been observed by earlier writers—Neubauer and Vogel,[1] A. Vogel,[2] Prattler,[3] Parkes,[4] Murchison. A large number of personal investigations directed to this point have yielded the same result. I have not at all rarely observed double the physiologic average amount of urea, and now and again even more than this. The processes responsible for the fever in cases of typhoid fever exert distinctly the most important influence upon the increased elimination of urea. The view that the elevation of temperature alone—that is, the increased heat of the body-tissues—is to be looked upon as the exciting factor must be rejected at the present day. Undoubtedly, increased elimination of urea and febrile elevation of temperature are co-ordinated manifestations, dependent upon the influence of the toxins upon the course of metabolism.

In the period of defervescence a reduction in the elimination of urea begins almost invariably, although at this time it is generally above the limits observed during health. During the period of convalescence the physiologic amount eliminated is generally again attained. In a

[1] *Anleitung zur Harnuntersuchung.*
[2] *Loc. cit.*
[3] *Loc. cit.*
[4] *On the Urine*, 1860.

number of instances I have observed even during convalescence—even where the mode of nourishing the patient in such cases did not differ from that in other cases of typhoid fever—a considerable, long-maintained increase in the elimination of urea. With this was constantly associated progressive reduction in the body-weight, a condition that appears to render such cases worthy of further investigation. It has been stated by some writers that even at the height of the attack in severe so-called adynamic cases, sudden reduction in the amount of urea may be observed, and that this manifestation is calculated to render the prognosis much more grave. I have personally not as yet made such an observation.

Like the urea, the uric acid is also almost unexceptionally increased in the febrile stage, and at times quite considerably. The elimination of uric acid is also diminished again with the commencement of convalescence, and returns to the normal during the period of recovery. The reports by Frerichs and Städler with regard to the presence of leucin and tyrosin are familiar and often cited; Griessinger also considers those substances as almost constantly present.

The chlorids, as in many other acute infectious diseases, are always greatly diminished during the febrile stage, to increase again considerably with the subsidence of the disease. The opinion of Jul. Vogel, that the diminution in chlorids is dependent solely upon the lessened amount of sodium chlorid ingested with the febrile diet, is no longer tenable. This phenomenon occurs now as formerly, although it has become customary in cases of typhoid fever to administer concentrated nourishment containing an abundance of sodium chlorid instead of a diet of watery soups. The more recent hypotheses with reference to the reduction in chlorids, however, also appear vulnerable, so that, as a matter of fact, it would appear worth while to undertake a new study of the question.

The appearance of albumin in the urine in cases of typhoid fever is of especial importance. The substances found under such circumstances are known to be serum-albumin and serum-globulin. Less commonly, and only under certain definite conditions, does peptone appear in the urine, as Gerhardt was the first to point out. We shall first take up the consideration of the elimination of albumin that occurs without profound disease of the kidneys, and is generally designated as febrile albuminuria. We shall return at a separate place to a consideration of the albuminuria due to actual nephritis.

Febrile albuminuria is one of the more common manifestations. According to my experience, it can be demonstrated in from 15 to 20

per cent. of cases of typhoid fever. I have reached this conclusion from the study of a large number of cases, including, naturally, mild as well as marked cases. In a number of extensive epidemics I have observed the proportion to be lower; for instance, in that at Hamburg in 1886–1887 only 10.7 per cent. of the cases exhibited febrile albuminuria.

The latter figures are approximated also by my Leipsic statistics, in which the proportion was 11.3 per cent. On the other hand, the statement of Gubler,[1] that albuminuria is constant during typhoid fever, is difficult of explanation. Other observers name higher figures than I do, as, for instance, Murchison,[2] who observed albuminuria in 93 of 282 cases—32.26 per cent. This is assuredly not the rule; possibly it may be explicable by the fact that Murchison's statistics are based upon a collection of smaller individual data (personal observation and that of six other writers), and that severe cases especially were taken into consideration. It is true also that Weil[3] and Griessinger give high comparative percentages. The latter believes that febrile albuminuria occurred in one-third of his cases.

Albumin was present at some stage of the disease in 616 of 829 cases (74 per cent.) treated at the Johns Hopkins Hospital (Osler[4]). This includes the cases in which the albumin was considerable in amount, as well as those in which the faintest possible trace of albumin was present.

The amount of albumin eliminated varies from traces to moderate amounts. The presence of a large amount should always lead to more careful examination for the presence of profound disease of the kidneys, which can almost always be demonstrated under such conditions. It can be stated definitely that only the more severe and the severest cases exhibit albuminuria. The condition is therefore one that makes the prognosis distinctly more grave, and the more so the earlier it appears, the longer it persists, and the greater the amount of albumin eliminated. Of 393 cases of febrile albuminuria that I have collected, death occurred in 107—27.2 per cent.—a mortality fully three times the normal.

As the period for the beginning of albuminuria I would designate the end of the first and the entire second week, in contradistinction from other writers (Murchison and Finger), who have never observed it before the sixteenth day, and most frequently between this time and the twenty-fifth day of the disease; its advent, however, is also quite frequent to the end of the third week, and upon this point I am in agreement with Weil. Its occurrence becomes less frequent after the third week; it has, however, come under my observation even quite late, up to the forty-eighth day of the disease. I consider late appear-

[1] *Dict. des sci. med.*, Art. "Albuminurie."
[2] *Loc. cit.*, p. 488.
[3] *Zur Pathologie und Therapie des Abdominaltyphus*, 1883.
[4] *Johns Hopkins Hosp. Rep.*, vol. viii., p. 467.

ance of albuminuria especially unfavorable from the prognostic point of view. I have observed it to be followed by death in an unusually large number of cases. In isolated cases I have observed albumin to appear in the urine during the first week, to disappear in the course of a few days, and then to reappear in varying amount and for a varying period. Striking as this fact is in itself, I have been unable to establish any relation between it and other deviations in course and termination. The observation that the albuminuria is likely to be increased or to reappear during relapses and recrudescences has been emphasized frequently.

The duration of febrile albuminuria in the individual case appears to correspond approximately with its intensity. In three-fourths of all cases it persists, in my experience, less than twelve days. A duration up to three weeks, exceptionally also longer, is not at all rare. Of 92 cases of febrile albuminuria that I have analyzed, I found the duration to be from one to three days in 5 cases; from four to six days in 25; from seven to nine days in 20; from ten to twelve days in 12; from thirteen to twenty-one days in 25; from twenty-two to twenty-seven days in 5.

Microscopic examination of the urinary sediment discloses in cases of pure febrile albuminuria, in addition to crystalline structures, especially uric acid and urates, isolated white blood-corpuscles and epithelial cells from the urinary passages, and generally a few hyaline, otherwise unchanged, tube-casts. In the presence of slight albuminuria their number is generally so small that they can be found only in the sediment obtained with the aid of the centrifuge. Osler[1] states that tube-casts were present in 391 of the 829 cases—47 per cent.; or, in other words, 63 per cent. of the cases showing albuminuria also showed the presence of tube-casts. Tube-casts of other kinds, and especially increase in the number of leukocytes, with evidences of increased desquamation on the part of the kidneys, are indicative of more profound lesions. In rare cases the albuminuria of typhoid fever may persist even throughout convalescence without having been referable in the course of the disease to nephritis, and it may give rise to a long-continued peculiar form of albuminuria, at times never wholly disappearing, which yet awaits thorough anatomic investigation.

I have observed such cases on several occasions, but have hitherto had no opportunity for anatomic investigation, so that I am without knowledge as to their nature. They are almost always characterized by the presence of a normal amount of clear urine of normal character and of normal specific gravity, with a small amount of morphologic elements: scarcely any epithelial cells from the uriniferous tubules, a small number of tube-casts

[1] *Loc. cit.*

exclusively of the hyaline variety, never any red blood-cells, and at most a few white corpuscles. Cardiac hypertrophy and edema apparently do not occur, and I have likewise failed to observe uremic manifestations. In some instances I have observed such albuminuria to persist, in a characteristic manner, for ten or twelve years after the attack of typhoid fever (treated by me), apparently without any further injurious effect upon the healthy-looking, functionally capable individual, who, on account of the results of examination of the urine, may become temporarily depressed or even permanently hypochondriacal—the only manifestation suggestive of the existence of disease. In isolated cases I have noted complete disappearance of this albuminuria, even after the lapse of years, with the persistent peculiarity, it is true, that slight transitory turbidity of the urine developed on the application of tests for albumin after active bodily exercise or after the ingestion of strong alcoholic beverages. I have observed a similar form of chronic albuminuria, the anatomic basis for which has not been clearly determined, following other acute infectious diseases also, especially dysentery, cholera nostras, and necrotic angina.

In addition to the more common changes in the state of the urine mentioned, a number of less common substances and reactions are worthy of mention. The increase of urobilin that occurs in the urine, and is at times so marked that the condition is appropriately designated urobilinuria (Tissier [1]), is interesting. Tissier and others are inclined to associate the manifestation with profound (typhoid) alterations in the liver and the biliary passages. According to Tissier, the most marked urobilinuria can be found only in severe cases, while that of moderate grade will be present in mild, but protracted, cases. I have no personal experience in this connection.

The appearance of moderate, and even of considerable, amounts of indican in the urine is quite frequent, and is an indication of derangement in proteid digestion and absorption. I am, however, by no means of the opinion that any direct relation exists between the amount and duration of indican-elimination and the severity of the attack of typhoid fever; and I am unable to attribute to it either diagnostic or special prognostic significance. I have often observed a more pronounced indican-reaction in mild cases of typhoid fever, especially when attended with profuse diarrhea, or, conversely, with obstinate constipation, than in severe cases. It need scarcely be mentioned, in view of what is known in general in this connection, that with the onset of general peritonitis and also of circumscribed peritonitis, particularly in connection with typhoid perityphlitis, especially marked elimination of indican takes place.

I have encountered true hemoglobinuria associated with hemoglobinemia in but 2 cases of typhoid fever. In one of these it occurred

[1] *Thèse*, Paris, 1890.

in the middle of the second, and in the other at the beginning of the third, week. Both cases terminated fatally with symptoms of most profound intoxication. Klemperer[1] has recently reported a case of hemoglobinuria after recovery from a severe attack of typhoid fever.

Roque and Weill[2] were the first to call attention to the presence of intensely toxic, probably specific substances in the urine of patients suffering from typhoid fever. Lépine and Guérin have reported most remarkable observations of a similar character. In the light of existing knowledge with regard to the presence of toxins and antitoxins in the circulating blood in cases of typhoid fever, these observations should stimulate further active investigation.

It is finally necessary at this place to refer to the diazo-reaction of Ehrlich with the urine in cases of typhoid fever, the principles of which and the method of eliciting it may be presumed to be familiar. Doubtless, this important reaction can always be obtained at the height of an attack of typhoid fever; it is permanently absent only in the milder cases. It is also undoubted that in severe cases, when improvement begins to take place, the reaction not rarely disappears, so that from this sign favorable conclusions may be drawn at a time when other symptoms are not indicative of improvement or are uncertain in this regard. It is noteworthy, also, that in relapses from typhoid fever the diazo-reaction, if it had already disappeared, generally returns, while it does not reappear when fever occurs during convalescence from typhoid fever as the result of organic disturbances due to other causes. In all these connections a certain degree of diagnostic and prognostic value is distinctly to be attached to the reaction, although it is not absolute. Thus, rarely, it is true, severe and even also anatomically demonstrable cases of typhoid fever have been observed in which the reaction was continuously absent owing to undeterminable causes. In addition, the reaction occurs with especial frequency, almost invariably, in other febrile diseases, and particularly such as offer difficulty in differential diagnosis, especially miliary tuberculosis and florid forms of pulmonary tuberculosis, typhus fever, certain varieties of profound pneumonia, malaria, and, finally, acute exanthemata, particularly measles.

The term typhoid bacilluria or bacteriuria has been applied to the condition in which typhoid-bacilli are found in the urine. This occurs in from 20 to 30 per cent. of all cases. The bacilli may be present in small numbers, or they may occur in enormous numbers, so as to render the urine distinctly turbid. Horton-Smith has laid special stress on the peculiar shimmer which is seen when a test-tube filled with such

[1] *Charité Annalen*, 20. Jahrg., 1895.

[2] *Rev. de Méd.*, 1891.

urine is held up to the light and gently shaken. In this way the condition can often be predicted without cultures and without microscopic examination. Usually, the bacilli do not appear in the urine before the fifteenth day, and they may persist for a variable length of time—even for months or years after convalescence (seven years in the case reported by Young[1]). The recognition of this condition is even of more importance from the hygienic standpoint than from the diagnostic. A patient voiding such urine is a source of constant danger to all those about him.

Associated with the bacilluria is frequently a moderate or even an extreme grade of pyuria. It is not uncommon for the urine of typhoid patients, especially if albuminuria be present, to contain a few pus-cells. If, however, the pus is considerable in amount, one should always suspect the presence of a typhoidal bacilluria. If, in addition to the pus, the patient complains of slight pain in passing the urine and slight frequency of micturition, it is probable that a mild grade of cystitis exists, which may pass into a more severe form or even become chronic. Thus, no hard-and-fast line can be drawn between bacteriuria and cystitis. Apparently, however, mere presence of the bacteria in the bladder is not sufficient to cause cystitis. Horton-Smith concludes that "the bacilluria is due to infection of the urine by a stray typhoid-bacillus, excreted by the kidneys from the blood, and its immediate multiplication in the bladder-urine. If, in addition, the bladder-walls have been in any way damaged, then true typhoidal cystitis follows."

Nephritis.—Emphasis has already been placed upon the fact that febrile albuminuria cannot be sharply differentiated from the nephritis not rarely attending typhoid fever, and, as it appears, etiologically related to this disease. Each may undoubtedly pass over into the other, and they are attributable in part to the same cause, namely, the action of toxins. The nephritis generally occurs in the form of acute parenchymatous inflammation, in part hemorrhagic, in part non-hemorrhagic. The nephritis generally occurs at the height of the disease, before the end of the third week; and it is much less common at a later period. I have, however, observed it appear on the thirtieth day, and in one instance even during convalescence. Cases of the latter variety are then likely to be prolonged for some time. Of 32 cases, I noted the appearance of nephritis before the end of the third week in 18. In 2 cases the onset of the complication was placed respectively at the beginning and the middle of the first week.

Age and sex exhibit little that is peculiar, although it appears to me

[1] *Johns Hopkins Hosp. Rep.*, vol. viii.

that men are attacked somewhat more frequently than women, and in this connection it is probable that the mode of life, especially alcoholism, plays a part. Of 84 cases of nephritis in adults (Leipsic and Hamburg statistics), 54 occurred in males. The proportion is more striking in the Leipsic statistics alone, where of 53 cases of nephritis, 41 were in males. In children, particularly during the early years of life, I have observed nephritis in but 2 cases. Among adults no special predisposition with regard to age appears to exist. During this period the frequency of nephritis is about the same as that of the predisposition of various ages to typhoid fever generally. Of 25 cases of nephritis, 3 were under sixteen years of age; 11 between sixteen and twenty-five years inclusive; 8 between twenty-six and thirty-five years; 1 between thirty-six and forty-five years; 1 between forty-six and fifty-five years; 1 above fifty-five years.

Numerous general statements have been made with regard to the macroscopic anatomy of typhoid nephritis, but relatively few with regard to the finer alterations. Besides findings similar to those attending acute inflammatory lesions of the kidneys, which are occasionally observed in association with other infectious diseases, numerous observers have reported cases pursuing an extremely pernicious course in which microscopic examination is said not to have disclosed any essential histologic alterations whatever. These observations, it is true, were made at an earlier period, and, if repeated with the aid of modern methods, they might perhaps yield more satisfactory results. An attempt has been made to separate from the ordinary cases of typhoid nephritis certain varieties that are characterized by the appearance especially early and in intense degree of the renal manifestations, and by the unusual duration of the same. These may, in fact, so thoroughly dominate the entire clinical picture that some French writers have devised the special designation nephrotyphoid for such cases.

Among the first of the cases of this character in the literature are 2 by Immermann,[1] in which nephritis, occurring at the height of the disease and accompanied by uremic manifestations, led to a fatal termination. The first to describe the condition as a special disorder was Gubler,[2] and he was followed by Legroux and Hanot[3] with statistical reports, and Robin, a pupil of Gubler's, who completed the description of his teacher and proposed the designation "nephrotyphoid." Amat[4] then elaborated the schematic limitations and description of this form of disease to a refined degree, and even believed that it presented special anatomic conditions, considerable enlarge-

[1] *Jahresbericht der Medicin. Abtheilung des Bürgerspitals zu Basel*, 1872.

[2] *Loc. cit.*

[3] "Observat. d'albuminurie dans la fièvre typh.," *Arch. gén. de méd.*, 1876.

[4] "Sur la fièvre typh. en forme renale," *Thèse*, Paris, 1878.

ment of the kidney, with evidences of acute interstitial inflammation, especially of the cortical structure. According to Amat, the urine is invariably characterized by its intensely bloody color and the presence of large amounts of albumin, with numerous tube-casts, blood-corpuscles, epithelial cells and their degeneration-products. In addition there is said to be from the outset remarkably high fever, with early, profound stupor, but with an absence of the usual abdominal symptoms of typhoid fever.

Kussmaul[1] was one of the first in Germany to direct attention to the Gubler-Robin type of disease, but with his customary penetration attributed to it its proper degree of importance. The 3 cases upon which his paper was based exhibited by no means complete agreement, and therefore cannot be used in support of the doctrine of a special form of nephrotyphoid in the sense of the French clinicians.

Personally, I am of the opinion that acute parenchymatous nephritis appearing early and pursuing a severe course during an attack of typhoid fever should be considered as a particularly serious occurrence. There is, however, no reason for the recognition of a distinct variety of nephrotyphoid, or for the separation of this from other, milder forms of nephritis, of shorter duration, occurring in the course of or toward the end of the disease. The differences and the contrasts are here not so sharp as was theoretically believed. On the contrary, if a series of distinctive cases are compared, a gradual transition will be noted. The urine contains a large amount of albumin, with numerous hyaline, granular, and epithelial tube-casts and a considerable amount of blood, and the disease in other respects pursues the typical course of typhoid, with marked abdominal symptoms; and these facts must be emphasized as opposed to the assumption of a separate condition exclusive of both typhoid and nephritis. Excessive stupor or other unusual nervous manifestations are, further, by no means always associated with such profound alteration in the condition of the urine. There is even no constant association of high fever with profound nephritis.

With regard to the frequency of true typhoid nephritis, if it be differentiated as sharply as possible from febrile albuminuria, it will be found, as has been said, to be not at all large. In my experience the condition occurs in scarcely 1 per cent. of the cases. The prognosis of typhoid nephritis is grave, and on this point it must be admitted that the French investigators are correct, but this is not so because the organism is especially affected by the severity of the disease of the kidneys, but rather because the occurrence of severe, especially hemorrhagic, nephritis is one of the local symptoms of unusually profound general intoxication. Almost half of all patients with typhoid nephritis die. In this respect my experience at Hamburg, where I observed a mortality

[1] Homburger, *Berlin. klin. Woch.*, 1881, Nos. 20, 21, and 22 (Mittheilungen aus der Kussmaul'schen Klinik).

of 50 per cent., differs little from that at Leipsic, with 44.4 per cent. Of 229 cases of typhoid fever at the Johns Hopkins Hospital,[1] there were definite evidences of an acute nephritis in 21. Of these 21, 7 died —33.3 per cent. Death occurs either—and this is the more common—amid symptoms of most profound general intoxication, or with the supervention of various complications. In 5 of the 7 cases above mentioned, death was due to perforation. In my experience actual uremia develops less commonly. I have in but 1 instance observed death to occur from uremia. This was in a young man, in the first half of the second week of an attack of typhoid fever, who developed convulsions and coma, after symptoms of hemorrhagic nephritis had existed for a few days only. In addition to the cases of Immermann that belong in this category, reference should be made to the report of Murchison. A case of Robert and Gaucher,[2] terminating in recovery, appears not to belong in this group.

The duration of cases of typhoid nephritis in which complete recovery takes place is variable. Most frequently it appears to be from one to two weeks. I have, however, also observed protracted cases that lasted as long as nine weeks. Incomplete recovery with transformation of acute nephritis into the chronic variety appears to be a rare exception, in contrast with some other infectious diseases in which this is well known to be not uncommon. In a large experience I have personally observed but 1 case that could be included in this category. No such case has occurred at the Johns Hopkins Hospital, and Osler[3] has never seen such a case.

Of other diseases of the kidney in the course of typhoid fever, virtually nothing is as yet known clinically. The multiple and the diffuse lymphomata of Wagner,[4] the exceedingly rare infarcts and multiple abscesses,[5] are attended in general with no symptoms, or at most with the appearance of albuminuria. Even noteworthy hematuria, in consequence of infarction, may be considered as exceedingly rare.

GENERATIVE ORGANS.

Male Genitalia.—Diseases of the male genitalia in the course of typhoid fever are not so frequent and important as are those of the female. As in other infectious diseases, especially variola, inflammatory affections of the testicle occur in the course of typhoid

[1] Hewetson, *Johns Hopkins Hosp. Rep.*, vol. iv. [2] *Rev. de Méd.*, 1881.

[3] *Ibid.*, vol. viii.

[4] *Arch. d. Heil.*, Bd. ii., and "Nierenkrankheiten," *von Ziemssen's Handbuch*, 2. Aufl..

[5] See the classic case of von Recklinghausen, *Verhandl. d. phys.-med. Gesellsch. z. Würzburg*, 1871.

fever. Not much can be said in general with regard to their frequency, as they have not as yet been so thoroughly and admirably studied as has the orchitis of variola (Chiari). Typhoid orchitis appears to occur rarely at the beginning of the disease, while it is almost always a manifestation of the last part of the febrile stage or the first part of convalescence. It begins with chilliness, or even, as I have observed in 1 case, with a chill. In any event, it is almost always attended with marked elevation of temperature. The testicle and the epididymis are, under such circumstances, often indurated and swollen, and the skin of the scrotum is reddened and occasionally edematous. The testicle is usually affected first, and often alone; less commonly the epididymis is affected first or alone (Eshner). The pains, which radiate in the course of the spermatic cord to the abdominal cavity, are generally severe, so that they deprive irritable individuals of sleep and rest. Termination in recovery is the rule. This was completed in from ten to fourteen days in all the cases under my observation. I have hitherto never observed termination in suppuration, which appears, on the whole, to be exceedingly rare. Quite exceptionally atrophy of the testicle develops. In a case under my observation sterility in the male, dependent upon azoöspermia, was with probability attributed to a previous bilateral typhoid orchitis from which recovery had taken place.

I have personally observed typhoid orchitis in 6 cases, and in all it was unilateral. In 4 instances the testicle alone was inflamed, and in 2 together with the epididymis. The affection appears not to occur in children. It develops chiefly in young men. Five of my patients were under thirty, and but one forty-five years old. An interesting study upon this subject has been made by Ollivier,[1] who analyzed 3 cases of his own and a considerable number from other sources. There may be mentioned, besides, among French observers, Cervelle[2] and Sorel,[3] and among German observers especially Liebermeister,[4] who observed orchitis in 3 cases among 200 of typhoid fever.

A late review of the cases of typhoid orchitis has been made by Eshner,[5] who collected 43 cases from the literature, besides reporting 1 of his own. Ten of these are mentioned as having gone on to suppuration, and from the pus of 5 of these cases the typhoid-bacillus was cultivated. From a study of these cases he concludes that in most instances the condition is dependent upon infection through the blood with typhoid-bacilli, although the possibility of infection by continuity through the urethra with typhoid-bacilli or other micro-organisms cannot be excluded.

The occurrence of emissions with abnormal frequency in convalescents from typhoid fever is worthy of mention, because at times of

[1] *Rev. de Méd.*, 1883.
[2] *Thèse*, Paris, 1874.
[3] *Gaz. méd. des hôp.*, 1889.
[4] *Loc. cit.*, 2d ed., p. 191.
[5] *Phila. Med. Jour.*, vol. i.

great practical importance. This was emphasized by Griessinger, and I have frequently observed it as a disturbing factor during convalescence. Changes in the penis appear extremely rare. Complete or partial gangrene of the organ, as has been mentioned by Andral, Pillmann,[1] and others, I have never observed.

Female Genitalia.—As is true of many other infectious diseases, so the beginning and course of typhoid fever have a definite influence upon the menstrual flow. It occurs quite frequently during the first days of the disease, and earlier than would have been expected during health. At times it is likely to be as free as usual, and at other times unusually abundant and protracted. In the latter event, careful examination of the genitalia should always be made, as abortion at the beginning of typhoid fever may be readily concealed behind the mask of abnormal menstruation.

If the normal time of menstruation is not due until two to three weeks after the onset of the fever, the flow usually does not take place. In general, absence of menstruation is the rule throughout the entire febrile period and during the first part of convalescence; at least, this is true of protracted cases and those pursuing a severe course. I believe that during these periods complete absence of menstruation may be expected in about 60 per cent. of the cases. In the remainder, transitory, slight, rarely profuse hemorrhage from the genitalia occurs in rather an irregular manner, even during the febrile stage.

After severe, long-protracted attacks of typhoid fever, menstruation is likely to be absent even after defervescence, often not appearing for two or three periods. After less severe and mild attacks it often recurs during convalescence. Profuse uterine hemorrhage at the height of the disease, without special local cause, is rare and of ominous import. It is analogous to a similar occurrence in cases of hemorrhagic smallpox, and occurs—rarely, it is true, in comparison with its frequency in the former disease—in cases of typhoid fever presenting other "hemorrhagic" symptoms. Toward the end of the disease or during convalescence, peri-uterine hematocele may occur, as Trousseau has pointed out. Still far less common than this is hematometra (Martin[2]).

So-called diphtheric and croupous affections of the uterine mucous membrane, which, undoubtedly, have nothing to do etiologically with true diphtheria, are of anatomic rather than of clinical interest, just as are the hemorrhage, the suppuration, and the necrosis of the ovary, all of which during life give rise to symptoms difficult of interpretation. More important are certain alterations in the external genitalia and

[1] *Loc. cit.*

[2] *Centralbl. f. Gynäk.*, 1881, No. 26.

the vaginal orifice. Edema of the labia minora, decubital ulceration of the greater and lesser labia and at the vaginal orifice, painful erosions at the mouth of the urethra, the latter being not rarely the cause of ischuria, are of not rare occurrence. A form of non-gonorrheal leukorrhea occurring with considerable frequency in the course of typhoid fever, and which still needs a thorough bacteriologic investigation, should be mentioned here.

In a number of instances I have observed acute inflammation and suppuration of the glands of Bartholin. Takaki and Werner[1] have reported such a case, from the suppurating gland of which they obtained the typhoid-bacillus in pure culture. Complete or partial gangrene of the vulva has frequently been reported at different times and in different epidemics (Hoffmann, Liebermeister, Spillmann[2]). I have observed this condition in 4 cases, twice in children and twice in adults. In one of the latter cases the gangrene was a sequel of bartholinitis. All clinicians agree that gangrene of the vulva is to be considered as a grave symptom, occurring almost only in exceedingly severe cases. In the rare cases in which it is possible to demonstrate a local cause, as in the case just referred to, recovery sometimes ensues, then generally with extensive cicatricial defects extending into the vulva, or even with vesical or rectal fistulæ.

Inflammation of the breasts in the course of typhoid fever, as has been described by Leudet,[3] appears to be quite rare. Slight transitory tumefaction, however, is in my experience somewhat more common. This may readily be overlooked, as it usually occurs in severe cases at the height of the febrile stage, with the termination of which it subsides, so that the patient is not really conscious of its presence, and it is rarely a source of complaint. Termination in suppuration appears, as in the case of the testicle, the thyroid gland, and the parotid gland, by no means to be the rule. Probably the bacillus of Eberth is the exciting agent of the inflammation in the majority of cases. It may be mentioned that I have observed slight mastitis in 2 cases of typhoid fever in young men.

The relation between **pregnancy** and typhoid fever is deserving of full consideration from both a clinical and a prognostic standpoint. Reference has already been made (under the subject of Etiology) to predisposition during gravidity. A study of the literature of this subject discloses differences, often actual contradictions, which are not, however, due in the least to the smallness of the statistics considered.

[1] *Zeit. f. Hyg.*, Bd. xxvii. [2] *Arch. de Méd.*, 1881.

[3] *Clin. méd.*

The majority of writers give unfavorable reports, stating that almost always abortion or premature labor occurs, with great danger to the life of the mother. In my experience the peril to pregnant women suffering from typhoid fever is not so great, certainly not comparable to the danger attending this condition in cases of small-pox. Nevertheless, gravidity is to be considered a serious complication of typhoid fever.

A number of patients pass safely through the attack of typhoid fever without interruption of pregnancy, while others recover, in spite of abortion or premature labor, in the latter event at times even with a living child. In other cases death occurs immediately after interruption of the pregnancy or occurs as a result of severe complications.[1] The cause of sudden death, often occurring within from twenty-four to thirty-six hours, is generally the large amount of blood lost. Among the complications, septic conditions with pseudodiphtheric and gangrenous changes in the uterine mucous membrane should be mentioned.

Müller states, however, that typhoid patients are not more liable than others to complications of labor, such as hemorrhage.

In my experience the age of the pregnant woman and the period in pregnancy have no considerable influence upon the interruption of the latter, as might be thought in advance. However, it may be said that if the interruption occurs in the later months of pregnancy, the prognosis is distinctly more unfavorable than if it takes place during the first eight or ten weeks. With regard to the occurrence of this complication in relation to the stage of the disease, it may be said that the danger is greatest during the febrile period, and that in the first week of this period abortion occurs far less commonly than in the second or third week. In protracted cases of typhoid fever with a markedly remittent or intermittent temperature-curve, I have observed this complication occur as late as the fourth week of the fever, and even later. If the febrile stage has been successfully passed, the outlook becomes more favorable. One should avoid, however, making definite promises for the period of convalescence. Even at this stage abortion and premature labor occur sometimes, especially in greatly reduced patients or with the onset of complications.

As an evidence of the remarkable variability in the statements of writers with regard to the course and prognosis of typhoid fever in gravid women, it may be mentioned that Murchison states that the prognosis is always grave in the presence of advanced gravidity, believing that a fatal termination to premature labor invariably occurs. Liebermeister also considers gravidity as exceedingly dangerous. Of 18 pregnant women, he observed

[1] See in the section on Etiology, the Conditions for Typhoid Fever in the Fetus.

abortion in 15 and death in 6, namely, in one-third of all. Of 5 pregnant women under the observation of Griessinger, 3 died, premature labor having occurred in all. From my Leipsic statistics, which, it is true, include only the small number of 14 cases, it appears that the gravidity was interrupted in all but 1, and death occurred in 5—35.6 per cent. My Hamburg experience, on the other hand, is quite favorable, and I would attach some importance to it, as it is more extensive and was obtained in the course of a severe epidemic. Of all the women coming under observation in 1886–1887, 38—3.4 per cent.—were gravid. Of these, 3 went to term and were delivered during convalescence of living children, while 14—42.1 per cent.—were discharged after recovery from the attack of typhoid fever without interruption of the pregnancy. Pregnancy was, thus, not threatened by the attack of typhoid fever in exactly half of my patients. Of the other patients, in whom abortion or premature labor took place, 3 died. The mortality during pregnancy was therefore 7.8 per cent. I had, besides, a similarly favorable experience at Berlin before the Hamburg epidemic. It should be mentioned, further, that results similar to my own have been reported from Kiel by Goth,[1] who among 9 patients observed abortion in 4 and death in but 1. Also, Betz[2] reports from Ziemssen's clinic at Munich that, of 9 pregnant women, abortion failed to occur in 5.

Sacquin[3] collected from various sources the statistics of 233 cases of pregnancy during typhoid. Abortion, miscarriage, or premature labor occurred in 150 of these cases. Death occurred in 37—16 per cent.

DIGESTIVE ORGANS.

Lips, Mouth, Tongue, Pharynx, Parotid Glands.—While during mild attacks these parts exhibit slight changes or alterations that are not characteristic, in the severe and worst cases they are likely to acquire so peculiar a character as to constitute an important part of the general clinical picture. Even early the mucous membrane of the mouth, lips, and tongue exhibits a tendency to dryness. At the same time the latter is more or less coated and swollen, with distinct and often deep impressions of the teeth. At the height of the disease the upper lip is likely to be retracted and the upper teeth exposed. The tongue and the lips then become covered with a dirty-brown, viscid deposit, rapidly undergoing desiccation. The dry mucous membrane of the lips becomes fissured, the gums are spongy and bleeding, and, in children who constantly pick at the sore lips, extensive eczematous and ulcerative processes readily develop, with marked swelling of the lips and the tissues about the mouth. In rare cases complete scorbutic detachment and ulceration of the gums take place, with at times pretty free hemorrhage.

The tongue at first is frequently covered only in the middle with a

[1] *Inaug. Diss.*, Kiel, 1886; and *Deutsch. Arch. f. klin. Med.*, Bd. xxxix., S. 140.
[2] *Deutsch. Arch. f. klin. Med.*, Bd. xvi., xvii., xviii. [3] *Thèse*, Nancy, 1885.

more or less heavy whitish or whitish-yellow deposit, while its swollen margins, marked with the impressions of the teeth, are greatly reddened. In some instances it may be completely covered as early as the first week by a thick coating, which at times is discolored dirty brown or even black by food and medicine. During the early period of the disease, at the beginning and the middle of the first week, the tongue is likely to be still moist by day, exhibiting a tendency to dryness only toward evening and night. In the second week of severe cases it can be kept moist only with great care; it is then extended with difficulty and is tremulous; it appears less, if at all, swollen, and in less well-cared-for patients is brown, dry, encrusted and fissured, and bleeds readily from the fissures. The coating of the tongue disappears at a time depending upon the character of the individual case, but usually at the end of the second or in the beginning of the third week, usually disappearing first at the tip in the form of a triangle and at the margins, then over the entire tongue, so that the organ then appears smooth, red, dry, and thin, and more pointed than usual.

Several factors are responsible for the ominous dryness of the tongue, namely, the febrile temperature, the diminution in salivary secretion, constantly keeping the mouth open, and the diminished desire of the somnolent patient to moisten the organ. Typhoid patients with a dry tongue always exhibit more or less marked derangement of consciousness. The tongue in cases of typhoid fever does not exhibit any distinctive morbid manifestations. Its alterations become characteristic only from the period of onset, the intensity, and the arrangement. An early appearance and a tendency to dryness of the tongue are of diagnostic importance. They represent a conspicuous associated feature of the typhoid state.

McCrae[1] has reported a case of glossitis coming on during convalescence from typhoid fever. The onset was on the twenty-fifth day of normal temperature, and with it occurred a typical relapse lasting two weeks. Recovery was complete. He has also collected several other cases from the literature.

Of peculiar changes in the mucous membrane of the mouth and the pharynx, deposits of thrush especially are to be mentioned. These occur only in extremely severe, protracted cases, or in patients who have been previously ill, and in whom the care of the mouth has been neglected. Under such circumstances I have seen the deposits extend down the esophagus to the region of the cardia, and even to constitute a serious obstruction to breathing. The occurrence of a severe case of

[1] *Johns Hopkins Hosp. Bull.*, vol. ix.

thrush in a hospital does not reflect creditably upon the medical care and the nursing.

The structures of the fauces exhibit various changes in cases of typhoid fever. Lymphoid swelling of the tonsils and the palatine arches—to which reference has already been made (in the chapter on Anatomy)—appears to me to be rarely demonstrable, at least clinically. Duguet and Chantemesse have observed such infiltrations undergo disintegration with the subsequent formation of ulcers, in the floor of which typhoid-bacilli were demonstrable—a process, therefore, that is probably comparable to the specific lesion in the intestines.

In the large majority of cases there is but slight involvement of the pharyngeal structures, namely, moderate swelling, and frequently cloudiness of the mucous membrane of the soft palate, the tonsils, and the posterior pharyngeal wall. In the second and third weeks the pharyngeal structures participate in the dryness of the remainder of the mouth. They are then profusely covered with exceedingly viscid mucus, readily desiccating into crusts and filaments, and occasionally becoming a serious obstruction to swallowing and breathing.

It is exceedingly important to realize that symptoms of angina may be present as early as the beginning of the first week of typhoid fever, and that, together with chilliness and slight elevation of temperature, may at times constitute the earliest and the only manifestation causing the patient any inconvenience. Under such circumstances the mucous membrane of the pharynx and the tonsils appears more or less markedly reddened and spongy. In addition there are not rarely present upon the soft palate, the palatine arches, and the tonsils isolated, rarely numerous, whitish, at times slightly elevated spots, varying in size from that of a lentil to that of a pea, which represent areas of circumscribed granular clouding and tumefaction of the uppermost layer of the mucous membrane. Generally in the course of a few hours superficial exfoliation takes place, leaving quite shallow reddish erosions, covered with a thin whitish deposit and surrounded by a flat, irregular, often vividly reddened margin, which is never infiltrated. If the parts are kept sufficiently moist and clean, the lesions do not further increase in size and depth, and they have almost always disappeared at the beginning of the second week.

At times this affection of the throat becomes so prominent as to give rise to error in diagnosis. I have in 2 instances observed such patients admitted to the hospital with a diagnosis of diphtheria and croup, respectively. In one instance incipient scarlet fever was suspected because of the associated presence of a slight initial rash. In another case in which

the affection of the throat existed together with an abundant roseolous eruption upon the trunk, a diagnosis of syphilis was made.

Typhoid angina was evidently known to earlier writers; at any rate, certain statements made by Louis, Jenner, and Chomel with regard to early involvement of the pharyngeal structures in cases of typhoid fever are indicative of this. Subsequently it disappeared for a time from the literature and the memory of physicians, in part, perhaps, because it varies extremely in frequency, at different times, and in different places. Thus, I observed it quite rarely in the years in which typhoid fever prevailed extensively in Hamburg, while it came under my observation with remarkable frequency and in marked degree at certain times in Leipsic. So far as I know, this variety of angina, which possesses a certain degree of importance as an early manifestation of typhoid fever, has not yet been studied bacteriologically. This might prove an interesting undertaking that would possibly yield diagnostic results.

Actual diphtheric affections of the pharyngeal structures, such as have been described by Griessinger, Oulmond,[1] and others, at the height of the disease, toward the close of the second or in the third week, are probably to be included among the true complications. In any event, they are extremely rare occurrences that yet require exact bacteriologic investigation. I have personally not as yet encountered a case of this kind. The extension of the affections of the throat above described to the nasopharyngeal space, the Eustachian tubes, and the middle ear will be considered at another place.

The alterations in the parotid gland, and especially the inflammatory lesions of this organ, in cases of typhoid fever are quite important, even though they are not so common as they are generally believed to be. As is so often the case with especially painful and conspicuous disorders, the frequency of parotitis has been greatly overestimated. I have personally determined that during the Hamburg epidemics only 0.3 per cent., and in Leipsic 0.5 per cent., of the patients exhibited inflammation of the parotid glands; and in the statistics of Hoffmann relating to the Basle epidemic, parotitis was noted in 16 of 1600 cases—1 per cent. Recently parotitis appears to have become even less common, and this is probably due, in part at least, to the greater care given generally to the mouth of the patients.

Parotitis develops generally on one side; rarely both glands are involved synchronously, while disease of both successively is more common. Parotitis is usually a manifestation at the height of the disease, toward the end of the second or the third week, although it may come under observation also later, and even during convalescence. Its clinical features are scarcely different from those of inflammation of the glands under other conditions. The affection usually occurs in very

[1] *Rev. de méd. et chir. de Paris*, July, 1855.

ill and already much reduced individuals, which fact has an important bearing on the course and symptoms of the complication. In the majority of cases the retromandibular portion first becomes swollen, after which, with few exceptions, the entire organ is involved. The affection is so painful that even profoundly soporose patients are conscious of its existence. But rarely, and then in cases of metastatic origin, it sets in with a chill, while a corresponding elevation of temperature without a chill is observed almost unexceptionally. The affection may, as I have repeatedly observed, subside without suppuration, even after considerable tenderness, swelling, and redness have been present. When suppuration occurs, as it does in most cases, it involves at times but one portion of the inflamed gland, and at other times the entire organ. In the latter event I have occasionally been able to extract from the incision wound large portions of the connective-tissue structure of the gland in the form of necrotic shreds.

With regard to the mode of origin of typhoid parotitis, the view of Virchow,[1] that it is due to extension of infectious processes from the mouth through the duct of Stenon to the gland, is certainly correct for some cases. In several cases I have observed parotitis occur in association with ulcerative stomatitis, especially in the vicinity of the papilla of Stenon. Above all, it should be kept in mind that the glands are more frequently directly involved in consequence of the action of the typhoid toxins than are other organs (see section on Anatomy). Also, the typhoid-bacilli themselves may in some cases be the direct excitants of the inflammation. At least 1 case has been reported (Janowski[2]) in which a pure culture of the typhoid-bacillus was obtained from the suppurating gland. In a number of other cases the typhoid-bacillus has been associated with the pyogenic cocci (Anton and Fütterer[3]). In a number of instances I have been able to demonstrate the presence of staphylococci exclusively in the pus obtained by puncture of the gland during life. Exceptionally, I have observed parotitis as one of the symptoms of a complicating general septicemia. Although earlier writers report the observation of this occurrence more frequently, this may be due to the fact that the term septicemia was given a wider interpretation than appears justified at the present day. I have also in a number of instances seen parotitis as the sole metastatic manifestation, without the development of general pyemia, particularly following suppurative enteritis in cases of typhoid fever. I can recall, for instance, having observed metastatic abscess of the parotid gland in

[1] *Charité-Annalen*, 1858. [2] *Centralbl. f. Bact.*, Bd. xvii.
[3] *Münch. med. Woch.*, 1888, No. 19.

2 cases following typhoid perityphlitis. In 1 of these cases the affection was bilateral.

In general, parotitis is one of the severe and dangerous complications of typhoid fever. Liebermeister,[1] among 210 fatal cases between 1865 and 1868, observed parotitis in 6—2.8 per cent. Of the 16 cases of parotitis reported by Hoffmann, to which reference has previously been made, death occurred in 9. Of 28 cases collected by Keen,[2] 8 were fatal. Among the serious consequences, thrombosis of the jugular vein and the cerebral sinuses and acute edema of the brain are to be mentioned. As a result of direct extension of the suppuration, periostitis and necrosis of the adjacent bones, suppuration of the masseters, burrowing of the pus between the superficial and deep fasciæ of the neck, in the latter event with the development of mediastinitis, may take place. Secondary pyemia is a possibility under such conditions. In 1 instance I observed incurable facial palsy (see also Griessinger and Liebermeister).

Stomach and Œsophagus.—Although it is extremely rare that the stomach and the esophagus exhibit specific alterations, and almost never give rise to characteristic symptoms, they do, especially at the beginning of the attack, play a certain *rôle*. It will, at any rate, be well to devote a few words to the consideration of such general and indefinite symptoms as the pain in the epigastrium, the nausea, and the vomiting. Nervous individuals frequently complain of a sense of dull pressure in the epigastrium from the prodromal stage into the first week of the disease. This sensation almost never attains to the intensity of the dominating pains, such as are characteristic of the first days of other infectious diseases, particularly variola. Severe pain in the epigastrium, therefore, at a period in the course of a febrile disease when the diagnosis is uncertain is against rather than in favor of typhoid fever. From the second week on, the complaints of epigastric oppression yield to the progressive somnolence.

Also, vomiting and nausea by no means play the *rôle* in the beginning of typhoid fever that they do in that of typhus fever and variola. I have observed them most frequently at the beginning of the disease in children, in nervous women or hysterical men; but under such circumstances they appear generally as a transitory feature, and almost never become severely spasmodic or colicky. In some instances the attacks of vomiting appeared not to be induced by irritation in the stomach, but by the anginose lesions previously mentioned. In such cases they may be continued into the second week. Severe and repeated vomiting at the height of the disease should suggest the possibility of certain

[1] Betke, *Inaug. Diss.*, Basle, 1870. [2] *Loc. cit.*

complications, such as meningitis and allied conditions, perforation of the bowel, peritonitis, and, finally, latent intestinal hemorrhage. After defervescence and during convalescence, nausea and vomiting are almost always referable to dietetic error. Some writers refer to the occurrence of severe, almost uncontrollable vomiting during convalescence, for which no adequate anatomic basis could be found at autopsy. I have observed this manifestation, which I believe to be extremely rare, only in cases of protracted course with severe complications. In 1 case, which from the other symptoms was to be considered as one of hemorrhagic typhoid, I found erosive gastritis with numerous ecchymoses as the anatomic explanation of the vomiting.

The appetite is wholly lost in most cases as early as the prodromal stage, and in all during the first week. The patients acquire an aversion, even a disgust, for the ingestion of food, and complain of a stale, pasty, acid or bitter taste, and of a sense of burning thirst. At the height of the disease these subjective manifestations disappear, and the patients swallow mechanically what is proffered them, at times, it is true, with some resistance. In a word, during the period of evolution and at the height of the disease, the state of the appetite is the same as in most infectious diseases. The conditions are different, however, during the period of involution and in convalescence. In children and in young adults a marked almost uncontrollable sense of hunger makes its appearance during the stage of steep curves. In nervous women and in elderly persons the appetite is, on the other hand, generally wanting at this period. During convalescence, however, impairment or want of appetite is the exception in all patients. Only exceedingly sensitive individuals and those who suffer from the consequences of certain severe complications are still indifferent or averse to food and drink at this time. Well known are the large eyes with which those convalescent from typhoid fever constantly look about for food and with which they follow anyone from whom they hope fulfilment of this controlling desire. The appetite, almost always prematurely large in relation to the state of the intestinal lesion, often brings the physician in conflict with the patient and injudicious relatives. Even in the physician there may be a struggle between the sense of duty and conviction and the feeling of sympathy.

I recall a boy, thirteen years old, who, during protracted convalescence from an attack of typhoid fever, was provided food to the utmost limit of the permissible, and then requested his sisters to come to his bedside to eat in order that he might at least be able to see them dispose of their huge slices of bread and butter.

In the consideration of the anatomic alterations reference was made to certain organic lesions in the stomach that are encountered in cases of typhoid fever. These are scarcely attended with special clinical manifestations.

Bouchard and his pupil, Legendre,[1] have called attention to the fact that typhoid fever and dilatation of the stomach are so frequently associated that a direct connection between the two must be thought of. Both of these writers believe not only that dilatation of the stomach may be the result of typhoid fever, but also that, conversely, existing dilatation of the stomach favors typhoid infection. The fact that individuals attacked several times by typhoid fever frequently suffer from dilatation of the stomach is thought to be especially convincing. So far as I know, these statements have not yet been confirmed in the German literature. Personally, from my own experience, I am unable to verify them.

Reference has already been made to the superficial erosions and ulcers sometimes seen in the esophagus after death. These rarely give rise to symptoms. In the case of esophageal ulceration reported by Mitchell,[2] however, for two days before death there was well-marked dysphagia. Several cases of esophagismus during typhoid fever have been reported, but it is not known whether this has any anatomic basis. No cases of hematemesis associated with esophageal lesions have been reported. Several cases of stricture of the esophagus following typhoid fever have occurred. This is usually a late sequel, but the onset of symptoms may be during convalescence, as in the case reported by Summers.[3]

Liver and Biliary Passages.—The liver and the biliary passages also play no prominent *rôle* in the ordinary symptomatology of typhoid fever. Especially subjective symptoms referable to them are extremely rare. Objectively, at the height of the disease, the region of the liver is occasionally tender on pressure, associated with enlargement of the organ, usually of moderate grade and probably due to hyperemia and cloudy swelling. It is further to be noted that, in a majority of all, even severe, cases of typhoid fever, providing they are uncomplicated, the liver generally does not continuously exceed its normal size. So far as is known, the focal necroses previously mentioned give rise to no symptoms.

Icterus is, in the opinion of most experienced observers, among whom Murchison, Griessinger, and Liebermeister may be mentioned, an especially rare manifestation in the course of typhoid fever—so rare that some, as, for instance, Fiedler, with reference to Weil's disease, considers this fact properly of significance in differential diagnosis. Possibly this manifestation, which is common in some other infectious diseases, and then principally due to duodenal catarrh, is so rare in cases of typhoid fever because in this disease the stomach and the upper por-

[1] "Dilatation de l'estomac et fièvre typhoïde," etc., *Thèse*, Paris, 1886.

[2] *Johns Hopkins Hosp. Rep.*, vol. viii. [3] *Phila. Med. Jour.*, Oct. 28, 1899.

tions of the intestine are but little involved in the morbid process. Also, another condition favoring the development of icterus in some infectious diseases, namely, marked acute swelling of the parenchyma of the liver and consecutive interlobular biliary stasis, is encountered with extreme rarity in cases of typhoid fever.

Liebermeister observed jaundice but 26 times in 1420 cases, and Osler has seen it but 5 times in 830 cases. Its frequency seems to vary in different epidemics, as Da Costa,[1] in 1898, reported 5 cases from the Pennsylvania Hospital, 4 of which he had seen within a few months. He[2] has analyzed 52 cases from the literature. The probable causes of the jaundice in these cases were: catarrhal, 4; pylephlebitis, 3; cholecystitis, 5; abscess, 6; acute yellow atrophy, 5; toxic, 24; uncertain, 5.

According to Osler,[3] the cases of jaundice occurring in typhoid fever may be grouped in four categories: (1) catarrhal; (2) toxic; (3) those associated with abscess; (4) those associated with gall-stones and cholangitis.

Catarrhal Jaundice.—Osler thinks that the slight jaundice in cases of moderate severity is of this form, and under this heading he includes 6 of the 8 cases reported by him. Da Costa, however, thinks that most of the cases are of toxic origin, as he includes only 4 of the 52 cases under the catarrhal. It is interesting, in this connection, that clay-colored stools are of rare occurrence. They were not clay colored in 4 of the 5 cases reported by Da Costa, and in only 1 of Osler's cases is the presence of clay-colored stools mentioned. In favor of many of these milder cases being of catarrhal, obstructive origin is the great frequency with which the bacilli are present in the bile. The quite constant occurrence of typhoid-bacilli in the gall-bladder in cases of experimental inoculation-typhoid in rabbits was noted by Blachstein[4] in 1891. After Gilbert and Girode[5] had demonstrated the typhoid-bacilli in the human gall-bladder, Chiari[6] showed the almost constant occurrence of the bacillus of Eberth in the gall-bladder—in 20 of 22 autopsies—often in enormous numbers. Chiari's observations have been confirmed by Birch-Hirschfeld[7] and others. In most cases they cause no damage to the gall-bladder or ducts. That they probably induce more severe forms of inflammation and may lead to the forma-

[1] *Trans. of Assoc. Am. Phys.*, vol. xiv. [2] *Ibid.*, vol. xiii.
[3] *Johns Hopkins Hosp. Rep.*, vol. viii.
[4] *Johns Hopkins Hosp. Bull.*, 1891, vol. ii.
[5] *Sem. méd.*, 1890, No. 58, and *Compt. rend. de la soc. biol.*, 1891, No. 11.
[6] *Prag. med. Woch.*, 1893, No. 22.
[7] *Path. Anat.*, Bd. ii., 4. Aufl., S. 694.

tion of calculi will be spoken of later. Whether they can induce a mild form of catarrh of the ducts, and so lead to an obstructive catarrhal jaundice, is not yet definitely settled. As we know, however, how the presence of typhoid-bacilli in the urine may give rise to the mildest form of cystitis, as shown only by the presence of a few pus-cells in the urine, as well as to the more severe grades of cystitis, it seems probable that a similar condition can occur with regard to the bile, and that a simple catarrhal inflammation may be set up that induces these milder grades of jaundice.

Toxic Jaundice.—In favor of the view that many of the cases are of this form, Da Costa presents these arguments: "Its occurrence, as a rule, as a late symptom and in grave cases; the character of the stools, which are but little modified; the general similarity to the jaundice noticed in other infective diseases and altered blood states, such as in pyemia. The condition of the liver itself does not give us much information. Yet where the organ has been carefully examined, it has been found to show degeneration of the liver-cells that has been likened by Frerichs even to the state found in acute yellow atrophy."

Such a case, running a course like acute yellow atrophy, with, at autopsy, a liver resembling that found in that condition, has been lately reported by Sauborin. Reference has also been made to this condition by Griessinger, Liebermeister, and Hoffmann. When this rare condition occurs at all—I am unfamiliar with it from personal observation—it is said to appear at the height of the typhoid process, at times in association with distinct painful tumefaction, and then rapidly progressive diminution in the size of the liver. Jaundice soon appears, together with hemorrhages from various organs, hematuria and albuminuria, cardiac weakness, and death in coma.

Abscess of the Liver.—Da Costa has collected 22 cases in which the association of abscess of the liver with typhoid fever seemed beyond doubt. Of these, only 7 had jaundice, but in 12 it is not mentioned at all. I know of no cases in which the abscesses are due to a localization of the typhoid-bacilli in the liver. Abscess of the liver may arise in three different ways: (1) As one of the manifestations of general secondary septicemia or pyemia complicating typhoid fever; (2) as a result of septic pylethrombosis, in connection with suppurative affections of the intestine, especially the cecum; finally, (3) in consequence of various inflammatory and ulcerative processes in the large biliary passages and the gall-bladder.

I have personally observed instances of all three modes of origin. An instance of the first variety consists in the case of a man, twenty-three years

old, who presented 3 abscesses, from the size of a pigeon's to that of a hen's egg, in the right lobe of the liver, doubtless due to a deeply undermined putrid bed-sore. A similar condition has been observed by Louis[1] and Chvostek,[2] the former in the sequence of suppurative parotitis, and the latter after perichondritis of the larynx. Osler has reported such a case, in which, in addition to the abscess of the liver, there occurred suppuration in the parotid gland, abscess of the gastrohepatic lymph-glands, and multiple lung-abscesses. I have observed 2 cases belonging in the second category, the first, in 1887, in private practice. In this case an abscess developed in the right iliac fossa as a sequence of typhoid perityphlitis, and it gave rise to an irregular, bulging abscess, as large as an apple, in the left lobe of the liver, attended with chills and characteristic intermittent fever, and terminating fatally. The second case, reported from my clinic by Romberg,[3] likewise originated from a suppurative perityphlitis, and gave rise to multiple abscesses of the liver in the distribution of the portal vein. Bacteriologic examination disclosed the presence of staphylococci only, and no typhoid-bacilli, in the pus. Klebs[4] has probably reported the first instance of the development of abscess of the liver from ulceration of the biliary passages. A case under my observation occurred in a woman, eighteen years old, with an encapsulated abscess at the side of, and behind, the gall-bladder, which communicated with it, extending to the size of a pigeon's egg into the substance of the liver. The condition had developed at the commencement of the fourth week of the attack of typhoid fever, and, what made the diagnosis most difficult, it was at the beginning unattended with jaundice, and later was attended with but slight jaundice.

The typhoid inflammatory affections of the gall-bladder and large biliary passages are deserving of thorough consideration. Such occurrences were mentioned by Andral, Louis, Jenner, and Leudet, and subsequently were described, especially by Rokitansky, as diphtheric affections of the gall-bladder. Later German and French writers also refer to them, generally as ulcerative pseudomembranous affections, terminating in abscess of the liver, perforative peritonitis, etc. Cholecystitis and cholangitis in typhoid fever have been more fully treated of in the past few years by Osler,[5] Mason,[6] Da Costa,[7] Camac,[8] Ryska,[9] and others. These authors have collected and reported numerous cases in which these conditions occurred either as complications or as sequels. As to the frequency of acute cholecystitis during the febrile attack, no considerable statistics have been collected, although quite numerous cases have been reported by the above-mentioned writers. With regard to

[1] *Loc. cit.*, 1841, 2d ed., vol. i. [2] *Allg. Wien. med. Zeit.*, 1866, No. 37.

[3] *Berlin. klin. Woch.*, 1890, No. 9. This article contains an extensive bibliography. Of similar cases, there are cited that of Tüngel, *Klin. Mittheil.*, Hamburg, 1862–1863; that of Asch, *Berlin. klin. Woch.*, 1882, No. 51; and that of Buckling, *Inaug. Diss.*, Berlin, 1868.

[4] *Handbuch der path. Anat*, 1868, p. 480.

[5] *Loc. cit.* [6] *Trans. Assoc. Am. Phys.*, vol. xii.

[7] *Loc. cit.* [8] *Johns Hopkins Hosp. Rep.*, vol. viii.

[9] *Münch. med. Woch.*, Bd. lvi., No. 23.

the etiology, it may be said that in a number of the cases in which bacteriologic examinations were made, pure cultures of the typhoid-bacillus were obtained. But, as from the work of Chiari and others, the almost constant presence of the typhoid-bacilli in the gall-bladder has been demonstrated, there must be some secondary factor. Recent studies leave no doubt that gall-stones render the biliary ducts and gall-bladder more receptive to infection. But while stones have been found in some of these acute cases, in the majority they have not been present. Of 74 cases of biliary infection collected by Keen, in 38 no gall-stones were found. In 34 cholecystitis, empyema, or ulceration was present without gall-stones, and from 11 the typhoid-bacillus was isolated. It is probable that in many cases the obstruction to the flow of bile is due to mucus; the growth of the bacteria being thus favored, an acute inflammation of the walls of the gall-bladder may be induced, leading to suppuration, distention, possibly ulceration and perforation.

The main symptoms of cholecystitis are localized pain and tenderness and the presence of a tumor. The tumor is usually located in the right hypochondrium, but may be much lower, even below the umbilicus. Jaundice may occur, but is by no means constant. Further and more complete observations as to the behavior of the leukocytes are needed. Surgical interference in these cases will be referred to in the chapter on Treatment.

Suppurative cholecystitis and cholelithiasis following typhoid fever are conditions requiring surgical treatment, and further consideration is not possible here.

The relation of typhoid-bacilli to the formation of **gall-stones** is an exceedingly interesting one. Richardson[1] has shown that the bacilli are frequently clumped in the bile, and he, Cushing,[2] and others believe that these clumps form the nuclei for stones. From the interior of stones the typhoid-bacilli have been isolated in a number of instances, and the experimental production of gall-stones by inoculation of typhoid-bacilli into the gall-bladder of animals has been successfully accomplished by Gilbert and Fournier,[3] Richardson,[4] Cushing,[5] and others.

It has been demonstrated that typhoid-bacilli may remain viable in the gall-bladder for years. Hunner[6] has reported a case of suppurative cholecystitis occurring eighteen years after the attack of typhoid fever, from the pus of which the typhoid-bacillus was isolated in pure culture.

Reference has been made in the anatomic section to the condition of

[1] *Jour. Boston Soc. Med. Sci.*, vol. iii. [2] *Johns Hopkins Hosp. Bull.*, vol. x.
[3] *Compt. rend. de la soc. biol.*, Oct. 30, 1897. [4] *Loc. cit.* [5] *Loc. cit.*
[6] *Johns Hopkins Hosp. Bull.*, vol. x.

the bile itself. This is known to be thinner, lighter in color, and of lower specific gravity (from 1010 to 1016, as compared with the normal, 1026 to 1030, Brouardel). With regard to the influence of this alteration upon the intestinal contents and the urine, nothing of a definite nature is known. Possibly the striking pallor or even the almost complete decolorization of the stools, of considerable duration, as I have observed, may be dependent upon that condition. The intimate connection between urobilinuria[1] occurring in cases of typhoid fever, which has, as yet, been but little studied, and the alterations in the bile and the functions of the liver in general, is a matter for future investigation.

Symptoms Referable to the Intestinal Tract.—The inexperienced observer is likely to assume an intimate relation, and, even as to details, an actual parallelism, between the conspicuous specific alterations in the intestine and the clinical manifestations. This may be correct with regard to certain less common or subordinate conditions. As to the severity, the extent, and the localization of the usual typhoid lesion of the intestine, however, most good observers, I believe, agree that the stages of the disease probably correspond in general with the occurrence and the development of the lesion, but that this is by no means true of the character of the manifestations, the severity and the duration of the abdominal symptoms in detail. Every experienced physician will recall walking cases of typhoid fever, with slight general symptoms, without meteorism, without abdominal pain, and without diarrhea, that terminated fatally from unexpected intestinal hemorrhage or perforative peritonitis, and occasioned surprise on anatomic examination on account of the unusual extent and severity of the typhoid intestinal lesions. Conversely, profuse diarrhea and other intestinal symptoms are not rare in the earliest stages, when the specific intestinal lesion has scarcely begun to develop. Every experienced physician will know of cases presenting predominant intestinal symptoms throughout which are in remarkable contrast with the slight anatomic lesions found at autopsy.

I shall never forget a case seen in consultation. A young woman died at the beginning of the third week of an attack of typhoid fever. She had not been compelled to go to bed until five days before death, and as late as a week previously had spent considerable time at an evening entertainment without special inconvenience. During the three weeks preceding death there had been only variable, generally diminished, appetite and no diarrhea, but rather constipation. Marked febrile manifestations had been noted only during the last six days. Post-mortem examination disclosed intestinal typhoid lesions throughout an extent that I have rarely since observed. In the lower two-thirds of the ileum almost all of Peyer's patches were infiltrated in part confluent, and in the stage of exfoliation of the sloughs; while

[1] Tissier, *Thèse*, Paris, 1890.

in the region of the ileocecal valve and the cecum itself there was scarcely a free area of mucous membrane, and the upper third of the large intestine was also densely occupied by lenticular ulcers, in part of unusual size. Still more surprising were the results of an autopsy on the wife of a physician, who apparently had died, in the opinion of the husband, in consequence of perforation of an ulcer of the stomach without previous noteworthy symptoms. In this case also the lesions of typhoid fever in the stage of exfoliation of the sloughs were found, likewise with extension of the intestinal lesion from the valve up to the middle of the ileum. Death had resulted from perforation of the vermiform appendix.

It will be seen, therefore, that it is better to study each case individually and to reserve a decision than to proceed upon schematic lines.

We shall begin the discussion of the individual intestinal manifestations with **meteorism.** Many, particularly older, works contain descriptions of the early onset, of the severity and the frequency, and even the constancy of this symptom, such as no longer correspond with the experience of the objective observer of the present day. On the contrary, I would assert that considerable meteorism occurring early scarcely belongs among the manifestations of a well-marked attack of typhoid fever pursuing a regular course. It is, in general, apart from local and special conditions, the less common the earlier the patient comes under observation and the greater the care given him. Under favorable conditions in private practice or in a well-conducted hospital, the milder and moderately severe cases, if received early, are likely to be unattended with meteorism, or at most to exhibit it in slight degree. More marked meteorism, if it develops in spite of good care and restricted diet, is a most ominous manifestation. It is indicative of the extreme severity of the course of the disease, and is dependent far less upon the intensity of the typhoid intestinal lesion than upon the intensity of the general infection which gives rise to paralysis of the muscular layer of the intestine, and thereby to gaseous distention. In further support of this view, it may be mentioned that severe intestinal manifestations, even rather persistent diarrhea, by no means always precede or accompany the meteorism; and also, conversely, obstinate constipation is by no means always associated with it. It generally appears, on the contrary, to be a sequel of the meteorism.

The individual portions of the intestine are involved in the gaseous distention in varied degree. As has been mentioned, the large intestine, and especially the transverse colon, is, as a rule, involved in most marked degree and most frequently. The small intestine is likely to be distended less markedly in comparison with the colon, often remark-

ably little. Decided meteorism, if it involve the small intestine at all, is located with preference in those parts that are, as a rule, less attacked by medullary infiltration, namely, the region of the jejunum and the upper portions of the ileum. Under such circumstances the transverse colon, unless displaced or exhibiting abnormal arrangement of its coils, may be seen beneath the abdominal walls, in the form of step-like loops passing transversely above and below the umbilicus.

In addition to the general there are not rarely severe local disturbances that give rise to the meteorism, and that are the more readily overlooked in the soporose patient, inasmuch as he does not by complaint suggest thorough local examination. In this category belong especially circumscribed peritonitis and intestinal hemorrhage, the latter of which is by no means always indicated at once by the evacuation of bloody stools. Incarceration of the bowel, volvulus or intussusception, which, it is true, occur rarely, must also be thought of. In a number of instances I have observed marked meteorism and symptoms of ileus in direct association with typhoid perityphlitis.

If, therefore, marked meteorism appears generally as a sequel or associated phenomenon of other serious conditions, it is by no means thereby implied that on its own account it may not exert injurious effects, especially by diminishing the capacity of the thorax and so interfering with the respiration, already so gravely threatened by the typhoidal disease of the respiratory organs. Abdominal tenderness, spontaneous or on palpation, is rarely present under ordinary conditions. In uncomplicated cases the patients complain, if at all, of scarcely more than a sense of tension and pressure. Only in the presence of meteorism of marked degree, even if not of inflammatory nature, will palpation often be attended with pain. Far more common than general tenderness of the abdomen is tenderness in the right iliac fossa, which is referable to the portion of intestine preferably the seat of the ulcerative process. In some cases this tenderness is constantly somewhat higher toward the liver, and this is possibly due to the congenital dislocation of the cecum upward (Curschmann), which is known to occur not at all rarely. McCrae has carefully studied 500 cases of typhoid fever at the Johns Hopkins Hospital with reference to abdominal pain and tenderness. He found that about two-fifths of the patients are free from pain or tenderness, rather less than one-fifth have tenderness only. Pain due to some condition other than the specific bowel-lesions was present in about 14 per cent. of the cases. It occurred with hemorrhage or perforation in about 5 per cent. of all cases. It was most constantly present with perforation, when it was usually sudden in

onset, severe in character, and paroxysmal in occurrence. In about two-fifths of all cases with pain no cause could be found.

In connection with the question as to whether there is pain associated with an inflamed serous surface over an inflamed Peyer's patch, he quotes an interesting case in which the severe pain, associated with other symptoms, led to a diagnosis of some acute abdominal complication, and an exploration was done under local cocain anesthesia. Just under the point where the patient had complained of greatest pain was a large Peyer's patch with the serosa much inflamed. With the handling of the intestine he made no complaint of pain, but even a gentle touch over this inflamed area made him cry out. Yet in other cases patients made no complaint when the serous surface over the ulcers was handled. It is questionable whether deep ulceration may be a cause of pain.

Since the time of Chomel, clinicians attach no little importance to the occurrence of gurgling and splashing, which it is said can almost constantly be induced by palpation of the cecal region in cases of typhoid fever—the *gargouillement* of the French. As to the occurrence of this phenomenon, and its striking frequency in cases of typhoid fever, there can be no doubt; but I would call attention to the fact that it should not—as is often the custom—be considered an important symptom of the disease. In my experience the phenomenon is so inconstant that I am not in the habit of attaching important diagnostic significance either to its absence or its presence. From the theoretic point of view also this inconstancy could scarcely be otherwise, for the development and the distribution of the specific typhoid intestinal lesions are so variable, as has been pointed out in the anatomic section, that the anatomic conditions in the lower portion of the ileum and the cecum that render the development of that symptom physically possible are not fulfilled with any regularity.

Finally, it may be mentioned, with reference to palpation of the abdomen, that care should be taken to avoid confusing circumscribed tenderness of the abdominal walls that may be associated with various changes in the abdominal muscles, such as lacerations, hematomata, etc., which are known to occur so frequently, with local inflammatory processes in the internal abdominal organs. I have observed the commission of such an error in a number of instances.

The Stools.—It is customary to speak of a "typhoid stool," and this designation is employed to describe a peculiar, and therefore diagnostically important, characteristic of the intestinal discharges. Undoubtedly the discharges which are spoken of as typhoid stools present a peculiar appearance. Apart, however, from the demonstration of

typhoid-bacilli, neither their physical nor their chemic condition presents anything specific. Their diagnostic value resides especially in their association with a number of other symptoms. It is well known that the so-called typhoid stools are thin, liquid, of ochre-yellow color, "pea-soup-like." They exhibit an alkaline reaction, and they possess at times, although by no means always, a peculiar ammoniacal odor. Both of these characteristics are attributed by Parkes and Lehmann to the presence of ammonium carbonate and a fixed alkali. It is characteristic for the stools, when permitted to stand, to separate soon into two layers, a lower, yellowish-gray, friable, flocculent, opaque one, and an overlying, watery, turbid, translucent one that contains remarkably little (only about 4 per cent.) of solid matter and is particularly deficient in albumin and mucus. It is evidently this deficiency of the fluid in mucus that renders it incapable of being emulsified and that favors the separation of the typhoid stools into layers.

Microscopic examination of the sediment of the stool discloses structures derived from the food, more or less altered intestinal epithelium, detritus, and smaller and larger particles of slough, and in the second and third weeks even larger shreds derived from exfoliation of the sloughs. In addition, white and red blood-corpuscles are always present in small number, and also masses of various micro-organisms. So long ago as the year 1834, Schönlein showed that in addition to all these, quantities of triple phosphates are almost constantly present. Although his opinion that these are specific constituents of the typhoid stool has not been confirmed, they are, nevertheless, undoubtedly more common in association with typhoid fever than with other diseases, and, therefore, are not without diagnostic significance. Concerning the presence of typhoid-bacilli in the stools, detailed statements have already been made in the chapter on Etiology. Their bearing upon diagnosis can be estimated from that section.

It must be emphasized that the stools just described are by no means so constant or so frequent as the inexperienced might believe, and that when the disease is accompanied by any diarrhea, the stools are, in general, not likely to be exceedingly numerous, particularly not so frequent as in the majority of cases of acute intestinal diseases, dysentery, catarrh, and allied conditions. From three to six thin stools in twenty-four hours may be considered as the average number in the diarrhea of typhoid fever. A larger number, up to twelve, is less commonly observed, and then only for a short time. Abnormal frequency of intestinal evacuations, when continued for a considerable length of time, justifies a fear that the disease will pursue a severe course—in this

connection my own experience is entirely in accord with that of Louis, Murchison, Trousseau, and others. In the absence of local disease at the anus, such as hemorrhoids, fissures, etc., the intestinal discharges of typhoid patients are almost always unattended with pain or tenesmus.

The time of the first appearance and the duration of the diarrhea exhibit wide variations. Not rarely thin stools occur as early as the prodromal stage, before the onset of the fever. They are often incorrectly attributed to simple intestinal catarrh, and occasionally also to the excessive and protracted action of laxatives, which had been administered to overcome existing constipation. At this time the discharges do not so readily form layers, and also are often dark in color, resembling ordinary diarrheal stools, thereby increasing the difficulty in diagnosis. This appearance may be due to the fact that the alterations in the secretion of bile, particularly the thinning and the lighter color of the secretion, which occur so constantly at the height of the disease, have not yet begun. This prodromal diarrhea may disappear with the beginning of the fever or after the first few days of fever, not to recur throughout the entire course of the disease; or followed for a few days by constipation, less commonly by normal evacuations, after which, at the end of the first or the beginning of the second week, the stools again become thin, and now present the characteristic pea-soup-like appearance. In some cases stools of this character persist throughout the entire febrile period, rarely beyond this, with approximately the same or varying frequency. In other instances diarrhea alternates with constipation or with normal discharges, or it disappears permanently. The patients then generally remain more or less constipated, or, what is much less common, the intestinal discharges occur regularly.

If an exact statement is desired as to the frequency with which diarrhea occurs in cases of typhoid fever, it may be said that diarrhea throughout the whole or the larger part of the febrile period of the disease is likely to occur in scarcely one-third of all the cases, while in about an equally large number diarrhea occurs but transiently or in alternation with solid discharges. Of 3835 cases that I have examined with regard to this point, 1289 belonged to the first, and 1359 to the second category, while 1187 were throughout free from diarrhea. These cases of typhoid fever "without typhoid stools" deserve especial consideration from the diagnostic standpoint. The novice is far too readily disposed under such conditions to doubt the existence of the disease. The experienced physician, however, may go still further, and maintain that of this large number of cases without thin stools more

than half actually suffer from constipation, frequently throughout the whole course of the disease, less commonly for a short time.

The following figures will illustrate these relations more accurately; and in this connection it may be mentioned that the Leipsic statistics, which include all the cases observed at the medical clinic during thirteen years, more nearly approximate the general prevalent conditions than the Hamburg statistics, which cover a single epidemic. Like many other clinical manifestations of typhoid fever, the variations in the intestinal discharges also exhibit not inconsiderable local and temporal differences. Nevertheless, a comparison of these figures discloses on the whole considerable agreement. Of 2240 cases during the Hamburg epidemic of 1887 that were investigated as to the state of the stools, diarrhea was present throughout in 809—36.1 per cent.; the stools were normal throughout in 116—5.2 per cent.; constipation was present throughout in 567—25.3 per cent.; normal stools alternated with constipation in 52—2.3 per cent.; transitory diarrhea alternated with normal stools in 202—9 per cent.; transitory diarrhea alternated with constipation in 424—18.9 per cent.; diarrhea alternated with constipation and normal stools in 39—1.8 per cent.

Of 1875 cases observed at the Leipsic medical clinic between the years 1880 and 1893, which were investigated from the same point of view,[1] there was found diarrhea throughout in 480—25.6 per cent.; normal stools throughout in 83—4.4 per cent.; constipation throughout in 307—16.4 per cent.; normal stools in alternation with constipation in 62—3.3 per cent.; diarrhea in alternation with normal stools in 144—7.7 per cent.; diarrhea in alternation with constipation in 550—29.3 per cent.

Bloody Stools.—The hemorrhagic discharges which are here especially referred to are those that take place from portions of intestine the seat of the specific lesions, and therefore stand in direct relation with the typhoid process. Care should be taken to avoid confusing these with the accidental admixtures of blood from the lower portions of the rectum or the anal region, due to hemorrhoids, fissures, and the like, which not rarely greatly agitate the layman and may occasionally lead the physician into error. Under these conditions the blood generally presents a fresh appearance or is found in coagulated masses or admixed with mucus; it is deposited upon or lies beside the fecal matter, and is never intimately admixed with it.

True intestinal hemorrhage is one of the most important events in the entire course of an attack of typhoid fever. The amount varies between slight admixture of blood, often distinguishable with difficulty, even on microscopic examination, and the most profuse hemorrhages, the blood being discharged from the bowel in liter-amounts and rapidly causing death by loss of blood. In accordance with the amount and the source of the blood, and the time that elapses between the extravasation and the discharge with the stool, the latter will present a variable

[1] *Inaug. Diss.*, Leipsic, 1893, by Berg.

appearance. If there be but slight admixture of blood, the stool is likely to be yellowish-red or brownish-red in color. If a comparatively large amount of blood is gradually extravasated and is not expelled at once, it will appear as a liquid, from dark brown to reddish black in color, or even as an almost wholly black, viscid, tar-like mass, often with a greenish tinge. If the hemorrhage takes place rapidly from one or several large vessels, and if the blood is soon expelled as a result of accelerated peristaltic movements, the stools acquire rather the character of simple coagulated blood, namely, reddish-black or blood-red, generally coagulated, masses, or not rarely dark clumps of blood in a liquid stool.

The usual time for the occurrence of this dreaded accident is often stated to be later than my experience indicates. Although local, temporal, and individual influences may be operative in this connection, I believe the statement is justified that fully 30 per cent. of all intestinal hemorrhages occur within the first two weeks of the disease, and then, naturally, the more frequently, the more nearly the close of the second week is approached. I have even noted periods (Hamburg epidemic of 1887) in which half of all the instances of hemorrhage (44.8 per cent.) were observed during the first two weeks of the disease, while 24.4 per cent. were seen in the third, and 13.4 per cent. in the fourth week. My experiences at Leipsic confirm these statements, and they are perhaps even more striking.[1]

The average conditions may be indicated by the following figures: In 148 cases of intestinal hemorrhage (Hamburg, 1886–1887), the bleeding occurred from the sixth to the ninth day in 12, from the tenth to the twelfth day in 23, from the thirteenth to the fifteenth day in 23, from the sixteenth to the eighteenth day in 31, from the nineteenth to the twenty-first day in 17, from the twenty-second to the twenty-fourth day in 9, from the twenty-fifth to the twenty-seventh day in 11, from the twenty-eighth to the thirtieth day in 10, from the thirty-first to the thirty-third day in 3, from the thirty-fourth to the thirty-sixth day in 4, after the thirty-sixth day in 5.

As there can be no question of extensive exfoliation of sloughs and the opening of large vessels before the end of the second week, these early hemorrhages must have some other source. As a matter of fact, they take place, as anatomic investigation shows, from the soft, spongy, exceedingly hyperemic and friable tissue of Peyer's patches, which is discolored dark red to black, and which may undergo this serious alteration as early as the beginning or the middle of the second week, in some instances even earlier. From this source, if numerous Peyer's patches are involved, the hemorrhage may be as copious as from eroded large vessels.

[1] See Berg, *Loc. cit.*, p. 18.

After the end of the second and the beginning of the third week the hemorrhages are naturally no longer due to these alterations, but to exfoliation of the sloughs from the affected Peyer's patches and solitary follicles. Depending upon the seat of the infiltration and the depth attained by it, one or more smaller or larger vessels are simultaneously eroded. Inasmuch as the process of infiltration and ulceration of the lymphatic intestinal apparatus—as anatomic observation shows—does not take place at a single stroke, but rather slowly, in stages, so also is the period in which hemorrhage is dependent upon it often quite long. Even at the time when all the ulcers may be thought to be clean, or in greatly reduced individuals many weeks after this period, hemorrhages, sometimes of fatal degree, may yet occur. These result from imperfectly thrombosed vessels in the floor of ulcers, often also, even when the intestinal lesions in general appear to be healed, from isolated slugglish ulcers, situated both in the small intestine and also relatively quite frequently in the large intestine. This intestinal hemorrhage may be observed to occur as late as between the thirtieth and the fortieth day of the disease, and even still later; I have observed it on the fifty-second, fifty-fifth, and fifty-eighth days, respectively.

Hemorrhages appear to be much less common during relapses than during primary attacks of the disease. Of 153 cases of hemorrhage that I have analyzed, this complication occurred in only 4 during relapses.

The number of bloody stools that occur in the individual case is, as a rule, overestimated, as it is usually stated from memory. In general, there may be from 1 to, at most, 4, which usually are expelled in succession at relatively short intervals. Much more rarely I have observed a larger number of bloody stools, from 6 to 10, and only in isolated instances more—up to 20. In the latter cases conditions of the so-called hemorrhagic diathesis are probably generally present.

Of 256 cases of intestinal hemorrhage observed at Leipsic and Hamburg that I analyzed, from 1 to 4 bloody stools occurred in 225, and a larger number in only 31; but of this latter number the cases with 1 and 2 stools preponderated. There occurred 1 bloody stool in 78 cases, 2 bloody stools in 57 cases, 3 bloody stools in 45 cases, and 4 bloody stools in 45 cases.

With regard to age and sex, the mature period of life is distinctly that at which intestinal hemorrhage most frequently occurs. It is much less common in children, and this statement, agreeing with that of Henoch and Rilliet and Barthez, as against opposite statements by a number of other observers, I can confirm positively upon the basis of a large number of cases. While in adults I have at certain times observed

intestinal hemorrhage in as high as 10 and even 14 per cent. of all patients, I have noted it in scarcely 1 per cent. in children. Doubtless this circumstance is related to the usually lesser extent and intensity of the typhoid infiltration of the intestine in childhood. I have been unable to note any material difference between the two sexes with reference to the frequency of hemorrhage. With regard, however, to the severity and the danger of this symptom, men appear distinctly to present the graver condition.

In adults, in my experience, the frequency of hemorrhage is quite limited up to the thirtieth year of life, although greater than in children. After the thirtieth year there is a noteworthy increase. The maximum is reached between the forty-fifth and the fiftieth year, although later life also is still exposed to risk. During some epidemics, it is true, exceptions to this rule appear to occur. Thus, in Hamburg in 1887 young persons suffered from intestinal hemorrhage with relative frequency, as the following figures show: From fifteen to twenty years, 27.7 per cent.; twenty-one to twenty-five years, 25.3 per cent.; twenty-six to thirty years, 21.7 per cent.; thirty-one to thirty-five years, 10.8 per cent.; thirty-six to forty years, 4.8 per cent.; forty-one to forty-five years, 5.4 per cent.; forty-six to fifty years, 1.2 per cent.; fifty-one to fifty-five years, 1.2 per cent.; fifty-six to sixty years, 1.2 per cent.

On the other hand, the year 1886 exhibited the following conditions: From fifteen to twenty years, 3.4 per cent.; twenty-one to twenty-five years, 4.9 per cent.; twenty-six to thirty years, 4.9 per cent.; thirty-one to thirty-five years, 7.1 per cent.; thirty-six to forty years, 14 per cent.; forty-one to forty-five years, 7.7 per cent.; forty-six to fifty years, 2 per cent.

The frequency of hemorrhage in relation to the number of cases is variously stated by different observers. Naturally, it makes a material difference whether one considers only large and copious hemorrhages or includes even the slightest admixture of blood. This circumstance may explain some extremely low as well as some extremely high estimates. Above all, it should be emphasized that the frequency of hemorrhage varies greatly in different places and at different times. In my experience, if those cases showing only a trace are not included, and the mean of many years' experience in different places is taken, the average frequency of intestinal hemorrhage is from 4 to 6 per cent.

In Leipsic, among 1626 cases of typhoid fever occurring in the course of thirteen years, I noted 103—6.3 per cent.—in which hemorrhage occurred. Among the much larger number of cases at Hamburg, hemorrhage occurred in 4.6 per cent. in 1886, and in 3.8 per cent. in 1887. These figures agree with those of Griessinger, who, among 600 cases of typhoid fever, observed hemorrhage in 5.3 per cent. Homolle collected the enormous number of 10,000 cases of typhoid fever from various sources (including, among others, Louis, Barth, Ragaine, De Céronville, Griessinger, Liebermeister, Golddammer, Jessen, Chvostek), and found intestinal hemorrhage to have occurred in 4.65 per cent. Liebermeister places the figure relatively high, namely, 7.3 per cent. The statement that has found its way into many books, that

Murchison had observed intestinal hemorrhage in 16.6 per cent. of cases, is based upon a misconception. The figures do not refer to patients at all. Murchison observed 14 among 84 deaths as a result of hemorrhage—16.6 per cent. The figures given in the reports of the Wieden Hospital for the years 1855–1857, namely, 2 per cent., are remarkably low. Of 829 cases in the Johns Hopkins Hospital, hemorrhage occurred in 6 per cent.

Among the exciting causes for intestinal hemorrhage, dietetic error, restlessness on the part of the patient, especially getting up too early, may be mentioned as the most frequent. These factors also certainly explain the fact that, in my experience, ambulatory typhoid frequently manifests itself by unexpected intestinal hemorrhage. The treatment of typhoid fever with cold baths may possibly intensify intestinal hemorrhage that has already occurred. It is, however, probably incapable of directly exciting the hemorrhage. During the period in which I still practised frequent and cold bathing I did not, on the whole, observe hemorrhage with greater frequency than since I have employed bathing less frequently, less cold, and with more regard to the individual case. Although Liebermeister observed hemorrhage in 8.4 per cent. of cases before the introduction of hydrotherapy, and after its introduction in only 6.2 per cent., the reduction being, according to him, due mainly to the use of hydrotherapy, I would point out that in Hamburg, with almost purely expectant treatment, at any rate with only the infrequent employment of baths, we observed hemorrhage in but 3.8 per cent. of cases.

With regard to the clinical manifestations of intestinal hemorrhage, it may be stated that its onset is rarely announced in advance in any special manner. On the contrary, the hemorrhage often occurs—"like a flash of lightning in a clear sky"—at a time when the patient feels entirely well, and the friends are most hopeful. Abdominal pain rarely precedes the hemorrhage. Only now and again have I observed severe colic and peristaltic unrest of the intestines for from one to several days before the onset of the hemorrhage, but I am inclined to attribute these symptoms rather to the ultimate (exciting) cause of the hemorrhage than to the latter itself.

McCrae,[1] in his analysis of 500 cases of typhoid fever with reference to abdominal pain, found that pain was present in 14 of the 36 cases in which hemorrhage occurred. Its importance is especially in reference to the differential diagnosis between this complication and perforation of the bowel. The frequency with which both complications occur simultaneously may be seen from the fact that of 30 cases of perforation in the Johns Hopkins Hospital, 6 were accompanied by hemorrhage.

[1] *Loc. cit.*

In a doubtful case, with pain, the blood-examination may show a marked drop in hemoglobin and number of red corpuscles before any blood appears externally. Thayer[1] has found that hemorrhage from the bowels may be followed by an increase in the number of leukocytes, reaching its maximum inside of twenty-four hours. In some cases, however, the hemorrhage has no effect on the number of leukocytes in the peripheral circulation.

In cases in which the patients are not already greatly reduced in consequence of antecedent disease or of the special severity and long duration of the attack of typhoid fever, slight or even moderately severe hemorrhages in small number cause no material alteration in the general condition.

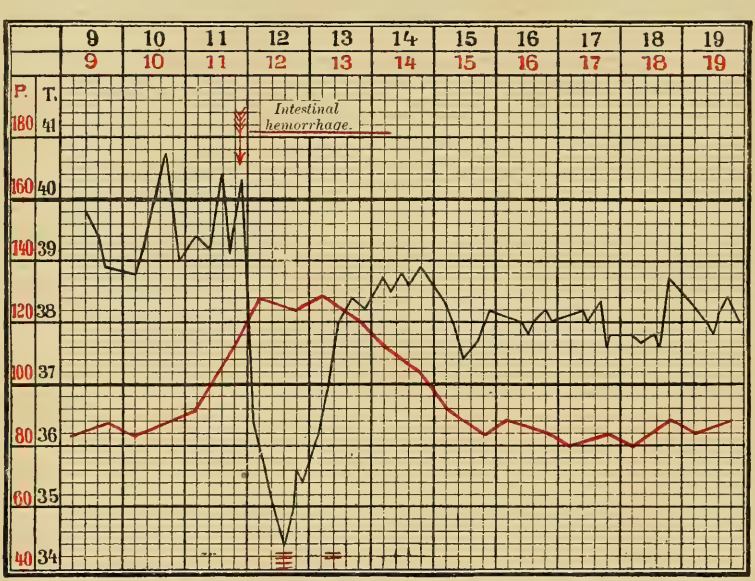

FIG. 24.

Profuse hemorrhage, however, is under all conditions a serious occurrence, to which the patient may succumb, in the course of a few hours, amid symptoms of most profound acute anemia. Fortunately, such a course is exceptional. In order that the patient should finally die as a result of hemorrhage, its repeated occurrence is necessary. The cases are especially pathetic in which it has been possible to sustain the patient in spite of copious loss of blood, but who nevertheless dies after the lapse of a few days in consequence of unexpectedly recurring and, at times, not even profuse hemorrhage. Such cases are at the same time strong evidence of the great degree to which the resistance of the typhoid patient is reduced in consequence of profuse loss of blood.

[1] *Loc. cit.*

In those cases in which the patient does not die during the first copious hemorrhage, the clinical picture becomes alarmingly altered. The skin acquires a waxy pallor, there is relaxation of the features, the pulse becomes small and shows greatly increased frequency, lividity and coldness of the extremities, and possibly syncope, appear. With the rapid increase in pulse-frequency there is generally associated a rapid reduction in the body-temperature. The curve may be observed to decline from 40° or 41° C. far below the normal—to 35° C. and below—in the course of a few hours. This characteristic intersection of pulse- and temperature-curves, of which an illustration is given, is of grave prognosis (Fig. 24).

Depending upon the constitutional condition and the impression that the disease has already made upon the organism, even slight hemorrhage may be attended with more or less marked depression of the body-temperature. The temperature-curve of the typhoid patient reacts in a remarkably sensitive manner to hemorrhage in far greater degree than the pulse, which, in the presence of moderate intestinal hemorrhage, by no means always becomes smaller and more frequent, in correspondence with the reduction in temperature. I have often observed the pulse but little influenced with reference to fulness, tension, and frequency when the hemorrhage was not repeated or was but small in amount. Quite rarely I have even seen the pulse-frequency fall parallel with the temperature-curve—a condition that is, without doubt, to be considered as a favorable prognostic sign.

It is an interesting and practical fact that even with the occurrence of profuse intestinal hemorrhage the extravasation and the evacuation of the blood externally by no means always take place in immediate succession. On the contrary, it more often happens that cases are observed in which the patient becomes profoundly anemic and emaciated, while the temperature rapidly declines and the pulse becomes smaller and more frequent—signs, therefore, of considerable internal hemorrhage are present—and, nevertheless, hours or even days may elapse before the resulting bloody intestinal discharge takes place. This appears to occur especially when the bleeding-point is situated high up in the bowel and the extravasation takes place slowly, particularly when the blood oozes from spongy Peyer's patches which are in a state of hemorrhagic infiltration. This condition is also favored by feebleness of intestinal peristalsis, such as occurs in the course of severe attacks, particularly if several considerable hemorrhages have already taken place. Patients dying from intestinal hemorrhage quite generally do not expel the last portion of blood extravasated. Under such

circumstances the affected portion of intestine is found after death filled with a tarry mass, which often is of viscid consistency. During life this condition not rarely gives rise to corresponding physical signs, namely, increased distention of the abdomen, with impairment of the percussion-resonance at all points, or even extensive dulness, together with diminution in the elastic tension of the abdomen to the point of doughy consistency, a peculiar tremulous sensation being sometimes imparted to the palpating hand.

The occurrence of intestinal hemorrhage is always an important and serious event. If the patient's strength be good and the other conditions favorable after the first hemorrhage, the physician may give only a doubtful prognosis. Fulminant, rapidly fatal cases are, fortunately, not common. Nevertheless, I have in a number of instances seen death occur in less than six hours after the first hemorrhage, and twice even during the first hour. A fatal termination in the course of two or three days is not rare, after repetition of the hemorrhage. In general, death, when it occurs at all, takes place in the course of from three to five days. In some cases death occurs in the course of a week or two weeks, or even several weeks, after the hemorrhage has ceased. In such cases examination of the body after death may also reveal nothing special, and the impression is gained that the patients have not died directly from the hemorrhage, but from the attendant loss of strength, from which they were unable to recover, in spite of the observance of all possible care.

The mortality from intestinal hemorrhage is, in general, quite high. On the average, from 20 to 30 per cent. of those attacked die. Griessinger placed the figure at 31.2 per cent., Liebermeister at 38.6 per cent., and Homolle, as a result of his collective investigation, which, it is true, is unfavorably influenced by the inclusion of a number of small groups of cases, made it as high as 44.3 per cent. My own analyses show 38.2 per cent. for Leipsic. In Hamburg I encountered remarkably low figures, namely, in the year 1886, 20.9 per cent.; in the year 1887, only 11.6 per cent. These figures confirm the observations of all physicians that not only the frequency, but also the danger, of intestinal hemorrhage may vary considerably from as yet unknown causes, as a result of temporal and local influences.

Whether sex has any influence on the prognosis of intestinal hemorrhage does not appear as yet to be definitely determined. In my experience the danger is greater in men than in women. From the character of the bloody stools—apart, naturally, from the absolute amount of blood—a prognostic guide can rarely be obtained. I should, however,

consider the discharge of blood in large coagulated masses as serious. This can be considered as indicative of erosion of a large vessel, and probably also that the origin of the hemorrhage is in the lower portion of the intestine, particularly the colon, from which a hemorrhage is often likely to be especially massive.

The view taken by a number of distinguished clinicians, such as Graves,[1] Trousseau,[2] and others, that intestinal hemorrhage is not a serious, but, on the contrary, a rather favorable occurrence, is most remarkable. While Graves based his opinion upon concrete instances, the ingenious Trousseau was led to a generalization of this view. It cannot be denied that moderate loss of blood, or even a single considerable intestinal hemorrhage which is not repeated, occurring in a robust, full-blooded patient with high fever, appears at times to influence the general condition favorably. The patient then becomes brighter, the temperature declines, while the pulse remains good. Even the spleen undergoes distinct reduction in size (Eichhorst, Curschmann), and if the occurrence takes place in the terminal stage of the disease, convalescence may at once set in. As opposed to such rare exceptions is the overwhelming preponderance of unfavorable results, so that, even from the most favorable aspect, the occurrence of hemorrhage cannot be looked upon as a desirable event. It should here again be pointed out, and cannot be too strongly emphasized, that even distinguished writers often base their conclusions upon insufficient statistics. I have noted periods in which only 2 of 50 successive cases of intestinal hemorrhage under observation terminated fatally.

Peritonitis is one of the untoward occurrences in the course of typhoid fever deserving of detailed consideration. It may remain circumscribed or, as is unfortunately more common, it may be general. In the large majority of cases both varieties occur as sequels of the intestinal lesion. It is the contamination of the peritoneum from the intestinal ulcers by the exciting agents of inflammation or the escape of intestinal contents into the abdominal cavity that, in accordance with special conditions, gives rise at times to circumscribed foci of inflammation, and at other times to general peritonitis.

The inflammation of the peritoneum is but rarely independent of the specific lesions of Peyer's patches and the solitary follicles. Now and again gangrene of the bowel from some other cause may be the underlying factor. Thus, in one instance, I noted such a condition to be caused by thrombosis of the artery supplying that portion of the

[1] *Clinical Lectures*, 1848, vol. i.

[2] *Clin. méd.*, 2d ed., transl. by Kunzmann, vol. i., p. 238.

bowel and of the accompanying veins. Perforation of other organs also may be the cause of peritonitis, as, for instance, rupture of the spleen or of the mesenteric glands in consequence of softening or abscess, rupture of the gall-bladder, of the larger biliary passages, or of an abscess of the liver which has developed in the course of the attack of typhoid fever.

The question as to whether a localized peritonitis may occur without perforation has been raised by Cushing,[1] who thinks that in certain cases the earliest symptoms of perforation may be due to "a little localized inflammation of the serosa, with or without the passage of microorganisms, and leading to a slight adhesive peritonitis." This he speaks of as the pre-perforative stage of ulceration. He mentions a case of Murphy's[2] in which there was peritonitis, but no perforation found; and also 5 cases of Gairdner's,[3] in which fatal peritonitis occurred without an absolutely complete perforation. Two of the cases reported by Shattuck, Warren, and Cobb[4] were said to show at operation "a general septic peritonitis, originating in damaged and necrosed areas of peritoneum over the bases of one or more typhoid ulcers."

The peritonitis associated with the specific lesion of the intestine is not only one of the most frequent, but also one of the most characteristic causes of a sudden dangerous and fatal change in the course of an attack of typhoid fever. There are very few other acute infectious diseases in which this complication occurs at all, and even then only as a rarity. At times perforative peritonitis, like intestinal hemorrhage, is the first distinctive manifestation in a case of ambulatory typhoid fever previously showing no symptoms, or at most attended with obscure disturbances. The occurrence is not at all rare, so that if individuals with perforative peritonitis, giving an uncertain history or none at all, are admitted to a hospital, this possibility should especially be kept in mind.

I have observed cases in which the first symptoms of peritonitis occurred in persons who had been previously apparently healthy in the form of intestinal colic or sudden collapse while walking about or while at work. A case under observation was brought to the hospital as one of volvulus; another, under the suspicion of having attempted suicide with arsenic; and a third, as a case of meat-poisoning.

These quite surprising and often unrecognized cases are comparable with those in which the symptoms of general peritonitis develop sud-

[1] *Johns Hopkins Hosp. Rep.*, vol. viii.

[2] Keen, *Surgical Complications and Sequels of Typhoid Fever*, Phila., 1898, p. 238.

[3] *Glasgow Med. Jour.*, vol. xlvi., p. 114.

[4] *Boston Med. and Surg. Jour.*, June 28.

denly in a case of typhoid fever of apparently mild course, with moderate fever, an absence of meteorism, and with other very mild intestinal symptoms. However important these cases may be, and however noteworthy from the diagnostic point of view, it should nevertheless be noted that it is principally the severe cases and those that pursue a grave course from the outset that are attended with perforative peritonitis. Among such cases, however, it is by no means only in those attended with severe, persistent diarrhea that perforative peritonitis occurs—a fact which confirms the general statement previously made, that the severity of the intestinal manifestation and the general course of the disease are by no means in accord. It is almost exclusively clinically uncontrollable and anatomically unfortunate accidents that give rise to perforation in the individual case.

That perforation is more likely, however, to occur in cases with diarrhea is shown from the statistics of perforation at the Johns Hopkins Hospital. Of 30 cases of perforation, 20 had diarrhea, 16 at the time of perforation. This becomes more striking when it is known that of the whole number of cases (829), only 19 per cent. had diarrhea during the course of the disease.

Generally, there is but a single point through which the intestinal contents escape. Now and then, 2 or 3 openings close together may be found; rarely, 2 widely separated points of rupture, as, for instance, in the ileum and the colon, are demonstrable. I have observed a larger number of perforations at the same time in only a few instances. The maximum numbers were, in one case, 10, in another 12, and in a third 15 perforations. Hoffmann refers to an autopsy in which 25 perforations were found.

As the perforation is almost exclusively confined to the specific lesions of Peyer's patches and the solitary follicles, its frequency, with regard to situation, likewise corresponds with that of these alterations in the individual portions of the bowel. Perforation, accordingly, is most frequent in the lower portions of the ileum, especially in the vicinity of the cecum. Rupture of the bowel at a higher level than the lower third of the ileum is observed less commonly. In a number of instances, it is true, I have encountered perforation in the upper portions of the ileum, but I cannot recall an instance of perforation of the jejunum, such as has been described by Hoffmann. The cecum, the parts adjacent to the valve, and the vermiform appendix are somewhat less commonly than the lower portion of the ileum, but still frequently enough, the seat of rupture. I have observed perforation of the colon at almost all parts, even down to the descending colon and the sigmoid

flexure; perforation has been noted even in the rectum by various writers, and I have likewise observed it. The ascending and the transverse colon, however, appear to be the favored seats of the lesion.

With regard to time, the occurrence of perforation coincides especially with the period of exfoliation of the sloughs. Its earlier occurrence, as is so frequently the case with hemorrhage, is extremely rare, and results only under exceptional conditions. The principal time for the occurrence of perforation of the bowel is therefore the end of the second and the third week of the disease. Anatomic investigation teaches that the accident occurs especially when the medullary infiltration is most extensive, and extends down to the peritoneum, or even involves this also. In this way the floor of the ulcer may come to be formed by a translucent membrane as thin as paper, that will be unable to withstand even the slightest mechanical influences. In some cases the infiltration and the sloughing are so deep that the peritoneum also is involved, and rupture ensues immediately upon the occurrence of sloughing. In the cases just referred to, in which, after clearing up of the ulcers, a greatly thinned area in the intestinal wall remains, perforation takes place either through rupture or through more or less gradual extension of the ulcerative process. The latter occurs especially in cases in which the peritonitis develops late—at the end of the third or in the fourth week.

The character of the resulting opening depends partly upon the preliminary alterations and the mode of development of the perforation. The perforations due to large direct loss of structure, which I have seen attain a diameter of from a quarter of an inch to one inch, are generally attributable to the exfoliation of large profound sloughs. The small cribriform openings, at times lying close together in considerable number, are often referable to slowly progressive ulceration, while ruptures due to mechanical influences are often distinguished, as I think I have been able to show, by the longitudinal, slit-like, ragged character of the openings. Among the mechanical influences giving rise to rupture of the bowel at the situations anatomically predisposed is gaseous distention of the intestine, especially if it undergo sudden augmentation in a single portion. Further, the condition is certainly often due to other mechanical influences, especially those exerted by the solid intestinal contents. That still other mechanical influences acting from within and without, such as vomiting, forced movements, especially too early sitting up or getting up, violent expulsive efforts and straining at stool and in micturition, may exert an injurious effect, can be comprehended theoretically, and the possibility of their exercising such

an action is, unfortunately, too often demonstrated at the bedside. Dietetic errors, with secondary gastro-intestinal catarrh and abnormally increased peristalsis, are with equal propriety to be held responsible in certain cases. All these points cannot be too clearly kept in mind by the young physician, in order that he may as fully as possible shield his patients from injury at a critical period. While in a few cases rupture must inevitably take place in consequence of the extent and the depth of the ulcerative process, in the overwhelming majority of cases the conditions are fortunately such that, under the most favorable circumstances, with careful observation of internal and external precautions, even deep ulceration may undergo cicatrization, and even minute perforations may be rendered harmless by timely adhesion with adjacent organs. It is a particularly disturbing fact that perforation may still take place at a late stage of the disease, after the usual period when exfoliation of the slough is completed, and even at a time when the patient appears almost convalescent. This unfortunate accident at times occurs in Peyer's patches and solitary follicles which exhibit a recrudescence of the specific lesions at a time when the majority of the ulcers are in process of healing or have already undergone cicatrization. In other cases imperfectly cicatrized ulcerated areas, especially those with very thin floors, may subsequently reopen and undergo perforation. Finally, the indefinitely protracted so-called sluggish ulcers may be a source of great danger. I have, for instance, observed perforative peritonitis develop after the fiftieth and the sixtieth day of the disease, in one instance even after the hundredth day—a warning for patients and their friends, who often charge the physician with pedantic rigidity of supervision during convalescence.

Such late perforations are emphasized also by other writers, namely, Louis, Murchison, Griessinger, Niemeyer, and others. Among these, Griessinger considers the sluggish ulcers as especially dangerous. That possibility of perforation exists throughout quite a long time is shown by the following figures:

Of 73 cases of perforation that I have analyzed, this accident occurred between the eleventh and the twentieth day in 23, from the twenty-first to the thirtieth day in 31, from the thirty-first to the fortieth day in 13, and after the fortieth day in 6.

The frequency of perforation of the bowel may, precisely like that of intestinal hemorrhage, be extremely variable at different times. I have observed epidemics in which the condition was quite rare, and others in which the cases were exceedingly common. This fact probably explains the extreme diversity in the statements of various writers. Upon what this temporal variation in frequency depends is as yet

unknown. The degree to which the number of cases of perforation may at times increase is shown by an analysis by Murchison, who noted perforation in 21.2 per cent. among 165 autopsies in cases of typhoid fever. Although Heschel[1] observed only 56 cases of perforative peritonitis (4.4 per cent.) among 1271 autopsies during the years from 1840 to 1849, this number is distinctly less than that usually encountered. Brouardel and Thoinot,[2] who analyzed 1721 autopsies from English, French, and German sources, found perforation in 190 cases—11.03 per cent. Griessinger noted perforation in 14—11.01 per cent.—of 118 autopsies made by himself. I have personally observed 93 cases—16.17 per cent.—among 575 autopsies (Hamburg-Leipsic). It will therefore not be an exaggeration to assume that in from 9 to 12 per cent. of all fatal cases of typhoid fever death results from perforative peritonitis.

The percentage of deaths due to perforation in the Johns Hopkins Hospital during the past ten years is considerably higher than this. Of 63 deaths, 20 (31.7 per cent.) were due to perforation.

Fortunately, the absolute frequency of perforation, making allowance for temporal and individual variations, is distinctly less than that of intestinal hemorrhage. I believe that under the most unfavorable circumstances perforation occurs in not more than 3 per cent. of all cases of typhoid fever. In my Leipsic statistics (1626 patients) the proportion was 2.2 per cent. In Hamburg it was 1.6 per cent. among 4094 patients. The estimate of Griessinger, who observed perforation in 14 cases—2.3 per cent.—among 600 of typhoid fever, is in agreement with my own.

Among 829 cases of typhoid fever in the Johns Hopkins Hospital, there were 23 (2.7 per cent.) cases of perforation. Twenty of these were fatal, and 3 recovered following operation.

Age, sex, and social condition do not occasion such marked differences with reference to the danger of perforation as some observers, upon the basis of an insufficient number of cases, state. In general the conditions are analogous to those in connection with intestinal hemorrhage. I believe that children, especially under the age of ten years, are less commonly attacked than adults, and I base my opinion both upon a rather large personal experience and upon the statements of Topin, Rilliet and Barthez, Rocher and Henoch. The probable reason for this is the generally slighter intensity of the intestinal affection in children, which has already been mentioned in the consideration of

[1] *Zeit. d. Gesellsch. d. Aerzte z. Wien.*, 1853.

[2] *La fièvre typhoïde*, Paris, 1895, p. 79.

hemorrhage. Among adults, those between eighteen and forty years of age are especially predisposed to perforation. After the fortieth year of life the occurrence is relatively less common. The contrary opinion, occasionally expressed, that later life is in turn more predisposed, is not in accord with my experience.

In general, men appear to be attacked by perforation more frequently than women. This is by no means dependent upon inequality in the development of the specific intestinal lesions in the two sexes, but probably upon the fact that, with equal chances, men are more unfavorably influenced during convalescence by reason of previous derangement of the digestive apparatus, due to diet and mode of life, than are women, and often also by coming under treatment late, as well as by greater impatience and carelessness during convalescence.

With regard to social position, perforative peritonitis undoubtedly occurs rather more frequently among the poorer classes, probably in consequence of the less favorable conditions of living and of nutrition among these classes, and also on account of the less efficient nursing and care devoted to them. This is in accord with my observation that the occurrence of perforation is more frequent among ambulatory and milder cases in the poorer classes.

Murchison and Griessinger probably emphasize unduly the predominance of perforation in the male sex. I have noted periods in which this difference, which I appreciate, was not present. Thus, in the year 1886–1887, in Hamburg, both sexes were affected almost equally, and in the year 1887 females even somewhat more frequently.

Symptoms of Perforation.—The complication often occurs quite suddenly and unexpectedly, without previous noteworthy injurious influences. At times it is preceded by more or less ill-defined disturbances, namely, increased abdominal tension, colicky pain, borborygmi, and diarrhea. Intestinal hemorrhage of greater or less amount is not rarely an indication of impending breach in continuity. That this is not rare is shown by the fact that of 30 cases of perforation in the Johns Hopkins Hospital, 6 have been preceded or accompanied by hemorrhage. The time when perforation occurs is at times quite definitely stated by intelligent patients. They complain of sudden stabbing pain, or even of an actual sense of laceration.

In the great majority of cases the perforation is soon followed by abdominal pain of rapidly progressive intensity, which can be recognized as due to peritonitis from the fact that it is greatly increased on breathing, on passive and active movement, and on pressure and palpation of the abdomen. In some cases the patients refer the

point of origin of the pain to the right hypogastrium. The majority, however, are unable to designate any definite situation. Simultaneously with the onset of the pain, frequently even preceding it, there occur distressing retching and vomiting, in consequence of which the gastric contents, which are more or less markedly changed, and often contain the ingesta to which the accident is due, are evacuated. Soon only small amounts of mucoid bilious matter are expelled with the distressing retching.

The abdomen now becomes progressively more distended, at times to an extreme degree, so that the cutaneous covering of the abdomen appears smooth and glistening. The markedly elevated position of the diaphragm thereby induced, in conjunction with the peritonitic pain, greatly interferes with breathing. The bowels are generally constipated from the outset and remain so; also, flatus is passed less frequently, if at all. The cause of these disturbances, the paresis of the muscular layer of the intestine, soon attains a high degree of intensity. The vomiting not rarely acquires a fecal character, so that the entire condition suggests the existence of ileus, and for which it may indeed be mistaken by those of limited experience. Although the symptoms described are generally attributed to the peritonitis alone, at times, especially when the peritonitic process originates in the vicinity of the ileocecal valve and the lowermost portion of the ileum, and is particularly localized in this situation, there may be actual occlusion of the lumen of the bowel, and thus true ileus.

The general condition of the patient changes approximately in correspondence with the local manifestations. The features become drawn, the nose pointed, the extremities livid and cold, and the face and the body are often covered with cold sweat. The condition of the pulse soon becomes poor, so soon that at times it may be the first indication of the grave significance of abdominal pain of sudden onset. The pulse becomes frequent, irregular, and small; then thready, scarcely to be counted, and frequently, at a time when the patient is still conscious and the friends are still hopeful, is no longer palpable at the radial artery. When perforation with general peritonitis is present, the body-temperature rises, as a rule, but little, in an irregular manner, or not at all. Only toward the end is rapid elevation to an extreme degree sometimes observed. Most frequently a more or less rapid, often abrupt, decline of temperature to far below the normal occurs, and persists until death. In some cases, especially those with subsequent elevation of temperature, I have observed a chill at the outset. How this is brought about in the individual case, and which kind of

patients exhibit high, and which low, temperatures, is not yet wholly clear to me.

In the severest cases, those in which the intestinal contents, poured out of large openings, soon deluge the entire abdominal cavity, the symptoms described, intensified to the maximum, occur synchronously. Collapse then appears to develop abruptly, the pulse becomes imperceptible during the first few hours, and the temperature falls below the normal with equal rapidity. Often the abdomen does not become distended, and the peritonitic pain is absent, a circumstance that greatly increases the difficulty of diagnosis even for the expert clinician. The majority of these patients, unfortunately, retain perfect consciousness, some until immediately before death, which may take place before the termination of the first twenty-four hours.

When the course of the peritonitis is less rapid, the patients may even recover somewhat from the primary shock, the pulse may again become fuller and slower, the temperature may again rise, though rarely, it is true, as has been mentioned, to any considerable height. Unfortunately, the hope thus aroused is almost always deceptive; only rarely does the peritonitis become locally circumscribed. It extends without restraint, and the local and general symptoms increase accordingly, until death occurs in profound collapse at the end of the second or the third or, at the furthest, on the fourth day. The cases of severe onset scarcely ever live beyond this time.

More protracted cases may occur in which, in consequence of the form or the seat of the perforation, as, for instance, when there is a single or a number of minute cribriform openings close together, minimal amounts of intestinal contents may slowly escape, and temporary adhesions prevent the diffusion of the infectious material throughout the entire peritoneal cavity. Under such circumstances, rapid progress and complete cessation may alternate. It is in such cases, also, that, in addition to the general peritonitis, one or several partly encapsulated foci of pus are found in the right iliac fossa, behind the liver, in the true pelvis, or in other portions of the abdominal cavity. Patients presenting such conditions may live for six or eight days. I have personally seen a few cases in which death occurred on the ninth or the tenth, even on the eleventh, day. Those are horrible days for friends and physician, with alternation between fear and hope, the latter being finally almost always unrealized. I cannot believe in spontaneous recovery from universal perforative peritonitis, such as has been reported by a number of observers. In a number of my own cases terminating favorably and suggesting this possibility, I would consider them rather

as cases of circumscribed, although at times quite extensive, peritonitic affections, which exhibited especial severity of the initial shock on account of individual causes.

Early Diagnosis of Perforation.—Considering the very promising results that have been obtained from operative interference in cases of perforation, and since good results are mainly dependent upon early recognition of the condition, it is extremely desirable that the physician should learn to recognize the symptoms of *perforation*, particularly of its onset, apart from those of the consecutive peritonitis. Of all early symptoms, pain is the most constant and important. McCrae [1] has most carefully studied the question of abdominal pain in typhoid fever with special reference to its character in perforation. Perforation occurred in 13 of his cases, and in all of them pain was present and seemed severe. In 10 of these cases the patients had been previously quiet and comfortable, and were suddenly seized with severe abdominal pain, which in 4 cases was severe enough to make the patient cry out. In the remaining 3 cases the pain was present for some days before the perforation occurred. In 14 cases of 21 reported by Shattuck, Warren, and Cobb,[2] "there was early warning pain—earlier by a definite number of hours than the severe symptoms." It may be said that a sudden onset of pain demands the most careful examination of the patient and careful noting of every symptom. After onset the pain is usually not constantly severe, but is paroxysmal. In some cases the pain may be present for several hours before the onset of tenderness and muscle-spasm. In many cases, however, with the onset of pain there is tenderness, usually localized, most often situated in the right hypogastrium. Associated with this tenderness there is usually some rigidity or spasm of the abdominal muscles, especially of the right rectus, and limitation of the abdominal respiratory movements. These latter signs, while not certain, are of the greatest importance when taken in connection with the other symptoms. A sudden fall of body-temperature, when present, is a very characteristic symptom, but its frequent absence, and the fact that it occurs frequently in other conditions, such as hemorrhage, make it an unreliable sign. Vomiting is an important symptom when present. Increasing distention, as shown by the gradual rise of the lower line of hepatic dulness, which should be marked out at short intervals in suspicious cases, is an important, though usually somewhat later, sign. It must also be remembered that the Hippocratic facies is not only a late occurrence, but that the pinched, drawn, anxious face may be one of the first suggestive signs to the

[1] *Loc. cit.*

[2] *Boston Med. and Surg. Jour.*, June 28, 1900.

experienced observer. Much attention has been given to the question of an early increase in the number of the leukocytes in the peripheral circulation following perforation. Many more observations will have to be made before an absolutely accurate estimation of the value of this sign can be determined. Thayer [1] concludes, from a study of this question, that perforation of the bowel is usually followed by an increase in the number of the leukocytes in the peripheral circulation. This increase may be considerable, or may be slight and appreciable only in comparison with previous counts; hence the great importance of frequent counts of the leukocytes during the course of the fever. Not infrequently, following the rise there is a fall; and in a number of cases there may be no rise at all, but there may even be a fall from the onset. Conditions such as these are indications of the malignity of the infection or the prostration of the patient.

Operative Treatment.—To Leyden in Germany and Wilson in America are due the credit of first ardently advocating operation in cases of perforative peritonitis. The American surgeons especially took up the subject, and have been most earnest advocates of the utility of this procedure (Finney,[2] Keen,[3] Cushing [4]). In 1899, Keen was able to collect from the literature 158 cases of operation for perforation in typhoid fever. The recovery-rate in the entire 158 cases is 23.41 per cent. When this is contrasted with the recovery-rate in unoperated cases (not over 5 per cent.), the value of the procedure is evident. Of 16 cases operated upon in the Johns Hopkins Hospital during the past few years by Finney, Cushing, and Mitchell, 6 recovered—37.5 per cent.

That operation, when performed early, especially if done under local cocain anesthesia, as advocated by Cushing,[5] is in itself not of great danger to the patient, even though at the time he is extremely weak from the effects of the disease, has been shown by numerous cases, and especially by several on whom exploratory laparotomy was done and no perforation found. These results have corroborated the statement of Mikulicz, made in 1884: "If suspicious of a perforation, one should not wait for an exact diagnosis and for peritonitis to reach a pronounced degree; but, on the contrary, one should immediately proceed to an exploratory operation, which, in any case, is free from danger."[6]

I have observed spontaneous recovery from perforative peritonitis

[1] *Johns Hopkins Hosp. Rep.*, vol. viii. [2] *Annals of Surgery*, March, 1897.
[3] *Jour. Am. Med. Assoc.*, Jan. 20, 1900.
[4] *Johns Hopkins Hosp. Rep.*, vol. viii. [5] *Phila. Med. Jour.*, March 3, 1900.
[6] Quoted by Cushing, *loc. cit.*

only in cases in which strong protective adhesions and encapsulation, formed about the site of perforation, separated this from the remaining larger portion of the peritoneal sac. Such forms of circumscribed peritonitis may also set in violently with profound manifestations of shock, and, especially when large fecal abscesses are present, may be attended with most grave symptoms. Recovery may follow under such conditions as a result of timely surgical intervention, or of spontaneous rupture directly outward, or into the intestine or other hollow viscus. The prognosis should, however, at best be dubious. Many of such cases die.

In a number of cases I have observed circumscribed peritonitis develop with very slight local and general symptoms, and progress quite slowly, often with remarkably little pain, and with remittent or even intermittent fever. Under such circumstances the conditions present consist principally in small abscesses encapsulated between adherent coils of intestine, situated, however, in parts of the abdominal cavity accessible to operative intervention only with exceeding difficulty. If, under such circumstances, spontaneous rupture with complete evacuation does not take place, this distressing condition may drag along until the patient is relieved by death due to some further complication, or after months of suffering.

An interesting position among the various forms of circumscribed peritonitis is occupied by the cases in which the process is localized to the right iliac fossa, and especially to the vicinity of the cecum, cases that can be appropriately designated as typhoid perityphlitis or paratyphlitis. These cases occur more frequently than is generally believed, and may be looked upon as typical processes, since they originate from portions of intestine especially involved in cases of typhoid fever. That in such cases minute openings of perforation, or even extreme ulcerative thinning of the intestinal wall without actual perforation, may permit the escape of the inflammatory irritants, is readily comprehensible in accordance with previous statements. It is interesting to note that the site of the lesions in question corresponds with that of the usual inflammation of the cecum. In the presence of typhoid perityphlitis, perforation of the vermiform appendix, which, it is well known, is quite generally involved in the medullary infiltration, plays an important *rôle*. Also, in the cecum itself, especially in the neighborhood of the valve, as well as at the junction with the ascending colon, I have in a number of instances found deep ulcers with minute perforations to be the cause of circumscribed inflammations in the right iliac fossa.

I have observed typhoid perityphlitis during all stages when peri-

tonitis is likely to develop, with greater relative frequency, however, in the later stages of the disease, and even during convalescence, in one instance on the eighteenth, and in another on the twenty-first afebrile day. Chomel and Gonzonnec[1] have made similar observations. The local symptoms are like those of ordinary inflammatory processes in the iliac fossa, namely, painful circumscribed infiltration, at times of moderate extent, at other times more extensive, occasionally quite indurated; this, it appears to me, more readily and more rapidly terminates in an abscess than in cases other than typhoid. Precisely as in these other cases, the affection may assume the characters of both perityphlitis and paratyphlitis, or of a combination of both. In one instance in private practice I observed the development of a retroperitoneal abscess, which was successfully evacuated through a lumbar incision.

Typhoid perityphlitis is not alone of theoretic interest, but it is also a condition of practical importance. This is true especially from the diagnostic standpoint, and here, above all, it is of importance when the affection occurs in association with slight, ill-defined, at times protracted cases of typhoid fever, or in the course of an attack of ambulatory typhoid fever.

Thus, I have observed cases in which, during residence in the hospital following a period of general malaise of from twelve to fifteen days' duration or longer, with irregular fever, unattended with diarrhea and roseolæ, but with recent enlargement of the spleen, perityphlitis developed, which then led to a correct interpretation of the condition. In other cases that came under observation with the simple diagnosis of perityphlitis, the history of a general febrile disease having preceded the local inflammatory process, and having lasted sometimes two or three weeks, first aroused suspicion of typhoid perityphlitis, which subsequently was verified either by the further typical course of the disease or by the occurrence of a characteristic relapse. I have observed cases of typhoid perityphlitis in Berlin and in Hamburg in private practice as well as in hospital practice. Unfortunately, no reference is made to this subject in the statistics of Schultz. Six of my cases from the Leipsic clinic are reported in the dissertation of Glos (1892). Further, Schönlein[2] and Rokitansky[3] mention the condition in question. Griessinger and Chvostek also were aware of its occurrence. Recently, it has been mentioned in the dissertations of Langheld, Schneller, and Hölscher.[4] Cases of typhoid perityphlitis, such as have been described by Besnier and Follet, belong in this category symptomatically, but not etiologically. These were cases of ordinary perityphlitis pursuing a septic course. They are capable, it is true, of causing great difficulty in differential diagnosis. Thus, I can recall a case under my observation in which, during the course of the disease, intercurrent unilateral parotitis appeared to be especially indicative of typhoid fever. It subsequently proved to be a septic metastasis from a purulent focus in the iliac fossa.

[1] *Thèse*, Paris, 1881.
[2] *Klin. Vorlesungen.*
[3] *Lehrbuch der pathologischen Anatomie.*
[4] *Loc. cit.*

Comparatively little is to be said concerning the cases of peritonitis in connection with inflammation, softening, and rupture of other abdominal organs, to which consideration has already been given. Some, particularly those due to rupture of the spleen and the mesenteric glands, almost always escape correct clinical interpretation. The rare instances of perforation of the large biliary passages or of secondary abscess of the liver can generally only be suspected.

ALTERATIONS IN THE RESPIRATORY ORGANS.

These are among the most frequent and the most varied disorders in the course of typhoid fever. They consist in part of actual complications and sequels, in part of specific alterations dependent upon the bacillus of Eberth and its products. A sharp differentiation between the two sets of conditions is not, as yet, possible; it is, however, probable that the extensive catarrhal and certain inflammatory alterations in the respiratory organs especially belong etiologically in the second category.

Alterations in the Nose and the Nasopharynx.—The nose and the nasopharynx quite generally exhibit at the beginning and at the height of the disease the condition of so-called dry catarrh. The mucous membrane of the nose is likely to be reddened and spongy, and it frequently exhibits a dark-red, velvety swelling, especially over the turbinated bone. The secretion is, under such conditions, quite moderate, and the orifice and anterior portion of the nasal cavity are often covered with a fuliginous deposit. If the nasal cavity be very narrow normally or in consequence of congenital or acquired change in shape, its permeability may be greatly diminished, with resulting pathologic mouth-breathing, the consequences of which are doubly injurious to the typhoid patient.

From the symptomatologic standpoint, it must be emphasized that the ordinary symptoms of coryza—sneezing, increased secretion, conjunctival catarrh—are among the greatest exceptions, at least in moderately severe and severe cases of typhoid fever, and may be thrown in the balance against a diagnosis of typhoid fever. Severe infectious conditions with a predominating coryza generally have some other significance. Under such circumstances typhus fever and influenza especially would have to be considered.

The hyperemia not rarely becomes so marked that even on merely blowing the nose bloody mucus is discharged, or small amounts of blood gain entrance into the nasopharynx, which, when expelled in the form of sanguinolent sputum, may give rise to unnecessary alarm. Quite

frequently the fragility of the blood-vessels of the nasal mucous membrane is so marked that actual profuse epistaxis occurs. This is observed by far the more frequently during the period of incubation and in the beginning of the febrile stage. I believe that 50 per cent. of all cases of epistaxis during typhoid fever occur at this time. Nose-bleed is less frequent at the beginning of the second week, while it is uncommon at the height of the disease, becoming again somewhat more frequent during the last days of the fever, in the period of steep curves, and during convalescence. Bleeding from the nose may be repeated several times within a short period, and it may occasionally be so profuse that, in spite of apparent amelioration of the condition of the patient at first, it may greatly depress him; and when it occurs at a late period in the febrile stage or during convalescence, it may be directly a source of danger.

In a number of instances I have observed patients under such conditions reduced to an alarming state of debility. In one case in private practice I was compelled to resort to subcutaneous infusion of blood, and in another to introduce saline infusion beneath the skin, in order to overcome the impending danger. Liebermeister has observed 2 fatal cases, and Strümpell 1. Tamponade of the nose, even from behind with Bellocq's cannula, is not at all rarely necessary.

It may be mentioned further that nose-bleed plays a not unimportant *rôle* in the cases of hemorrhagic typhoid fever, which, fortunately, occur but rarely, and are attended with such a grave prognosis. Apart from these hemorrhagic cases, which may occur at any age, young persons are particularly likely to be attacked with nose-bleed; children under the age of ten years less commonly, it is true, than older ones. Epistaxis, in my experience, rarely occurs after the fortieth or forty-fifth year, and it then occurs almost solely in persons presenting other predisposing conditions, either local or general, as, for instance, chronic alcoholism. With regard to the frequency of epistaxis in general, it may be stated that I have observed it in 6.5 per cent. of 1700 cases investigated as to this point—a proportion that approximates that found by Liebermeister (7.5 per cent.).

Croupous and diphtheric affections of the nasal mucous membrane, which are rather frequently mentioned in older writings, I have observed with extreme rarity in cases of typhoid fever. When present at all, they occurred almost exclusively in association with similar processes in the pharynx and upon the tonsils, in which they likewise occur but exceptionally.

Larynx, Trachea, and Bronchi.—If these structures of patients with typhoid fever are frequently examined, some sponginess

and redness of the mucous membrane will not rarely be found in the region of the false vocal bands and the arytenoid cartilages, probably also slight discoloration of the true vocal bands, especially at their points of attachment, and rather at the posterior than at the anterior portion. The laryngeal mucous membrane also presents an appearance of dryness. The voice of the patient under such circumstances is weak, uncertain, and somewhat hoarse. More pronounced catarrhal laryngitis with especially marked symptoms is, on the contrary, not frequent—in fact, it is almost as rare as marked coryza. This must again be emphasized in contrast with typhus fever, in the diagnosis of which nasal and laryngeal catarrh is generally of importance.

Of great importance, on the other hand, in cases of typhoid fever, are more profound affections of the larynx, ulceration of the mucous membrane, and perichondritis. The occurrence, seat, form, and course of these conditions are so typical that the question arises, Are they, from the etiologic standpoint, a part of the typhoid fever itself? Although little is as yet known in this connection from the bacteriologic standpoint, an affirmative conclusion with regard to some of the alterations is most probable for a number of reasons. As is known, there have been demonstrated (Cornil and Ranvier, and others) in cases of typhoid fever, upon the posterior wall of the larynx, between the points of attachment of the vocal bands, in the vicinity of the arytenoid cartilages, and upon the epiglottis, especially at its base, formations which are to be looked upon as recently infiltrated lymph-follicles, comparable with similar lesions in the intestine and in other portions of the body. As previously mentioned (see section on Pathology), Schultz has been able to demonstrate the typhoid-bacilli in these follicles in the larynx. Like the follicles in the intestine, these exhibit a marked tendency to undergo necrotic destruction, so that thereby a means is afforded for the development of more or less deep and extensive ulcers. The frequency with which ulceration of the larynx takes place in this manner, and how often it is due to other causes, can at present not be decided. It is certain, however, that diphtheric and pseudodiphtheric affections, which often were held responsible by earlier writers, have gradually become less frequently a cause of this condition.

Another mode of origin for ulceration of the larynx, however, appears quite frequent. The condition then results from small, at first shallow, fissures and erosions upon the postero-internal wall of the larynx, between the arytenoid cartilages and the points of attachment of the vocal bands, which lesions, obviously, develop as a consequence of the hyperemia and dryness of the mucous membrane and the increased

respiratory activity and frequent cough.[1] When such small fissures and epithelial excoriations have once developed, the process, owing to the tendency to tissue-degeneration at the height of severe attacks of typhoid fever, readily extends, and if unfavorably situated and accompanied by other complicating conditions, attains a considerable depth.

Both the ulcers resulting from the necrosis of follicles, and those due to fissures and erosions, may involve and penetrate the mucous membrane to a varying extent. When they involve its entire thickness, perichondritis with perichondritic abscesses, and even rather extensive necrosis of cartilage, with correspondingly severe, dangerous, and, under the most favorable circumstances, protracted sequels, may result.

Whether such deep ulcers can, by reason of their mode of origin, be designated decubital in the strict sense (Dittrich)—as has been done by earlier writers—does not appear to be definitely determined. I believe that at the present day a correct conception cannot be formed of the mechanism by which such ulceration is brought about.

The seat of the laryngeal ulceration is constant, almost typical. As has been mentioned, it is most frequently situated upon the posterior wall of the larynx, extending at times to the contiguous portions of the attachments of the vocal bands, in the latter situation, it is true, almost solely in the form of slight erosions. With this seat of predilection for the ulceration is associated the fact that secondary perichondritis and necrosis of the cartilage involve in the majority of cases the cricoid and arytenoid cartilages. Typhoid ulcers appear to be quite rare at other situations in the interior of the larynx. I have in one instance observed, in association with ulceration upon the posterior wall, erosion of the left ventricular band.

Ulceration occurs not much less commonly upon the epiglottis than it does upon the posterior wall, but in general it is there much less deep and less extensive. Under such circumstances laryngoscopic examination often discloses numerous small shallow, ragged, ulcers occupying the margin of the epiglottis. I have frequently observed them in association with follicular swelling and ulceration in the throat, especially with the peculiar erosive inflammation of the soft palate and the tonsils previously mentioned. Quite commonly the ulcers extend down to the cartilage and cause exfoliation of small portions. Only exceptionally does extensive necrosis of the epiglottis take place, leaving large defects. Especially severe cases of this kind have been recorded in the literature by Moore,[2] West,[3] and others. I have personally observed at autopsy

[1] See also Störk, *Klinik der Krankheiten des Kehlkopfes*, Vienna, 1880, pp. 259, 260.

[2] *Trans. Path. Soc.*, 1883, vol. xxxiii., p. 38.

[3] *Ibid.*, p. 37.

in one instance destruction of one-third of the epiglottis by necrosis, and in another instance necrosis of more than half. Nevertheless, apart from these extensive lesions, affections of the epiglottis are by no means so dangerous as those of the interior of the larynx. They are often not even noticed by the stuporous patient, and often become appreciable only through difficulty in swallowing. Only in cases in which the constitutional condition is grave, or where very extensive defects exist in the epiglottis, does aspiration-pneumonia develop.

The much more frequent profound disturbances due to ulceration of the interior of the larynx are of varied kind. Before the ulcerative process extends deeply—more frequently, indeed, if this is the case—edema of the glottis may develop. At times it appears quite unexpectedly, and then increases with such rapidity that even in hospitals suffocation has occurred before tracheotomy could be performed.

A further serious danger resides in the possible development of perichondritic abscess and necrosis of cartilage. The cricoid cartilage, which is most frequently involved, may be destroyed throughout almost its entire extent. Next to it in frequency the arytenoid cartilages are involved, and are frequently bathed in pus and partially or wholly exfoliated. In one instance I observed expectoration of an entire arytenoid cartilage; this sometimes occurs also in cases of typhus fever. That such perichondritic processes are more likely than simple ulcers to cause marked tumefaction of the mucous membrane and stenotic edema of the larynx is obvious. If, however, in such cases the impending danger to life is averted by tracheotomy, the patients are still exposed to the most serious consequences due to extensive ulceration and corresponding loss of cartilage. The slightest of these disturbances consists in the necessity of wearing a cannula for a considerable length of time, and the persistence for a further period of a certain degree of hoarseness. When severe cicatricial stenosis of the larynx develops, some patients must continue to wear a cannula permanently; or in favorable cases some degree of improvement may be secured by long courses of dilatation with bougies.

Fortunately, secondary suppuration and gangrene in the cellular tissues of the neck and its vicinity are rare in connection with suppurative perichondritis. In one instance I observed purulent posterior mediastinitis, and in a number of instances burrowing of the pus into the anterior mediastinum. Quite exceptionally (Wilke), extensive cutaneous emphysema, involving the larger portion of the body, has been described in the sequence of perforation of the thyroid cartilage.

Whether typhoid perichondritis may develop directly and independ-

ently without antecedent ulceration of the mucous membrane, as is believed by Dittrich and others, is as yet undemonstrated. But with our recent knowledge with regard to typhoid osteomyelitis and periostitis, the question can by no means be ignored. I have personally encountered a case in which, on careful laryngoscopic examination, the arytenoid cartilages, the epiglottis, and the entire interior of the larynx were found clear, while circumscribed inflammation of the thyroid cartilage, attended from the outset with swelling of the anterior portion of the neck, developed. There resulted suppuration, burrowing of the pus between the deep muscles of the neck, and exfoliation of a portion of cartilage about three-quarters of an inch in diameter, followed finally by uncomplicated recovery without stenosis or impairment of the voice. On the whole, the thyroid cartilage appears to be by far the least frequently involved of all.

The literature contains a large number of isolated cases of extensive typhoid necrosis of the larynx. Extensive necrosis of entire cartilages or of individual portions of cartilage have been recorded by Pachmayer,[1] DeBroeu,[2] Gilliard,[3] Sekretan,[4] Dutheil,[5] and others. A collective report of the cases of severe typhoid involvement of the larynx (200 cases), together with 14 personal cases, has been made by Lüning.[6] He found affections of the larynx in almost one-tenth of all cases of typhoid fever that came to autopsy. Half of these consisted in simple superficial ulceration; the others in more profound ulceration, in part with necrosis of cartilage. The statements of various writers with regard to the frequency of laryngeal ulceration vary quite remarkably. While Murchison, who bases his opinion upon the observations of Jenner, Trousseau, Louis, Bartlett, Wilks, and others, as well as his own, designates it as an "occasional," evidently not frequent, condition, Hoffmann observed laryngeal ulceration at Basle in 28 of 250 autopsies, and Griessinger in 26 per cent. of his fatal cases. In Hamburg we observed extensive ulceration of the larynx in 37 of 349 autopsies.

With regard to the frequency of ulceration of the larynx in accordance with age and sex, children appear to be rarely attacked. Men exhibit ulceration of the larynx far more frequently than women. Two-thirds of the cases under my observation occurred in men. In this connection antecedent predisposing influences probably play an important *rôle*, especially chronic pharyngeal and laryngeal catarrh, such as occurs predominantly in men, largely as a result of smoking and of alcoholism.

It is doubtful whether ulceration of the larynx occurs with especial

[1] *Verhandl. d. Würzburger med. Gesellsch.*, 1869.

[2] *Presse méd. Belg.*, 1869, No. 21.

[3] *Ibid.*, No. 20.

[4] *Rev. méd. de la Suisse Rom.*, August, 1883.

[5] *Thèse*, Paris, 1869.

[6] "Die Larynx- und Tracheastenosen im Verlaufe des Abdominaltyphus und ihre Behandlung," *Arch. f. klin. Chir.*, 1884, Bd. xxx.

frequency in certain countries and localities. Quite striking differences in frequency, however, may be observed at certain times and during certain epidemics. This is true of typhoid fever as well as of the laryngeal ulceration of typhus fever, which at times may be a very conspicuous feature of the epidemic; for instance, during the last epidemic of typhus fever at Berlin, when 4 per cent. of all the typhus patients under my observation presented more or less marked involvement of the larynx.

The time of onset and the duration of laryngeal ulceration in the course of typhoid fever are extremely difficult to determine, inasmuch as the milder lesions, as well as those that subsequently pursue a severe course, are likely to be almost free from symptoms at the outset. The deeply stuporous patients do not complain, and the physician, under such conditions, has little reason and opportunity for examination of the larynx. It may be said in general that ulceration of the larynx occurs chiefly at the height of the disease and in the latter part of the febrile stage, principally at a time when exfoliation of the sloughs and cicatrization of the ulcers in the intestine are taking place. In isolated instances I have observed, both by laryngoscopic examination and at autopsy, ulceration of the larynx as early as the beginning of the third week; in one instance, even at the beginning of the second week, there was a deep ulcer upon the posterior wall of the larynx.

When the affections of the larynx give rise to symptoms, these will be most variable—local pain, difficulty in swallowing associated with aspiration of food into the air-passages, irritative cough on speaking and on deep breathing, hoarseness, and even aphonia. At times the symptoms of acute edema of the glottis may set in quite suddenly, before there is any reason for thinking of serious disease of the larynx. Every typhoid patient with laryngeal symptoms should therefore be subjected to special observation. This applies particularly to the throat and larynx in severe cases where the patients are stuporous. With every increase in respiratory frequency, with the development of dyspnea and cyanosis, involvement of the larynx should, among other things, always be thought of as a cause. More than one unfortunate case is known in which superficial observers attributed such symptoms to bronchitis, lobular pneumonia, or to the existing infiltration of the lungs alone, and in which the autopsy showed that death was due to edema of the glottis, for which tracheotomy should have been performed promptly. In contrast with the profound conditions just referred to, it is comforting to know that in the large majority of cases ulceration of the larynx remains superficial, extends but little, and heals without sequels. The laryngeal affection should not therefore be considered as of too grave prognostic significance.

Following the suggestion of Rokitansky, some writers, especially the French, have applied the designation "laryngotyphoid" to those cases in which extensive laryngeal symptoms appear quite early. I considered this designation arbitrary and scarcely justified. Some remarks upon paralysis of the vocal cords will be made in the succeeding chapter.

Trachea and Large Bronchi.—In these parts also dry catarrh or catarrh attended with but scanty secretion plays a certain *rôle*. At autopsy tracheitis and bronchitis are among the conditions most constantly found (see Anatomy). These conditions are manifested clinically by dry cough, tenderness, and a sense of soreness behind the sternum, and these symptoms are more frequently complained of since the tracheitis is likely to appear at the end of the first and the beginning of the second week; therefore, at a time when intelligence is still preserved. On auscultation, coarse, dry râles, sonorous and sibilant, can be heard. The superficial erosions of the mucous membrane that are encountered on post-mortem examination give rise to no special clinical symptoms.

Diphtheric affections of the trachea and the large bronchi are still more rare than those of the nasopharynx and larynx. Griessinger refers to pseudomembranous affections of the larynx and the trachea in cases of malignant course, but I have never observed such conditions. Eisenlohr[1] has described a form of fibrinous bronchitis developing as early as the end of the second week, which extends into the smallest bronchi and heals without complication. A fatal case of this character is mentioned by Brault.[2]

Involvement of the bronchial glands is often observed at post-mortem examination, and is well known. It is doubtless analogous to that of the mesenteric glands, and is probably specific, due to the bacillus of Eberth. In the cadaver recent medullary swelling of the glands is quite generally found, at times of such considerable extent that the possibility of compression of the trachea or of the large bronchi in consequence can readily be conceived. In some instances in severe cases of typhoid fever I have, in fact, observed remarkably enfeebled, soft breathing upon one side, when no adequate explanation could be based upon disease of the lungs or the pleura, and which persisted so long that neither occlusion by mucus nor other transitory influences could be considered the cause of the condition. The respiratory murmur became normal again with subsidence of the fever. I have lost no case of this kind, and therefore do not venture to consider the condition as

[1] *Berlin. klin. Woch.*, 1876, No. 31. [2] *Progrès méd.*, 1881, No. 19.

with certainty one of bronchial stenosis due to glandular enlargement. In a fatal case of empyema I was able to demonstrate purulent-putrid disintegration of a mass of bronchial lymphatic glands as the point of origin of the complication.

The **catarrh of the medium-sized and smallest ramifications of the bronchial tubes** is a direct continuation of the catarrhal conditions present in the larger air-passages. By reason of the constancy of its occurrence, the peculiarity of its symptoms and its course, I believe that it can be definitely looked upon as a specific typhoid symptom, and may be attributed directly to the action of toxins or of the bacilli. Although Murchison and subsequent writers do not attach to it this significance, and although the former even believes that he observed bronchitis far more frequently in cases of typhus than in those of typhoid fever, this position is not wholly in accordance with the facts. The bronchitis attending typhus fever pursues its course with much more pronounced symptoms, particularly more marked cough and more abundant secretion; while in cases of typhoid fever, by reason of the slight degree of swelling and sponginess of the mucous membrane and the small amount of secretion, cough is less frequent and less severe, and expectoration is almost always wanting. If, however, the patients are examined carefully at the height of the febrile stage, physical signs of bronchitis and bronchiolitis—at times, it is true, but slight—will always be demonstrable in some degree. As early as the end of the first or the beginning of the second week, and from this time on throughout the entire febrile period, roughened, frequently enfeebled, vesicular inspiration is audible, at times with prolongation of expiration, and sometimes with an abundance, and at other times with a scarcity, of dry râles of sonorous and sibilant quality.

The seat of such catarrhal conditions is especially in the lower lobes. Not rarely, and especially in severe cases, they extend throughout the entire lung. In those situations in which extensive bronchiolitis is present, marginal emphysema may develop. Rarely, the anterior and upper portions of the lungs are involved first and most markedly. Such cases should be viewed with suspicion, and be investigated for complications with especial care.

It has been stated that by no means all cases of bronchitis are attended with cough, and that when patients do exhibit a short, dry cough there may be only a scanty, vitreous, viscid expectoration, if any. More violent and more frequent cough, or abundant mucopurulent expectoration, demands careful investigation for the presence of other alterations.

In general the catarrhal manifestations are of considerable significance both from a diagnostic and from a prognostic standpoint. In diagnosis the detection of diffuse bronchitis is especially of significance because other infections that may readily be confounded with typhoid fever, as, especially, febrile protracted intestinal catarrh, are unattended with it. On the other hand, it is noteworthy in the diagnosis of typhoid fever, and under some conditions decisive, when apparent intestinal catarrh, even of slight intensity, is from the outset associated with extensive bronchitis. It is to be noted that the degree and the extent of the bronchitis in cases of typhoid fever need by no means correspond with the severity of the case in general. There are mild cases with markedly predominant bronchitis. The reverse, it is true, is less common. From a prognostic point of view it is also noteworthy that after intense catarrhal conditions of early onset, severe involvement of the lung immediately adjacent is likely subsequently to occur.

In addition to simple typhoid bronchitis, the rare occurrence of putrid bronchial disorders is worthy of note. I have repeatedly observed them, and have noted their disappearance without traces at the termination of the attack of typhoid fever. In isolated cases, on the other hand, they probably give rise to small bronchiectases or circumscribed destruction of pulmonary tissue, occasionally with consecutive putrid pleural exudates. The atelectasis and the lobular pneumonia that are so frequent in the course of typhoid fever are intimately related to the bronchitis, particularly to the capillary variety. Clinically these conditions are often recognizable with difficulty if at all, and this is especially true of atelectasis.

Bronchopneumonia, which occasionally manifests itself by increase in the fever, change in the character of the expectoration, and occasionally also by distinctive auscultatory signs, has been little investigated from the etiologic point of view. In the majority of cases this condition is doubtless to be included among the true complications. In the small number of cases thus far investigated, principally the pyogenic bacteria, streptococci, and staphylococci have been found. Without doubt, bronchopneumonia may also be of specific typhoid character, as is shown by the investigations of Polynère,[1] Finkler,[2] and others, who were able to demonstrate the bacillus of Eberth as the exciting cause of the inflammation. The extremely grave cases of acute edema of the lungs, which are fortunately rare, are also dependent upon extensive

[1] *Thèse*, Paris, 1889, cited by Finkler.

[2] *Die acuten Lungenentzündungen*, Wiesbaden, 1889.

bronchopneumonia and cardiac weakness with acute onset, or with acute intensification.

Bronchopneumonia likewise constitutes the usual basis for the **hypostatic congestion** of the lower lobes of the lungs that occurs so frequently in the latter part of the febrile stage; its development is also favored, however, by the weakness of the heart and the influence of the posture of the body upon the distribution of the blood. From all that has been said, it will appear that hypostatic congestion occurs only in debilitated individuals with severe attacks, and it therefore forms an important link in the chain of unfavorable occurrences in the course of typhoid fever. In patients presenting especially severe infection and already much reduced, the hypostasis develops as early as the first half of the febrile stage or at its height, and it is then of especially unfavorable omen. It is more common, it is true, particularly in cases of protracted course, toward the end of the febrile period, or even at the beginning of convalescence. I have occasionally observed it also during relapses with prolonged course following an antecedent severe attack. In the absence of systematic careful examination of the patient, for which there is often no special indication, this hypostasis may be readily overlooked, as in itself it gives rise neither to elevation of temperature, pain on breathing, nor to increased cough, and by no means always to changes in the frequency and the character of the respirations. On the other hand, physical examination will at once yield the desired information. There will be found slightly tympanitic or even markedly impaired resonance, posteriorly and inferiorly, at first often confined to one side, though subsequently usually marked upon both sides. The vocal fremitus is generally moderately increased if the patient can be induced to submit to investigation of this phenomenon, but not rarely it is enfeebled and even absent when the bronchi are filled with secretion. The respiratory murmur is accordingly indistinct, soft, no longer vesicular, and expiration is prolonged, with a bronchial character. If the congestion progresses further, the respiratory murmur becomes markedly bronchial and the râles amphoric. Not rarely inspiration is completely obscured by crepitant or subcrepitant râles.

With improvement in the remaining symptoms of the disease such consolidation usually undergoes resolution, as a result of appropriate treatment or without special intervention, and is usually followed by no sequels. In some cases, with continued progress of the disease the symptoms of consolidation may increase and extend. Considerable elevation of temperature may occur associated with repeated chilliness or even a marked chill. Under such circumstances a condition of

hypostatic pneumonia may appropriately be spoken of. This is undoubtedly dependent upon the secondary invasion of exciting agents of inflammation, principally through the inspired air; less commonly through the circulation. Whether the typhoid-bacillus plays an etiologic *rôle* in these complications, and if so with what frequency, is as yet unknown.

Hypostatic pneumonia is one of the most dangerous complications of typhoid fever. Death occurs in the majority of cases. Should recovery ensue, slow disappearance of the physical signs; with a protracted course for the entire process, is the rule. Local complications—abscess of the lung, gangrene, and pleurisy with effusion—appear to me to be less common after hypostatic pneumonia than after other inflammatory processes in the lungs.

Of 1830 cases of typhoid fever of which I have notes, signs of consolidation or inflammatory congestion of the lower lobes were present in 121. In the overwhelming majority of cases the onset of the condition occurred in the second and the third week, most frequently between the end of the second and the middle of the third week; and of the patients in question, 65 died. The observations of Liebermeister differ but little from my own. He found among 1420 cases, 100 of hypostatic congestion, with 50 deaths. It is noteworthy that congestion and hypostatic pneumonia are far less common in children than in adults. This is no doubt partly due to the shorter duration and the generally slighter intensity of the attack of typhoid fever in children, but especially to the fact that the determining cause in adults, namely, the weakness of the heart, is much less commonly effective in children. Especially convincing in this connection also is the fact that lobar pneumonia, the onset of which is due less to the cardiac weakness than to the infection itself, is in my experience no less common in children than in adults.

Lobar pneumonia is less frequent in the course of typhoid fever than hypostatic congestion or consolidation. Among the different varieties true croupous pneumonia plays the principal *rôle*, and is one of the more important actual complications of the disease. It is almost exclusively dependent upon the Fränkel-Weichselbaum diplococcus; with extreme rarity upon the bacillus of Friedländer. It occurs, as a rule, at the height or toward the end of the febrile period. It occurs very rarely, according to my experience, during convalescence or in the course of relapses of considerable duration.

Although the onset and the course of genuine fibrinous pneumonia are usually most characteristic, the symptoms when it occurs as a complication of typhoid fever are exceedingly inconstant. Even the manner in which it manifests itself is extremely variable. Generally it sets in with a single or repeated chilliness, or a true chill, although these symptoms may be wholly wanting. The absence of chilly symptoms is

observed especially in previously debilitated or in elderly persons, or when the pneumonia develops at a late stage in severe protracted cases. Under such circumstances even noteworthy elevation or characteristic course of the temperature may be wanting.

As a rule, the onset of the pneumonia is attended with rapid rise in the body-temperature, which may then continue for days at an abnormally high level, in the form of a remittent continued fever. When the pneumonia develops during the last portion of the febrile period and the resolution coincides with the termination of this period, there may occasionally be a definite critical decline in temperature. If, on the other hand, the pneumonia undergoes resolution in the course of the fastigium, the critical decline is wanting, as a rule, and defervescence by lysis takes its place.

All cases of pneumonia, even those that do not give rise to marked elevation of temperature, are attended with considerable increase in pulse-frequency; and in debilitated persons are generally associated with reduction in size and considerable lowering of tension of the pulse. A corresponding increase in frequency of respiration and in cyanosis are naturally quite common. There is therefore all the more reason to look for these symptoms in cases of suspected pneumonia during typhoid fever, because under these circumstances subjective complaint, particularly of pain in the side, as well as of cough and expectoration, is often wanting. The absence of pain and the slight character of the cough are probably dependent upon the lessened irritability of the patient, associated with the obscuration of consciousness; and the absence of expectoration upon the fact that the patient expels the sputum imperfectly and swallows it again, in part possibly also upon its secretion in relatively small amount. When the patient ejects the sputum, it may be characteristically viscid, rusty, or even more hemorrhagic. I have an impression that the last mentioned peculiarity is more frequent in cases of pneumonia complicating typhoid fever than in those of genuine pneumonia.

With regard to its seat and the physical signs, fibrinous pneumonia attending typhoid fever differs little from that arising independently. As to the course, the height of the infiltration appears to me to be at times reached more slowly, and resolution also is not rarely completed more slowly than in the independent form. A considerable number of cases do not advance beyond the symptoms of congestion. That they, nevertheless, are cases of fibrinous pneumonia, I have repeatedly been able to establish both by puncture of the lung during life and by the demonstration of the characteristic encapsulated cocci in the sputum.

Fibrinous pneumonia is not one of the more common complications in the course of typhoid fever. Its occurrence, however, doubtless exhibits great variations in accordance with the season of the year, the locality, and the character of the epidemic. I am personally not in possession of large statistics, and would draw conclusions with care from those of other writers, as a large proportion of the cases hitherto reported have not been studied with sufficient care from the bacteriologic standpoint, and the results of study of the remainder are unreliable. Even the older anatomic statements are to be accepted with reservation, as in cases of typhoid fever, in consequence of certain histologic conditions, the pneumonia dependent upon encapsulated cocci may, upon section, exhibit an unusual color and a smooth or slightly granular surface.

Age and sex exert no influence upon complication with croupous pneumonia, which occurs, as has been indicated, with scarcely less frequency in children than in adults.

The *rôle* played by the diplobacillus of Friedländer, as compared to the Fränkel-Weichselbaum coccus, in the development of pneumonia in the course of typhoid fever, is obscure. In those cases in which examination has been made as to this point, the diplococcus especially has been found, and only in rare instances the bacillus of Friedländer, which I have personally been able to demonstrate in only 1 case.

Other Varieties of Lobar Pneumonia.—In addition to hypostatic and true fibrinous pneumonia, other varieties of lobar pneumonia certainly occur. They have, as yet, not been thoroughly investigated, and a portion of that which is said to have been surely demonstrated needs still further investigation. This is true, above all, of the cases of lobar pneumonia attributable to typhoid-bacilli (Bruneau,[1] Chantemesse,[2] Polynère,[3] Finkler[4]). Thus, Polynère found, in addition to the lobular pneumonia already mentioned, extensive consolidation due to the bacillus of Eberth. Early occurrence, rapid development, and tardy subsidence of the infiltration are considered as characteristic clinically of this form of the disease. Recently, even the bacteriologic diagnosis of the specific typhoid affections of the lungs and the pleura has been rendered additionally difficult by the fact that the Bacterium coli, which in some respects closely resembles the bacillus of Eberth, has under such conditions been repeatedly found as the exciting agent of the inflammatory process.

It is also objected by opponents of the view that specific typhoid affections of the lungs occur, that in the cases where pure cultures of the typhoid-bacilli have been found, the cultures were made so late that the primary invader had died out (see section on Pathology).

The conditions are not much clearer with regard to the lobar pneu-

[1] "De la nature des complic. broncho-pleuro-pulmonaires de la fièvre typhoïde," *Thèse*, Paris, 1893. [2] *Loc. cit.* [3] *Loc. cit.* [4] *Loc. cit.*

monia due to streptococci or staphylococci than with regard to that due to typhoid-bacilli. Undoubtedly these micro-organisms play an important *rôle* in the mixed infections that frequently are associated with the development of pneumonia in the course of typhoid fever. They have been observed both in association with pneumococci and with the bacillus of Eberth (Karlinsky [1]). Streptococci appear to be the sole or the principal cause of pneumonia more frequently than staphylococci. They give rise to both lobular and lobar inflammation,[2] the latter obviously the result of the confluence of multiple contiguous lobular foci. Probably they are also the principal micro-organisms causing the secondary inflammatory changes attending simple hypostatic congestion.

Streptococci and staphylococci certainly play a *rôle* also in the development of the so-called aspiration-pneumonia of typhoid fever. I have reason to believe that the former are especially responsible for the severe pneumonia following typhoid ulceration of the larynx and perichondritis of the larynx. Apart from all these, the streptococcic pneumonia of typhoid fever is doubtless to be most frequently considered as one of the manifestations of general secondary septic infection. Under such circumstances other lesions due to this organism can be found in the body after death, and often even during life. Only recently we were able to demonstrate in a man twenty-five years old embolic abscesses of the kidneys, associated with bilateral pure streptococcic pneumonia in addition to pleuritic effusion.[3]

Just as septic processes generally appear at a late stage in the course of the disease, owing to their mode of development, so also the pneumonia dependent upon streptococci and other pyogenic organisms occurs late. It is almost exclusively the late febrile period or that of convalescence in which it occurs. Its source under these conditions is often a bed-sore, or phlegmonous inflammation of the skin and the subcutaneous connective tissue, or it may, of course, follow still other purulent processes, as, for instance, phlebitis and circumscribed peritonitis.

Clinically, streptococcic and staphylococcic pneumonia, apart from microscopic and bacteriologic examination, can be differentiated from the other varieties only with very great difficulty. Recently, numerous attempts have been made, with the aid of the exploratory needle, to obtain

[1] *Fortschr. d. Med.*, 1889, Bd. viii.

[2] See also the communications of Neumann, *Berlin. klin. Woch.*, 1886, No. 6; Finkler, *Verhandl. d. Cong. f. inn. Med.*, 1888 and 1889; and Karlinsky, *loc. cit.*

[3] See Koch, *Inaug. Diss.*, Leipsic, 1897.

material from the lung during life for examination. I have personally availed myself of this method repeatedly without injury to the patient, but would advise great caution in its application.

It should be emphasized as of importance from the clinical, and especially from the diagnostic, point of view, that pneumonia may occur even at an early period in the course of typhoid fever, at times so early that it may at first be considered as an independent condition. Thus, pneumonic infiltrations have frequently been observed in the first week of typhoid fever, even in the first days, before any of the characteristic features of typhoid have been manifested. At times they set in with one or more chills or repeated chilliness. Unilateral or bilateral consolidation then rapidly follows; in my experience, often more rapidly than in the case of uncomplicated frank pneumonia. Not rarely, under such circumstances, there is no expectoration whatever, or the sputum is but scanty and is not characteristic, containing no blood, encapsulated cocci, or fibrinous coagula; in other cases the sputum is blood-tinged or actually prune-juice-like in character. Certain of the subjective manifestations also are more inconstant than in cases of genuine pneumonia. Nevertheless, headache of unusual severity and more or less marked stupor are soon noticed, and at the same time or a few days later the enlargement of the spleen appears. If suspicion now arises that the condition may not be one of ordinary fibrinous pneumonia, —at this time influenza-pneumonia is frequently thought of,—the situation soon becomes clear, especially if at the proper time, after the disease is of from seven to nine days' duration, critical defervescence, or, in fact, any remission in the symptoms does not take place, but the pneumonia instead remains stationary, and a continuance or an increase in the enlargement of the spleen, roseolæ, meteorism, pea-soup-like stools, and bronchitis in the previously uninvolved portions of the lungs make their appearance. Such cases, in analogy with those of nephrotyphoid previously mentioned, have been designated pneumotyphoid. Rokitansky[1] and Griessinger,[2] subsequently Gerhardt[3] and Rindfleisch,[4] have directed attention to cases pursuing this peculiar course.

Strictly speaking, the designation pneumotyphoid should be employed only when the bacillus of Eberth has been demonstrated as the sole, or at least as the principal, cause. As a matter of fact, such cases possibly occur (Lépine[5] and others. See section on Pathology, p. 116).

[1] *Loc. cit.* [2] *Loc. cit.*

[3] *Thüringisches Correspondenzbl.*, 1875, No. 11, and *Handb. d. Kinderheilk.*, 1874, Bd. ii., S. 388. [4] Garpagni, *Inaug. Diss.*, Würzburg, 1875.

[5] *Rev. de méd.*, 1878, and *Nouv. dict. de méd.*, Jaccoud, 1880, t. xxviii.

As yet, however, not much is known concerning them. Further bacteriologic investigation will be required before it is definitely decided whether such cases occur, and if they do, with what frequency. If it be shown that pneumonia may be caused by the typhoid-bacilli alone, it will then be necessary to determine whether there is any support for the theory, previously mentioned, that a direct invasion of the typhoid virus through the air-passages may occur, or to what degree the pneumonia is to be considered as due to an unusually early and rare primary localization of the contagium which has gained entrance into the body through the customary portals. Between such cases and those in which the pneumonic consolidation occurs at a later period are those in which, after an attack of ambulatory typhoid fever, a recrudescence or a relapse sets in with specific pneumonic infiltration.

We shall in the future probably have to differentiate from pneumotyphoid in the true etiologic sense those cases in which other microorganisms—pneumococci, streptococci, and staphylococci—likewise give rise to pneumonic infiltration in the initial stage of typhoid fever. Such conditions represent true complications during a period in which complications rarely occur, and in these cases the clinical picture of typhoid fever may be strangely altered and at times even wholly obscured. I have personally observed cases in which pneumonia due to pneumococci developed during the first week of an attack of typhoid fever, while roseolæ and splenic enlargement appeared only subsequently, and then helped to clear up the situation.

Interesting clinical evidence in regard to these atypical forms of pneumotyphoid has been furnished by E. Wagner,[1] but neither he nor his predecessors were able, on account of the state of knowledge at the time, to make an etiologic differentiation of their cases. To be sharply discriminated from the cases thus far mentioned—and this has not always been done, even until within a recent period—are those forms of genuine pneumonia which, in consequence of the malignity, in the symptomatic sense, of their typhoid-like course, have been designated pneumotyphoid, or, at times, typhoid pneumonia. The condition present is undoubtedly one of inflammation of the lungs, which pursues a particularly unfavorable course, in consequence of individual circumstances, or because it constitutes one of the manifestations of one of the other severe infectious disorders, among which septicemia, particularly the cryptogenetic variety, is to be mentioned above all. In addition to septic pneumonia, the mixed infections of tuberculosis with the pyogenic agents that have been repeatedly mentioned have been considered as pneumotyphoid or typhoid-pneumonia.[2]

Abscess of the lung is considered an exceedingly rare complication of typhoid fever. Abscesses are probably encountered most fre-

[1] *Deutsch. Arch. f. klin. Med.*, Bd. xxxv. and xlii.

[2] See the statistics of E. Wagner.

quently as metastatic phenomena associated with complicating general pyemia; they also exceptionally occur as sequels of lobar, fibrinous pneumonia. Two cases of the latter variety have come under my personal observation. As they occur, like the primary disease, especially in the later stages of typhoid fever, they give rise under the most favorable conditions to considerable retardation of convalescence, if they do not act as the cause for a fatal termination of the disease. Without doubt, the latter is more likely to occur as a result of abscess of the lung following typhoid fever, than it is after abscess following simple fibrinous pneumonia. Whether pneumonia due to the typhoid-bacillus may be followed by the formation of an abscess has not yet been established, but it is entirely probable, as the typhoid-bacillus is well known to be an independent pyogenic agent.

Symptoms of **pulmonary infarction,** which consists essentially in the development of an acute afebrile consolidation, with hemoptysis, I have observed repeatedly. It is most frequently attributable to the detachment of marantic thrombi in the right side of the heart, especially in the auricle and the auricular appendix. Occasionally, it is true, the thrombus is derived from the peripheral veins. In stuporous patients infarction occurs now and again without noteworthy subjective manifestations; this is more likely to be the case since such patients do not expectorate properly. Most frequently acceleration of the pulse and of respiratory frequency are also observed.

While infarction occurs in some cases without a chill and without elevation of temperature, in others it sets in with a chill, and subsequently the temperature-curve shows septic characteristics. I have observed the latter kind of symptoms especially during convalescence. These symptoms are either the first manifestations of a pyemic disorder or are due to emboli in the course of such a disorder, and these cases almost always pursue an unfavorable course. Under the most favorable conditions these lesions are followed by circumscribed gangrene of the lungs with putrid pleurisy or even by pneumothorax.

Embolism of large branches of the pulmonary artery, which fortunately is rare as a cause of sudden death, has been referred to (see Anatomy).

Pulmonary gangrene appears to be somewhat more frequent than abscess and infarction in the course of typhoid fever. Excluding the cases of septic embolism just referred to, pulmonary gangrene occurs most frequently as the termination of lobar pneumonia of most diverse origin, especially of fibrinous pneumonia. The condition belongs almost unexceptionally among the complications of the late period, since, in

addition to the activity of the special micro-organisms concerned, weakness of the heart and general emaciation play a determining *rôle* in its development.

In 1 case I observed pneumonia dissecans occur in the sequence of complicating fibrinous pneumonia. Fortunately for the patient, the lesion ruptured into the pleural cavity, and the sequestrum was discharged into it. A resection of the ribs enabled me to evacuate the consequent putrid empyema, together with the gangrenous portions of lung, and so to bring about a permanent cure.

The cases of pulmonary gangrene resulting from the aspiration of decomposed infectious material, derived especially from the mouth, the nares, and the pharynx, are also important. In this connection a special *rôle* is played, according to my experience, by the more superficial and also by the more profound ulcerative form of purulent tonsillitis, and especially by the cases of laryngeal ulceration and perichondritis.[1] In deeply stuporous patients such conditions remain concealed from the physician so long as the lesions are still small, and become distinct only after they have attained a certain extent. In addition to the infectious materials mentioned, aspiration of particles of food is also occasionally the cause of pneumonia with secondary gangrene. It should not be forgotten in this connection that aspiration of particles even of considerable size by profoundly stuporous patients need not give rise at once to special symptoms.

I have observed gangrene of almost the entire lower lobe of the right lung in a young man, the cause for which was disclosed only upon post-mortem examination by the discovery of a piece of decomposed meat impacted in a large bronchus. As subsequently appeared, the patient had received meat surreptitiously at the height of the febrile period, while he lay in a stuporous state, and the time when a portion of this was aspirated was not even noted by the neighboring patients.

Liebermeister has observed cases of extensive gangrene of the lung without antecedent inflammation of the organ or aspiration of foreign bodies, and he has attributed the condition to the unusual severity of the general disturbance of nutrition. In view of the large experience of this observer, these cases are especially noteworthy. I have, fortunately, not as yet encountered such cases.

It is peculiar that Murchison considered gangrene of the lung an extremely rare complication of typhoid fever. He saw but 1 or 2 cases which followed pneumonia in the course of typhoid fever. On the other hand, Liebermeister encountered gangrene in 14 among 230 fatal cases. It is quite remarkable that 9 of his cases occurred in the course of three months, during which the hospital was greatly overcrowded and it was impossible to provide suita-

[1] See also Curschmann, "Das Fleckfieber," *Ziemssen's Handbuch d. klin. Med.*, Bd. ii., 3. Aufl.

ble hygienic conditions. Griessinger has observed gangrene in 7 of 118 cases examined post mortem. In my Leipsic statistics it is recorded in 10 instances in 228 autopsies.

That the frequency of the **pleurisy** is variously stated by different observers is probably dependent upon different interpretations of the term. If every circumscribed pleuritic friction, every fibrinous deposit upon the pleura in cases of lobar and lobular pneumonia or other focal disease of the lung, is included in this category, then pleurisy is almost as frequent a disease as the affections of the pulmonary parenchyma itself. If, however, as appears to be more practical, principally those cases are kept in mind that appear more or less independently, especially those attended with the development of moderate or large effusions, then the condition is a rare occurrence. When it occurs at all, it is a manifestation of the late febrile period or of convalescence. I have exceptionally encountered pleurisy during the first week which was such a prominent feature of the case that the designation pleurotyphoid might be employed in the same way that French investigators[1] have used pneumotyphoid and nephrotyphoid.

In a number of cases the typhoid-bacillus has been obtained in pure culture from the serous or purulent pleuritic effusion, and its primary etiologic significance in a number of these cases seems fairly well established (see section on Pathology). Pleurisy in typhoid, just as under other circumstances, is probably generally secondary to affections of the lungs or of other contiguous structures. Cases of empyema especially I have been able to trace to antecedent disease of the lung. A number of hemorrhagic effusions that I have encountered proved to be tuberculous. Certain serous effusions possibly have a more independent origin; these, however, in my experience, rarely become large, and therefore but exceptionally demand the performance of thoracocentesis. If direct intervention is not undertaken, these are usually of longer duration in cases of typhoid fever than when there are complications of other diseases. Now and again, it is true, pleuritic effusions of considerable size disappear rapidly without especial interference. Only recently I observed in a student suffering from typhoid fever a large left-sided, serofibrinous effusion, with considerable displacement of adjacent organs, which, nevertheless, underwent absorption in the course of two weeks.[2]

[1] Lécorché and Talamon, *Études méd.*, 1881. Germain Sée, *Die einfachen Lungenkrankheiten*, German translation by Salomon. Charrin and Roger, *Soc. méd. des hôp.*, April, 1891. Fernet, *Ibid.*, May, 1891.

[2] It may be considered noteworthy that in this case the fluid obtained with the exploratory needle exhibited a characteristic agglutinating effect upon bouillon-cultures of typhoid-bacilli in the same degree as the blood-serum of the patient.

The prognosis of serous exudates in the course of typhoid fever is, according to my experience, not particularly unfavorable. That it has been considered so upon the authority of Louis is due to the fact that the individual varieties have not been adequately differentiated. Naturally, pleurisy is of far graver significance if purulent, hemorrhagic, or even putrid effusions are included under that term.

Pneumothorax is an extremely rare complication of typhoid fever, and is to be considered merely as an accidental occurrence, generally in conjunction with disease-foci in the lungs, pulmonary abscess, pulmonary gangrene, etc.

Pulmonary tuberculosis bears various important relations to typhoid fever as a complication and a sequel. Even earlier writers were aware of this. Contrary to the opinion of these early writers, however, the view is generally held at the present day that when tuberculous processes appear in the sequence of typhoid fever, the condition is not due to an intercurrent disease, but almost always is the first manifestation, or represents the progression, of an earlier process which had hitherto been more or less concealed.

The appearance of tuberculosis is confined almost exclusively to the later period of typhoid fever. Even in the latter half of the febrile period it is less common than during convalescence, and in some cases the symptoms become distinct only after the patients have left their beds and are apparently convalescent. Cases of the latter character led earlier writers to believe that typhoid fever might terminate in pulmonary tuberculosis by the direct caseation of inflammatory foci developed during its course.

Tuberculosis occurs in various forms in the course of typhoid fever. I have observed miliary tuberculosis as a complication only with relative rarity, and then especially during the last part of the febrile period or the first part of convalescence. Under such circumstances there is danger of confusing this condition with intercurrent cerebrospinal meningitis, which, as experience has shown, may occur at this time (see Nervous System). Noting the considerable acceleration of respiratory frequency which attends the nervous manifestation, careful observation of the changes in the physical conditions of the lungs and examination of the eye-grounds will help to clear up the situation. Positive results from examination of the sputum under such circumstances, are less to be expected than when miliary tuberculosis occurs independently. On the other hand, positive results are more to be expected in the extremely rare cases of mixed infections of fibrinous pneumonia and tuberculosis in cases of typhoid fever, which exhibit nothing distinctive

from the physical-diagnostic standpoint. In 1 such case I was able to demonstrate tubercle-bacilli in moderate number in the sputum, in addition to the Fränkel-Weichselbaum diplococci. Exceptionally, I have observed the tuberculous process to appear in the form of acute or subacute peribronchitis. A case of this kind under my observation began as early as the third week; 2 others—and this appears to be the more usual—during convalescence. As direct examination of the lungs under such circumstances, particularly at the beginning, yields only uncertain results, such cases may be the source for various errors, especially the assumption of simple recrudescences or relapses. Such patients also expectorate but little, if at all, and the sputum, in my experience, rarely contains bacilli. Of diagnostic importance on the one hand are the increase and persistence of the fever, without enlargement of the spleen or presence of fresh roseolæ, and, on the other hand, considerable rapid increase and extension of the bronchitic symptoms, with pulmonary emphysema, subjective and objective dyspnea, cyanosis, and sweats.

Quite rare also, but important on account of the danger of confusion with other varieties of lobar pneumonia occurring in the course of typhoid fever, is acute tuberculous infiltration of considerable portions of the lungs, especially of the lower lobes. This condition may set in with a chill, pain in the side, severe cough, and blood-tinged sputum, just as do other forms of pneumonia. Nevertheless, the persistence of the fever and the imperfect resolution will soon arouse suspicion, which becomes converted into sad certainty by the demonstration of elastic fibers and tubercle-bacilli in the abundant mucopurulent sputum, and probably also by the physical signs of breaking down of the pulmonary tissue.

The onset, the first symptoms, and the course of subacute or chronic tuberculosis of the ordinary kind complicating typhoid fever are different in every individual case, and are to be valued in diagnosis and prognosis accordingly. Fortunately, the association is by no means frequent, and the outlook for checking the tuberculous process is, in my experience, not so gloomy as some clinicians believe.

NERVOUS SYSTEM AND ORGANS OF SPECIAL SENSE.

Typhoid fever is, not without cause, known popularly as nervous fever. The physician must admit that this designation is appropriate in view of the prominent nervous symptoms of the disease. In fact, the disturbances on the part of the nervous system in cases of typhoid fever are especially frequent and varied. They occur from the earliest period

throughout all stages, and threaten the patient far into convalescence. Even in the period of incubation and in the initial stage nervous symptoms are marked. These include general malaise, mental depression, dragging sensations and cutting pains in the extremities in the course of the large nerve-trunks, sacral pain, vertigo, roaring in the ears, and headache.

Headache is probably one of the most constant symptoms of the initial period—far more constant than the sacral pain. It is at times referred to the forehead or to the occiput, less commonly to one side of the head. At other times it exhibits an intense stabbing, boring character. At still other times—and this is true of the majority of cases—it is described as a dull, heavy pressure, or is like a band tied about the head. True neuralgic pains as an initial symptom of typhoid fever are worthy of mention, especially pains in the distribution of the supra-orbital, infra-orbital, and occipital nerves,[1] although in my experience they are quite rare.

Toward the end of the first or at the beginning of the second week, in cases of moderate or severe course, the complaint of headache and the remaining subjective nervous symptoms generally lessen. The patient, now becoming stupid, is no longer capable of appreciating his condition, and his statements cannot be relied upon. It is even urgently advisable, when a typhoid patient still complains of headache or vertigo at the height or toward the end of the febrile period, or begins to make new complaints of headache at that time, that attention be directed to complications, especially meningitis and other intracranial alterations.

In the first stage of the disease, almost coincidently with the complaint of headache, there is generally complaint of sleeplessness also. This becomes less pronounced with increasing stupor. Naturally, a sharp distinction must always be made between sopor and sleep in a sick person. Every experienced clinician knows that a stupid patient may actually sleep or may be sleepless. On further examination it may be found that the sleeplessness, although the patient may no longer complain of it, persists in varying degree throughout the entire febrile stage. The majority of patients sleep, if at all, for only short periods, with frequent interruptions. The relatively early occurrence of profound, long sleep is a favorable sign.

Toward the end of the first week the severe and the moderately severe cases almost regularly begin to exhibit that condition of the nervous system which is designated as the actual typhoidal state; which is attended with obtunding of consciousness and dulling of the special

[1] See O. Rosenbach, *Deutsch. Arch. f. klin. Med.*, Bd. xvii.

senses. The complaints lessen gradually, the interest of the patient in his surroundings diminishes, and the desire for food and drink becomes progressively less. The patient lies in an apathetic state in a relaxed dorsal decubitus, but still reacts sluggishly to loud speaking, to questions, and to active sensory impressions. His statements are still fairly rational, but even slight demands upon mental activity are speedily followed by fatigue. After making brief replies, he relapses into his stuporous condition, in which he is likely to be annoyed by dream-like hallucinations, which constantly reappear as soon as the eyes are closed, or even during the half-waking state.

With the progress of the disease, generally at the beginning or the middle of the second week, in severe cases or in irritable individuals earlier, the dream-like hallucinations become transformed toward evening and during the night into actual delirium. This is generally not violent and aggressive at first, but the patients rather work and talk aimlessly in a quiet manner concerning matters related to their usual pursuits and experiences, being influenced immediately and markedly by auditory, visual, and sensory impressions. At times the hallucinations are of an alarming nature. Some patients complain of nightmare-like conditions, while others cannot get rid of peculiar hallucinations with regard to certain parts of the body. They have an impression that the head or entire members are shrunken or have disappeared, or, on the contrary, have grown to enormous size and then have become moderate in size.

Some patients exhibit a tendency to get out of bed. Under such circumstances they rarely injure themselves or others. Wild, dangerous delirium, with threats against attendants, attempts at flight, etc., such as are quite commonly observed in cases of typhus fever and variola, are very much less frequent in cases of typhoid fever. In drinkers the mental disturbance generally resembles that seen in alcoholic delirium. True delirium tremens, such as almost always occurs when hard drinkers are attacked with the other severe infectious diseases, as, for instance, fibrinous pneumonia and erysipelas, and which sets in with rapid elevation of temperature, occurs with relative rarity in typhoid fever. At the middle or end of the second week the delirium, which at first was noticeable only toward evening or during the night, begins to persist also during the day. The patients can still at this time be awakened at times, and their attention attracted, and temporarily even be convinced of the groundlessness of their excitement. Soon, however, the abnormal delusions and hallucinations become more and more fixed and consciousness more obscure; and the patients enter upon a state in which

they take no notice of their surroundings, and are day and night in a dreamy state, unconscious of their condition. The features are relaxed, expressionless, even somewhat drawn; the eyes are wholly or half-open, stare directly forward, and are no longer fixed on any definite object. The patients murmur and are quietly restless, but become more actively so toward evening and night. In uncomplicated cases which are not of extreme severity this condition persists into the third week, and even to the end of this week, then, with the beginning of convalescence, undergoing gradual improvement. The patients now become quieter, and again at times conscious; they begin to sleep, and with a reduction of the temperature to the normal or below, often even during the stage of steep curves, they become completely rational, except during sleep, especially at night, when dreams occur that are forgotten with difficulty. It can readily be understood that the disturbances above described exhibit the most diverse variations in accordance with the severity of the attack, and especially in accordance with the temperament of the patient. Irritable persons, children, women, and delicately constituted men naturally exhibit marked disturbance of consciousness, when those of strong nerves are wholly unaffected. In extremely severe cases, however, the most robust individuals may enter, even during the first days, into a state of delirium, which soon, occasionally as early as the beginning or the middle of the second week, passes into deep sopor and into coma. Such patients exhibit the appearance of most profound intoxication, with paralytic relaxation of the entire body —an open mouth with dependent jaw and dry, encrusted mucous membrane of lips, tongue, and mouth, and labored, stertorous breathing. They cannot be completely awakened, and they can only at times, and then by active interference, be induced to make transitory, indistinct statements. Even the swallowing reflex can be elicited only with difficulty. The urine and the stools are generally voided in bed. This condition may, in severe cases, continue throughout the third week, and it may persist even longer, under which circumstances it is especially to be mentioned that the gravity of the general condition is by no means constantly attended with corresponding elevation of temperature. On the contrary, remarkably low temperature with a curve of most irregular course is at times found in association with a most serious and most alarming general condition.

With the more profound conditions of stupor, peculiar motor manifestations of most varied character and severity, from the simplest tremor to spasmodic twitchings and convulsions, are also quite commonly associated. This does not imply that such motor disturbances do not

also occur in cases of moderate and mild course. They are merely more frequent and more pronounced in the severe cases, but they vary with regard to their character, duration, and extent, in accordance with the individual irritability.

Simple tremor occurs in debilitated, irritable persons quite commonly as early as the initial stage. This is the case also in more robust alcoholic individuals. More intense motor disturbances generally appear as transitory manifestations in the later febrile stage in the lighter and moderate cases. They occur early and persistently almost solely in the severe cases, and, as a result, acquire a degree of prognostic significance not to be underrated. Among these more severe disturbances picking at the clothing (floctitation) is first to be mentioned, as it probably is the mildest and least significant from the prognostic point of view. The soporose patient, lying quietly, moving the lips uninterruptedly, murmuring incoherently, pulls constantly with tremulous hands at the clothing and bed-covering. In fact, the analogy with the pulling of wool, the plucking of down, and the like, is most appropriate. At times the tremulous, jerky movements exhibit peculiarities suggestive of the previous occupation of the patient. However marked the manifestations may be in the arms and the hands, there is often no particular movement in the lower extremities, or at most a certain amount of tremor.

With the progress of the disease, and in serious cases, the tremor and floctitation are often soon associated with rather violent muscular twitching, which is also more marked in the trunk and the upper extremities than in the lower extremities. This may displace the true tremor entirely, and appears especially in the forearms and the hands, as a jerking prominence of the muscles and tendons and the related fingers—tendon-jerking (subsultus tendinum). In some cases, especially in patients who are exceedingly restless and have vivid dreams, more or less marked twitching throughout entire muscle-groups may become associated with floctitation and subsultus, especially when a purposeful movement is attempted. This is then highly suggestive of true intention-tremor. At times all these manifestations occur over the trunk, the four extremities, and even the face, naturally always with a preponderance in the arms, so that the clinical pictures acquire close resemblance to a severe choreic condition. Such phenomena were obviously in the minds of those writers who—in my opinion incorrectly—spoke of a combination of typhoid fever with true chorea at the

[1] The occurrence of true chorea minor during convalescence, as has been observed repeatedly by Barthez and Rilliet, and others, and also by myself, naturally has nothing to do with the condition under consideration.

height of the febrile stage.[1] The further supervention in adults of trismus and a tetanus-like condition—grinding of the teeth, tonic contracture of the extremities and of the muscles of the back and the nape of the neck—is quite alarming and, fortunately, not very frequent. Such attacks are more frequent and of slighter significance in irritable children. In adults they are the expression either of a most profound toxic action upon the central nervous system or of especially severe complications, among which meningitis, miliary tuberculosis, and septic or uremic conditions are especially to be mentioned. In children I have observed general convulsions without severe complications, and not rarely the cases terminated in recovery. In adults they are, in any event, extremely rare. If they occurred, I should invariably suspect complications, or raise the question whether the diagnosis of typhoid fever is still to be adhered to.

Because of the variability and the combinations of cerebral and spinal disturbances, especially of the abnormal motor manifestations and the psychic symptoms of depression or excitement, the earlier physicians distinguished a number of different varieties of typhoid fever, to which, naturally, only superficial significance can be attached. The best known of these varieties are the following: "Febris nervosa stupida," that variety in which the patients lie in a soporose state—murmuring, tremulous, with floctitation; and "febris nervosa versatilis," in which, as the name implies, the disturbance of consciousness is associated with especial restlessness, subsultus tendinum, choreiform twitching, active delirium, up to conditions of most marked excitement with attempts at flight and violence.

It has been pointed out, and it must here be emphasized again, that the conditions hitherto described are, as a rule, not dependent upon anatomically demonstrable lesions. I have noted the condition of the brain at numerous autopsies in various stages of typhoid fever. There is present generally some serous infiltration of the cerebral tissue, rarely marked hyperemia or anemia. Especially is there no confirmation for the statement which one hears and reads now and then that conditions of excitement are associated with hyperemia, while the "febris nervosa stupida" is more frequently dependent upon anemia or serous infiltration of the substance of the brain. Marked cerebral edema, with more or less marked dropsy of the ventricles, which is so often made responsible for profound comatose states, I have rarely encountered, and it was then by no means always associated during life with profound stupor.

The opinion of Liebermeister,[2] that the febrile temperature alone

explained the severe general disturbances on the part of the central nervous system which have hitherto been discussed, has not proved entirely satisfactory. It is true that quite generally the previously impaired intelligence is observed to improve and return in the sequence of cold baths, and also that certain complications attended with reduction in temperature, as, for instance, the profuse intestinal hemorrhages from the bowel, already mentioned, have the same effect; but, upon the other hand, the character and the manifestations of cerebral disturbances, especially the varying degree of stupor, do not correspond with the height and the intensity of the fever. On the contrary, the most profound cerebral disturbances may occur with quite low temperature; while cases of afebrile typhoid fever are at times attended with symptoms of most pronounced nervous depression.

Another factor, namely, the action of the toxins upon the central nervous system, is far more important than the temperature. This factor alone, however, does not determine the character and the severity of the disturbances in question. These behave and are modified rather in accordance with the remaining, especially the individual, conditions; on the one hand, in accordance with age, sex, constitution, heredity, and antecedent diseases; and, on the other hand, in accordance with the general condition of the patient or that of individual organs as influenced by the typhoid disease and by its stage.

With reference to age and sex, it can readily be understood that women, children, and the aged react differently than robust, previously healthy men, if all are exposed to the action of similar influences upon the central nervous system. Anemic and plethoric individuals also will exhibit different manifestations. Among conditions present antecedent to the attack of typhoid fever which predispose to profound nervous disturbances are especially neurasthenia, hysteria, and mental or physical injuries of long standing, and, above all, emotional disturbances and conditions of depression, bodily overexertion, excesses in food and toxic substances, such as morphin, bromids, chloral, coffee, tea, and especially alcohol.

Psychoses.—Although the actual mental disturbances occurring in the course of typhoid fever are often directly related to the febrile delirium, and are often not sharply separable from it, and frequently even appear to arise out of it, nevertheless the character and peculiarity of their onset and course render necessary their special consideration.

At times as early as the second, more frequently in the third week, peculiar illusions and delusions and associated abnormal acts stand out prominently in some patients from among the general symptoms of the

febrile stupor, and are worthy of special consideration by reason of their independence and peculiarity. In part they soon subside with the remaining febrile symptoms of the attack of typhoid fever, in part they persist independently and obstinately for a variable length of time after defervescence, and even after convalescence has been completed. As has already been pointed out with regard to the ordinary forms of febrile delirium, the mental conditions under these circumstances are very rarely states of excitement with aggressive tendencies, but more frequently consist in acts and delusions that exhibit the character of mental depression, of fear or anxiety, with or without hallucinations. One patient may occupy himself with groundless self-accusation, and laments a life which, from a religious or other standpoint, has been wasted; another may hear voices or see figures that depress, persecute, or threaten him; and still another may lie rigidly in bed, not eating or drinking or reacting at all, believing himself motionless or even dead. Still others believe they have amassed great fortunes, which they fear they may lose, or they search for and lament the loss of valuables.

Although, as has been mentioned, these delusions often disappear with defervescence, nevertheless they frequently persist thereafter and become fixed far more frequently than in the sequence of most other acute infectious diseases. The mental depression and confusion, or only certain morbid conceptions, may then persist in the presence of an otherwise apparently intact sensorium into the period of convalescence, or even extend far beyond it. Some patients, after they have been out of bed for a long time and appreciate the nature of the disease from which they have recovered and the delirium that was associated with it, are still unable to free themselves from certain imperative ideas. In other respects they make an impression of mental quietude and intelligence, and themselves admit that on one point thought and speech are morbid, but they are constantly irresistibly impelled thereto.

Thus, I observed a young journeyman tailor who was unable to free himself from the belief that a benevolent woman had presented him with a good deal of money, and had concealed it for him behind a closet in the ward. Long after the patient had gotten out of bed this thought could only temporarily be dispelled. Even after he had improved remarkably in physical condition, and mentally appeared entirely clear, he was only half-convinced with regard to his delusion. He had some diffidence in speaking of it, but every now and then, in an unwatched moment, he glanced longingly toward the corner occupied by the promising chest. In another case, a servant-girl, eighteen years old, during the febrile stage was possessed by the delusion that she had been visited by her uncle, who suddenly became so greatly distended as to burst. While during the febrile stage she lamented bitterly the fate of her uncle, she laughed during convalescence at the

thought of his peculiar method of dying, but even after she had been free from fever and out of bed for weeks she could not rid herself of the idea that he had at least died. Another patient, a stone-setter, forty years old, became incessantly excited during the last week of the fever concerning his child, which he thought had been stolen from him by neighbors, and had been cut up and burned upon a sand-heap. The harassing thought followed him into convalescence. Attempts were made without avail to relieve him of this delusion by bringing the child, which was entirely well, to him. A few hours after the departure of the child the delusion would return.

In addition to the form of psychic disturbances just mentioned, those occurring in individuals who have hysteric tendencies deserve special mention. I have observed, principally in young women and men, conditions of more or less marked catalepsy occurring as early as the second week, and from this time on to the period of defervescence—only exceptionally in the afebrile period. The patients lie motionless and completely unresponsive, apparently unconscious, with eyes wide open, without sleeping day or night, taking no food or drink, and voiding the urine and stools in bed. Such cases are considered by the inexperienced as of especial severity; and the most profound typhoid intoxication with deepest coma, or even meningitis, or extensive meningeal hemorrhage, is assumed to exist. If, however, such patients are observed more critically, it will be found that they react to very strong auditory and visual stimuli, even to a loud call, with a sigh, increased frequency of winking, co-ordinated voluntary movements of the eyes, sudden acceleration of pulse-frequency, or the development of an emotional erythema. One can see that the patients, though conscious, have their powers of expression greatly inhibited, and lie in a state of plastic flexibility which is one of the most certain signs of the existence of the cataleptic state. After this clinical picture has been seen a few times in its most characteristic form, it will become apparent that slighter degrees of hysteric stupor, with more or less marked catalepsy and plastic flexibility of the muscles, are not at all rare in predisposed individuals. Far less common than the foregoing disturbances are, in my experience, cases of actual hysteric insanity. In those patients in whom I have observed this condition it did not occur during the febrile period, but in the earlier stage of convalescence.

Among 4000 cases of typhoid fever, I have observed more or less well-developed psychoses at the height of the fever or during convalescence in 42. In 35 cases the mental disturbance occurred during the febrile stage, in 2 during the period of irregular temperature, and in 5 during convalescence. These patients were exclusively adults, and women were more frequently affected than men. I noted 27 of the former and 15 of the latter. In 32 of the cases states of melancholia or quiet delirium were present, with

or without hallucinations; while in the remainder, conditions of more or less marked excitement and even maniacal states were observed. With regard to hysteropsychic disturbances, and especially the cataleptic variety, which I have observed far more frequently, I have, unfortunately, no statistics.

Owing to the field of my activity, the conditions that I have hitherto been able to describe from my personal observation belong almost exclusively to the period of the actual disease and the patient's residence in the hospital up to the time of complete recovery and dismissal. Alienists are, however, familiar with cases of mental derangement that develop much later, but which occur undoubtedly in consequence of the attack of typhoid fever. These cases following typhoid fever are quite common as compared with those following the other infectious diseases, and they often exhibit marked severity and obstinacy and protracted duration. Under these circumstances the condition is usually one of depression or melancholia, with self-accusation, fear and anxiety, stupor, and often hallucinations; though not much less common are quieter conditions, with peculiar ideas, especially delusions of grandeur; and more rarely, commonly, conditions of excitement up to the point of mania or acute dementia (Krafft-Ebing[1]).

The prognosis of typhoid psychoses appears in general to be favorable. Of the cases under my observation, previously mentioned, which developed during the febrile period and early in convalescence, only 2 persisted beyond the period of convalescence; the one terminated in recovery after six months, the other, after nine months. The severer psychoses also, which necessitate treatment in hospitals for the insane, appear in general to pursue a not unfavorable course. According to Krafft-Ebing, the prognosis is almost always favorable in conditions of quiet delirium. Quiet or even stuporous melancholia may last for months, but in 65 per cent. of the cases it terminates in recovery; recovery from conditions of maniacal excitement and from acute dementia occurs in from 50 to 65 per cent. of the cases.

Before leaving this section it appears worthy of mention that in exceedingly rare cases marked psychic disturbances may be present at the very onset of the attack of typhoid fever, even as early as the first day, or, at least, at the beginning or the middle of the first week, and they may then exhibit the characteristics of an independent disorder. Such cases are well calculated to give rise at first to error in diagnosis. I have observed 2 cases in which patients of this kind were at once sent to a hospital for the insane, where the true nature of the disease first became manifest when, after the lapse of eight and twelve days,

[1] See the text-books on psychiatry by Kraeplin, Krafft-Ebing, and others.

respectively, enlargement of the spleen, diarrhea, and distinct roseolæ made their appearance.

The fact that the previously insane, if exposed to the possibility of infection, are attacked by typhoid fever almost as frequently as healthy individuals, should likewise be considered in this connection. Under such circumstances the course and termination of the disease vary, as in other cases, in accordance with the constitution of the patient, the severity of the infection, and such complications as may be present. It has been stated that in a number of such cases after recovery had taken place from the attack of typhoid fever considerable improvement, or even complete recovery from the psychosis, occurred. Unfortunately, this is the exception and not the rule.

Nervous Disturbances with Demonstrable Organic Lesions.—Although the affections of the nervous system thus far described have been classed separately from a number of others which are known to be dependent upon macroscopically and microscopically demonstrable anatomic lesions, it will readily be understood that distinction is not final, but is only an expression of the present state of our knowledge. Without doubt the so-called functional disturbances will also in the course of time become more and more accessible to anatomic investigation.

Alterations in the Meninges.—Among these, meningitis, which is usually not confined to the brain alone, but far more frequently is cerebrospinal in distribution, should be mentioned first on account of its importance. During certain epidemics of typhoid fever and in certain places profound nervous disturbances, which can be ascribed only to acute inflammatory processes involving the membranes of the brain and the spinal cord, occur in the course of the disease with varying frequency, at times in large numbers of cases. At the onset and during the course of these cases, the stupor, in contrast with the remaining symptoms, is slight, if present at all. Under such circumstances the patients complain—as is unusual at the height of the attack—of most severe, persistent headache, vertigo, roaring in the ears, and photophobia. At the same time or soon after sacral pain and pain at the back of the neck set in, with painful rigidity of the vertebral column, especially the cervical portion, and characteristic opisthotonos. Even touching or movement or concussion of the dorsal and sacral cervical region induces loud expressions of pain. In addition, twitching and pains in the extremities are present, and great tenderness of the skin and muscles on pressure. The patients are deprived of rest and sleep by day and night, and complain and groan constantly. The sensory as well as the tendinous

reflexes are generally considerably increased, and the elicitation of the latter is especially painful to the patient. In some cases there is polyuria, with difficulty in micturition. Facial herpes, which under other circumstances is rare in the course of typhoid fever occurs with remarkable frequency. This symptom-complex may occur in both severe and mild cases. The intensity of the attack, it should be expressly pointed out, is not proportionate to the severity of the meningitic symptoms. A mild attack of typhoid fever may be attended with severe and, conversely, a severe attack with slight, at times transitory, meningitic manifestations.

The duration of meningitis during typhoid is exceedingly variable. At times it is from four to twelve days; at other times it persists throughout the greater portion of the febrile period. Occasionally it even appears to prolong the latter considerably. I have observed cases of from three to three and a half weeks' duration. Bernhard[1] also refers to a case of twenty days' duration. I have never observed renewed appearance of the meningitic symptoms during a relapse of typhoid fever.

I have often had opportunity for anatomic investigation of cases of typhoid fever which had showed symptoms of cerebrospinal meningitis, both those in which the symptoms referable to the central nervous system were slight as compared with the symptoms to which death was directly attributable, as well as those in which death undoubtedly resulted directly from cerebrospinal meningitis. The first group is characterized by the slight, almost negative, anatomic evidence. One may find at most more or less marked hyperemia of the soft membranes of the brain and the spinal cord, with or without turbidity. A marked advance in the interpretation of such cases is furnished by the interesting observation of Fr. Schultze[2] that, although under such circumstances no coarse anatomic lesions appear to be present, nevertheless small-cell infiltration is demonstrable in the membranes of the brain and spinal cord in the course of the vessels, and also microscopic foci of similar character in the tissue of the central nervous system. In 5 cases presenting unusually well-marked cerebrospinal symptoms, which were doubtless the direct cause of death, I was able at autopsy to demonstrate the familiar anatomic picture of purulent cerebrospinal meningitis. In 3 of these cases especially the pia-arachnoid, particularly on the convexity and lateral aspects of the brain, was involved, and in less degree that of the spinal cord; while in the 2 other cases the membranes of the brain and the spinal cord were equally involved.

[1] *Berlin. klin. Woch.*, 1886, No. 50. [2] *Loc. cit.*

In these cases the condition had developed between the second and the fifth week in the course of attacks of typhoid fever of severe onset, with in part an unusually long febrile stage, and the disease had terminated fatally after a duration of from six to ten days. What relation these cases bear to those previously mentioned in which there was no suppuration must remain uncertain until further thorough bacteriologic investigations have been made. To me it seems probable that in part at least they differ from one another only in degree. In any event, I was able in my purulent cases to exclude with certainty any underlying complications, either general septicemia or purulent affections in the immediate vicinity of the skull (ear, nose).

My cases, which were observed at the beginning of the decade 1880–89, were not thoroughly examined bacteriologically. No doubt various micro-organisms, possibly also mixed infection, will, in the course of time, be found to be the cause of the meningitis. In this connection attention will have to be directed especially to Staphylococcus and Streptococcus pyogenes, to pneumococci, and particularly also to the specific micro-organisms of epidemic cerebrospinal meningitis. I would direct attention particularly to this point, because in Hamburg on two occasions I observed the striking fact that severe meningitic disturbances in the course of typhoid fever were especially well marked and frequent at a time when idiopathic cerebrospinal meningitis raged in the city. Besides those cases probably due to the pyogenic cocci or meningococci, it is now quite well established that a certain number of cases are due to the localization of the typhoid bacillus itself in the meninges. Within the past few years a number of such cases have been reported, and have lately been collected by Hofmann.[1] Leaving out of consideration the doubtful cases, at least 10 have been reported in which the typhoid-bacillus was definitely obtained from the meningeal exudate in pure cultures. Ohlmacher[2] has reported 2 such cases in which the typhoid-bacillus was most carefully identified, and the histologic changes described. A positive observation has also been made by Quincke,[3] who saw death occur in a workman on the fourteenth day of an attack of typhoid fever, amid symptoms of severe cerebrospinal meningitis, and was able to demonstrate the bacillus of Eberth in the meningitic exudate as the sole pyogenic agent. In most of the cases reported as due to Bacillus typhosus, the condition has been one of a purulent leptomeningitis. In the case reported by Hofmann, however, there was simply an increase in the amount of cerebrospinal fluid with a round-cell infiltration about the vessels of the pia and arachnoid. The meningeal symptoms, however, were most marked, with clonic convulsions during the six hours preceding death. This case brings forth the interesting question as to how often the less-marked meningeal symptoms, frequently seen in typhoid, are due to the presence of the typhoid-bacilli in the brain, cord, or cerebrospinal fluid. An interesting case in this connection is one which occurred lately at the Johns Hopkins Hospital, in which, following quite marked meningeal symptoms, including stiffness of the neck and delirium, a lumbar puncture was performed, and from the cerebrospinal fluid, which was macroscopically quite clear and con-

[1] *Deutsch. med. Woch.*, July 12, 1900. [2] *Phila. Med. Jour.*, August 28, 1897.
[3] Stühlen, "Ueber typhöse meningitis," *Berlin. klin. Woch.*, 1894, 15.

tained only a very few pus-cells, the typhoid-bacillus was obtained in pure culture. After several days the meningeal symptoms entirely cleared up. That in the future resort will more frequently be had to spinal puncture, which is also not rarely indicated for therapeutic purposes, for the etiologic explanation of the meningitic symptoms, need only be indicated at this place. It is an interesting fact that meningitic symptoms occasionally occur with great frequency in certain epidemics and in certain places, and that they may then occur in groups of individuals in the same house or the same family. Thus, I observed recently in the Jakobsspital 5 nurses stricken in quick succession with typhoid fever, probably in consequence of infection through milk, and in all the cases meningitic symptoms predominated from the first week to such a degree that in the first case the diagnosis was as a result not a little obscured.

The fact that cerebrospinal symptoms occur in a considerable number of cases in the late febrile period, in the stage of irregular temperature, and the first part of convalescence, was long ago noted by Ducheck, Griessinger, Buhl, Leyden, Erb, and myself. Undoubtedly, these cases of meningitis arising in the later period of the disease are among the more severe, and they attracted attention therefore relatively early. The fact, however, that marked meningitic symptoms may appear in the earliest period of typhoid fever, and may so thoroughly dominate the clinical picture that the greatest difficulty in diagnosis may arise, was practically unknown before I called attention to it.[1]

I have exceptionally observed cases in which remarkably severe headache with rigidity of the neck and hyperesthesia existed even during the period of incubation of typhoid fever. More frequently I have observed the symptoms in question appear on the first or second day after the commencement of the fever, at times naturally suggesting genuine cerebrospinal meningitis, and the real nature of the condition being recognized only when enlargement of the spleen, diarrhea, and roseolæ appeared at the end of the first or the beginning of the second week of the disease. Undoubtedly, if one wishes to classify such cases, they might be designated meningotyphoid.

I have also observed meningitic symptoms appear on all the subsequent days of the first week as well as in the second week. At times their onset was marked by a chill or by repeated chills, and the surprising development of facial herpes. I have observed these cases of early occurrence far more frequently than those that set in during the

[1] *Sitzungsbericht d. Cong. f. inn. Med.*, Bd. v., S. 469; and F. Wolff (Report from my department in the Hamburg General Hospital), *Deutsch. Arch. f. klin. Med.*, Bd. xliii. Fritz alone (*Études cliniques sur diverses sympt. spinaux observ. dans la fièvre typhoïde*, Paris, De la Haye, 1864) had referred to this condition before I did. This latter publication is but little known; my own attention was directed to it by Bernhard only after the appearance of my own paper.

third week or later. They appear to be more varied with regard to severity and course, but, on the whole, milder than the latter.

Symptoms of meningitis during the course of an attack of typhoid fever are seen almost exclusively in young individuals, in males less commonly than in women and children. I have observed this condition only twice in patients over thirty-five years old. Among 38 cases of which I have notes, 23 were in women, 10 in men, and 5 in children.

If, as has already been mentioned, in cases of typhoid fever with profound stupor, symptoms of meningitis develop, especial attention should be directed to the possibility of the symptom being due to a primary purulent process. Thus it is not rare for existing old inflammation of the middle ear to undergo exacerbation during, and perhaps in consequence of, an attack of typhoid fever, with subsequent extension of the process to the meninges. I have personally observed this in a number of instances, and in 2 cases was compelled to recommend immediate trephining of the mastoid process. Meningitic symptoms have been observed also in the sequence of recent suppurative inflammation of the middle ear, which was dependent upon typhoid fever (Louis, Peacock [1]).

Cerebrospinal meningitis is quite rare as one of the manifestations of septicemia complicating typhoid fever. I have observed 2 cases in which such a condition developed during convalescence in consequence of pyemia, following extensive, deep bed-sores. In one of these cases purulent sinus-thrombosis developed, and in the other an abscess of the brain as large as a pigeon's egg, and two smaller purulent foci in the external layer of the hemisphere, were present.

I have observed tuberculous meningitis exceptionally, and only during convalescence, then occurring either as the cerebrospinal form alone or as one of the manifestations of a complicating general tuberculosis. Attention has been called to this by other writers also, as, for instance, Trousseau.[2]

Meningeal hemorrhage not of inflammatory origin occurs, on the whole, quite rarely. It is either circumscribed or extends over a considerable extent, mainly upon the surface of the brain. The circumscribed hemorrhages, when they give rise to symptoms at all, fall into the category of focal lesions. They may then give rise to hemiplegia, especially cortical monoplegia with muscular twitchings upon one side or in circumscribed areas; at times there is aphasia. Less commonly the latter occurs alone. Extensive meningeal hemorrhage has been observed but exceptionally. I have personally seen 2 cases in markedly alcoholic men of middle age who presented a hemorrhagic

[1] *Med. Times and Gaz.*, 1856. [2] *Loc. cit.*

course of the disease in general. Death occurred in one at the end of the second, and the other in the middle of the third, week. In both the symptoms set in in an apoplectiform manner, and they persisted for two and three days, respectively, until death.

Alterations in the Cerebral Tissue and its Vessels.—It has been mentioned in the anatomic section that symptoms dependent upon coarse lesions of the cerebral tissue and its vessels are not frequent. When they are present, they occur principally during the later stages of the disease, in the last part of the febrile period, during convalescence, or even later, so that they may with especial propriety be designated sequels. We have observed hemorrhages, embolism, and thrombosis of the large, moderate-sized, and small cerebral vessels, with circumscribed and profuse softening, and rarely abscesses, as anatomic features. Among the clinical phenomena to which they give rise, and which often during life are difficult of correct interpretation with regard to the anatomic basis, hemiplegia, with facial and hypoglossal paralysis, and right-sided palsy, occasionally with aphasia, may be pointed out.

I have personally observed 2 cases of this character. In the one, which terminated fatally in the course of eighteen hours, the condition was dependent upon recent hemorrhage into the left lenticular nucleus and its vicinity; while in the second case, which likewise terminated fatally in the course of a few days, embolism of the left Sylvian artery was present. A case probably susceptible of a similar explanation has been reported by Clarus.[1] Two other cases of right-sided hemiplegia with aphasia and choreiform twitching, particularly in the arms, which were under my observation, terminated in complete recovery. I am uncertain whether hemorrhage into the cerebral tissues or into the meninges was the underlying condition in these cases. Other writers also, especially Griessinger,[2] Jackson,[3] Benedikt,[4] Berger,[5] Nothnagel,[6] and Strümpell,[7] report cases of cerebral hemorrhage in the course of typhoid fever.

Osler[8] has reported the case of a young man who, during a mild attack of typhoid fever, on the ninth day of his illness suddenly developed general bilateral clonic convulsions, which, though general, were more intense on the right side. The convulsions continued at intervals up to his death, ten hours later. At autopsy there was found thrombosis of the ascending parietal and parietotemporal branches of the middle cerebral artery. In a second case, that of a man aged forty-six, in the third week of a moderately severe attack of typhoid fever, there was a gradual onset of paralysis of the left side. Death occurred four days later, and at autopsy an area of thrombotic softening in the internal capsule was found. In two other cases of hemiplegia with sudden onset, one of them with convulsions, there was recovery

[1] *Inaug. Diss.*, Würzburg, 1874, and *Jahrb. f. Kinderh.*, Bd. vii.

[2] *Loc. cit.*

[3] *Edinb. Med. Jour.*, 1867.

[4] *Wien. med. Presse*, 1868.

[5] *Berlin. klin. Woch.*, 1870.

[6] *Deutsch. Arch. f. klin. Med.*, 1872. The paper of Nothnagel contains a complete collection of the literature up to 1872 on the nervous sequels of typhoid fever.

[7] *Lehrbuch.*

[8] *Johns Hopkins Hosp. Rep.*, vol. viii.

from the fever with only partial recovery from the hemiplegia. Welch[1] mentions 4 other fatal cases of thrombosis of the middle cerebral arteries. Hawkins[2] has made a most careful study of hemiplegia in typhoid and has collected 17 cases from the literature. Two of the cases died, and in both of these there was a thrombosis of the middle cerebral artery.

I have observed abscess of the brain but twice in the course of typhoid fever. The cases were those previously referred to (p. 121), which were dependent upon septicemia and were attended with purulent meningitis of the convexity; the clinical symptoms and course being those of the latter condition.

In addition to aphasia dependent upon profound disease of the brain, disturbances of speech of cortical origin in the course of typhoid fever are deserving of special mention, since they form a special group and are characterized by the fact that they occur alone or at least with only circumscribed paralysis, and generally terminate in recovery with comparative rapidity. If they are attended at all with motor disturbances in the trunk or the extremities, these are generally of the character of tremor or ataxia. On account of the rapid, favorable course, these cases can hardly be attributed to other causes than to slight anatomic alteration not permanently injuring the speech-centers. It is peculiar, further, that these cases occur almost solely during convalescence, and especially in children and young persons.

I have personally observed the following cases of this character: The first occurred in an irritable, spoiled girl ten years old, with a neurotic predisposition, who, during convalescence from a severe and protracted attack of typhoid fever, was suddenly seized on the fourth afebrile day with almost complete loss of speech after slight disturbances had been noticed on the previous day. The condition was one of ataxic aphasia. Consciousness and the remaining functions of the body were preserved; I would note especially that no paralysis of the extremities developed. After this condition had persisted unchanged for two weeks the disorder of speech began to improve, and after the lapse of five weeks complete recovery had ensued.

The second case occurred in a merchant's apprentice, fifteen years old, whose mother had died in a hospital for the insane, and who prior to the onset of a severe attack of typhoid fever had engaged in excessive physical activity; he likewise was suddenly seized at the end of the third week of the disease, in the stage of steep curves, in the daytime, with ataxic aphasia which was accompanied by considerable transitory elevation of temperature. Consciousness remained wholly undisturbed from the beginning of the disorder. Improvement began within a week, and in the course of three and a half weeks almost complete recovery had taken place, except for slight difficulty in forming words and syllables, which difficulty persisted for months. While still in bed, and after getting up, ataxic disturbances were demonstrable in the lower extremities; sensation, however, being undis-

[1] *Abbutt's System of Medicine*, 1899, vol. vii., London.

[2] *Clin. Soc. Trans.*, vol. xxvi.

turbed and the patellar tendon-reflexes normal. These ataxic disturbances had also completely disappeared in the course of about ten weeks.

References in the literature to this peculiar variety of aphasia date back to a comparatively early period. After Klusemann,[1] Baudelocque,[2] Weise,[3] and Trousseau[4] had called attention to it, Clarus[5] and Kühn[6] engaged in a more thorough study of the subject. Among 28 cases collected by Kühn, 25 were in children, and the remaining 3 were also in young persons. Except for the presence of ataxia in 2 cases, Kühn does not refer to any other associated nervous disturbances in his cases. Death occurred in but 1, while complete recovery ensued in the remainder in from three to six weeks, rarely later.

Other forms of cerebral monoplegia involving the arms, the legs, or only certain groups of muscles, have likewise been recorded exceptionally in the literature.[7] They have, however, not been carefully investigated, and the condition, especially in the older cases, cannot be distinguished from certain varieties of peripheral neuritis.

Hemorrhage and inflammatory softening of the medulla oblongata deserve special mention.

The case of this kind reported by Kümmell[8] is interesting, as it pursued the course of an acute ascending paralysis, as did also the case of softening of the bulb with capillary hemorrhages which was under my observation (see Anatomy, p. 121). The latter occurred in a man, thirty years old, who was brought to the hospital from the harbor, profoundly ill, in a comatose state, without any history. There were high fever, moderate meteorism, palpable enlargement of the spleen, rigidity of the neck, and stiffness of the entire vertebral column, hyperesthesia of the whole body, extensive labial herpes, but no roseolæ. Death occurred on the second day of residence in the hospital. The autopsy disclosed the lesions of an attack of typhoid fever at the end of the third week, and, in addition to the bulbar lesions mentioned, marked hyperemia of the pia-arachnoid of the brain and the spinal cord, with slight turbidity of the cerebrospinal fluid.

The cases reported by Eisenlohr[9] may also best be cited here. He described 3 cases of conspicuous involvement of the bulbar nerves in the course of typhoid fever, which were characterized especially by dysarthria, paralysis in the distribution of the facial nerve, and in part of the motor distribution of the trigeminal nerve (weakness or spasm in the masseter muscles). All 3 patients exhibited evidences of profound infection and were attacked with the nervous symptoms during the febrile stage. In 2 cases recovery ensued with comparative rapidity, while death occurred in the third, and the autopsy disclosed as the cause for the trouble invasion of the medulla oblongata by organisms resembling Staphylococcus citreus and by peculiar bacilli. As in my case of invasion of the spinal cord by typhoid-

[1] *Preuss. med. Vereinszeitung*, 1854, No. 12.

[2] *Compt. rend. de la Soc. de Biol.*, 1860.

[3] *Jour. f. Kinderh.*, 1864.

[4] *Gaz. des Hôp.*, 1864.

[5] *Loc. cit.*

[6] *Deutsch. Arch. f. klin. Med.*, Bd. xxxiv. This contains also detailed reference to the literature.

[7] See Nothnagel, *loc. cit.*

[8] *Zeit. f. klin. Med.*, Bd. ii., Heft 2.

[9] *Deutsch. med. Woch.*, 1893, No. 6.

bacilli, so also in Eisenlohr's fatal case, scarcely any actual destruction of tissue in the medulla oblongata was demonstrable.

A case under my observation in the year 1884, to which my attention was again called only after the appearance of Eisenlohr's report, may be included in this group. It occurred in a servant-girl, nineteen years old, suffering from an attack of typhoid fever of moderate severity. At the end of the third week disturbances of speech similar to those described by Eisenlohr suddenly appeared. The sensorium was clear, there was no other paralysis, and the muscles of mastication were, according to my notes, intact. Complete recovery gradually ensued in the course of four and a half weeks.

Certain cerebral nerves appear to be involved but rarely in the course of typhoid fever. Facial or hypoglossal paresis is mentioned exceptionally. Possibly the few reported cases of paralysis of accommodation during convalescence (Gubler,[1] Kittel[2]) belong in this group.[3] The occurrence of paralysis of the vocal cords is, in part at least, to be included here; while another portion of the cases are attributable directly to local disease of the larynx, such as inflammatory swelling of the mucous membrane and the submucous tissues, and ulceration (see p. 239 and the succeeding pages). The condition present in the first class is undoubtedly one of innervational disturbance in the distribution of the recurrent laryngeal nerve. Bilateral or unilateral paralysis of all the muscles supplied by this nerve has but rarely been observed; more frequently, paralysis of certain groups of muscles, especially of the abductors of the vocal cords, and somewhat less commonly that of the adductors.

The earliest reported case is probably the well-known one of Traube,[4] in which paralysis of the vocal cords, together with other severe nervous manifestations, developed during the first week of the disease. Türk and Nothnagel (who gives the earlier literature) have reported similar cases. An extensive study has recently been published by Boulay and H. Mendel.[5] Lublinsky[6] also deserves credit for his investigation of this subject. Other cases,[7] especially of paralysis of the crico-arytenoideus posticus, have been reported by Lüning,[8] Rehn,[9] Jourasse,[10] and Pel.[11]

Sensory disturbances in the distribution of the cranial nerves appear to be even more infrequent than motor disturbances. Trifacial neu-

[1] *Arch. gén. de Méd.*, 1860. [2] *Wien. med. Zeit.*, 1865.

[3] See further at a later page the dissenting opinion of Förster and Knies (p. 285).

[4] *Gesammelte Beiträge*, Bd. ii. [5] *Arch. gén. de Méd.*, Dec., 1894.

[6] *Deutsch. med. Woch.*, 1895, No. 26.

[7] The monograph of Przedborski (Volkmann's *Sammlung klin. Vortr.*, May, 1897, No. 182), which appeared while this volume was in press, attempts to show that paralysis of the vocal cords in the course of typhoid fever is a quite frequent occurrence. Further observations will be required to determine to what extent this striking statement, which is contrary to the opinions hitherto held, is correct.

[8] *Langenbeck's Archiv*, Bd. xxx. [9] *Deutsch. Arch. f. klin. Med.*, Bd. xviii.

[10] *Deutsch. med. Woch.*, 1879, Nos. 14 and 15. [11] Virchow-Hirsch, 1879.

ralgia, persisting into convalescence, is referred to by various observers, among others by Strümpell. I have personally observed no case of this character.

Affections of the Spinal Cord.—These also are doubtless quite rare, much rarer than was believed at a time when peripheral neuritis and its clinical manifestations were little known, and paraplegia, particularly of the lower extremities, was, without further consideration, classed among the spinal diseases. For this reason the earlier literature[1] cannot be accepted without qualification. Cases of myelitis definitely confirmed by anatomic observations have, however, been observed in a number of instances. Such a case was recently observed in my clinic.

I may at this point refer also to the case described by me in 1886 (see also p. 121), in which a strong man, thirty-one years old, died in the first half of the second week of an attack of typhoid fever, with most marked symptoms of acute ascending (Landry's) spinal paralysis (or, if that term be preferred, myelitic acutissima). Microscopic and careful bacteriologic examination of the spinal cord disclosed beyond doubt invasion by typhoid-bacilli, which could be demonstrated both in transverse sections and in cultures.

A case almost identical with my own had been described by Leudet[2] in 1861. His patient was seized, in the third week of a mild attack of typhoid fever, after she had actually entered upon convalescence, with acute spinal paralysis, ascending from the lower extremities, which terminated fatally in the course of seven days, with symptoms of asphyxia, and in which consciousness was preserved throughout.

A somewhat similar case, proving fatal at the end of eighteen hours, has been reported by Schiff.[3] The examination of the cord in this case showed an acute hemorrhagic transverse myelitis at the level of the fourth and fifth cervical segments. Cultures in this case were negative.

I know of no other similar case. They thus appear to be quite rare. Whether in future cases bacilli will be demonstrable, as they were in my case, in the tissue of the central nervous system, cannot be stated in advance, and their presence is possibly only of subordinate significance. It is readily conceivable that toxic effects of especial severity may give rise to similar symptoms. It is noteworthy, further, that quite similar severe conditions of acute ascending paralysis have been described in the course of other infectious diseases also; for instance, in cases of variola by Gubler, Bernhardt, and others, by Landry in cases of diphtheria and cholera, and by the latter and Leyden in cases of pneumonia.

Still other clinical pictures undoubtedly of spinal origin have been observed. Thus Westphal,[4] upon the basis of a case terminating in recovery, has called attention to a peculiar variety of marked ataxia following typhoid fever, associated with tremor in the lower extremities, without actual impairment of gross strength or of sensibility. The

[1] See the monograph of Nothnagel. [2] *Gaz. méd. de Paris*, 1861, No. 19.
[3] *Deutsch. Arch. f. klin. Med.*, 1900, Bd. lxvii.
[4] *Arch. f. Psych. u. Nerv.*, Bd. iii., Heft 2.

condition was associated with disorders of speech of the bulbar type resembling those attending multiple sclerosis. A similar condition has apparently been observed by Eichhorst and Strümpell.[1]

Multiple insular sclerosis has also been observed clinically, and in a number of instances anatomically, in cases of typhoid fever. In comparison with its occurrence in other acute infectious diseases, this condition appears to be not extremely rare in typhoid.

Pierre Marie[2] observed, among 25 cases of insular sclerosis dependent upon infectious diseases, 11 in which this condition was a sequel of typhoid fever. The military-sanitary report of the French campaign of 1870–71 likewise refers to similar cases. Ebstein[3] was one of the first to call attention to this interesting complication. His patient exhibited bulbar disturbances of speech and ataxia, without any other impairment of motor power or sensation. Anatomic examination disclosed insular gray degeneration of the spinal cord and the bulb.

Cases of spinal paralysis of childhood have been mentioned by a number of writers as of rare occurrence in the course of or toward the close of the attack of typhoid fever. The earlier reports are not based upon anatomic examination.[4] Recently Richardier[5] has published a report of 2 cases of this kind, which, however, I have not yet been able to obtain in the original.

In concluding this section, a few words may be stated with regard to the state of the reflexes in cases of typhoid fever. In Germany only Strümpell has hitherto discussed them, while French investigators appear to have made extensive observations. I have personally made some observations at various times and in an irregular manner, but which, nevertheless, have yielded certain data. Like Strümpell, I have found in severe cases in patients who were greatly reduced, toward the end of the fever or during convalescence, marked exaggeration of the patellar tendon-reflexes. Often I was even able to elicit slight or even a marked Achilles tendon-reflex. In mild and moderately severe cases the patellar tendon-reflex is exceedingly variable at the height of the disease. Rarely it is entirely wanting, but in the great majority of cases it remains normal or is somewhat enfeebled. Toward the end of the attack and during the period of convalescence, even in mild cases, I have observed now and again moderate exaggeration of the reflexes.

[1] Mentioned in their text-books.

[2] *Vorlesungen über Krankheiten des Rückenmarks*, German translation by Weiss, Vienna, 1894.

[3] *Deutsch. Arch. f. klin. Med.*, Bd. ix. and x.

[4] See, for instance, Benedikt, *Lehrbuch der Nervenkrankheiten.*

[5] *Thèse*, Paris, 1885, cited by Marie, who appears himself to have made no similar observation.

In children I have observed enfeeblement and absence of the reflexes with relatively greater frequency than in adults.

General Neuroses.—Chorea minor, to which Rilliet and Barthez have called attention, is rarely mentioned as a sequel of typhoid fever.

I have personally observed a woman, thirty-one years old, who acquired severe, chronic chorea minor in her twenty-fifth year, during convalescence from typhoid fever. The history relating to this point was based upon the statement of a most trustworthy physician, who treated the woman during her attack of typhoid fever. I have also observed choreic conditions in 3 children in the course of typhoid fever. In one case, which developed during convalescence from an attack of typhoid fever prolonged over six weeks, the condition was principally one of unilateral choreic twitching, recovery from which took place in the course of six weeks. The second child, in whom the characteristic twitching appeared during the third week of the attack of fever, recovered two and a half months after convalescence. With regard to the third case I have no further notes.

In a case at the Johns Hopkins Hospital of a young woman who had had chronic chorea for a year before the onset of typhoid fever, there was a disappearance of the choreic movements during the height of the fever, with a gradual return during convalescence.

Of other neuroses, reference may be made to the occurrence of paralysis agitans (Benedikt). I have personally observed this complication but once, in a woman, forty-six years old, occurring late during convalescence, and then persisting without change. Exophthalmic goiter has been mentioned by Waldenburg as a sequel of typhoid fever. Eichhorst and others have seen diabetes insipidus occur in connection with typhoid fever. I have personally encountered no case of either complication. In 1889, Gibney described a sequel of typhoid fever which he called "the typhoid spine," and which he regarded as a perispondylitis. Osler has since reported a number of quite similar cases, most of which he regards as examples of a painful neurosis, analogous to the painful condition met with in the "hysteric spine" and the "railway spine." It usually comes on during convalescence in neurotic individuals, and the slightest bending movements of the back may elicit expressions of the most acute pain.

Lesions of the Peripheral Nerves.—The peripheral nerves, especially those of spinal origin, appear to be involved more frequently than the spinal cord. As in other infectious diseases, the condition is usually one of neuritis, which may manifest itself as an atrophic paralysis of certain muscles, muscle-groups, or an entire extremity, or even as a paraplegia, or, in still wider distribution, with the clinical picture of pronounced polyneuritis.

Both the clinical and the anatomic knowledge of neuritis itself, and the observation of its occurrence in the course of typhoid fever, are

still comparatively recent. It is possible, however, as has been previously intimated, that not a few cases of paralysis supposed to be of spinal origin were actually due to neuritis. In this category belong the cases of atrophic paralysis in which the muscles exhibited a reaction of degeneration and loss of electric irritability, with tenderness on pressure, associated with subjective and objective disturbances of sensation, and in which, even in advanced cases, recovery or material improvement took place. Leyden early referred to the probability of the more frequent occurrence of peripheral neuritis in cases of typhoid fever in his book on *Diseases of the Spinal Cord.* Neuritic paralysis occurs less frequently at the height of the disease than toward its close, and into late convalescence. I have observed neuritic paralysis of both lower extremities develop as late as the twenty-ninth day after defervescence, after the patient had already gotten out of bed. Such late occurrence is, it is true, still more usual after diphtheria than after typhoid fever.

Paralysis due to neuritis, both when extensive and more particularly when circumscribed, appears to involve the lower extremities more frequently than the trunk and the upper extremities when it occurs in cases of typhoid fever. Among my cases are 2 of paralysis in the peroneal region, and 1 each of paralysis of the adductors of the thigh and of the quadriceps. Paralysis of the latter has been mentioned also by Krafft-Ebing,[1] as well as by Nothnagel and Surmay.[2] Of other forms of neuritic paralysis, that of the long muscles of the back, the serratus (Eulenburg), as well as that of the ulnar and the median, has been recorded in the literature.

Among the cases of paraplegia of the lower extremities, 4 cases reported by Nothnagel deserve mention. Alexander[3] has also reported such a case in an adult. I have personally seen neuritic paralysis of both lower extremities in a boy, eight years old, which began as early as the second week of a mild attack of typhoid fever, and from which recovery ensued after a duration of six months. Cadet de Gassicourt[4] and Henoch[5] had previously called attention to this complication during childhood. Finally the fact may be mentioned that neuritic processes may develop also without atrophic paralysis; in fact, almost wholly without clinical manifestations, as Buhl and Bernhardt[6] and recently Pitres and Vaillard have demonstrated anatomically.

Sensory disturbances on the part of the spinal nerves are not quite so frequent as the motor paralyses. Cutaneous anesthesia is mentioned by Duchenne,[7] Griessinger,[8] Gubler,[9] and subsequently by numerous other writers, as, for instance, Krafft-Ebing[10] and Bäumler.[11] It

[1] *Beobachtungen und Studien über Abdominaltyphus*, 1871.
[2] *Arch. gén. de Méd.*, 1865, T. 1.
[3] *Deutsch. med. Woch.*, 1886.
[4] *Traités clir. des mal. de l'enfance*, 1882, T. ii.
[5] *Charité-Annalen*, 1892.
[6] *Loc. cit.*
[7] *De l'électrisat. locale*, 1861.
[8] *Loc. cit.*
[9] *Loc. cit.*
[10] *Loc. cit.*
[11] "Klinische Beobachtungen über Abdominaltyphus," *Deutsch. Arch. f. klin. Med.*, Bd. iii.

has occurred also in several instances in my experience, and is manifested in part by impairment or complete abolition of sensation throughout the distribution of certain nerves or in quite circumscribed areas of the skin. So far as I can recall, the various forms of sensation were equally impaired. Cases of cutaneous anesthesia, such as are observed during convalescence, especially in adult females, involving extensive areas, without being confined to definite nerve-areas, appear to belong to the group of hysteric disorders, which are not rarely encountered in the sequence of typhoid fever.

More frequent than the simple derangements of sensation, and especially more vexatious, are the neuralgias. Among these, neuralgic pains in the toes and the heel, and also in the remaining portions of the sole of the foot, have occurred in my experience with particular frequency. Comparatively rare at the height of the disease, they are likely to appear especially during the stage of defervescence and the first part of the period of convalescence, to the great distress of the patient and also of the physician, to whom the obstinacy of the disorder soon becomes apparent. At times the patient, under such circumstances, is unable to rest the foot upon the heel, so that this must be placed upon a concave surface; while at other times the bed-clothing must be supported by means of hoops, in order that it may not exert pressure upon the painful toes. Fortunately, the pains eventually disappear, generally without special intervention. Nevertheless, I have exceptionally observed them to persist for a considerable period of time, in one instance for a year and a half, and in another for more than two years. In both instances neuralgia of the heel was present.

Neuralgia of the sole of the foot and of the toes has been long and generally known. Among those who have referred to it are Ducheck,[1] Liebermeister and Hagenbach,[2] Jürgensen,[3] Nothnagel,[4] Fritz,[5] and Krafft-Ebing.[6] It is mentioned also in the *Sanitary Report of the German Armies for 1870–71.* Sciatica appears to be much less common (Benedikt, Nothnagel). I have never encountered it. I have observed in a woman, forty-one years old, who had a neurotic tendency, an extensive, severe neuralgia in the distribution of the brachial plexus, in association with persistent fibrillary muscular contractions in the deltoid and the triceps, but without atrophic paralysis. Recovery ensued in the course of three months.

I have observed intercostal neuralgia in 2 cases, in 1 associated with herpes zoster; occipital neuralgia in 3 cases, the first developing during

[1] *Loc. cit.* [2] *Loc. cit.* [3] *Loc. cit.* [4] *Loc. cit.* [5] *Loc. cit.*
[6] *Klinische Studien über de Behandlung des Abdominaltyphus.*

the period of irregular temperature, and the other two during convalescence. Recovery ensued in all 3 cases, in 1, it is true, only after the lapse of five months, but in the other 2 in the course of a few weeks. Neuralgia in the distribution of the lumbar and the crural nerves, which has been mentioned in the literature, I have not observed.

The state of the sensory reflexes in the course of typhoid fever has hitherto been but little investigated. The literature contains but scanty reference to the subject, and my own observations also are few. According to these, the sensory reflexes appear to be generally much diminished during profound coma, while in moderate and in mild cases they less commonly exhibit alterations. I have frequently found them normal, or diminished rather than increased, even in cases of moderate severity showing marked tremor.

Undoubtedly, considerable increase in the sensory reflex activity occasionally occurs, and this may persist for weeks and months after the attack of typhoid fever, especially in the lower extremities, the soles of the feet, and the abdominal wall. In some patients the friction of the clothing in walking, the wearing of woolen stockings, and the like, give rise to an annoying sense of tickling. In 1 case under my observation, occurring in a man who was highly nervous before the attack of typhoid fever, there persisted such a degree of general cutaneous hyperesthesia of the lower half of the body, with punctate anesthesia and exaggeration of the plantar, cremasteric, and abdominal reflexes, that the patient for a long time could be permitted to walk only when a closely applied silk protective which did not scratch the skin was placed beneath the outer clothing.

Diseases of the Ear.[1]—The organ of special sense by far most frequently involved in the course of typhoid fever is the ear. Among 1243 cases of typhoid fever analyzed by Bezold,[2] impairment of hearing occurred in 4 per cent. in the course of the disease. Other aurists also emphasize the frequency of this occurrence. Thus Bürkner[3] states that in 1.8 per cent. of all cases presenting impairment of hearing, he was able to determine typhoid fever as the cause of the disorder; while Zaufal found a similar etiologic factor in 0.7 per cent., and Kramer in 2.5 per cent., of their cases.

[1] See Moos, Schwartze's *Handbuch d. Ohrenheilkunde*, Bd. i. Schwartze, "Erkrankungen des Gehörorgans im Typhus," *Deutsch. Klinik*, 1861. *Ibid.*, "Typhöse Taubheit," etc., *Arch. f. Ohrenh.*, 1864 and 1867. Anatomic references can be found in the paper of C. E. Hoffman, *loc. cit.*

[2] "Ueber die Erkrankungen des Gehörorgans bei Ileotyphus," *Arch. f. Ohrenh.*, 1884.

[3] "Beiträge zur Statistik der Ohrkrankheiten," *Arch. f. Ohrenh.*, Bd. xx.

The disorders of hearing thus far observed are most variable with reference to their seat and character. With regard to the external ear and the auditory canal, the rare cases of gangrene of the auricle are to be borne in mind (p. 168). Periostitis of the external auditory canal and perforation of abscesses of the parotid gland into the cartilaginous portion of the canal are more frequent. Furunculosis of the external auditory canal is also frequently mentioned. I have observed it in a number of instances as one of the manifestations of multiple furunculosis of the skin during convalescence from typhoid fever.

Among the disorders of the internal ear a distinction is generally made between purely nervous or functional disorders and those dependent upon organic causes. The purely functional disorders are by no means rare. A portion of these make their appearance at the beginning of the attack, and while they are possibly less conspicuous at the height of the disease, it is only because the profoundly soporose patients make no complaint. Among these disturbances is to be included especially the extremely annoying, subjective sensation of sound, as of roaring and ringing, which is often present during the first period of the disease. Probably the almost characteristic impairment of hearing at the height of the disease is also in many cases due solely to nervous disturbances. At least, it is often impossible to demonstrate any causative lesion with most thorough investigation. The prognosis of these disorders is favorable. They disappear with subsidence of the fever, or at any rate with the end of convalescence. While formerly the causes of these disturbances were thought to consist in hyperemia or anemia of the brain and its membranes, or even of certain parts of the middle ear itself, at the present day the action of toxins upon the parts in question is properly made responsible.

The disorders of the middle ear dependent upon anatomic lesions are referable principally to extension of inflammatory processes from the structures of the nasopharynx through the Eustachian tube to the middle ear. Not rarely mucopurulent infectious matter gains entrance mechanically to the cavity of the tympanum. The possibility of dissemination of excitants of inflammation from remote organs and their lodgment in the ear is probably of subordinate significance. The microorganisms of etiologic significance in all these inflammatory processes have not yet been adequately determined. Especially it has not yet been made out to what extent the bacillus of Eberth itself plays a part in this connection.

The course of the affections of the middle ear varies between the mildest cases and those which are the most severe and are directly

dangerous or are attended with sequelæ which persist throughout the rest of life. For instance, purulent sinus-thrombosis or periostitis and caries of the petrous bone may develop. Fortunately, these profound disturbances are far less common in the course of typhoid fever than in some other infectious diseases, as, for instance, scarlet fever and diphtheria. Far more frequent are the milder disturbances that are readily overlooked in their incipiency unless the physician examines the profoundly soporose patient frequently and thoroughly, and which are recognized only after they have given rise to suppurative inflammation of the middle ear, with perforation of the drum-membrane and otorrhea. In addition to inflammatory lesions of the middle ear, hemorrhages into the cochlea and the vestibule have been observed as the cause of severe, and at times permanent, impairment of hearing. Moos[1] also mentions small-cell infiltration of the membranous labyrinth.

Disorders of the Eyes.[2]—These are, on the whole, rare in cases of typhoid fever; at any rate, they are much less common than diseases of the ear. Gangrene of the tissues has exceptionally been observed in the immediate vicinity of the eyes and of the lids, and has been attributed to endarteritis and thrombosis of the external carotid artery and its branches (p. 168). True noma complicating typhoid fever is also mentioned by earlier writers as a cause for extensive destruction of the eyelids.

Paralysis of the extra-ocular muscles occurs most commonly during convalescence. Knies believes that certain varieties of these extra-ocular paralyses are nuclear in origin and are to be attributed to a chronic nephritis. Unilateral and bilateral ptosis has been observed (Nothnagel, Henock). Cases occurring during the height of the fever are very rare in the absence of intracranial complications. Ptosis and abducens palsy have been recorded in the third week of the disease by Nothnagel. In a case at the Johns Hopkins Hospital oculomotor paresis of the left eye developed on the eighth day of the disease. In this case there was paralysis of both intra-ocular and extra-ocular muscles, and the condition was probably due to a slight local meningitis. In children symptoms of meningitis and strabismus may occur

[1] *Loc. cit.*

[2] See Förster, *Beziehungen der Allgemeinleiden und Organerkrankungen zu Veränderungen und Krankheiten des Sehorganes*, Leipsic, 1877; and Knies, *Die Beziehungen des Sehorganes und seiner Erkrankungen zu den übrigen Krankheiten des Körpers und seiner Organe*, Wiesbaden, 1893. Also, de Schweinitz, chapter on "Ocular Complications" in *The Surgical Complications and Sequels of Typhoid Fever* by Keen, Phila., 1898, *Phila. Med. Jour.*, March 3, 1900.

early, but it is questionable whether they are associated with a true meningeal inflammation.

Paralysis of the intra-ocular muscles is also most common during convalescence. Förster, with whom Knies agrees, considers the paralysis of accommodation and mydriasis as essentially part manifestations of the general exhaustion; far less frequently they are due to circumscribed disease of the affected nerve-paths.

Among the changes in the eyeball itself, conjunctivitis should first be mentioned. A catarrhal form of conjunctivitis occurs frequently in deeply soporose patients during the febrile period, but by no means so frequently as typhus fever and small-pox, or even measles. Probably this conjunctivitis is not specific, but is dependent upon or favored by the fact that the dull patient winks infrequently and closes his eyes imperfectly and possibly also by the diminished secretion of tears. During convalescence, and sometimes in the later stages of the disease, a true phlyctenular conjunctivitis may appear. A phlyctenule may break down and form an ulcer, or without this origin ulcerative keratitis may arise. These ulcers are rarely so large as to give rise to extensive leukoma and considerable impairment of vision. True keratomalacia, which was early described by Trousseau, is, fortunately, an extremely rare manifestation of profound marantic or septic conditions (see my own case, pp. 291 and 292). According to Knies, iritis, cyclitis, choroiditis, and chorioretinitis also occur; less commonly, however, than in other infectious diseases, as, for instance, relapsing fever. They may give rise to permanent profound impairment of vision, as the cases of Arens and Trélât, cited by Knies, show.

Though extremely rare, the transitory and the permanent forms of amaurosis are worthy of mention. The transitory forms, whose nature and causes have not been adequately studied, occur almost solely in youth and childhood (Eberth, Nagel, Fréminau, Förster). I have personally observed such a case develop in a girl, eleven years old, without demonstrable lesion of the eye-ground, in the course of typhoid nephritis, and disappear within seventy-two hours without leaving a trace. Uremia must be thought of as the cause in such cases. The persistent forms of amaurosis,[1] which may be either unilateral or bilateral, generally depend upon atrophy of the optic nerve. The seat of the disturbance is to be sought either in the brain or in the optic tract itself. Among the causes of the disturbances in question, hemorrhage and sclerotic or other variety of focal disease have been mentioned. Probably meningitic exudates, with their injurious secondary effects,

[1] The literature is given by Förster.

are also often operative, as Knies and Förster, especially, have pointed out.

Optic neuritis during typhoid is usually associated with meningitis. However, according to de Schweinitz, an optic neuritis may occur which is entirely unconnected with intracranial complications, and is analogous to the neuritis occurring in the nerves elsewhere in the body.

According to Bull, retinal hemorrhages are not infrequent during the height of typhoid fever, being most common about the third week. A perverted quality of the blood, a weakened condition of the blood-vessel walls, or a microbic invasion of the vascular coats may explain these hemorrhages (de Schweinitz).

VARIATIONS IN SYMPTOMATOLOGY AND COURSE.

The character and the severity of the course, and the symptomatology, of typhoid fever represent the expression of two principal factors, namely, the mode of action of the bacillus of Eberth upon the body, particularly the degree of its virulence; and the special conditions of the invaded organism itself. These conditions are, naturally, extremely variable. As to the nature of these conditions, a part is already known, at least empirically, while a part is still entirely undetermined. Among the more important determining conditions are, first, the factors relating to individual, namely, age, sex, constitution, occupation, and mode of life, and the degree of susceptibility and power of reaction. Further, of importance in shaping the cause of the disease are special prominence of symptoms on the part of individual organs or systems, and the not uncommon associated activity of the typhoid-bacillus with other pathogenic micro-organisms. In addition to the special conditions, general conditions also play a *rôle*, and these affect the individual only in part, but in far greater degree influence the preservation, development, dissemination, and the degree of virulence of the virus; these are especially the local conditions, habitations, state of cultivation, modes of intercourse, and water-supply, and, finally, the geographic situation, climate, and season. The varieties of clinical picture, course, and termination of typhoid fever resulting from all these various influences are so diverse, often so completely opposed, and, on the other hand, at times so running together, that any exhaustive description is impossible. Every case, therefore, is different from every other, and any description can serve only as a guide in the midst of this variability, and determine the most important points of view. A

considerable number of facts in this connection have already been referred to in the clinical section.

It will be best to begin the description with a recital of the simplest conditions: the varieties of typhoid fever that result in accordance with the severity and the mildness of the attack, as well as those varieties depending upon the duration of the disease in general, or of its different stages. It may be emphasized in advance that severity and long duration of the disease do not coincide any more than do brevity and mildness. Although such coincidence occurs frequently in the individual case, the severity and the duration of the symptoms are, in general, wholly independent of each other. The best evidence of this is afforded by the study of the variety to be described first.

The Short, Malignant Variety (*Malignant or Fulminant Typhoid Fever; Hyperpyretic Variety*).—This variety, which, fortunately, is rare, represents, as its designations indicate, a form of typhoid fever of most severe course. Some of the cases begin after a longer or shorter period of incubation, which is not free from symptoms. The patients complain for days in advance of great malaise, headache, vertigo, and sleeplessness, and often exhibit nausea and vomiting, and not rarely diarrhea. The pulse, also, at this time may be abnormally frequent, and the temperature temporarily elevated. In another group of cases the disease sets in suddenly, without prodromal manifestations, with a single chill or repeated severe chilliness.

Almost always the stage of ascending fever is considerably shortened, so that within from twenty-four to forty-eight hours the level of constant fever is reached. At times this occurs at once, at other times with one or two slight remissions. The temperature-level then reached is not rarely an unusual one, so that as early as the evening of the second to the fourth day of the disease the thermometer may register from 40.5° to 41° C. (Fig. 14). The temperature then remains at this level, generally with slight fluctuations, for the next few days, or it rises still higher, preserving the character of a continued or remittent continued fever (Fig. 25).

The pulse, even in robust men, is from the outset excessively frequent, at first still full and tense. Soon it becomes softer and dicrotic. The differences between the morning and evening pulse-frequency are, like those in the temperature, remarkably slight. Shortly before or at the height of the fever, at times even during the ascent, the patients become stupid. They are delirious at night and sometimes by day, and lie in a state of relaxation, in passive dorsal decubitus, with the mouth open, exposing the dry, fissured tongue and lips. Subsultus tendinum,

floctitation, and grinding of the teeth, in young persons even convulsions, increase the gravity of the clinical picture. Not rarely rigidity of the back with opisthotonos and other cerebrospinal symptoms are present besides.

The state of the spleen is variable. Generally it is distinctly demonstrable quite early, even at the time of admission of the patient, on the second or the third day of the disease, and often the organ is converted into a large, soft, and sensitive tumor. Less commonly enlargement of the spleen occurs later, or is not demonstrable throughout the entire course of the attack. The abdomen early becomes greatly distended,

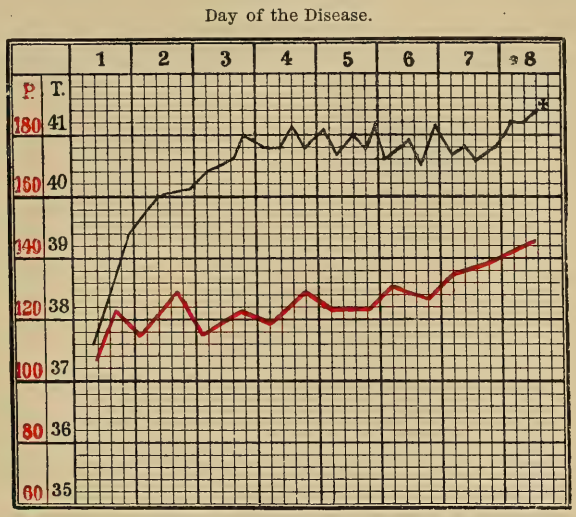

FIG. 25.—Temperature-chart from a fulminant case of typhoid fever in a woman, thirty-five years old, terminating fatally on the eighth day. This was the third case in a house-endemic. The attack began with a chill. Intestinal lesions were marked, especially in the region of the cecum and the lower third of the ileum. Peyer's patches were in a state of medullary swelling, in part greatly disintegrated, and in a state of congestion. No complication was present.

and in some cases acquires a considerable degree of tension, which is an ominous sign. The stools are at times diarrheal, at other times constipated; the urine generally contains albumin during the first few days, at the same time being scanty, concentrated, and high-colored. While ischuria occurs at first, with the commencement of deep stupor, the urine and the stools are passed involuntarily into the bed.

The termination is in most cases fatal, following progressive loss of strength, and at times associated with extremely high degrees of temperature (hyperpyretic form). Only the minority of patients survive. In the latter event the severity of the general symptoms subsides toward the end of the second week, the temperature-curve declines to a lower

level, with simultaneous improvement in the pulse; and after a longer or shorter period the patient becomes afebrile. Convalescence is always unusually severe and protracted; this often occurs in consequence of recrudescences and relapses.

The symptoms in the presence of which death takes place are those of most profound intoxication. Only exceptionally do early intercurrent intestinal hemorrhages accelerate the fatal termination. Post-mortem examination discloses, in accordance with the short duration of the attack, that the lesions in the small and the large intestine are still in a state of medullary swelling, and only here and there is there beginning sloughing. Their extent and intensity do not, by any means, always correspond with the severity of the clinical picture. Although severe degrees of intestinal involvement are more frequent, cases also occur with remarkably slight specific intestinal lesions. The large, soft, diffluent spleen is often the seat of recent extravasations of blood. The liver and the kidneys are in a state of marked cloudy swelling. Fortunately, as has been stated, this variety is quite rare. It occurs principally in adults up to the fortieth year, while children and old persons are attacked much less frequently. With reference to the duration of the process, the fulminant form, which may terminate fatally at the end of the first week, and rarely persists until the end of the second, is to be contrasted with the severe forms of protracted course.

Severe and Moderately Severe Cases of Protracted Course.—Detailed reference need not again be made here to the course of such cases, as this has been fully done previously (General Clinical Picture). At this place we wish merely to point out that the conditions and the forms of the prolonged attack are extremely variable. Thus, the prolongation may be due to the fact that the individual stages of the disease are extended beyond the usual period. This applies with especial frequency to the fastigium, which may persist for as long as four weeks, and even much longer. The fever has then less commonly or only in the first stage the character of a continued or remittent continued type. Very early or even from the outset, the temperature is likely to exhibit marked fluctuations, and may assume the character of an intermittent type or even become wholly irregular. Next in frequency the stage of defervescence is prolonged. The characteristic steep curves are then obscured or are entirely absent, and the increase in temperature takes place gradually, with a more or less protracted, remittent, or wholly irregular course, in which there are not infrequently causeless remissions and exacerbations. After defervescence has finally

taken place, the stage of convalescence may be unusually long. The patients remain weak, and often exhibit marked instability of pulse and temperature, so that transitory increase may take place without obvious cause or upon slight provocation. Cases are also frequent in which convalescence is unusually prolonged in consequence of recrudescences and relapses (recrudescent form).

The moderately severe and mild forms may, not less than the severe form, be unduly protracted, and yet give no cause for especial anxiety at any time in the course of the attack. The fever is then from the outset not very high, and is quite irregular or remittent, or so markedly intermittent from the beginning that the temperature-chart in consequence acquires an appearance which seems remarkable to the inexperienced observer, and may readily give rise to false conclusions. These cases are also frequently prolonged by recrudescences and relapses, which, in course and intensity, resemble the primary attack or are even more severe. While severe and moderately severe cases generally pursue their course in from four to five weeks, protracted cases may keep the patient in bed for from three to four months, and even longer.

Among these protracted cases, those terminating fatally from marasmus, which fortunately are of extreme rarity, are deserving of special mention. In these cases the disease, which is generally severe from the outset, is then prolonged unduly, there is often an irregular temperature-curve, and when defervescence has finally taken place, the patients do not convalesce, but their condition becomes progressively worse. The appetite is not restored, but, on the contrary, there is distaste for food, especially for meat, bouillon, and milk. Some patients who eat even fairly well fail, nevertheless, to make progress. The bowels are constipated in all these cases; the abdomen is hard and retracted. The skin appears dry and scaly, and the hands and feet are cyanotic and cold. Emaciation progresses uninterruptedly, although most careful examination fails to disclose any special organic lesion, and life is terminated with the most profound marasmus. Post-mortem examination in such cases discloses what clinical examination had already rendered probable, namely, the absence of complications or any special organic change. Murchison, who directed especial attention to this form of the disease, states that Rokitansky attributed it to shrinking of the mesenteric glands, together with disappearance of the intestinal villi and lymph-follicles.

A characteristic case of this remarkable variety, to which even experienced clinicians make no reference, came under my observation in consultation, occurring in a girl twenty-one years old, who lived amid the most

favorable conditions. After an attack of typhoid fever of eleven weeks' duration, with irregular and on the whole low fever, the patient appeared about to enter upon convalescence. The temperature became subnormal, and soon reached an unusually low level—33.5° or 34° C. in the morning. The pulse remained unusually small, thready, and retarded, and became progressively slower, so that finally only 38 or 40 beats could be counted in the minute. At the same time the patient wasted in a frightful manner, and upon the thin skin stretched over the bones bed-sores gradually appeared in the most varied situations—over the sacrum, the vertebræ, at the heel, even over the iliac spine, the upper extremity of the fibula, and the ankles; and, after suffering for a long time, the patient finally died, total necrosis of the left and beginning necrosis of the right cornea having also developed in the last few days of life. At the autopsy there was no noteworthy alteration of the internal viscera, with the exception of the intestine, which contained numerous smooth, pigmented cicatrices in the ascending colon, and in the ileum in the vicinity of the ileocecal valve, in place of the Peyer's patches, so that even the pathologic anatomy was unable to answer the question as to the cause of death.

Well-characterized Cases Pursuing a Moderate and Mild Course.—While definite external or individual conditions or special organic disease often give their impress to cases of this group, they are in general distinguished from one another principally by their duration. In a number of the cases the duration is shorter than is the average in the well-marked severe cases, while others pursue equally as long but a mild course. Among the cases of the first kind, those are especially characteristic in which the individual stages of the disease are regular and maintain their normal proportions, although they are shorter, so that the temperature-chart, except as to the duration of the various stages, entirely resembles that of the typical variety (Fig. 11). Other cases exhibit a favorable course in that certain individual stages of the disease are considerably shortened or remain almost undeveloped. Thus, the initial stage may be almost entirely wanting, and the height of the fever may be reached at a single bound in from twelve to eighteen hours; or, as occurs with especial frequency, the stage of steep curves is considerably shortened or is not at all marked. In the latter event the febrile stage is often terminated by a critical decline. Considerable shortening of the amphibolic stage, with complete development of the initial period and that of convalescence, is less common.

The cases of moderate and mild degree, which are unabbreviated, but, on the contrary, are often greatly prolonged, appear to pursue a wholly irregular course. Under these circumstances the febrile stage maintains in general a lower temperature-level. The curve is at the same time likely to exhibit a markedly remittent or wholly irregular course. The general symptoms are likely to be exceedingly mild, and

the nervous system especially is but little involved. From the diagnostic point of view, these cases, apart from the fact that the fever-curve frequently gives no aid, may further be a source of considerable difficulty because of the absence of splenic enlargement or its unusually late development, because of the scantiness of the roseolæ, or inability to demonstrate them, throughout the entire course of the disease, and occasionally also because of the insignificant character of the intestinal symptoms. Such cases are probably the same as those that earlier physicians designated as gastric fever or as mucous fever, and separated etiologically from typhoid fever. It is only a step from these moderate and mild cases to those pursuing an especially short and frequently also an especially mild course. These are really separable only superficially, for they are actually connected by all possible transitional forms.

Atypical Cases of very Short and Mild Course (*Typhus Abortivus, Typhus Levissimus, Typhoidette* (*Brouardel*).—In earlier times these cases were, still less than the preceding forms, considered as examples of typhoid fever. Although Lebert[1] occupied himself with their study and contributed something to the knowledge of them, it remained for Griessinger[2] to demonstrate beyond doubt their nature and their relation to typhoid fever. He was followed by Jürgensen,[3] Bäumler,[4] and others, who helped to give clearness and force to the new doctrine. All the cases included in this group are characterized by the especial shortness of the course, and frequently also by the marked mildness. Mildness is, however, as has been mentioned, by no means always a characteristic feature. On the contrary, the well-developed cases may be classified, according to the suggestion of Liebermeister, into mildest cases (Typhus levissimus), including all cases characterized by mildness and by brevity, and into a second class (Typhus abortivus), which includes those cases in which, although the course is short, the character of the disease may at times be quite severe and even alarming.

If the manner in which the mild and the abortive cases of typhoid fever make their appearance be more minutely observed, it will be found that they exhibit in varying degree the evidences of imperfect development of the disease. We have observed that in the mild cases one or another stage of the disease is often abbreviated, but in the cases under consideration this shortening often attains a most extreme

[1] *Prag. Viertelj.*, 1857, Bd. lvi.

[2] Schmidt, *Inaug. Diss.*, Zurich, 1862; and *Infektionskrankheiten*, 1864.

[3] *Volkmann's Sammlung klin. Vortr.*, 1873, No. 61.

[4] *Dublin Med. Jour.*, Nov., 1880; and *Deutsch. Arch. f. klin. Med.*, Bd. iii.

degree. All the stages may be considerably shortened in their course or may be so abridged as to be unrecognizable. As in the cases of moderate severity, so also in the mildest, this abbreviation may affect the initial and the terminal stages especially, sometimes in the form of an abrupt rise or a critical decline, or there may be a quite gradual commencement or subsidence of the fever. It should be pointed out that considerable shortening of the initial stage and critical decline of the fever occur more frequently in cases of abortive typhoid than in those of the mildest variety. The fastigium of the disease, which likewise is frequently more or less greatly shortened, may exhibit all possible varieties of temperature-curve, from that of the regular remittent continued course, which is decidedly the least common, to that of the pure intermittent or wholly irregular course, with low or moderate temperature.

The pulse is likely to be particularly accelerated and to be unstable only in irritable women and children, while in less sensitive, more robust individuals it exhibits scarcely any acceleration throughout the entire course of the disease. Even in the abortive cases with high temperature at the outset, the slight degree of increase in the frequency of the pulse is at times especially striking (Fig. 29).

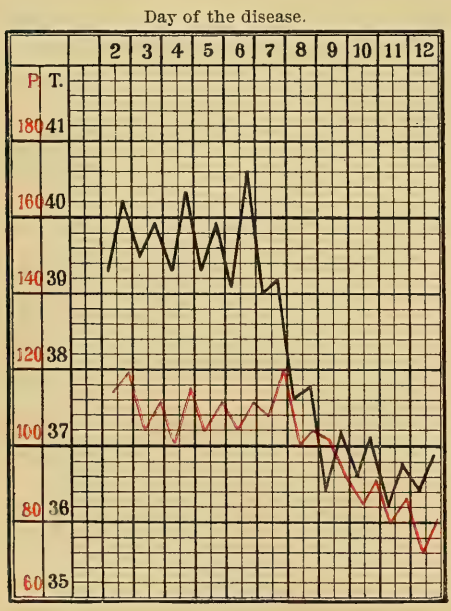

FIG. 26.

Before passing to a consideration of the remaining symptoms of the abbreviated and the mildest cases, a few histories with temperature-tracings may be briefly given to illustrate the various forms of course.

The following case may be considered as one of abortive typhoid fever: A compositor, nineteen years old, after several days of headache, anorexia, and prostration, was suddenly seized with a chill. On the day of admission (second day of the disease) enlargement of the spleen was distinctly demonstrable. Between the fourth and the fifth day a small number of roseolæ made their appearance upon the chest, the abdomen, and the back, and were followed by others up to the ninth day. On the second day of the disease the evening temperature was 40.2° C., and from this time on until the

sixth day, on which the evening temperature reached 40.6° C., there was comparatively high continued fever, which then declined rapidly in two stages, and complete defervescence occurred after the eighth or the ninth day (Fig. 26). The pulse during the febrile period ranged between 100 and 120, and was full and of high tension. Convalescence was uncomplicated, and the patient was dismissed after three and one-half weeks ready to return to work.

The temperature-chart shown in Fig. 27 is from a case with nine days of fever, on only two or three of which the temperature was high, but which, nevertheless, exhibited a severe, even alarming, aspect. The patient was an obese assessor, thirty-six years old, who had drunk a good deal of beer and had eaten generously, though engaged in but slight physical activity. He was seized with a chill on a return journey from Italy. As early as the second day of the disease a large, palpable, sensitive, splenic tumor was present; on the third day, an abundance of roseolæ on the trunk, the upper arms, and the

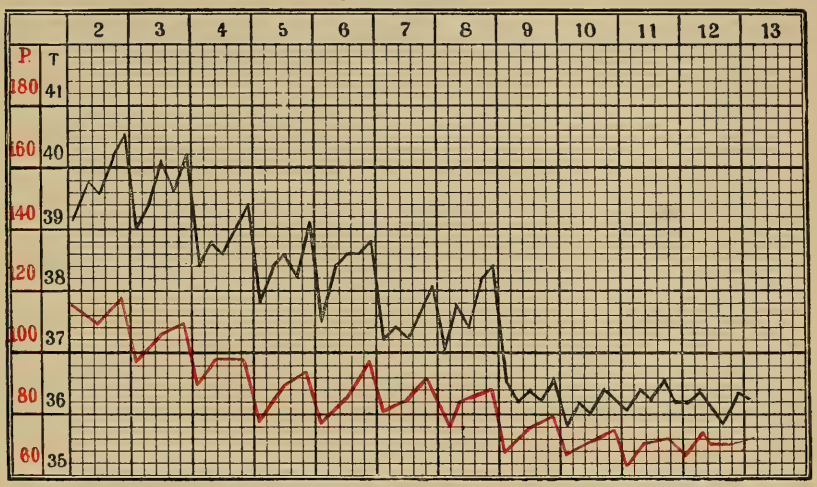

FIG. 27.

thighs. From this day on there were stupor and, toward evening and in the night, active delirium with attempts at flight. From the fourth to the tenth day there was moderate albuminuria, at first even with slight admixture of blood and of hyaline and epithelial casts, and a small number of blood-casts. As will be seen from the temperature-chart, the fever subsided gradually. Complete defervescence was attained between the night of the eighth and the morning of the ninth day by a sort of critical decline, which was attended with profuse sweating. The state of the pulse was from the outset quite favorable, being intermittent now and again during the first few days, but never especially small or frequent. Convalescence was unusually protracted, so that the patient, in spite of the short duration of the actual febrile stage, was not able to get out of bed until after four and one-half weeks, and then with a loss of weight of 19 pounds.

By the side of this case may be placed that from which the tracing shown in Fig. 28 was obtained. This occurred in an embroiderer, twenty-one years old, who was admitted on the fourth day of the disease, and entered

upon defervescence on the thirteenth day. The clinical picture was severe until the eleventh day of the fever, with marked apathy, somnolence, and slight delirium. The course of the temperature exhibited the character of a rather obstinate, remittent, continued fever of moderate degree. Systematic treatment with baths was required, the effect of which was but slight and of short duration. On admission a large palpable splenic tumor was present, and—what made this case appear especially remarkable—there was an unusually profuse eruption of roseolæ, which continued to multiply until the evening of the fifth day, so that as many as 700 could be counted upon the back and the extremities. The pulse remained relatively good, even at the height of the fever, being always full, regular, and tense, but being more than 120 only on the first evening, and thereafter ranging about 100 and below.

The following case exhibits a certain contrast to the 2 severe cases just mentioned; it likewise was attended with fever of moderate degree, but it

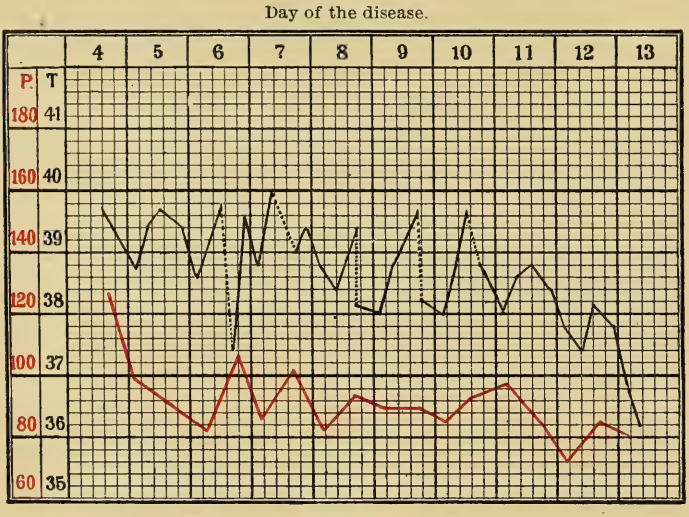

FIG. 28.

did not for an hour exhibit any severe or alarming symptoms even at the height of the disease. It occurred in an extremely robust hostler, twenty years old. The fever lasted altogether for nine days, the markedly remittent and intermittent curve rising generally in the evening to from 39° to 39.7° C., and finally exhibiting a peculiar and rare variety of critical decline in two stages. Between the ninth and the tenth day the temperature fell from 39° to 37° C., then fluctuated for two days between 37° and 37.6° C., to decline again suddenly below normal between the eleventh and twelfth days, and persisting at this low level during the first part of convalescence (Fig. 29). As the temperature-chart shows, the pulse in this case was from the outset unusually slow, although always full and tense; at no time was the sensorium of the patient in any degree affected, and he complained of hunger even before the subsidence of the fever; after a brief, uninterrupted convalescence he was restored to his full capacity for work with remarkable rapidity.

The following case pursued, on the whole, a severe course, with various

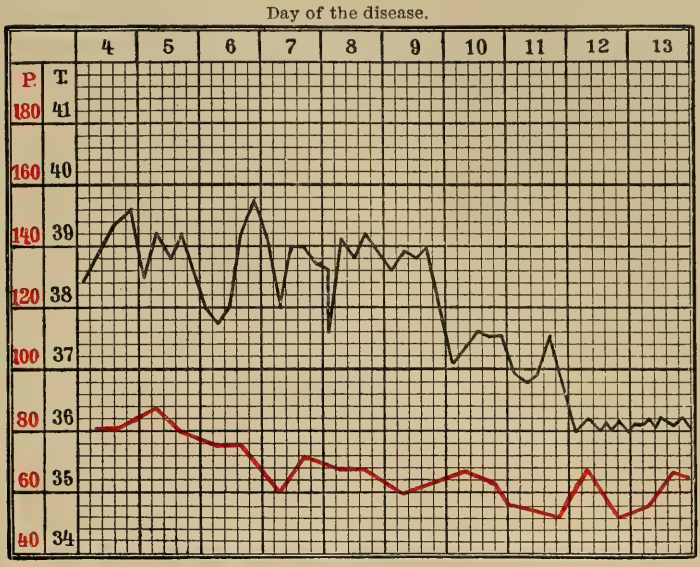

FIG. 29.

subjective complaints and for days a small, although not unduly frequent, pulse. This is an example of almost complete intermittence of the tempera-

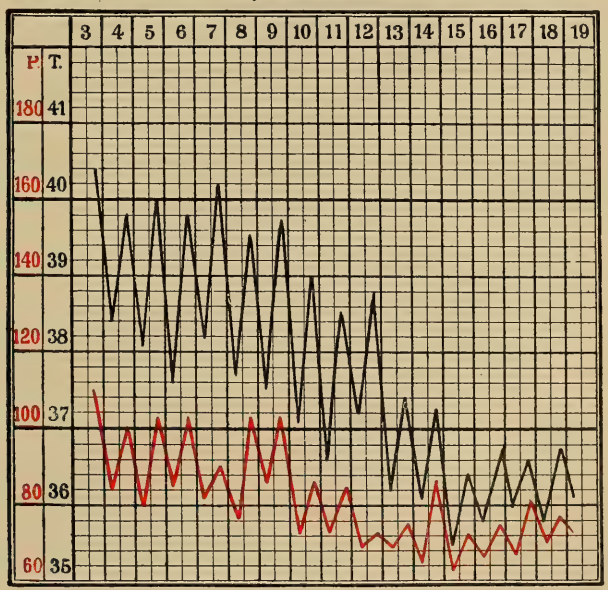

FIG. 30.

ture-curve from the first day of observation, and probably from the beginning of the fever (Fig. 30). The patient was a girl, fifteen years old, in whom enlargement of the spleen was demonstrable on the fifth day, with moderate

distention of the abdomen and slight tenderness in the ileocecal region, and from the seventh to the thirteenth day two or three thin, pea-soup-like stools were passed daily. The mother of the patient had died shortly before from an attack of the gravest form of typhoid fever, with intestinal hemorrhage.

The following case will serve as an example of true typhoid fever of the mildest type. The patient was a man, forty-one years old, who had been under treatment in the hospital for months for tabes dorsalis, but otherwise he was robust and well nourished. The onset of the disease, which was not preceded by prodromes, was attended with chilliness. As early as the first day enlargement of the spleen was demonstrable by percussion, and on the third day as well by palpation. A small number of well-developed roseolæ appeared relatively late—between the sixth and the ninth day. Throughout the entire course of the disease there was no diarrhea, but, on the contrary, constipation. Convalescence progressed rapidly, and at its close the

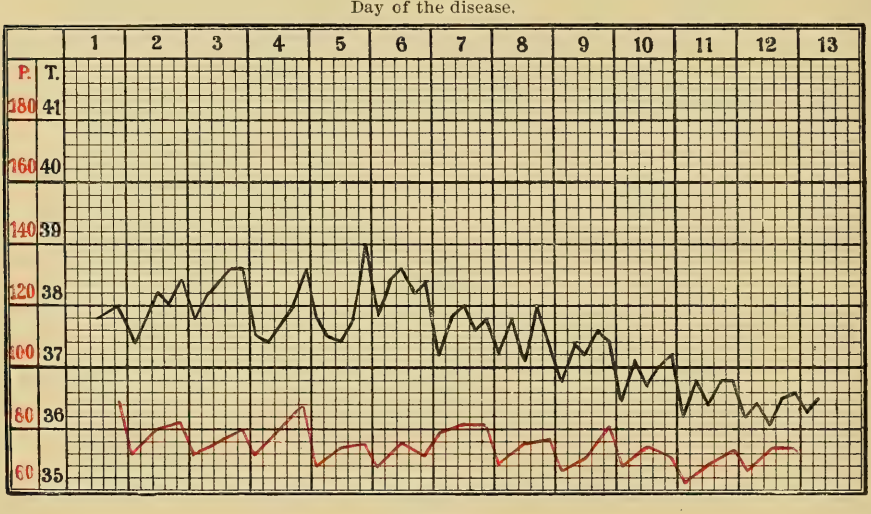

FIG. 31.

patient weighed five and a half pounds more than a week before the beginning of the disease (Fig. 31). The temperature-chart of the case is, as is so frequent in the mildest cases of typhoid fever, wholly uncharacteristic. The temperature, alternately remittent and intermittent, but once reached 39° C.

With regard to the course of the incompletely developed, abbreviated cases in general, it has been pointed out—and of this the case last related affords a good illustration—that many, in addition to the brevity, are characterized besides by unusual mildness of the symptoms, so that they well deserve the qualification "mildest." These cases set in either unexpectedly with a chill or a feeling of chilliness, or after slight prodromes, and then the maximum temperature is reached either gradually or more rapidly, occasionally before the end of twenty-four hours. In all, the general condition is but slightly disturbed. The patients are

at most somewhat apathetic, restless and sleepless at night, but almost wholly without delirium. The pulse remains good throughout, and is often remarkably slow. Complications and unusual localization of the typhoid process are extremely rare. After the fever has lasted from six to ten days, the patients recover rapidly and completely.

A number of cases that should likewise be included in the category of the mildest form of typhoid fever exhibit during the first few days severe but transitory general manifestations, with somewhat higher fever, but the course subsequently assumes a mild character, terminating in uncomplicated convalescence. We may also, with a certain degree of propriety, include in the class of mild cases those which exhibit relatively high remittent fever, which persists for days, but which is not accompanied by corresponding acceleration of the pulse-frequency or by especial disturbance in the general condition, and in which convalescence begins in the course of six or eight days, the fever subsiding by crisis or rapid lysis. They occupy a position midway between the "typhus levis" and the "typhus abortivus" of Liebermeister, constituting a transition between these groups, and in their typical form they illustrate the saying "Parturiunt montes, macetur ridiculus mus." Such cases generally begin with abrupt elevation of temperature following a chill, and are marked at times by quite severe symptoms of general intoxication at the height of the fever, which at night may attain a level of 40° C. or more; they also occasionally show especial involvement of the internal viscera, such as particularly severe diffuse bronchitis and albuminuria and nephritis of early onset. These cases almost make the impression that all the severe symptoms of typhoid fever were being crowded into a short time; and they not rarely give rise to anxiety, which, however, is soon dissipated by a critical or at least rapid subsidence of the temperature, often accompanied by sweats. Evidence of the fact that severe disturbances have taken place in the body even during the short duration of the disease is afforded by the fact that convalescence is often disproportionately protracted, strength is but slowly regained, and the loss of weight is at times very considerable (see the case illustrated by Fig. 27).

The course of these true abortive cases is generally as long as that of the mild and very mild cases. Even more markedly than in the latter, one may note that the incompleteness in development is at the expense of the initial stage and the period of defervescence, so that the duration of the fastigium with relatively high fever is often rather protracted. With regard to the course of the fever during the latter period, the remittent continued type predominates, but complete inter-

mittence and absolute irregularity in the temperature-curve may exist together with alarming general manifestations.

While, as has been emphasized, the general manifestations in the mildest cases of typhoid fever, as well as those referable to single organs, are likely to be extremely mild, in abortive typhoid fever, in spite of the short duration, certain organs are at times seriously affected —a further evidence of the severity of the infection under certain circumstances. Thus the case illustrated by Fig. 27 showed that albuminuria may be present as early as the fourth day of the disease, although in severe cases of the ordinary type it is not likely to appear before the

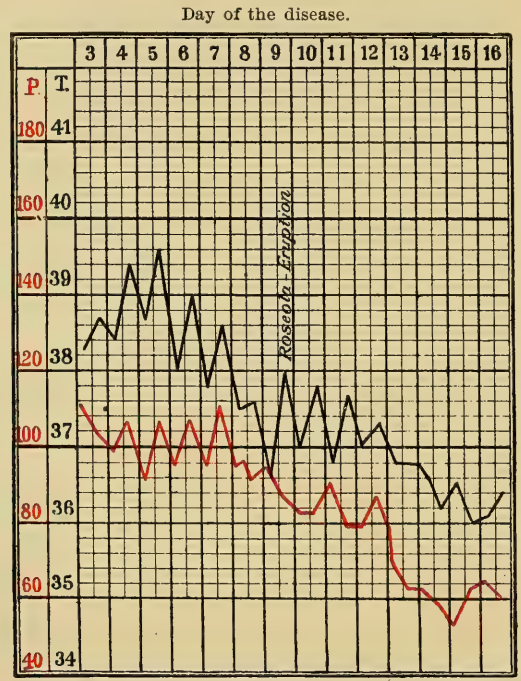

FIG. 32.

middle of the second week. Still more instructive is a case of abortive or mild typhoid fever which was under my observation, the onset of which was attended with nephritis, and which pursued its course amid the clinical manifestations of the latter condition, and which therefore may be appropriately called an example of nephrotyphoid.

A saleswoman, twenty years old, was admitted for hemorrhagic nephritis after she had been ill for two days. The amount of urine was considerably diminished, and the secretion was dark and bloody and contained an abundance of albumin, large numbers of epithelial cells, and hyaline and blood-casts. The temperature (Fig. 32), which was 38.7° C. on the evening of

the third day of the disease, rose on the following three days to between 39.4° and 39.6° C. In addition to this degree of elevation of temperature, which was considerable for a case of acute nephritis, the palpable enlargement of the spleen that was present on admission was striking. On the ninth day of the disease distinct roseolæ made their appearance upon the chest and abdomen, with rather abundant new crops up to the eleventh day. The nature of the attack was thus established. Defervescence set in between the eleventh and the twelfth day of the disease. Convalescence was thereafter uninterrupted. The albumin had disappeared from the urine upon the sixteenth day, while blood and epithelial casts were no longer demonstrable after the eighth day.

With regard to the individual symptoms characteristic of typhoid fever, the occurrence of enlargement of the spleen is quite as frequent in all abbreviated mild or abortive cases as in those that are completely characteristic. According to my observations, the enlargement of the spleen occurs more frequently at a comparatively early period—in the first days of the fever or even before its commencement—in the mild and abortive cases than in the completely characteristic ones. It has been especially in these cases, which later pursued an abortive course, that the complaint of the patient of tenderness in the splenic region, even before the onset of fever, has led me to examine the spleen.

The roseolæ seem to be, on the whole, less profuse and less constant in the abbreviated cases than is the enlargement of the spleen. In some cases they appear remarkably early, during the first few days of the fever; while in others their presence is synchronous with the enlargement of the spleen or shortly afterward. Not rarely their appearance is delayed, and sometimes they appear after the fever has subsided. I have even in a number of instances observed the first roseolæ only after defervescence, on the eighth or the ninth day of the disease, therefore at the time when they would have appeared in ordinary, completely developed cases. Complete absence of the roseolæ seems to me to be more frequent in the abbreviated cases than in those pursuing a regular course—a circumstance that contributes in no small degree to the increased difficulty in diagnosis. Unusual profusion of the exanthem is rare, but the case previously referred to (p. 296) demonstrates the possibility of its occurrence.

Sudamina are comparatively rare in cases with relatively low temperature, but I have often observed them during the period of defervescence in abortive cases with high and long-continued fever. Meteorism is frequently absent in cases of mild or very mild character, and is generally slight when it occurs in abortive typhoid fever. Characteristic diarrhea appears to be less common in these than in the well-developed cases. As has repeatedly been pointed out, this absence of diarrhea

naturally does not prove much with reference to the degree of development of the specific intestinal lesions. On the contrary, in some cases, which apparently afford no ground for anxiety, the most undesirable surprises are experienced, for instance, sudden intestinal hemorrhage or peritonitis.

Under such circumstances I have seen peritonitis occur in different forms. In a few cases in which, during attacks of typhoid fever of mild onset, irritative symptoms in the right iliac fossa with perityphlitic exudate appeared, the course was relatively favorable. Cases of fatal perforative peritonitis have been mentioned on page 226. Sudden intestinal hemorrhage also may convert mild, perhaps ambulatory, cases into serious ones. I have seen instances of this kind in which the occurrence of intestinal hemorrhage gave the first suggestion that typhoid fever should be looked for. One of my patients, a man forty years old, was admitted on account of sudden, severe bloody diarrhea, with a diagnosis of duodenal ulceration. It was stated that he had been quite healthy before the occurrence of the accident, and had continued at his work without interruption. A few days following his admission, after the bloody discharges had been replaced by thin, pea-soup-like stools, the temperature, which on admission had been subnormal, rose in the evening to 39° C. This was followed by remittent fever of moderate severity for a period of eight days, with decline of the temperature by lysis. The suspicion that the condition was one of typhoid fever with hemorrhage from the bowel was completely verified, but only when, after an afebrile interval of eleven days, a severe relapse of fifteen days' duration occurred, with enlargement of the spleen, distinct roseolæ, and again with thin stools. In a second case under my observation in which the hemorrhage had occurred after an indefinite illness of several days' duration, attended with slight fever, a fully developed relapse confirmed the suspicion of its typhoid origin. Cases of mild and abortive typhoid fever with intestinal hemorrhage are mentioned also by Liebermeister, who cites similar observations by Louis[1] and Vallin.[2]

Diffuse bronchitis is not rare in cases of abortive typhoid fever, as is evident from the clinical histories already detailed, and I consider it one of the most valuable diagnostic symptoms if its onset can be shown to have occurred simultaneously with the remaining symptoms. Pneumonic complications have occurred in my experience with extreme rarity in cases of abortive typhoid fever. Complications and sequels localized in other organs are no less rare in the abbreviated forms of typhoid fever than in the ordinary form.

With reference to convalescence, it has been stated that in correspondence with the mildness of the symptoms it is frequently remarkably short and uncomplicated, and attended with considerable increase in weight—often beyond the previous weight. The cases of severe onset and early high fever are, however, often followed by quite a long period

[1] *Loc. cit.*, T. ii., p. 332.

[2] *Arch. gén. de Méd.*, Nov., 1873.

of convalescence with considerable emaciation and rather slow restoration of the previous body-weight.

It is worthy of especial mention that the mild and abortive cases are followed by recrudescences and relapses with particular frequency, possibly with greater frequency than the severe cases. In addition, the secondary attacks are generally more intense, of longer duration, and more characteristic than the primary attack. Thus, it is not rare for the nature of a case to be obscure or altogether unrecognized during the first febrile period, and not to be viewed in its proper light until the occurrence of a relapse, with its characteristic symptoms, roseolæ, enlargement of the spleen, etc. In not a few instances the attack is not terminated with a single relapse. I have observed two and even three relapses and recrudescences following a mild primary attack.

With regard to the total duration of the imperfectly developed cases, the brevity of the attack is, as was emphasized at the outset, the most characteristic feature of these cases. A duration of the fever for more than ten or twelve days is extreme. Often enough it is only from three to six days. When convalescence is rapid and uncomplicated, not a few cases terminate within three weeks, but even cases of only fourteen days' duration or slightly more occur. On the other hand, at the beginning of even mild cases the possibility of the course being protracted or convalescence being prolonged owing to recrudescences and relapses must be kept in mind in expressing an opinion as to the probable duration.

Symptoms due to Typhoid Toxins.—Although almost all writers who have studied the atypical, abbreviated forms of typhoid fever have expressed an opinion as to the conditions attending its development, none of the theories hitherto put forward appears to be sufficient. It is easy to say that the conditions are dependent upon the action of attenuated bacilli, or upon a quantitatively slight infection (*"Typhe en petite dose"* of the French), or upon slight susceptibility of the organism, or, on the other hand, upon marked eliminative capacity on the part of the body. Although these statements may contain much that is true, so far as actual knowledge is concerned, these hypotheses are only formulated problems. The solutions must be gained step by step by means of painstaking experimental investigation.

Considering the question from this point of view, one may go still further with reference to the production of certain cases, and ask—May not all the peculiar symptoms in human beings be induced by the action of typhoid toxins, just as can be done experimentally in animals, as has been demonstrated with certainty by Fränkel and Simmonds,

Kitasato and Wassermann, Sirotinin, Baumgarten, and others? Undoubtedly abundant possibility and opportunity are afforded for such intoxication. It would be necessary to consider in such cases especially the accidental ingestion of greatly infected articles of food in which the contained bacilli, after having greatly multiplied, had been destroyed by heating, cooking, baking, and the like, and their toxins alone remained active.

That the human organism—presupposing favorable personal and external conditions—reacts to the introduction of such poisons does not appear to me to be in the slightest degree doubtful. As a matter of fact, I have repeatedly observed in the course of house and family endemics during periods when typhoid fever was severe, in addition to characteristic cases of varying severity, others whose explanation was most readily furnished by the assumption of the exclusive action of toxins upon the organism. These were more or less severe, at times quite severe, cases which generally occurred in young individuals, servants, cooks, etc., and had a duration of from twenty-four to forty-eight, and not more than seventy-two, hours. The patients complained of severe headache and vertigo, shooting pains in the sacral region and in the lower extremities, with marked cutaneous and muscular hyperesthesia. They were restless and sleepless, and toward the evening and at night even slightly stuporous. Almost all the patients exhibited from the outset marked nausea and vomiting. In addition to total anorexia or even disgust for all food, they suffered from burning thirst. The tongue was heavily coated throughout, at times to such a degree in the course of a few hours that it appeared as if boiled.

At the same time severe diarrhea occurred in many without the characteristic pea-soup-like color of the stools. Quite exceptionally distressing tenesmus with mucous and bloody stools was observed—a manifestation that recalled forcibly to my mind certain lesions of the large intestine induced experimentally in animals by means of typhoid toxins. In the majority of cases there was slight meteorism. I have observed enlargement of the spleen in a number of instances, but have never seen roseolæ. At times, in the course of from twelve to eighteen hours after the onset of the disease, there was moderate albuminuria, which invariably soon subsided, with a small number of hyaline tube-casts, but without other characteristic morphologic elements, and particularly without blood.

Generally the cases were attended with fever, setting in with repeated sensations of chilliness or a definite chill, the temperature reaching 30° C. in the morning, and at times 40° C. or above in the

evening. I have not as yet observed death as a result of this form of the disease, although the condition in some instances appeared quite alarming, and impressed even the laymen as a state of profound intoxication. The subsidence of the symptoms occurs in the course of from twenty-four to seventy-two hours at the latest, and is almost always associated with rapid decline in the temperature, accompanied by profuse sweating. Even after the disappearance of all other morbid symptoms there often remain unusual prostration and languor, which keep some patients in bed or in their rooms for more than a week. Such instances require only to be mentioned in order to remind other physicians of similar cases in their own experience. For further studies it would certainly be worth while to compare again the clinical picture observed in human beings with the results of the experimental action of toxins in animals.

To what extent, if at all, the shortest of the atypical cases described in the preceding section depend upon the action of toxins alone or upon a combination of this with that of attenuated cultures; whether certain especially violent severe cases of short course are possibly to be considered as examples of "toxin-typhoid fever," are questions which must for the present remain undecided. It appears quite interesting to me in this connection that Chantemesse[1] found, on puncture of the spleen in cases of abortive typhoid fever, that the splenic juice was free from the bacilli of Eberth, and he attempts to explain this circumstance by assuming that in these cases the bacilli penetrate less deeply into the tissues.

THE LATENT VARIETIES.

Ambulatory Typhoid Fever; Afebrile Typhoid Fever.—Among the latent varieties might be included also those cases in which the attack of typhoid fever begins and continues amid severe but unusual symptoms, so that at the onset, and not rarely throughout, its nature may be unrecognized—nephrotyphoid, pneumotyphoid, pleurotyphoid, typhoid fever setting in with meningitis or psychoses. These varieties, however, will be more appropriately considered at some other place. Those cases will be considered as belonging to the latent varieties in the strict sense of the word that are characterized by absence or mildness of the fever or such slightness of other symptoms that the patient is not really conscious of the existence of a serious disorder.

Ambulatory Typhoid Fever.—The qualification ambulatory was introduced by Griessinger, and is generally employed especially in

[1] *Traité de Méd.*, p. 771, and *Sem. méd.*, Nov., 1889.

Germany. In France, where its existence is actually denied by some writers (Brouardel), the qualification latent, which in my opinion is less distinctive (Louis, Chomel, and others), is more commonly employed. The qualification ambulatory applies naturally to the most conspicuous feature of the clinical picture: the patients do not go to bed, but continue more or less fully in the pursuit of their usual occupations. This presupposes that the symptoms are at the outset and throughout the course so slight that the patient either does not complain at all or makes but little of his ill-defined discomfort. Some patients, it is true, suffer more; they are conscious of being ill and feverish. They, however, resist the disease, and in this are encouraged by their friends, since, as not rarely occurs under unfavorable external conditions, they are frequently considered as simulators or malingerers.

The course of events as elicited from the complaints of the patient or determined subsequently are usually as follows: The disease generally begins gradually, insidiously, at times with a feeling of chilliness, which may be repeated in the further course of the attack. The patients complain of progressively increasing languor, and are prostrated, especially toward evening. They tire at work, and during the day readily fall asleep, while during the night they are hot, perspiring, sleepless, or disturbed by frightful dreams. The face becomes pale; the mental state is depressed, at times irritable. Generally the tongue is somewhat coated, and almost always the appetite is lost and the sense of thirst increased. Irregular action of the bowels, with flatulence, alternates with diarrhea, or there is persistent constipation. Some patients complain of slight anginose symptoms, while others exhibit bronchitic manifestations and believe themselves to be suffering from a "cold" or from influenza.

Temperature-observations are naturally made irregularly, if at all, in private practice, in cases of ambulatory typhoid fever; and as the patients are seldom sent to the hospitals, a thorough study is as yet wanting. According to my observation, the temperature-course may be of several varieties. Thus, there may be simple remittent fever at a low level, so that in the morning the temperature rises little above the normal, if at all. Quite commonly also irregular variations occur, with a sudden elevation during the morning or in the middle of the day, as a result of excitement, overexertion, etc., or without obvious cause. Other cases pursue an afebrile course throughout, or at least for several days. An intermittent febrile course is least common, in which elevation of the temperature may take place daily, with a chill or with feelings of chilliness. In a number of instances I have observed that

under such conditions this ascent takes place not toward evening, but regularly at a time when the patient is most actively engaged; it is therefore in the nature of a reaction to external influences. Thus, I recall the case of a physician who during an attack of ambulatory typhoid regularly exhibited chilliness with marked fever after his consultation-hour at about noon, while during the remaining time the temperature was normal, however often observations were made. Another patient under my care, an attorney, had his attacks of fever in the morning during the sessions of court. The physician referred to believed himself suffering from malaria, until a relapse, with characteristic temperature-curve, diarrhea, and roseolæ, cleared up the nature of the attack; while in the other patient, who voided remarkably high-colored, dark, brownish-red urine during the febrile period, paroxysmal hemoglobinuria was at first suspected.

The pulse appears in almost all cases to be remarkably frequent from the beginning, relatively more so than in typhoid patients who have gone to bed. Whether dicrotism occurs or not, I do not know. In a considerable number of patients the action of the heart appears to be even more unstable than the state of the body-temperature, so that some complain only of attacks of palpitation. The physician previously referred to had himself detected intermission of the pulse, and had conceived all possible hypochondriacal ideas in regard to it, although no special change in the heart could subsequently be demonstrated.

Even at the primary examination in cases of ambulatory typhoid fever distinct enlargement of the spleen is not rarely found. Occasionally the patients themselves direct attention to this by complaints of abnormal sensations in the left hypochondrium. Roseolæ also are not infrequently found on careful examination, although generally in small numbers. I have personally been able to demonstrate them in patients who consulted me in my office—once, for instance, in a young woman from Russia, who had been sent to Franzensbad on account of "chlorosis with hysteric symptoms," and becoming herself doubtful, had consulted me *en route*.

With regard to the course and the duration of ambulatory typhoid fever, naturally no definite statement can be made for the majority of cases. Undoubtedly two principal varieties occur in this form of the disease. The one includes the well-developed cases of typhoid fever of usual duration. In these the disease extends over from four to six weeks, when recovery occurs. If such developed cases unexpectedly terminate fatally,—as unfortunately not uncommonly occurs, particularly from hemorrhage and perforative peritonitis,—they often occasion sur-

prise at post-mortem examination on account of the unusual development and extent of the intestinal lesions and other characteristic visceral changes.

The second group of cases more closely approximates the conditions present in the undeveloped, mild cases, and might equally well have been discussed in the preceding chapter. By reason of their short duration and the circumstance that the slight disturbances rarely restrain the patients in their accustomed occupations, they certainly often escape recognition, especially when they occur isolated and without any distinct connection with well-developed cases of typhoid fever. Not a few cases of "cold," "angina," "acute gastro-intestinal catarrh," or "influenza" may belong in this group. Other cases of the ambulatory type—exactly as was mentioned as occurring in cases of mild typhoid fever—are recognized only when, after slight symptoms have been present for days, there occurs a recrudescence or a relapse, accompanied by roseolæ, enlargement of the spleen, and characteristic intestinal symptoms. It should be expressly emphasized at this place that even the apparently mild, ambulatory cases of short duration may, though apparently seldom, reveal themselves by intestinal hemorrhage and peritonitis, and terminate fatally therefrom.

With regard to age and sex, I believe the statement is justified that ambulatory typhoid fever occurs more frequently in adults than in children. Among the former, in my experience, the young and older individuals seem to be about equally predisposed. I have even observed ambulatory typhoid fever in debilitated, elderly individuals. With regard to sex, men are distinctly more commonly affected than women. They are more resistant, less sensitive, and, among the lower classes, often secure relief by the use of alcohol from symptoms that would cause others to take to their beds.

Some persons with ambulatory typhoid fever may perform surprising tasks. A salesman who had already been ill between two and three weeks had daily continued at his work without interruption, and had walked four hours on the day of his admission to the hospital, the reason for his coming having been a slight intestinal hemorrhage while going about. On admission, enlargement of the spleen, slight meteorism, and a profusion of roseolæ were demonstrable. Another patient under my care, a pilot, forty-two years old, had continued in service uninterruptedly throughout the entire journey from New York to Hamburg, although he had for a number of days suffered from anorexia, diarrhea, occasional headache, and vertigo; he had even remained almost constantly at his post during the last stormy days in the English Channel. On the day of his arrival at Hamburg the sudden development of symptoms of circumscribed peritonitis compelled his entrance into the hospital. On admission he presented moderate fever, but no other than the local manifestations. It was not until after the disappearance of the peri-

tonitic symptoms, twelve days after admission, that a marked recrudescence, lasting fourteen days, with high fever, enlargement of the spleen, and roseolæ, rendered certain our suspicion that the case might be one of ambulatory typhoid.

Afebrile Typhoid Fever.—Although with increasing knowledge of the nature and manifestations of typhoid fever some symptoms which were earlier considered pathognomonic of this condition were found not to be so, it was nevertheless believed—and this was still the opinion of Griessinger and Wunderlich—that there could be no typhoid fever without elevation of temperature. The modern conceptions of the infectious diseases, however, must of necessity have led to the belief that typhoid fever also might be wholly or almost wholly unattended with elevation of temperature, just as occurs in other infectious diseases, as, for instance, scarlet fever, measles, and variola.

Every experienced physician—the family physician more frequently than the hospital physician—will be able to recall that during the endemic prevalence of typhoid fever there occurred under the same roof, and amid the same general conditions, side by side with well-characterized cases of the disease, others in which individuals suffered for a considerable time with marked languor and malaise, with headache and vertigo, irregularity in the action of the bowels, diarrhea, or obstinate constipation with flatulence, and were compelled to remain in bed and in their room, and recovered but slowly, but in which, during the entire attack, there was no fever. In some of these patients examination fails to disclose any special organic change throughout the entire course of the disease. Loss of weight of from 8 to 10 pounds in the course of two weeks, however, indicates emphatically that some serious condition must have been present. One cannot relieve himself of the impression that the patient, who, in marked contrast with the negative organic changes, has been so greatly reduced in weight, must have been under the influence of some infectious process whose nature, in view of the coincidence with pronounced cases of typhoid fever, can scarcely be doubted. In other cases one need not make a diagnosis by exclusion. There may be present bronchitic symptoms, meteorism, characteristic diarrhea, isolated roseolæ, or, what is not rare and is especially important, recent enlargement of the spleen.

The frequency of such afebrile cases is, in view of the uncertainty and variability of their symptomatology, naturally difficult of estimation. Probably it is variable during different epidemics. Whether a certain age or sex especially predisposes to the condition is not known to me from personal experience, and, so far as I know, the question has not

been considered by other writers. The differentiation of the cases in question from superficially similar, afebrile morbid conditions particularly simple gastro-intestinal catarrh, will, in the future, by means of the Gruber-Widal reaction, be rendered more certain than has been possible in the past. Probably, also, bacteriologic examination of the blood, the urine, and the stools will lead to more definite results. It would naturally be artificial to separate the afebrile cases of typhoid fever into a rigidly distinct group. They gradually pass over into those cases in which, during a long afebrile course, only moderate elevation of temperature occurs temporarily or for days. Afebrile typhoid fever certainly contributes its contingent of cases to the ambulatory form.

I can personally give no statistical data with reference to the afebrile form of typhoid fever, although I have seen a considerable number of such cases. Most valuable contributions, however, have been made by Liebermeister,[1] who, agreeing with the practitioners of Basle as to diagnosis, observed many cases of afebrile typhoid fever. He noted in 1869, in addition to 206 cases of more or less well-developed typhoid fever, 29 of febrile and 139 of afebrile abdominal catarrh; in 1870, 26 cases of febrile and 11 cases of afebrile abdominal catarrh, in addition to 161 cases of marked typhoid fever. The statement of Liebermeister is also interesting in this connection, that in Basle at that time individuals who died of other diseases or as a result of accident frequently exhibited after death the unexpected condition of slight swelling of Peyer's patches.

An instructive case of afebrile typhoid fever under my observation in which a post-mortem examination was made may be reported. It occurred in a laborer, eighteen years old, who had been in the hospital for two weeks on account of "intestinal catarrh," and whose temperature, taken three times daily, was found to be completely normal, with the exception of one evening, when, after a visit which disturbed him considerably, it rose to 38.2° C. He exhibited also no especial local symptoms. He was only remarkably languid, entirely without appetite, prostrated, and was unwilling to get out of bed. On the fifteenth day of the disease, quite without provocation, without elevation of temperature, symptoms of mental disturbance appeared, with hallucinations and delusions of fear. In an unguarded moment the patient sprang from a window, and died instantly in consequence of fracture of the base of the skull. The autopsy disclosed a recent enlargement of the spleen of moderate degree, hyperemia, and firm medullary swelling of Peyer's patches in the lower portion of the ileum, almost down to the valve, and upon one of these a still adherent central slough, perhaps half an inch in diameter. This observation was made before the discovery of the typhoid-bacillus, but the diagnosis may nevertheless be considered as definitely established.

While a number of cases of afebrile typhoid fever may, by reason of their atypical and mild course, be included among the mild and the mildest variety, others, fortunately the great minority, belong to the severe form, even that with a fatal termination. The credit is due

[1] *Loc. cit.*, 3. Aufl., S. 174, 175.

especially to Strube[1] and Fräntzel[2] for having directed particular attention to this subject. My own experiences are entirely in accord with those of the observers named. I can confirm the statement that severe fatal cases of typhoid fever in elderly, decrepit persons, or in those debilitated by overexertion, alcoholism, or chronic disease, may be entirely unattended with fever, or may even be accompanied by a subnormal temperature.

SEVERE AND MODERATE CASES OF ATYPICAL COURSE AND SYMPTOMATOLOGY.

In this section will be discussed the essential facts with regard to such cases of typhoid fever as present deviations from the usual symptomatology of the disease by reason of peculiarities in their course in general, or on account of the predominant *rôle* played by certain systems or individual organs. The literature of different periods and countries exhibits the greatest variation in this connection. While in earlier times especial weight was attached to the variable general picture of typhoid fever, and accordingly, as is thought to-day, the disease was far too schematically divided into a mass of different forms, modern conceptions keep in mind rather the distinctive predominance of certain organic lesions, so that the French literature especially is thus rich in varieties established on this basis.

The Varieties with Atypical General Characteristics.— These may at the present day be disposed of in a comparatively small amount of space. It is scarcely worth while to repeat all the designations that have arisen and have been employed in the progress of time. We have previously mentioned the so-called gastric and the mucous fever (*Forme mucuese* of the French), and have pointed out that, according to the suggestion of Griessinger, these names had better be wholly abandoned at the present day, and be replaced by those of mild and moderately severe typhoid fever.

Not much more can be said of the designations gastric-bilious fever or bilious fever, which were formerly frequently considered as the third variety of the "abdominal forms." Under these designations were included those cases of typhoid fever in which, usually in conjunction with a moderately severe or a severe course, gastric disturbances, a bitter taste, with a heavily coated tongue, obstinate nausea, and the vomiting of bilious fluid, with severe pain in the epigastrium, predominated from the beginning. Some writers mentioned in this connection the frequent association of jaundice. These cases especially, on

[1] *Berlin. klin. Woch.*, 1871, No. 30. [2] *Zeit. f. klin. Med.*, Bd. ii.

account of the well-known great rarity of jaundice in cases of typhoid fever, are to be viewed with particular care. A considerable number of them are not to be attributed to infection with the bacillus of Eberth, but from the etiologic standpoint they are rather to be grouped with other morbid conditions, among which septic processes and Weil's disease are probably the most important.

Reference is very frequently made in earlier writings to versatile nervous fever and to stupid nervous fever. These were long undisputed as special varieties. As a matter of fact, cases are frequently observed in which the special symptoms indicated by these names so predominate that the names may be retained as short and appropriate. It should not, however, be overlooked that the differences indicated by these names are not essential, but rather superficial, and in large part individual, and that, besides, the great diversity of mixed and transitional forms demonstrates how little importance can be attached to any such strict systematic differentiation.

The designation versatile nervous fever is applied to cases in which symptoms of nervous excitement predominate at the height of the disease, at times also throughout the entire febrile period: Great restlessness, with marked motor and sensory irritability, delirium, appearing early, persisting into the day, with vivid, generally frightful, illusions and hallucinations, even crying and shouting, with a constant tendency to get out of bed, and occasionally attempts at flight. Tremor, floctitation, and subsultus tendinum, even convulsions, in children and irritable adults complete the clinical picture, which is most alarming to the friends.

In contradistinction to this condition, the cases included under the designation stupid nervous fever justify that name by reason of the depression which characterizes their course and symptoms. From the outset, or at least during the fastigium, the patients are greatly depressed physically and mentally, dull, unresponsive to stimulation, and without will-power. Sleepless, with eyes open or half-open, they preserve a relaxed dorsal decubitus in bed, with a constant tendency to slip downward. Without being entirely unconscious, often being but slightly stuporous, they are indifferent both to individuals and to events going on about them. They ask for neither food nor drink, but swallow badly and slowly that which is offered them, or permit it to flow again from the mouth. Not rarely, especially in young women with a nervous predisposition, the condition of stupor becomes increased to the development of symptoms of catalepsy. I have more than once been able to demonstrate cataleptic rigidity with plastic flexibility in indi-

viduals who were considered by their attendants as completely stuporous, and even in whom the typhoid fever was thought to be complicated by meningitis.

The form of stupid nervous fever just outlined is approximately identical with the variety of typhoid fever described by the French and English as the adynamic form; while they employ instead of versatile nervous fever the expression ataxic or irritative typhoid fever. It has been mentioned that transitions between these forms may occur and various clinical pictures be produced. The French literature gives expression to this with its ataxo-adynamic variety, in which the symptoms of excitement and depression may be present in varying degrees simultaneously or successively. The ataxo-adynamic variety also resembles that designated the hyperpyretic variety, which is characterized by the fact that after the disease has pursued a relatively short and severe course, with depression and irritative symptoms side by side, the fever, which from the beginning was considerable, rapidly rises to an excessive height, when the majority of patients succumb. Cases of this kind, pursuing an especially severe course, closely resemble, in turn, the clinical picture of the fulminant variety previously described.

It is not clear what cases earlier prominent physicians (Murchison, Trousseau) included under the designation of the inflammatory variety. They appear thereby to aim at the description less of a special variation in the general course rather than to include under this term such cases of typhoid fever as are attended, especially at the beginning, with severe fever, a tense, full, unusually frequent pulse, a hot, dry skin, an intensely reddened, swollen face, with injection of the conjunctivæ, a burning thirst, and great dryness of the mouth, tongue, and lips.

While the consideration of the varieties just described was intended to make clear the differences between the past and the present methods of classification of the different forms of typhoid, one of these varieties may now be referred to, which even yet appropriately occupies a distinct position. This is the so-called **hemorrhagic typhoid fever** (hemorrhagic putrid fever of Trousseau), that variety that is so strikingly and alarmingly characterized by hemorrhages in all possible portions of the body. In a number of rare cases it constitutes a form of termination of the fulminant variety, while in other cases it makes its impress upon the disease at the height, or may even occur in the later stages of cases, which at first exhibited an entirely typical course, or which had even pursued a protracted course (Wagner,[1] Gerhardt[2]). This dangerous tendency may be first manifested during a relapse, and

[1] *Deutsch. Arch. f. klin. Med.*, Bd. xxxii., xxxvii. [2] *Zeit. f. klin. Med.*, Bd. x.

this, so far as I know, was first pointed out by Gerhardt and myself on the basis of personal experience.

Such an instance has occurred at the Johns Hopkins Hospital, and was reported by Hamburger. In this case the hemorrhages first appeared on the fourteenth day of a relapse, the original attack having been of moderate severity. There was quite profuse bleeding from the gums, and numerous petechiæ and a few larger purpuric spots were scattered over the body. Notwithstanding this complication, the patient made a complete recovery.

The first hemorrhages appear to take place generally from the nose. Immediately thereafter, at times simultaneously, hemorrhages occur from the discolored, spongy gums. Then petechiæ appear upon the skin of the trunk and the extremities, scattered between the roseolæ, which occasionally do not become hemorrhagic or become only slightly so. In especially malignant cases profound extravasations of blood into the subcutaneous connective tissue, even beneath the scalp, may occur (E. Wagner). A considerable number of these patients are, besides, seized with meningeal and cerebral hemorrhage. Even more frequently, indeed in the overwhelming majority of all cases, intestinal hemorrhage occurs; at times being in such abundance and occurring with such frequent repetition that it may be considered the direct cause of death. In one case, which terminated fatally as early as the sixth day, in the course of a profuse hemorrhage from the bowel, I found, as the anatomic basis for the latter, that the Peyer's patches in the lower portion of the ileum were exceedingly spongy, friable, and infiltrated with reddish-black blood.

Not quite so common as the forms of hemorrhage mentioned is that from the urinary tract and the genitalia. Pregnant women seized with the hemorrhagic variety of typhoid fever invariably abort, and then die as a result of uncontrollable uterine hemorrhage. Hemoptysis appears to be the least constant form of hemorrhage, and when it occurs, it may be attributed either to infarction or simply to bleeding from the bronchial, tracheal, and laryngeal mucous membrane. In the further course of the disease gangrenous processes may be added to the hemorrhages: Ulcerative destruction of the gums and other parts of the buccal mucous membrane, pulmonary gangrene, generally, it is true, in conjunction with infarction, and pseudodiphtheric lesions of the uterine and vesical mucous membrane.

With regard to the nature and the mode of origin of this extremely malignant variety, which is fortunately rare, nothing is as yet known. If the modern clinician sneers at the expression "dissolution of the blood," employed by his predecessors, he should bear in mind that he has not as yet provided a better substitute. At present we do not

know whether special characteristics and mode of action of the typhoid-bacillus or whether certain conditions of the body or the effects of certain complications play the most important *rôle* in this connection. Earlier writers (Trousseau) claimed to have established that in the cases in question there occurred a special alteration in the blood, characterized by a remarkably dark color and deficient coagulability. I have personally, in the examination of one case during life, not been able to demonstrate either these macroscopic peculiarities or noteworthy histologic changes in the blood. In the case above mentioned as occurring at the Johns Hopkins Hospital, however, the coagulation-time of the blood, during the periods when hemorrhages were occurring, was increased to ten minutes, but during convalescence it again became reduced to four minutes. It should especially be emphasized, however, that neither in any of my cases nor, so far as I can learn, in the literature, has hemoglobinemia with hemoglobinuria been observed. Careful examination of the blood-vessels, particularly the capillaries, which possibly may show alterations of more importance than changes in the blood itself, has yet to be made.

With regard to the general etiologic conditions in the cases in question, childhood, as well as youth and adolescence, appears to be more predisposed than the later periods of life. Of 6 cases under my own observation, 3 occurred in childhood. The oldest of my patients was thirty-six years of age. Wagner and Gerhardt also emphasize the predisposition exhibited by children. The constitution and the mode of life apparently do not play the *rôle* that might *a priori* be attributed to them. Gerhardt and Griessinger include scorbutic states, deficient nourishment, and living in overcrowded rooms among the contributory causes. In my cases, however, nothing of this character appeared in the histories. Of great importance, however, appears to me to be previous alcoholic excess. Of my 3 adult patients, 2 were notorious drunkards.

With regard to the frequency of occurrence of the hemorrhagic variety, it may be repeated that I have personally observed only 6 definite cases. Liebermeister noted but 3 among 1900 cases of typhoid fever in the epidemic at Basle; and Weil but 1 among 150. Among 829 cases at the Johns Hopkins Hospital, only 1 case, that above mentioned, occurred. Slightly marked, mild hemorrhagic cases, however, appear to be not at all rare. Thus, in persons greatly exhausted in the sequence of protracted, severe attacks of typhoid fever, or in those with special predisposition, as in abnormally obese individuals, women and children, and especially in beer-drinkers, there is not rarely observed at

a late stage of the disease a marked tendency to hemorrhage from the nose, the gums, the corners of the mouth, and fissures of the lips. Such individuals exhibit a tendency to extensive hemorrhages into the skin, the subcutaneous connective tissue, and even into the muscles, as a result of the slightest traumatic influences—such as the pressure of the nurse's hand in moving him, or of the pressure of articles of clothing or of the sheet.

The prognosis in the well-marked hemorrhagic variety is in general the more unfavorable the earlier the hemorrhages appear and the more extensive they are. All my 6 cases terminated fatally. Wagner lost but two-thirds of his patients. The prognosis in the slightly marked cases depends upon the other associated conditions.

TYPHOID FEVER IN WHICH SYMPTOMS REFERABLE TO CERTAIN ORGANS OR SYSTEMS PREDOMINATE.

The majority of the cases to be considered in this section have already been referred to in connection with the analysis of the individual symptoms. It will be useful, however, particularly with regard to the diagnosis, to review these clinical pictures, and to complete the detailed description.

Typhoid Fever in which Symptoms Referable to the Central Nervous System Predominate.—Cerebral, spinal, and cerebrospinal varieties may be distinguished. These have previously been fully considered, so that at this place it will suffice to refer again only to the cases that set in with severe cerebrospinal symptoms and are even characterized by a predominance of these (meningotyphoid), and to those in which a complex of severe spinal symptoms resembling acute (Landry's) ascending paralysis obscure the picture of typhoid fever wholly beyond recognition (Leudet, Curschmann).

Of the so-called cerebral variety, only those cases will again be referred to that are quite early associated with severe mental disturbances. The greatest diagnostic difficulty may attend those cases, which are rare, it is true, in which the attack of typhoid fever sets in with the symptoms of a psychosis, and the characteristic manifestations of the underlying disease—the roseolæ, enlargement of the spleen, and diarrhea—do not appear for days and even for a week after the onset. It is a matter of expediency to specify such cases with the designation cerebral typhoid.

Among the **disorders of the respiratory organs** that at times give an unusual character to the course of typhoid fever, those of the larynx, the lungs, and the pleura are the most important. Among these,

those of the larynx are the rarest and the least conspicuous. Cases in which the entire clinical picture is dominated by the early onset and unusual development of the typhoid lesions of the larynx are extremely rare, and the designation laryngotyphoid is artificial and superfluous.

Of far more significance are the terms *pneumotyphoid* and *pleurotyphoid*. For the justification of the designation pneumotyphoid Gerhardt, Potain, Lépine, E. Wagner, and recently Eggert[1] have furnished abundant evidence. This condition is observed in those cases of typhoid fever in which symptoms of pneumonia appear during the first days, so that the first week is either dominated entirely by a typical clinical picture of inflammation of the lung, or the latter is attended with other symptoms unusual to it, but which are for a time of undetermined significance. Such cases may, as has been pointed out, be wholly unrecognized at first, and be correctly interpreted only toward the end of the first or even in the beginning of the second week of the disease, when the pneumonic symptoms recede and those characteristic of typhoid fever come more into the foreground. Undoubtedly, the majority of such cases are to be considered as due to a mixed infection. Among the associated organisms, probably the diplococcus of Fränkel-Weichselbaum occurs the most frequently. The cases are likely, just as those of genuine fibrinous pneumonia, to begin with a chill, with subsequent marked elevation of temperature, and to be followed by the rapid development of dense lobar, generally unilateral, infiltration of the lungs, often with characteristic rusty sputum. It is possible, however, that the typhoid-bacillus may also independently cause inflammatory alterations in the lungs (as claimed by Lépine, Chantemesse and Widal), and such cases would, as has been pointed out, be examples of pneumotyphoid in the strictest sense of the term. Further work is needed, however, before it can be considered as established that such cases ever occur (see page 116). It has been claimed that such cases are characterized by frequent absence of the initial chill, by delayed involution and absence of the characteristic rusty sputum, and by less rapid ascent of the temperature-curve and less dense infiltration of the lung than occurs in the cases due to the pneumococcus. It is maintained by some that in such cases the intestinal symptoms are frequently but slightly marked, if at all, and the development of roseolæ is altogether wanting. Our experiences in this connection appear to me to be too small as yet to justify such general statements.

As an instance of pneumotyphoid I may cite the case of a man, twenty-eight years old, in whom a moderate grade of infiltration of the lower lobe

[1] *Inaug. Diss.*, Erlangen, 1888.

of the left lung, associated with chilliness and a step-like elevation of temperature, occurred. Associated with this there were marked dryness of the tongue, palpable enlargement of the spleen, and slight meteorism, but no diarrhea or roseolæ. At the end of the third week of the disease, after the pneumonic consolidation had existed for two weeks, the temperature fell to normal. Sixteen days later there developed the symptoms of a typhoid relapse, with a characteristic febrile course of three weeks, with renewed enlargement of the spleen, copious and frequent pea-soup-like stools, and a well-developed roseolous exanthem on the trunk and the upper portions of the extremities.

The course of pneumotyphoid appears to be in general not so severe as would *a priori* be expected. Gerhardt early emphasized this. In one of my cases death occurred from pulmonary gangrene. This case was not examined bacteriologically. In another, due to the Fränkel-Weichselbaum diplococcus, empyema developed, but the case finally terminated in recovery. Although the variety known as pneumotyphoid is, on the whole, rare, it does, nevertheless, at some time and during certain epidemics appear to be more frequent (Gerhardt, E. Wagner). I have personally observed 2 cases of pneumotyphoid at Berlin and 1 at Hamburg at times when genuine fibrinous pneumonia prevailed.

Pleurotyphoid.—Just as during the course of typhoid fever, pleurisy occurs much less frequently than pneumonia, so also does the symptom-complex that may be designated pleurotyphoid appear to be still less frequent than pneumotyphoid. Nevertheless, experienced clinicians will be able to recall cases in which symptoms of pleurisy developed, generally associated with chilliness and subsequent, more or less marked, remittent continued fever. These cases were then at first considered as of independent, so-called rheumatic, or of other etiologic origin, until headache, progressive stupor, enlargement of the spleen, diarrhea, and meteorism, as well as roseolæ, established the existence of an attack of typhoid fever presenting itself in this peculiar and rare manner.

I have personally observed 4 cases of this character. In 3 copious effusions developed rapidly, being in 2 of a purely serous character, while in 1 it was serohemorrhagic. The fourth case was unattended with effusion. I shall briefly sketch this last case and one of the cases with effusion. I saw the case without effusion in the year 1886, during the typhoid epidemic in Hamburg. It occurred in an assessor, thirty-one years old, who, after having previously been entirely well, was seized during a session with chilliness and severe pain in the right side. Two days later the patient showed, in addition to the symptoms of slight diffuse bronchitis, extensive pleuritic friction over the lower lobe of the right lung. In view of the moderate elevation of temperature, the occurrence of considerable stupor, dryness of the tongue, and a large, palpable splenic tumor was striking. On the fifth

day following (seventh day of the disease) distinct roseolæ made their appearance upon the abdomen, chest, and back. Considering the temperature-course and the remaining symptoms, there was now no further doubt that the case was one of typhoid fever whose first marked symptoms were referable to the pleura. The course of the attack was favorable. The patient was free from fever after the lapse of four weeks, and he recovered rapidly and completely. The pleuritic friction persisted until the eighth day of the disease. Signs of adhesion of the affected portions of the pleura were absent at an examination made a half-year later.

The other case occurred in a merchant, twenty-seven years old, who was admitted to the clinic on the fifth day of the disease, and related that cough, with pain in the side and a difficulty in breathing, had been the first symptoms of the attack. On admission, a large right-sided serohemorrhagic pleural effusion was discovered. The left lung was intact, with the exception of a few bronchitic râles. The spleen was not enlarged, meteorism was not present, and there were no roseolæ. The only remarkable feature for a case of simple serous pleurisy was the unusual temperature-course, which was that of a continued fever of moderate degree, with but slight daily fluctuations. Not until the eighth day did characteristic pea-soup-like stools appear. At the same time enlargement of the spleen could be demonstrated, but roseolæ failed to appear either at this time or subsequently during the course of the disease. Our suspicion that the case was one of pleurotyphoid was confirmed by the positive results yielded by the Gruber-Widal agglutination-test. The case terminated in recovery after a most protracted course. The effusion, which had to be evacuated by thoracocentesis on the twenty-eighth day, did not reaccumulate.

My own cases were, unfortunately, not examined bacteriologically. It is certain, however, that the typhoid-bacillus alone may cause pleurisy.[1] The cases in which this has been demonstrated fulfil the most rigorous requirements that could be demanded for the establishment of pleurotyphoid as an especial variety.

The so-called **nephrotyphoid** has also been previously considered (pp. 192, 193). It was there mentioned that its sharp differentiation by Gubler and Robin, and especially the schematic classification of Amat, had, on closer study, proved untenable. Nevertheless, the designation nephrotyphoid may be applied to certain cases as describing briefly and well a peculiarity of their course. This is permissible —just as has been pointed out with regard to pneumotyphoid and pleurotyphoid—when the commencement, as well as the first, and even the second, week of the attack is dominated by the clinical picture of

[1] Compare the French literature on this point, p. 257 (see also p. 118). In addition, the papers of Netter, *Bull. de la Soc. méd. de Paris*, May 16, 1890. Loriga and Pensuti, *Riforma med.*, 1890, No. 206. Weintraud, *Berlin. klin. Woch.*, 1893, No. 15. Spirig, *Mittheil. a. klin. Instit. d. Schweiz*, 1894, 1 Reihe, Heft 9. Sahli, *Ibid.* In all these cases the typhoid-bacillus gave rise to purulent effusions. That it may, however, give rise also to serofibrinous effusions is shown by the case of Fernet, previously mentioned.

severe acute hemorrhagic nephritis. Further classification, however, so as to include cases in which the usual typhoid lesions of the viscera assume clinically, and even anatomically, a very subordinate position, or are even absent entirely, appears to me unjustified. I have observed cases of nephrotyphoid in which, at the end of the first or at the beginning of the second week, characteristic diarrhea, together with numerous roseolæ and enlargement of the spleen, first appeared; and I can recall another case that during life appeared to be free from intestinal involvement, but which at autopsy exhibited abundant infiltration of Peyer's patches in the lower third of the ileum as low as the ileocecal valve. The statement also that the cases in question almost always terminate fatally is not correct, and is probably based upon insufficient data.

I have described on page 300 a case of typhoid fever of abortive course which exhibited perfectly the clinical picture of nephrotyphoid. Only recently I observed a second case of the same character. A merchant, twenty-six years old, in whose family 3 well-defined cases of typhoid fever of moderate severity had occurred within a short time previously, was seized with sensations of chilliness, followed by a step-like elevation of temperature. After the second day, bloody urine containing large amounts of albumin, with great numbers of hyaline, epithelial, and blood-casts, was voided. The amount of urine was greatly diminished—from 300 to 400 c.c. in twenty-four hours—and the specific gravity was between 1022 and 1028. Although during the first few days, in the absence of other conspicuous symptoms, nothing else than an acute hemorrhagic nephritis could be assumed to be present, nevertheless the persistence of the fever, the dry tongue, and enlargement of the spleen, demonstrable by palpation on the fifth day, together with the occurrence of the other cases in the same house, raised the question as to whether the condition might not be dependent upon typhoid infection. The appearance of roseolæ on the ninth and tenth days of the disease, and their continued appearance in abundance up to the fourteenth day, converted the suspicion into certainty. The fever persisted in a moderate, continued, remittent form until the eighteenth day, after which the temperature abruptly declined to 36.3° C. within twelve hours. From this time on, convalescence was uninterrupted. The blood had disappeared from the urine on the eleventh day of the disease, and albumin and tube-casts could no longer be demonstrated after the seventeenth day. Both cases may be considered as typical instances of nephrotyphoid of mild course. If I am not mistaken, similar cases have been but rarely described heretofore. Possibly writers have been too much influenced by the conception of a very severe course that is considered typical of the disease.

The position etiologically of cases of nephrotyphoid is as yet unknown. Trustworthy bacteriologic examinations directed especially to the participation of the typhoid-bacillus in the kidney-lesions have not as yet been made.

ASSOCIATION OF TYPHOID FEVER WITH OTHER DISEASES.

Naturally, the question here of especial significance, and the one to be considered above all others, is as to the relation between the other acute infectious diseases and typhoid fever, or, more definitely expressed, the manner in which the organism under the influence of the typhoid-bacillus responds to the action of the specific exciting causes of those diseases. It has previously been emphasized in the General Section (p. 65) that the existence of typhoid fever, especially at the period of its febrile height, affords pretty certain protection against the invasion of other acute infectious diseases. As a matter of fact, the following statements will show that this is entirely true with regard to some, while with regard to others, even though with extreme rarity—*exceptio firmat regulam*—a coincidence of the disease with the fastigium of the typhoid can be made out. The possibility of infection during the stage of convalescence, and also during the period of incubation, is less to be excluded, as such infection appears to be distinctly more frequent at this time than at the height of the fever.

Typhoid Fever and the Acute Exanthemata.—The question as to the coincidence of the acute exanthemata with typhoid fever is still obscure in many respects. The older literature contains far more numerous positive statements than the more recent literature. Many of the earlier reports are to be accepted with great caution, not alone on account of the often most indefinite description of the exanthemata, but also on account of the uncertainty in the diagnosis of typhoid fever itself; for, as has been pointed out, typhus fever and typhoid fever were, until within recent decades, not sufficiently differentiated, particularly in England. It can at the present day be stated with considerable certainty that a number of acute exanthemata may definitely be associated with typhoid fever, while this can be denied of others, or, at least, the question is still doubtful.

The coincidence of scarlet fever and typhoid fever has been recorded by numerous observers: Taupin,[1] Forget,[2] Murchison,[3] and recently by Eichhorst[4] and Gläser.[5] Murchison presents the large number of 8 personal observations, all on patients in the London Fever Hospital, who were infected with scarlet fever from other patients in the same ward.

The following history by Murchison[6] may serve as an illustration:
A police-officer, twenty-three years old, was admitted to the London

[1] *Jour. des conn. méd. chir.*, 1839.
[2] *L'entérite follicul.*, Paris, 1840 (both cited by Murchison).
[3] *Loc. cit.*, and *Trans. Path. Soc.*, 1859, vol. x.
[4] *Lehrbuch.* [5] *Deutsch. med. Woch.*, 1885, No. 11, and 1886, No. 46.
[6] *Typhoid Diseases*, p. 522, translated by Zülzer, Berlin, 1867.

Fever Hospital, Nov. 9, 1857, after an illness of from two to three weeks' duration. He exhibited all the symptoms of typhoid fever: a red, glazed, and fissured tongue, tympanites, profuse watery diarrhea, and an abundant roseolous exanthem. Fresh spots appeared constantly. Eight days after admission they were still quite numerous and the diarrhea persisted. There now appeared in addition a general scarlatinal eruption identical with that of scarlet fever, together with a strawberry-tongue, with greatly enlarged papillæ, angina, and redness of the fauces. After two days the roseolæ were still quite numerous, and the scarlatinal eruption persisted. Two days later the latter faded, while the typhoid eruption persisted for a few days more. A week after the disappearance of the scarlatinal eruption there was abundant desquamation. The patient recovered rapidly.

Among the cases of Gläser, one that terminated in the death of the patient is especially instructive. In addition to the typhoid fever, which was characterized sufficiently by roseolæ and palpable enlargement of the spleen, symptoms of scarlet fever appeared at the beginning of the second week. The well-marked and characteristic exanthem, which persisted for five days, had been preceded immediately by angina, with dark-red discoloration of the mucous membrane. The patient died in consequence of scarlatinal nephritis. Examination of the intestine disclosed, in the neighborhood of the ileocecal valve, the lesions of a terminated or healed typhoid process of slight extent.

I have personally not as yet encountered the coincidence of the two diseases, probably because I have always practised the rigid isolation of typhoid patients, even of adults, from patients suffering from scarlet fever. With regard to the order in time in which the diseases succeed each other, apparently in the great majority of instances scarlet fever occurs secondarily. It then generally appears in the later stages of typhoid fever, often only during convalescence, but even in these cases the onset is frequently so early in convalescence that the period of infection must be referred to the febrile stage of the typhoid fever. From a diagnostic point of view, the combination in question presents considerable difficulty. It is easily conceivable that certain cases of hemorrhagic variola with a scarlatiniform initial exanthem and a typhoid course, and also certain scarlatinoid erythemata, especially those attending cryptogenetic septicemias, may be confused with the combination of diseases now under discussion.

The coincidence of rötheln with typhoid fever has been mentioned by Taupin, Barthez and Rilliet, and others. With all due regard for the acumen of these observers, especial caution would seem necessary in this connection, particularly on account of the danger of confusion of this condition with transient punctate erythemas, and especially with drug-exanthemas. It is doubtful whether measles and typhoid fever may occur together.

In my experience[1] variola and typhoid fever appear almost to

[1] See Curschmann, "Die Pocken," *von Ziemssen's Handbuch*, 2d ed., 1878. Th. Simon, *Berlin. klin. Woch.*, 1872, No. 11.

exclude each other during the febrile stage of each disease. I have repeatedly seen convalescents from typhoid fever attacked by small-pox, but whenever the beginning of the attack of variola was determined, it could be established that the infection must have taken place in the afebrile period of convalescence from typhoid fever, even admitting the longest possible period of incubation for the variola.

Of 6 convalescents from typhoid fever infected with small-pox whom observed in the year 1870–71 in the hospital at Mainz, which at that time was overcrowded, the primary stage began in 2 on the nineteenth, in 2 others on the seventeenth, and in 1 each on the sixteenth and the fourteenth day after they had exhibited the last febrile elevation of temperature attributable to the typhoid fever. A case, apparently of actual coincidence of variola and typhoid fever, has been reported by Th. Simon, who in the same communication states that it is his impression that during the epidemic of small-pox that prevailed in Hamburg at that time, the cases of typhoid fever which occurred exhibited usually well-marked development of the roseolous exanthem.

I have personally observed vaccine-pustules during the febrile stage of typhoid fever in a few cases. The patients were individuals who had, during the period of incubation of typhoid fever, a greater or less time before the appearance of its first symptoms, been subjected to protective vaccination. These cases prove that at a period in which the organism is already under the influence of the typhoid infection, even though in but a latent degree, the activity of the excitants of vaccinia is not abolished.

Typhoid Fever and Other Acute Infectious Diseases.—The Septicemic Variety.—This severe form of disease, which has as yet been but little investigated, appears to be the result of mixed infection with Bacillus typhosus and Streptococcus pyogenes. The cases are said to be characterized by high fever, unusually marked disturbance of the general condition, considerable and early enlargement of the spleen, the mesenteric and the bronchial glands, with, it has been stated, often only slightly developed, and, according to some writers, at times even wholly absent, specific intestinal lesions. The pathogenic micro-organisms are demonstrable especially in the spleen and the lymphatic glands. They have been repeatedly found also in the liver, the brain and the meninges, the lungs, and in the blood, especially the blood of the lungs. In all the cases heretofore reported the invasion with streptococci appears to have been secondary. Generally, purulent processes and tonsillar angina, otitis media, phlegmons, and the like, due primarily and solely to the streptococci, can be demonstrated after death; while in other parts, as, for instance, the spleen, the mesenteric glands, and the liver, both varieties of pathogenic micro-organisms may be found

together; and in still other organs, as, for instance, the intestinal follicles, typhoid-bacilli are frequently found alone.

The course of the cases in question appears to be most virulent. Almost all the cases hitherto observed have terminated fatally. It is correctly maintained, especially upon the basis of experimental observation, that the combined activity of both micro-organisms is especially dangerous—far more so than that of either alone. I have personally no experience with this variety of typhoid fever. The first and most important statements relating to it emanate from French investigators—Chantemesse and Widal, Vaillard and Vincent,[1] and others. They appropriately designate it as the *Forme septicémique généralisée.* In Germany, Wassermann[2] has published similar observations. He was able to demonstrate the streptococci in the blood during life. Further investigation will have to determine whether, as is highly probable, a considerable number of cases of typhoid fever of malignant, fulminant, hemorrhagic, or hyperpyretic course do not belong etiologically in this category. The cases, however, in which the agminate and the solitary follicles of the intestine are found entirely free from specific infiltration, although at the same time typhoid-bacilli, together with streptococci, are said to be present in the other organs, require, in my opinion, careful reinvestigation, which should be directed especially to possible confusion of the typhoid-bacillus with the Bacterium coli.

These cases are to be separated from those cases of typhoid fever which, during the defervescence of the fever or during convalescence, acquire a secondary general infection with one of the varieties of pyogenic cocci. The general infection is probably favored by the lowered general resistance of the patient. The point from which the organisms gain entrance to the general circulation is usually some localized focus of inflammation. In a case lately occurring in the Johns Hopkins Hospital the patient, during the end of an attack of typhoid fever, suffered from a large carbuncle on the back. Cultures taken from the blood during the height of the attack of typhoid showed the presence of typhoid-bacilli, but cultures taken ten days after the onset of the carbuncle showed a pure growth of Staphylococcus aureus. Cultures were repeatedly taken, with similar results, before death, which occurred after several weeks with symptoms of general septicemia.

Of other conditions allied to septic processes, **erysipelas** is worthy of special consideration. The occurrence of this, as has previously been

[1] See Chantemesse, "Typhoid fever," *Traité de méd.*, publ. par Charcot, Bouchard et Brissaud, t. i. Brouardel and Thoinot, pp. 293, 294. Vincent, *Ann. de l'Institut. Pasteur*, 1893, No. 2.

[2] *Charité-Annalen*, 1894, t. xix.

mentioned, is not excluded by the presence of typhoid fever. Typhoid patients at any stage may, on the contrary, be attacked by erysipelas. If this is more common toward the end of the febrile period and during convalescence, the principal reason for this circumstance resides in the fact that at this time bed-sores and other ulcerative processes constitute especially favorable starting-points for the process. I have observed facial erysipelas develop only with considerable rarity at the height of the disease. This rarity is especially striking in view of the frequency with which erosions occur at the nasal orifice and the lips, and the way in which these are maltreated at the hands of the patient himself. Whether this rarity is due, in part at least, to the fact that in cases of typhoid fever at the height of the pyrexia the erysipelatous infection is somewhat more severe than in healthy individuals, may for the present be considered undecided. Griessinger[1] also has noted fatal erysipelas in but 2 per cent. of 500 cases observed at Zurich.

The coincidence of typhoid fever with **Asiatic cholera** is mentioned especially by Trousseau and a number of modern French clinicians. If, however, the subject be investigated, the condition appears in most cases to be only one of infection with cholera of convalescents from typhoid fever, or, conversely, of typhoid infection in persons who a short time previously had recovered from cholera. Actual coincidence of both diseases appears, on the other hand, to be extremely rare, if it occurs at all.

Of the simultaneous existence of **dysentery** and typhoid fever we have knowledge only through medical reports from the tropics. Here, also, the condition appears to consist essentially in an invasion of dysentery during convalescence from typhoid fever. Cases in which dysentery has developed at the height, or in the second half, of the febrile stage should be accepted with great caution in the absence of careful post-mortem examination. Colotyphoid with typhoidal intestinal lesions extending far down to the rectum may, as I have personally observed, give rise to symptoms simulating those of dysentery.

The coincident occurrence of **diphtheria** and typhoid fever, particularly during severe epidemics, is mentioned frequently, especially by older writers. Doubtless the throat condition is principally one of diphtheria in the older anatomic sense. Adequate recent bacteriologic investigation has, so far as I know, not yet been made. I have personally not seen diphtheria—in the current etiologic sense, with the demonstration of the bacillus of Löffler—occur as a complication of

[1] *Loc. cit.*

typhoid fever. I would warn especially against confusion with the specific typhoid angina previously mentioned.

A not insignificant *rôle* is played in the tropics, in North America, China, and Japan, and in malarious regions on the continent of Europe, by cases that have been attributed to mixed infection with typhoid fever and **malaria**, and that have in France been designated typhomalarial fever. From the existing descriptions (Kelsch and Kiener, Scheube, and others [1]), the cases represent an admixture of typhoid symptoms —roseolæ, pea-soup-like stools, stupor, diffuse bronchitis—with the febrile course peculiar to intermittent fever. Accordingly as the one or the other of the two affections predominates or recedes temporarily or during the entire course of the disease, the most varied clinical picture, often difficult of interpretation, develops. The course of this form of disease appears to be quite severe, and its prognosis is said to be far more grave than that of simple typhoid fever.

Lyon,[2] who has studied the question of combined typhoid and malarial infection and the so-called typhomalarial fever, concludes that in regions where both are common, it is probable that combined infections not infrequently occur, but that such cases are certainly not the ones that have been described in the United States under the name "typhomalarial" fever. It is certain that cases of intermittent fever are incorrectly included in this group, that, without the influence on the body of the typhoid-bacillus in addition to the plasmodia, are attended with typhoid symptoms, stupor, delirium, prostration, etc.; and, conversely, some physicians practising in malarious regions are in the habit of considering cases of typhoid with a predominant intermittent type of fever as influenced by malaria. It should be emphasized that before such combined infection is considered as demonstrated, the plasmodia should be found in the blood, as well as a positive Gruber-Widal agglutination-test obtained. Italian physicians and, in France, Jaccoud [3] have described as the sudoral type of typhoid a form of disease occurring especially in Italy and Malta, in which, in addition to febrile and typhoid symptoms, intermittent sweating assumes a prominent position. Jaccoud considers it, with good reason, as a peculiar variety of typhomalarial fever. Canine fever also—fièvre des chiens—which has been described in Bosnia and Herzegovina by a number of observers (Pick, Karlinski), appears also to belong in this category. Probably the condi-

[1] *Maladies des pays chauds*, Paris, 1889. Scheube, *Krankheiten der warmen Länder*, Jena, 1896. See the rather extensive literature in the papers of both writers.

[2] *Johns Hopkins Hosp. Rep.*, vol. viii.

[3] *Clin. méd.*

tion is one of typhoid fever in individuals who, a short time previously, had recovered from malaria.

Karlinski[1] has described an interesting case of **anthrax** combined with typhoid fever, which was subjected to careful bacteriologic examination.

Cases of the coincident existence of **rheumatic polyarthritis** with typhoid fever, which have exceptionally been reported, are to be viewed skeptically, because, on the one hand, we are without pathognomonic signs of the first-named disease, and especially without knowledge of its specific exciting factor; and, on the other hand, it must always be borne in mind that typhoid fever itself, and other conditions closely resembling it superficially, may at times be attended with multiple inflammatory affections of the joints. Among the latter conditions certain cases of cryptogenic septicopyemia and infectious osteomyelitis should especially be kept in mind. I have never been able to convince myself of the occurrence of cases exhibiting a coincidence of true rheumatic polyarthritis with typhoid fever.

Chronic Diseases and Typhoid Fever.—Numerous references have previously been made to the relation between chronic diseases and typhoid fever. I may again call attention especially to the statements with reference to diseases of the nervous system, the circulatory organs, the lungs, and especially to tuberculosis. Among constitutional diseases, special attention has been paid to the combination of **diabetes mellitus** with typhoid fever.[2] As occurs in the majority of diseases attended with chronic emaciation, so even severe cases of typhoid fever in diabetic patients may be attended with remarkably low temperature. I have personally observed such an instance in a patient, forty-three years old, who died as the result of the attack of typhoid fever at the beginning of the third week; no special complications occurred, and the temperature throughout the entire course of the attack did not exceed 39° C., and reached this level only on three evenings. Low temperature in these cases is therefore not in itself to be considered as of favorable significance. Of 6 cases collected by Ebstein, death occurred in 4. It is worthy of note that the excretion of sugar undergoes little change during the course of the attack of typhoid fever, and generally lessens only toward the fatal termination.

[1] *Berlin. klin. Woch.*, 1888.

[2] Griessinger, *Arch. d. Heilk.*, 1862, 3. Jahrg. Bamberger, *Würzburg. med. Zeit.*, 1863, Bd. iv. Gerhardt, *Correspondenzbl. d. ærztl. Vereins f. Thüringen*, 1874, Bd. iii. Ryba and Plumer, *Prag. Viertelj.*, 1877. Ebstein, *Deutsch. Arch. f. klin. Med.*, Bd. xxx. (This paper contains a complete clinical discussion of the subject, together with full reference to the literature.)

On the other hand, the iron-chlorid reaction of Gerhardt appears to undergo a considerable intensification with the commencement of the fever (Gerhardt, Ebstein).

Among the **chronic intoxications,** reference may be made to morphinism and alcoholism. So far as I know, attention has hitherto not been called to the behavior of persons addicted to morphin toward typhoid fever. I have studied carefully 2 cases of typhoid fever in such persons, and have been impressed especially with the lessened powers of resistance of such individuals. Both patients—the one a woman, thirty-two years old, and the other a man, thirty-seven years old—died as a result of the disease on the fifteenth and the eighteenth day, respectively. The absolute sleeplessness from the beginning, the constant marked restlessness, and the early and unusually pronounced subsultus tendinum and floctitation, so that in the case of the woman the condition was strongly suggestive of a case of chorea, were conspicuous and, of course, easily explainable. The temperature, in comparison with the severity of the attack in other respects, was low, just as in the combination of diabetes and typhoid fever.

Chronic alcoholics are seriously threatened when attacked with typhoid fever. In them, also, the temperature-course, unless complications exert an elevating influence, generally pursues a rather low level. This fact, however, just as in the case of diabetics and persons addicted to morphin, in nowise alters the prognosis. Alcoholics also exhibit diminished resistance to the disease, and generally succumb to it within a short time. I have observed a mortality of 34 per cent. for drunkards suffering from typhoid fever at Hamburg. The lessened powers of resistance in these patients are especially appreciable in the action of the heart. Even from the beginning the pulse is likely to be disproportionately frequent, and often becomes distinctly smaller, feebler, and irregular as early as the middle or close of the first or the beginning of the second week. Dilatation of the heart also develops quite early.

With regard to the vascular system, the special tendency to hemorrhages is to be considered. Drunkards exhibit more frequently than other patients copious nose-bleed, and are often attacked unusually early by severe intestinal hemorrhage, the source for which is eventually found to consist in sponginess, friability, and hemorrhagic congestion of the patches that have not yet undergone sloughing. That the excessively severe cases of hemorrhagic typhoid fever occur with especial frequency in drunkards has been previously mentioned.

As a further peculiarity of typhoid fever in alcoholics, the unusually profound involvement of the entire nervous system is yet to be men-

tioned. The clinical picture of the "ataxic adynamic variety" appears early under these conditions, with the early development of profound disturbance of consciousness, great restlessness, and severe delirium. Symptoms of actual delirium tremens, however, occur—in comparison with their frequency in erysipelas, pneumonia, and other acute infectious diseases—with extreme rarity. It may further be mentioned at this point that albuminuria, not rarely also hemorrhagic nephritis, occurs especially early and in marked degree in drunkards. Under the deleterious influence of early cardiac weakness, the latter may readily give rise to fatal uremia.

VARIATIONS IN COURSE DEPENDING UPON CONSTITUTION, SEX, AND AGE.

Constitution.—Although definite knowledge is wanting with regard to the intimate nature of that which is designated constitution, it may nevertheless be stated that the course of an attack of typhoid fever stands in a most remarkable relation to that which in general is so designated. It has been seen that young vigorous individuals of good constitution are attacked with especial frequency by typhoid fever, although they recover most readily and uninjured after a longer or shorter course. Tough—that is, the spare, muscular—individuals with healthy internal viscera exhibit an especially favorable relation in this connection. On the other hand, the obese are especially threatened, as every experienced physician knows. Only too often have the friends of a corpulent young man or a blooming, flourishing young woman placed too much dependence upon this deceptive appearance. However much the physician tries to suppress his anxious fears, he sees them confirmed over and over again, as such persons, when attacked with typhoid fever, do not hold out. They often exhibit unusually high and uninterrupted fever, and they are early overcome by sopor, coma, and other severe symptoms referable to the central nervous system. The most unfavorable feature is the behavior of the heart, which, often as early as the first week, exhibits signs of deficient power, so that the course of the disease is almost from the beginning dominated by the signs of cardiac weakness. Upon this is dependent the fact that the typhoid bronchitis of the obese early attains a severe degree and a wide distribution, and that a special tendency to the development of pulmonary stasis and hypostatic pneumonia exists.

Sex.—General experience teaches that no material difference between the two sexes appears to exist in regard to the tendency to be attacked by typhoid fever. My own experience, based upon a large

number of cases, agrees with this. Also with reference to the prognosis of the disease, no radical difference can be discovered to exist. While Liebermeister at Basle observed a mortality of 12 per cent. in males and of 14.8 per cent. in females; in the medical clinic at Munich,[1] for the years from 1874 to 1877, on the contrary, the mortality among the males was considerably greater. Goth also reports from the clinic at Kiel a mortality of 5.4 per cent. in males and of 4.5 per cent. in females. I have personally found this relation to vary in different cities. Thus, at Hamburg we had a mortality of 9.9 per cent. in males and of 8.5 per cent. in females; while our statistics at Leipsic disclosed 14.7 per cent. for the former and 15.2 per cent. for the latter.

In certain cities and in certain classes of society, on the other hand, differences in nutrition, in mode of life, and in occupation appear to cause appreciable differences with regard to the character of the course and the termination of the attack in the two sexes. In this connection, the important *rôle* that alcoholism plays in men is especially to be considered. In women, naturally—although this, on the whole, makes no impression on the statistics—the sexual functions are of considerable influence. It has already been seen how greatly threatened are pregnant and puerperal women attacked by typhoid fever. Also during the first period of lactation the powers of resistance have appeared to me to be somewhat diminished, while at a later period of lactation otherwise well-constituted women react to the disease as those not lactating do.

Age.—The differences dependent upon age are far more important. In general it may be said that the course and the termination become progressively more unfavorable with increasing years, so that children—except during the earliest period of life—occupy by far the most favorable situation; while as early as the beginning or middle of the fifth decade the influence of age begins to make itself manifest. The moderate course of the disease occurs between the fifteenth and thirty-fifth years. The so-called typical picture of the disease is generally drawn from cases during this period. The peculiarities of typhoid fever in children and those of the disease in advanced life deserve especial consideration.

Typhoid Fever in Childhood.[2]—Apart from the earliest period of life, which will receive special consideration later, children are not much less predisposed to typhoid fever than adults. This predisposition begins

[1] Beetz, *Deutsch. Arch. f. klin. Med.*, Bd. xvi., xvii., xviii.

[2] The personal experience upon which the following statements are based is derived from the records of 613 cases, and upon the careful observation and treatment of 295 cases in hospital and private practice.

slowly to make itself noticeable as early as between the fourth and the fifth year. A further considerable, and from this time on progressive, increase in the morbidity generally occurs between the ninth and the tenth year.

Attention should be called to the fact that the experiences of private practice and the statistical statements referring to the general population are far more reliable in this connection than the data obtained from general hospitals. Naturally, relatively more children than adults are treated at home, and of those attacked, a considerable number in large cities enter the children's hospitals. Accordingly, the figures exhibited by the general hospital statistics are too low.

The character of the disease in children is, on the whole, milder than in adults. They are more resistant to the intoxication, and overcome its effects more readily and more completely. With this correspond the especially frequent abbreviation of the disease in children, particularly of its febrile stage, and the much larger number of recoveries, even in protracted, severe cases.

The cases in which the disease is of shorter duration manifest themselves in various ways. In a portion of the cases, the shorter duration appears to be dependent upon the fact that the individual stages, although they exhibit their typical development, pursue a shorter course. A still larger number belong to the varieties of typhoid fever that have been designated abortive, mild and mildest, which have already been adequately described. Cases of typical or greatly protracted course are less common in children.

With regard to the febrile symptoms, and especially the height of the body-temperature, the curve appears in general to pursue a somewhat lower level. In general the elevations of the temperature are less in young children than in older ones. After the twelfth year of life, the curve, with relation to its form and height, progressively approaches that of adults. The tendency to a markedly remittent curve, which makes itself apparent in the cases of abbreviated course and of moderate severity, and especially in those of protracted course, is noteworthy of typhoid fever in children. Cases, however, in which from the beginning the curve exhibits such marked and regular fluctuations as to be suggestive of malaria are distinctly less common in children than in adults. The older, particularly English and French, clinicians (Abercrombie, Wendt, Chomel, and others) early described as infantile remittent fever a symptom-complex occurring, as the name suggests, preferably during childhood. This was at first considered a special disease, but was subsequently recognized, through the labors of Taupin, Barthez and Rilliet, West and Murchison, as typhoid fever of peculiar course. At that time,

when the real nature of infantile remittent fever was not understood, and also the abortive and mild forms were but imperfectly known, typhoid fever in children was considered rare.

In contrast with the usual behavior of the body-temperature, the pulse-rate is from the beginning exceedingly high, especially in early childhood. Only in older children, after the twelfth year, does the pulse-frequency again approach that of adults. In such children dicrotism is occasionally observed in the course of the second or the third week, while I have with only extreme rarity encountered this manifestation in younger children. The condition of the heart, of all the organs, exhibits most distinctly the greater resisting power of the child to the action of the toxins. Cardiac weakness occurs much less commonly, and only in cases of especially long and severe course. Irregularity of the heart's action, as well as irregularity of the pulse in force and rhythm, is observed almost only in the quite exceptional cases complicated by endocarditis, myocarditis, or pericarditis.

With regard to the manifestations on the part of the skin, especially the roseolæ, they exhibit little deviation from those in adults. I know well that most diverse statements have been made by writers on pediatrics, so that, for instance, Rilliet and Barthez consider them as rare, while Taupin and others consider them as occurring with almost greater frequency than in later life. Probably these differences are attributable to accidental local and temporal conditions. During some epidemics or endemics the roseolæ appeared also to me to be less pronounced, while at other times they were especially constant and abundant. If, however, I take the average of many years' observation, I believe I am unable to appreciate any difference from the conditions in adults. Possibly it may be stated as noteworthy that the roseolæ generally appear somewhat later in children, generally in slighter or but moderate profusion, but in individual instances often more markedly developed. I have been struck, in a number of children between the ages of five and ten years, by the especial size of the roseolæ and their more marked elevation above the surface of the skin, and by their tendency to become confluent.

Almost the same that has been said of the roseolæ is applicable also to sudamina. Particularly in middle childhood, between the fifth and tenth years, I have not rarely observed upon the chest, the abdomen, and down to the thighs, rather abundant, in part even confluent, miliaria, with subsequent desquamation of the skin during convalescence, the desquamation being often of a branny character, and here and there even occurring in sheets of considerable size.

Bed-sores are much rarer in well-nursed children than in adults. Noma was formerly noted rather frequently as a complication, especially in young children, while at the present day the condition is scarcely ever referred to. Upon the tendency on the part of children suffering from typhoid fever to pick at the nose and at the lips is dependent the fact that extensive bleeding fissures and excoriations covered with crusts frequently occur.

The abdomen is more likely to be distended in children, but generally only in moderate degree, and rarely so greatly as in adults. Children complain more frequently than the latter of abdominal pain. Vomiting and retching are not very rare manifestations of the first few days of the disease in young children. With reference to the number and the consistency of the stools, the conditions in children exhibit little peculiarity. Possibly diarrhea is somewhat more constant than in adults.

Distinct peculiarities exist, however, with regard to the serious intestinal manifestations of hemorrhage and perforative peritonitis. Both are less common in children, especially in early and middle childhood, than somewhat later in life (Taupin, Rocher, Rilliet and Barthez, Henoch, Gerhardt, Biedert). While among adults I have at times encountered hemorrhage in 10 per cent. and even more, in children I have observed it in only 1 per cent. Biedert also states that in a collection of 435 cases of typhoid fever in children he found intestinal hemorrhage in not quite 4 per cent. Perforative peritonitis is comparatively even rarer. This peculiarity finds a satisfactory explanation in the anatomic conditions in the bowel. In children the infiltration of the agminate and solitary follicles is in general far less marked. Accordingly, sloughing and ulceration will occur under such circumstances more rarely, and, if at all, in slighter extent and to a lesser depth; but, on the other hand, it undoubtedly more frequently happens that the medullary swelling undergoes involution through absorption without disintegration. The mesenteric glands are also, in general, less markedly swollen, and only with extreme rarity are found in a state of softening.

The condition of the spleen exhibits no material difference from that which occurs in mature life. It may possibly be stated that enlargement of the spleen at an early period—that is, before the beginning or the middle of the second week of the disease—is less common in children than in adults, and that it does not frequently exceed moderate proportions. In my experience, actual persistent absence of splenic enlargement or of the possibility of its demonstration has been rather less common in children than in adults.

Among affections of the respiratory organs, typhoid bronchitis does

not differ with reference to frequency and extent from that of later periods of life. In children also it is one of the more valuable diagnostic symptoms of the disease. It is associated rather frequently with atelectasis and lobular pneumonia, especially in debilitated children. Simple and inflammatory hypostasis of the lungs is, however, all the more rare—a fact that sheds a strong light upon the favorable state of the heart-power in children that has been repeatedly pointed out. True lobar, fibrinous pneumonia I have observed but exceptionally in children. Pleuritis and empyema also are, according to the statements of most observers and my own experience, relatively uncommon. The same statement is applicable also to affections of the larynx, both simple ulceration of the mucous membrane and perichondritis and necrosis of the cartilage. As has been pointed out with regard to a considerable number of other conditions, these laryngeal affections become somewhat more frequent again in later childhood.

The symptoms on the part of the nervous system usually vary in accordance with the severity of the attack. In mild and even moderately severe cases they are relatively slight—generally far less marked than in adults. In the early period the children are ill-tempered, irritable, and lacrimose; they subsequently become dull, apathetic, and more or less stupid. The severe cases, however, sometimes set in with convulsions, and even during their course, especially in older children, often exhibit alarming symptoms. Among these symptoms, severe headache, rigidity of the neck and back, general hyperesthesia, with sluggishness, dilatation, and even inequality of the pupils, and profound stupor progressing into deep coma, should especially be mentioned. Nervous sequels, such as spinal affections, neuritis, and cerebral disturbances, especially psychoses, are, on the other hand, comparatively rare in children. Neuralgic disorders also—for instance, the distressing pains in the heels and toes so frequent in adults—have practically not come under my observation in children. Reference may here be made again to the as yet unexplained transitory aphasia (pp. 275 and 276) occurring almost exclusively in childhood, which, although mentioned by earlier observers, has recently been again pointed out, particularly by Gerhardt (Clarus Diss.) and Kühn.

With regard to the condition of the organs of special sense in cases of typhoid fever in childhood, little is known, so far as I am informed, with regard to the eyes. Typhoid affections of the ear, both those of nervous origin and those associated with affections of the nasopharynx and Eustachian tube, appear to be not less frequent than in adults.

The kidneys are comparatively resistant during childhood. Febrile

albuminuria is distinctly less common at this time, and, if present at all, is slighter and of shorter duration. Actual nephritis appears to occur but exceptionally. I have personally observed no case of the kind in a child. The diazo-reaction of Ehrlich is, apparently, almost never absent in childhood—a fact to which, in view of the limitations previously mentioned, not inconsiderable diagnostic significance is to be attached.

The duration of typhoid fever in childhood is, as has been previously indicated, on the whole, shorter than in adults. Undoubtedly, the mild and abortive cases are even more common in children; and the well-developed cases of severe onset generally terminate earlier than they do in later life. The abbreviation affects all stages of the disease, both the febrile period and convalescence. The febrile period in well-developed cases is likely to be shortened at times in all its stages, while at other times only one or another stage is shortened, especially that of ascending temperature or that of defervescence. It is interesting that the duration of the fever in well-marked cases appears to be shorter, on the whole, the younger the child. In children below the age of six years the duration much less commonly exceeds three weeks than it does in older children; and even in the latter, differences in relation to age are likely to make themselves distinctly manifest in the manner indicated.

The following table, based upon the cases observed at Hamburg from 1886 to 1887, is most instructive. Of 443 children between the ages of two and fourteen years, the duration of the fever was:

	2 to 5 years.	6 to 10 years.	10 to 14 years.
Up to 21 days	92 per cent.	71.8 per cent.	60.8 per cent.
Between 22 and 33 days .	4 "	18.6 "	25.7 "
More than 33 days . . .	2 "	7.7 "	11.8 "

The shorter duration of the fever, the greater resistance to the action of the toxins, and the lesser frequency and severity of complications are responsible for the fact that convalescence is in general completed earlier in children than it is in adults. This applies not only to restoration of the structure of the affected organs, but also to restoration of the former state of nutrition, especially a return to, and not rarely even an increase beyond, the former body-weight. With reference to the latter, children exhibit a peculiar relation. After severe and moderate attacks they lose flesh in the febrile stage with comparatively greater rapidity, and in general in somewhat greater degree than adults, but even in the worst cases they do not suffer the extreme loss of weight that occurs in the latter. While the greatest loss of weight that I have observed in severe cases in adults was in one instance 32 per cent.,

9 per cent. was the maximum encountered in children under the age of twelve years. On the other hand, the minimum loss of weight observed in children with severe and moderately severe attacks was 2.5 per cent. of the body-weight, and the least among adults under the same circumstances only 1.5 per cent.

The general rule, that relapses are likely to be the more frequent the younger the patient, is applicable also to childhood. The tendency to recrudescences and relapses is, without doubt, more pronounced at this period of life than in later years. Exceptional contradictory statements are based either upon too small statistics or upon exceptional epidemics and endemics, which, as a matter of fact, may occasionally exhibit a deviation from the rule.

Thus, in Hamburg, in the year 1887, although I observed not actually fewer relapses in children, the percentage of relapses was, nevertheless, disproportionately lower than in adults; while the figures for the year 1886, and those for fourteen years at Leipsic, agree with those that I believe to represent the usual state of affairs. There occurred in Hamburg in 1886: Relapses in adults in 13.4 per cent.; in children in 19.5 per cent.; in Leipsic, relapses in adults in 12.5 per cent.; in children in 19.1 per cent.

It is interesting that even in relapses in children the preponderant occurrence in the female sex—which almost constantly occurs in adults—is at times distinctly exhibited, as the following statistics of Hamburg show:

	Boys.	Girls.	Total.
Relapses, 1886	15.5 per cent.	23.8 per cent.	19.1 per cent.
Relapses, 1887	11.9 "	15.0 "	13.4 "

A fatal termination of the disease in childhood is, in general, less frequent than in adults, as is almost obvious from all the foregoing observations.

All estimates based upon large statistics confirm this. In Hamburg, for instance, the mortality among adults in the year 1886 was 11.5 per cent.; that among children, 7.3 per cent. In the year 1887 the mortality among children was 6.8 per cent., with an average mortality later in life of 8.8 per cent.

If these conditions are scrutinized somewhat more carefully, the remarkable fact will become apparent that this low mortality applies especially to children up to the tenth year. From the tenth to the fourteenth year the mortality approximates that of the next age-period —from fifteen to twenty.

A tabulation of the related figures from Hamburg shows: Between the second and the fifth years, a mortality of 4 per cent.; sixth and the tenth years, 6.4 per cent.; eleventh and the fourteenth years, 8.1 per cent.; fifteenth and the twentieth years, 8.7 per cent.

In **infants,** and in general during the first two years of life, up to

the third, typhoid fever appears to be distinctly less common than in later childhood. It is true, as has been seen, that intra-uterine transmission may take place, although this, in relation to the number of typhoid mothers, is to be considered as most exceptional, and is dependent upon certain definite conditions. I have often seen infants and children between one and two years old remain healthy, in spite of constant and intimate association with a typhoid mother. A final opinion as to the relative frequency of the disease in the earliest years and in later childhood is, naturally, not to be formed from ordinary statistical data. The picture of moderate and mild attacks in infants is so entirely uncertain and ill-defined that more cases are certainly overlooked at this period than in later childhood.

Conclusions based upon large statistics may be reached from the reports of the Elizabeth and Oldenburg Children's Hospitals of St. Petersburg. In the former there were, from the year 1844 to 1896, 3504 cases of typhoid fever among 352,370 children treated in the dispensary. These cases are divisible according to age as follows:

1-6 Months.	6-12 Months.	1-2 Years.	2-5 Years.	Over five years.
9—0.26 per ct.	35—0.99 per ct.	173—4.94 per ct.	1481—42.3 per ct.	1806—51.3 per ct.

In the outpatient service of Rauchfuss at the Oldenburg Children's Hospital there were, among 77,073 sick children, 647 with typhoid fever, of the following ages:

1-6 Months.	6-12 Months.	1-2 Years.	2-6 Years.	Over six years.
2—0.31 per ct.	5—0.77 per ct.	14—2.15 per ct.	213—32.9 per ct.	413—63.8 per ct.

Ollivier[1] had among 611 cases of typhoid fever in children only 3 under the age of two years. My own 3 patients were nine and eleven months and one and three-quarter years old respectively.

The clinical statements that have hitherto been made with regard to typhoid fever in infants are based especially upon severe well-developed cases. Also, my 3 cases of that character, the only certain ones that I have seen, pursued a severe course, 1 terminating fatally. Moderately severe and mild cases have been reported but exceptionally. Among these belongs the well-known observation of Gerhardt[2] of a case of typhoid fever in a child three weeks old, probably infected within the uterus from the mother.

The beginning of the attack of typhoid fever in young children can but rarely be determined even in well-marked cases, probably even less commonly than during the subsequent years of life. Only excep-

[1] *Leçons clin. sur les mal. de l'enfance.*

[2] *Handb. d. Kinderkrankh.*, Bd. ii. In this book the earlier literature of typhoid fever in infancy has been carefully collected.

tionally in young children does the disease appear to set in abruptly and the fever to rise rapidly. When it has been possible to observe the initial stage, the curve generally was step-like, indeed somewhat

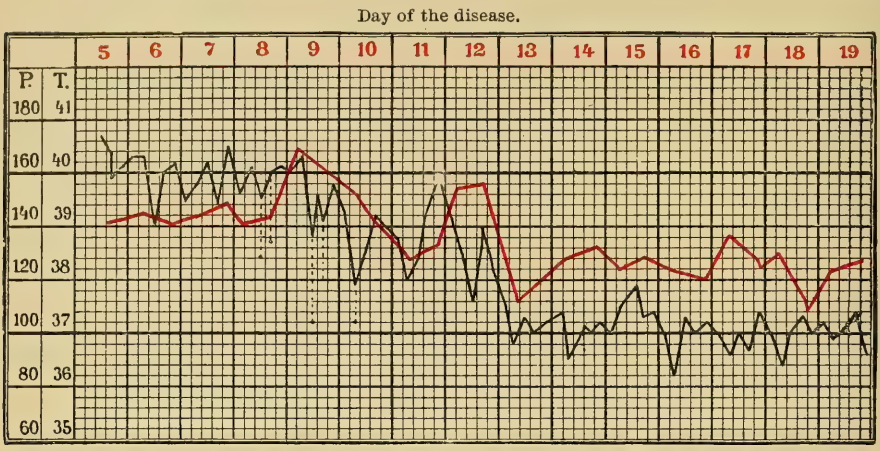

FIG. 33.

shortened, as in Gerhardt's case. Also the fastigium, and with it the entire febrile period, appears to be generally of relatively short duration, although exceptional cases have been observed that were protracted for

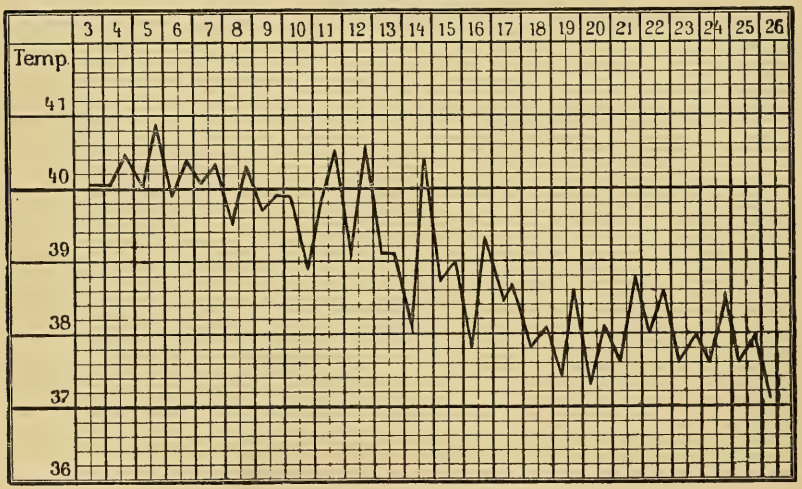

FIG. 34.

as long as twenty-seven and even thirty-one days before defervescence occurred (Filatow [1]). It is noteworthy that in severe cases of typhoid

[1] *Vorlesungen über Acute Infektionskrankheiten im Kindesalter.* Translated into German from the second Russian edition, Vienna, 1897.

fever in infancy the temperature is quite high at the fastigium, in general higher than during the succeeding years, and the temperature-curve is likely to resemble that of remittent continued fever. In the period of defervescence the type of steep curves not rarely makes itself manifest also in infants. As an illustration, I present the curve from a child one and three-quarter years old under my care (Fig. 33), and one from a little patient of Filatow's (Fig. 34) eight months old.

The pulse is, as would be anticipated, remarkably frequent and variable in cases of typhoid fever in infancy, without the number of pulse-beats being in itself of especial prognostic significance. Enlargement of the spleen is generally, although not constantly, demonstrable; but, on account of the frequency of its occurrence in connection with all possible conditions during early childhood, it is in itself of much less diagnostic importance than in later years. Roseolæ appear to be generally few in number, and are oftener wholly absent in young children than in older ones. In one of my cases—in a child eleven months old—which was under clinical observation from the very beginning until its fatal termination, and was examined anatomically after death, roseolæ were at no time demonstrable. Exceptionally, however, they have been found in great profusion, as, for instance, in Gerhardt's case.

Thin, watery stools appear to be quite frequent—more constantly so than in older children. The daily number of stools is at the same time comparatively small, and this fact may be a guide in the differentiation from other conditions of early childhood which are attended with diarrhea. The meteorism is said by almost all observers to be slight. One of my cases—in a child eight months old—in which recovery ensued, at one time throughout the entire course of the disease exhibited distention of the abdomen.

Vomiting is particularly frequent in the initial stage and at its inception. Also, during the further course of the disease it is often repeated. In association with the rigidity of the neck and back, which is not rarely present from the beginning of the fever, the crying, and the twitching, increasing to the point of convulsions, it is well calculated to excite suspicion of meningitis, which is the disease most frequently confounded with typhoid fever in early childhood. With the progress of the fever, and at the fastigium, these symptoms usually subside, to be replaced by more or less marked stupor and sopor.

Bronchitis appears in general to be mild in infants, while lobular pneumonia is particularly frequent, and is one of the common direct causes of death.

The duration and prognosis of well-marked typhoid fever in infants

are distinctly unfavorable in comparison with those of the succeeding years, and are the graver, apparently, the younger the child. Marfan[1] estimates the mortality in early childhood at 50 per cent. In addition to bronchopneumonia and severe toxemia, which are by far the most frequent causes of death, perforation of the bowel (Drewit) and ulceration of the larynx (Lewy) exceptionally act as direct causes of death, even in the youngest children.

Typhoid Fever in Later Life.—As early as the fortieth year of life the slighter susceptibility to the disease becomes apparent. The predisposition still further diminishes after the fiftieth year, so that typhoid fever in old age may really be designated as a rare occurrence.

Among 5306 cases of typhoid fever observed at Leipsic and Hamburg, I found 177 between forty and fifty years of age; 41 between fifty and sixty; 14 between sixty and seventy; and 5 over seventy. There were 1885 between the ages of fifteen and twenty-five years, however.

The influence of later life with reference to the course and the prognosis of the disease is exceedingly unfavorable. As early as the second half of the fourth decade the disease in its general course, or in relation to special features, is likely to assume a serious and even an alarming character. Above the fortieth year the mortality increases enormously, so that in the years between fifty and sixty it reaches from three to five times that between fifteen and twenty-five.

The mortality in Hamburg in 1886–1887 was, in the age-period from twenty-one to twenty-five, 7.7 per cent.; twenty-six to thirty, 12.3 per cent.; thirty-one to thirty-five, 11.5 per cent.; thirty-six to forty, 14.9 per cent.; forty-one to forty-five, 18.5 per cent.; forty-six to fifty, 26.1 per cent.; fifty-one to fifty-five, 23 per cent.; fifty-six to sixty, 37.5 per cent.

The statistics of the clinic at Leipsic (1880–1893), with, it is true, a higher average mortality, disclose similar relations. The mortality was, in the age-period from twenty to twenty-four, 13.8 per cent.; twenty-five to twenty-nine, 12 per cent.; thirty to thirty-four, 15 per cent.; thirty-five to thirty-nine, 28.3 per cent.; forty to forty-four, 29.2 per cent.; forty-five to forty-nine, 31 per cent.; fifty to fifty-nine, 40 per cent.

In the majority of cases in senile individuals the beginning of the attack and the ascent of the fever are gradual. When the beginning of the febrile period is attended with chilly sensations, these are likely to consist generally in repeated chilliness, only quite rarely confined to a single chill; in the latter case the course is usually abnormal in other respects also.

The further evolution of the entire clinical picture is marked by the evidences of lessened powers of resistance of the senile body to the

[1] *Traité des maladies de l'enfance*, 1897. This work contains also numerous bibliographic references, especially to recent French publications.

intoxication. In marked contrast to the period of youth, this lowered resistance is frequently exhibited in the general condition, and particularly in the condition of the nervous system. Great prostration is present from the beginning. Among the special nervous disturbances, symptoms of excitement are much less frequent than those of depression. The patients become stupid at an early period. Not rarely they are profoundly soporose or deeply comatose at the beginning of the second week. At the same time, or a little later, great asthenia, accompanied by tremor, subsultus tendinum, and floctitation, sets in. The patients under such circumstances are restless, often wholly sleepless, but generally without severe delirium. Pallid, with relaxed features and half-open eyes, murmuring feebly to themselves, they occupy a relaxed dorsal decubitus, the picture of the adynamic febrile course of earlier writers.

This character of relaxation or adynamia is exhibited in the course of the fatal cases, as well as in that of the severe cases that eventually terminate in recovery. The latter are generally unusually long in duration, not alone with reference to the febrile stage, but in comparatively still greater degree with reference to the stage of convalescence. The fever, under such circumstances, does not, in the majority of cases, attain the same height as is likely to be attained in severe cases during adolescence. On the contrary, the temperature-curve is very frequently observed to pursue a relatively low level, just as the afebrile cases of most severe course, as was previously mentioned, principally occur in debilitated senile individuals. In addition, the form of the curve is far more frequently irregular, markedly remittent, at times intermittent, and marked by attacks of true or false collapse than occurs at any other time in life. Often the stages of the disease are imperfectly, if at all, marked in the temperature-curve, so that neither the step-like ascent at the beginning, nor the continuance of a considerable average elevation of temperature in the severest period of the disease, nor yet a marked stage of steep curves, is present. Not a few cases, on the contrary, pursue so anomalous a course that the form of the curve furnishes no diagnostic information whatever, but rather may lead to incorrect conclusions.

The slowing of the pulse, which is so frequent and characteristic in young vigorous individuals, is extremely rare in the aged, and in my experience almost only occurs when the senile character of the disease is also less marked in other respects. The pulse in elderly individuals is, on the contrary, usually frequent from the outset—on the average more so than the height of the temperature warrants; and, what is indicative especially of a marked toxic effect upon the heart and the

vasomotors, is the fact that the pulse is early of low tension, irregular, and, when arteriosclerosis is not present, is soft, but seldom dicrotic.

The cardiac weakness that so early appears in the foreground is also responsible in considerable degree for the state of the respiratory organs. On account of the impaired propulsive power of the right side of the heart, the typhoid bronchitis early attains a considerable degree of intensity and extent. The associated hypostatic congestion which, in comparison with its frequency in early life, very commonly occurs in elderly persons, is dependent upon the same cause. The onset of this hypostatic congestion constitutes one of the indications of a fatal outcome in senile typhoid fever. The occurrence of bronchopneumonia is associated with the prevalence of bronchitis, and occurs with almost equal frequency in childhood and in later life. Elderly patients suffering from typhoid fever are not less frequently attacked by croupous pneumonia than younger patients, while pneumonia due to streptococci appears to me to occur more frequently in the former. The greater tendency to gangrene and abscess in association with pneumonia in older patients is noteworthy. That the chronic bronchial and pulmonary affections often existing in old persons before the development of the typhoid fever give to this disease a grave aspect needs scarcely be especially pointed out.

The anatomic and clinical manifestations on the part of the intestinal canal exhibit no radical differences from those in other adults. This is applicable especially to the number and the character of the stools. The meteorism, which not rarely is marked, sets in relatively early. In contradistinction to the conditions in childhood, elderly individuals—and this applies especially to the period between the thirty-fifth and the fortieth years—exhibit a somewhat greater tendency to intestinal hemorrhage. Elderly persons also succumb more readily to this accident. Even slight hemorrhages that would exert scarcely any, or but a transitory, influence upon younger persons, constitute a source of considerable danger for older ones. Perforative peritonitis appears to me to be, on the whole, by no means more frequent in advanced life, but rather less common than during adolescence.

The increased difficulty in the diagnosis of typhoid fever in elderly persons, in consequence of the variability and irregularity in the fever-curve, is still further augmented by the state of the spleen and the roseolæ. Enlargement of the spleen in elderly persons is, on the whole, distinctly less common than at other periods of life. In none of these earlier periods have I observed total absence throughout the entire course of the disease nearly so frequently as during the later periods of

life. Experience at the autopsy-table affords adequate explanation for this. The involution of the organ associated with advanced life, antecedent disease of the spleen and its capsule, extensive or multiple cicatrices resulting from infarcts, diffuse connective-tissue hyperplasia, and perisplenitic thickening of the capsule are all to be mentioned especially as factors which explain the infrequency of splenic enlargement. If these prevent the occurrence of enlargement of the spleen in a portion of the cases, the difficulty in the demonstration of the enlargement, even when it exists, is still further increased by displacements and adhesions, dependent upon disease at an earlier period in life, which naturally are more common in older individuals. Also, the rare cases in which, at the height of the disease, I have observed anatomically entire inexplicable absence of enlargement of the spleen, occurred almost solely in elderly persons.

While the typhoid roseolæ do not, in my experience, occur less commonly in advanced life, the eruption is, on the whole, less profuse, and often extends over a shorter period of time. In addition, the individual roseolæ are, in general, smaller, less bright in color, and of shorter duration—peculiarities that are apparently associated with the senile alterations in the skin. The same explanation probably also holds for the less common appearance of sudamina, and, conversely, for the greater tendency to bed-sores.

With regard to the changes in the kidneys, typhoid nephritis appears to me to be distinctly less frequent; while the occurrence and the symptomatology of febrile albuminuria exhibit no differences from those of the same condition at other times of life.

With reference to typhoid fever in the aged in general, it should be emphasized that in the event of recovery it has the most frequently, of all the varieties, a long-drawn-out and protracted course. Severe complications are not numerous or diverse, for the simple reason that aged persons almost always succumb to the first that appears. Of the special varieties of the disease previously mentioned, the hyperpyretic and the hemorrhagic forms are distinctly less common in later life. The preponderant early involvement of particular organs, giving the disease a special character, appears also to be less frequent. Cases that could be designated nephrotyphoid, meningotyphoid, or pleurotyphoid have in my experience but rarely occurred in older persons. Pneumotyphoid, however, appears to me to be not less common than during adolescence.

With reference to relapses and recrudescences, it is noteworthy that their frequency diminishes distinctly with increasing years, but their prognosis is far more grave than in younger individuals. That death

occurs at a comparatively early period is in no small degree due to the lessened bodily resistance. But, on the other hand, death may often occur in elderly individuals after attacks which were in themselves apparently not severe, but which were of unusually long duration. The impression is gained that such patients are no longer able to resist. The incomplete, mild, or abbreviated attack—mild typhoid fever, abortive typhoid fever, etc.—doubtless occurs also in advanced life. The exact relation its frequency bears to that during earlier periods of life is unknown to me, and, so far as I am aware, has not yet been determined.

RECRUDESCENCES AND RELAPSES.

In cases of typhoid fever of any variety or course it may happen that before the onset of final convalescence there may occur, without any other general or visceral disease, once or even several times, febrile states whose course and associated phenomena may more or less closely resemble those of the primary febrile period. They are designated, for obvious reasons, as relapses, if the first period of the disease is separated from the renewed elevation of temperature by a completely afebrile interval, and as recrudescences, if the reascent occurs during the period of involution, before the declining temperature has completely returned to the normal.

Clinically and anatomically, relapses and recrudescences represent recurrences, in more or less complete degree, of the typhoid morbid process. As to the question whether they are to be attributed to renewed infection or to a revival of the primary process, it may be said that at the present time it has been definitely settled that they arise in the latter manner. Undoubtedly, their development is to be attributed to the re-entrance into the circulation of living typhoid-bacilli which, after the primary attack, were left behind in various organs; and associated with this more or less complete redevelopment of the local and general typhoid lesions occurs. The patients then again exhibit fever, often in a most characteristic manner, with re-enlargement of the spleen, roseolæ, meteorism, and diarrhea, and, in fatal cases in which post-mortem examinations are made, newly developed specific intestinal lesions, especially recent infiltration of Peyer's patches, are found in addition to the healed lesions.

As little of a definite nature is as yet known with reference to the manner in which the typhoid virus is retained and the organs that are especially to be taken into consideration in this connection, as with regard to the manner and the special conditions under which the bacilli

again gain entrance into the blood. Probably the spleen, together with the lymph-glands and bone-marrow, and possibly also the gall-bladder, play an important *rôle* in this connection (see p. 207).

From the course, and especially the severity, of the primary disease, no conclusion can be drawn as to the probability of the occurrence of a relapse. Apparently, the predisposition to relapse is even greater in the milder than in the severer cases. In my experience, only from 25 to 35 per cent. of relapses occur after severe primary attacks, while all others follow moderate and mild attacks. It is quite common for atypical cases of typhoid fever—the mildest, abortive, or ambulatory—to be followed by severe, long-continued, and well-developed relapses, so characteristic that the previously uncertain diagnosis is first made positive by them (see Fig. 36).

Our Leipsic statistics show that of 210 relapses, 75 per cent. occurred after moderate and mild attacks. Also, Ziemssen observed among 108 relapses, only 28, thus about one-quarter, following severe attacks. Goth arrived at similar results. That this relation may be altered at times in some epidemics is shown by my Hamburg statistics, according to which 236 relapses were observed after severe, and 260 after mild, primary attacks.

It has been seen that for the recognition of a relapse in the strict sense of the word an actual afebrile period must have intervened between the termination of the primary attack and the beginning of the secondary elevation of temperature. Naturally, this interval is not necessarily measured by days. Undoubtedly, from twelve to twenty-four hours may even suffice, and therefore it is quite obvious that there exists only a gradual transition, and no essential difference between that which is designated as a recrudescence and that which is designated as a relapse.

The time that elapses between the primary attack and the beginning of the relapse is extremely variable. No relation between the duration of this interval and the character and severity of the primary attack can be demonstrated. In my experience, which coincides with that of most observers, the largest number of relapses occurs before the fourteenth to seventeenth day after the primary defervescence. Within this limit the duration of the afebrile period is quite variable. The beginning of the relapse is likely to be somewhat less common during the first few afebrile days, while after the third or the fourth day the onset is observed almost as frequently as on the subsequent days. About 10 to 12 per cent. of relapses begin after the seventeenth day, and the majority of these occur before the thirtieth day. Even after this interval, however, relapses may exceptionally occur. The longest time that I have observed to elapse before the onset of the relapse was fifty-three days.

Before considering the clinical symptoms of relapses and recrudescences in detail, it may be stated in general that with regard to course, duration, and severity, they vary almost as much as does the primary attack. It has been seen that the latter is, in the large majority of cases, unattended with slight or no manifestations during the period of incubation. With this fact corresponds the common view that the afebrile interval up to the beginning of the relapse is generally free from any symptoms that might point to the impending condition. To this, however, there are some exceptions which are of diagnostic importance.

Attention was called some time ago by Gerhardt[1] to one fact that I can completely verify—that is, the incomplete subsidence of the enlargement of the spleen after the primary defervescence. So long as the enlargement of the spleen has not disappeared, the physician is not relieved from anxiety with regard to a relapse. In the overwhelming majority of such cases he will, on the contrary, observe its occurrence. I believe also, however, that careful attention should be given to the state of the temperature and the pulse during convalescence with regard to the same point. I have pointed out that after all severe and moderately severe, not rarely after even apparently mild, cases, the temperature falls soon after defervescence, not only to the previously normal level for the individual, but for a certain time even below this. Well-marked cases in which, after defervescence, the course of the curve does not become subnormal are not to be considered as concluded, but, on the contrary, the possibility of an impending relapse should be suspected; and the suspicion should be stronger if the temperature at this low level exhibits causeless, abnormally marked, daily fluctuations.

This premonitory character of the temperature in the face of an impending relapse is almost always associated with a similar peculiarity of the pulse. It is likely under such circumstances, in spite of perfectly quiet, careful behavior on the part of the patient, to exhibit, in addition to relatively great frequency, more frequent and unusually marked fluctuations.

If a large number of curves from cases of relapse are analyzed, it will be observed—as appears to me not to have been sufficiently emphasized heretofore—that in the majority this peculiar premonitory character of the pulse-curve, which is analogous to that of the temperature-curve, is present in more or less distinctly marked degree. Even the cases in which, in spite of a subnormal course of the temperature after the primary defervescence, relapse occurs, the onset is frequently preceded by the important diagnostic character of the pulse mentioned.

[1] *Deutsch. Arch. f. klin. Med.*, Bd. xii.

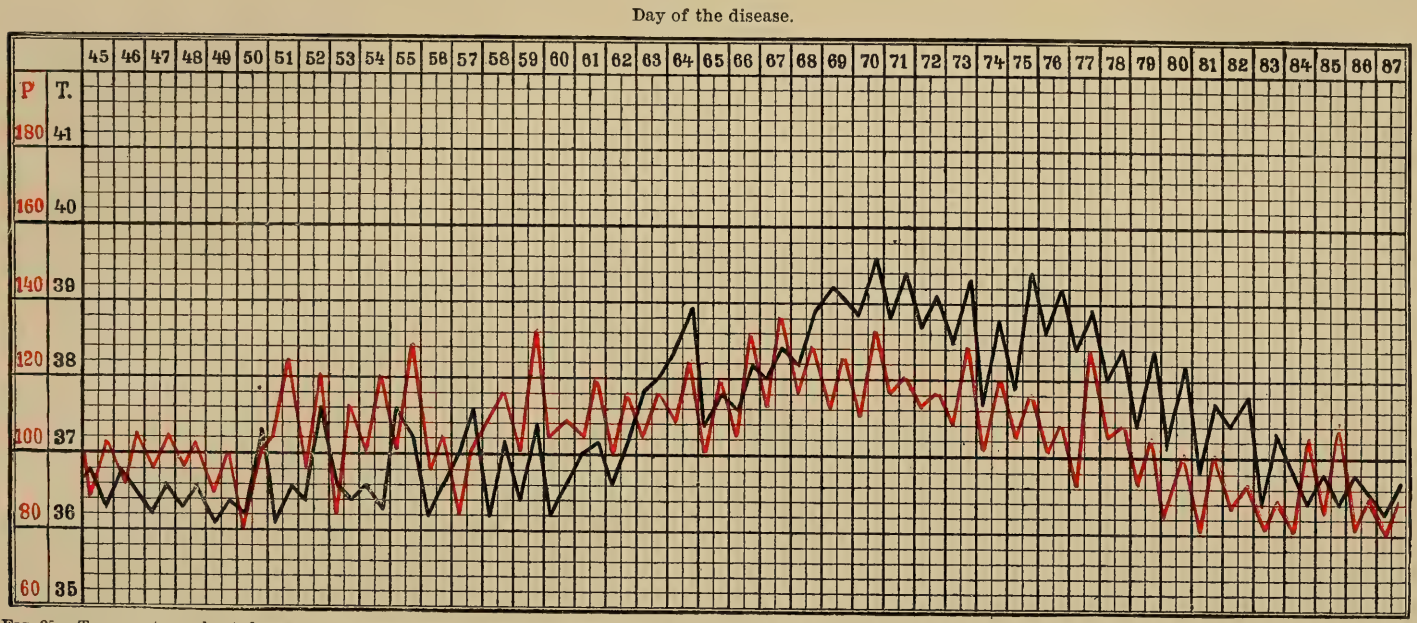

FIG. 35.—Temperature-chart from a servant-girl, twenty-eight years old. Relapse lasting twenty days, occurring twenty-six days after defervescence. Premonitory fluctuations in pulse and temperature.

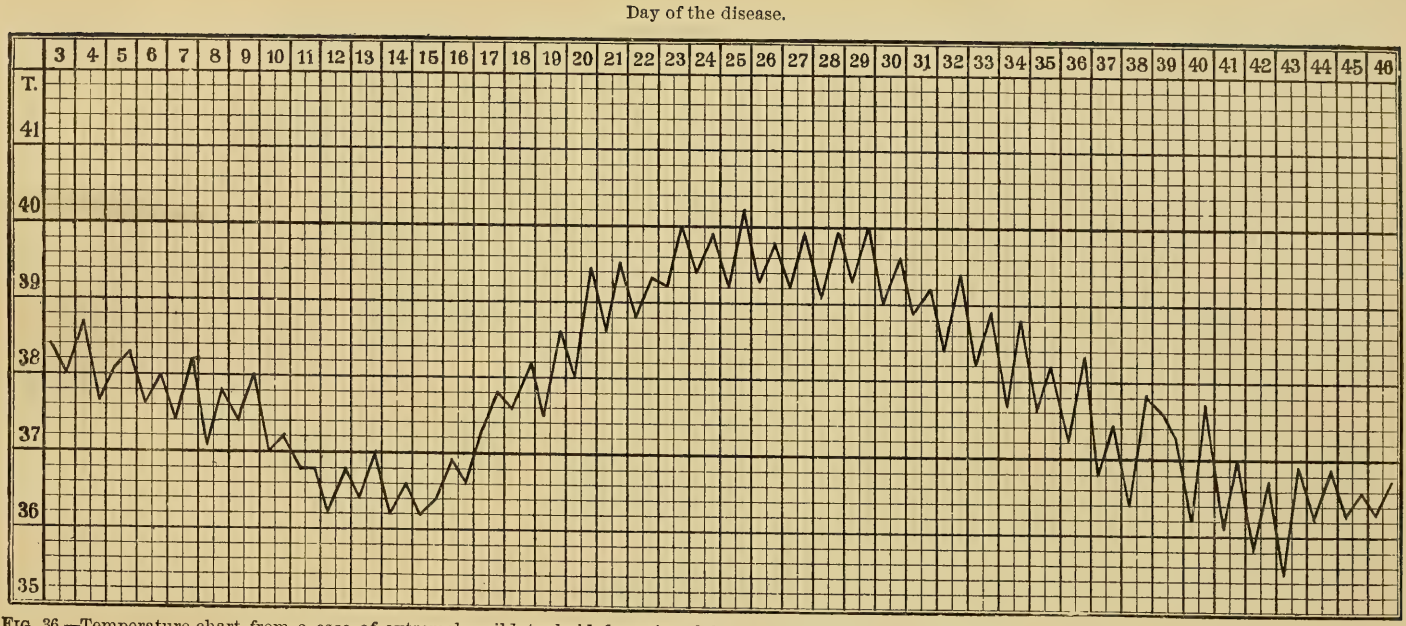

FIG. 36.—Temperature-chart from a case of extremely mild typhoid fever in a laborer, thirty-one years old, admitted on the probable third day of the disease. Seven days after defervescence a relapse of moderate severity began with a typical temperature-curve.

If this be compared with the rather rare cases in which it was possible to make observations of the pulse as early as the period of incubation, a striking coincidence of the pulse-tracing before the beginning of the primary attack with that preceding the relapse will be disclosed. There will also be found a resemblance between the relapse and the primary attack, manifested in the temperature-curve,[1] and in many other features besides.

An instructive instance of a mild relapse with the characteristic features of pulse and temperature just discussed is afforded by Fig. 35.

With regard to the state of the temperature during the febrile period

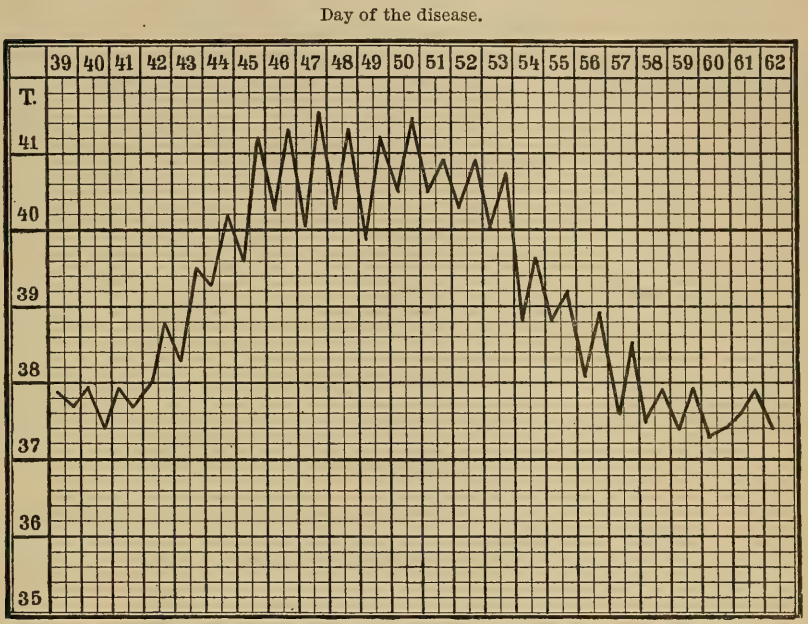

FIG. 37.—Temperature-chart from a moderately severe, protracted case of typhoid fever in a servant-girl nineteen years old. A relapse set in on the forty-first day of the disease, with step-like ascent of the temperature.

of the recrudescence and the relapse, both the duration of its elevation and the character of the curve are extremely variable, just as in the primary attack. Relapses may occur with fever-periods of from eighteen to twenty days, and even longer. They not rarely exhibit (Fig. 36) almost exactly the same course as moderately severe or mild, typical attacks of typhoid fever.[2] Relapses of much shorter duration (Fig. 37) may likewise exhibit distinctly all the usual stages.

In addition to these varieties, relapses pursuing a mild course, of greater or lesser duration, often quite considerably protracted, with

[1] See Figs. 8, 9, and 13.

[2] Compare Fig. 11, p. 140.

irregular, at times entirely uncharacteristic, temperature-curves, are in general rather frequent. The short and the shortest relapses finally reproduce, with reference to character and course, all the features that we have become familiar with as belonging to the symptomatology of mild, mildest, and abortive cases of typhoid fever. In many the fastigium is but of brief duration, and in some cases it is entirely wanting, in that the temperature remains but temporarily, often for a few hours only, at the highest level reached, and then declines. Not less varied is the character of the ascent and the decline of the curve in the mild and short relapses.

It is particularly interesting that the character and the peculiarities of the curve in the primary attack are frequently reproduced both in the recrudescence and in the relapse, at times even in a more clearly defined manner. This applies especially to the markedly remittent or intermittent type of curve, of which Fig. 38 constitutes an illustration.

If, further, the character of the individual parts of the curve in relapses be investigated, a similarity will be found to the conditions usually present in primary attacks. The form of the ascending curve is most frequently step-like in the customary manner, generally somewhat shortened in comparison with the same stage of the primary attack, less commonly of equal duration.

In other cases the temperature reaches its acme at a single bound or with but one or two brief intermissions (Figs. 38, 39, and 46). Under these circumstances the onset of the relapse with a chill, which is otherwise very rare, is frequently observed. Other rare cases exhibit the peculiar feature of one or several marked fluctuations in the temperature, with considerable evening elevation, before the stage of definite ascent begins (Figs. 35 and 40).

In addition to the foregoing varieties of curves, there occur, especially at the beginning of relapses pursuing an irregular course, a number of others which are distinctly related to the like forms of fever-ascent in the primary attack. It need only be mentioned further in this connection that the onset may be attended with abnormally marked remissions in the temperature-curve, which may justify the expectation of the same or of a wholly intermittent character of all the succeeding portions.

The course of the temperature at the height of the fever is in relapses, as has been emphasized, in many respects like that in the primary attack. When the fastigium has persisted for a considerable time, the temperature-charts will exhibit, just as in the primary attack, the characters of remittent continued fever or of the more marked remittent or

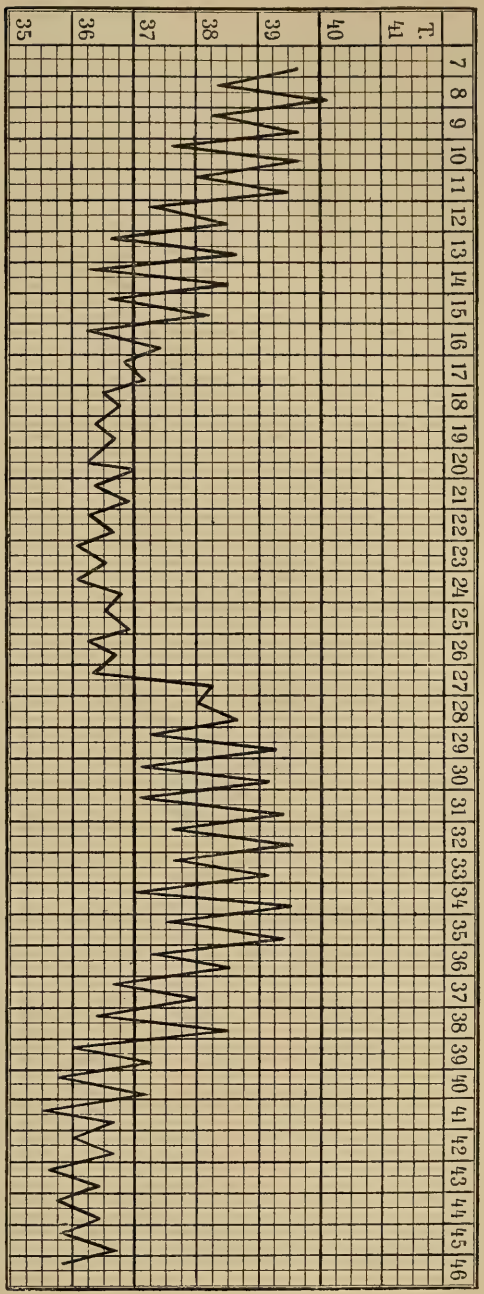

FIG. 38.—Temperature-chart from a mild case of typhoid fever in a servant-girl, twenty-four years old. As early as the beginning of the second week the temperature was markedly remittent. On the twenty-seventh day of the disease a relapse lasting thirteen days began, with a temperature-curve of the same character as that in the primary attack.

the almost intermittent forms of fever (Figs. 38 and 39). The period of onset, entirely like that of the primary attack, is usually characterized by step-like or characteristic steep curves (Figs. 36 and 37).

Termination of the relapse by critical decline is relatively rare. A gradual, entirely uncharacteristic decline, with an irregular, often protracted course, or subsidence with marked intermissions, is more frequent; this occurs again especially in cases in which also the preceding stage exhibited a similar character of curve (Fig. 39).

The pulse is generally more frequent in the relapse than in the primary attack. In women and children, and in men debilitated by the antecedent attack, the number of pulse-beats is even likely to be unusually high. A pulse of 120 in the evening is then not a rare occurrence, and, if the condition does not persist for too long a time, it is not

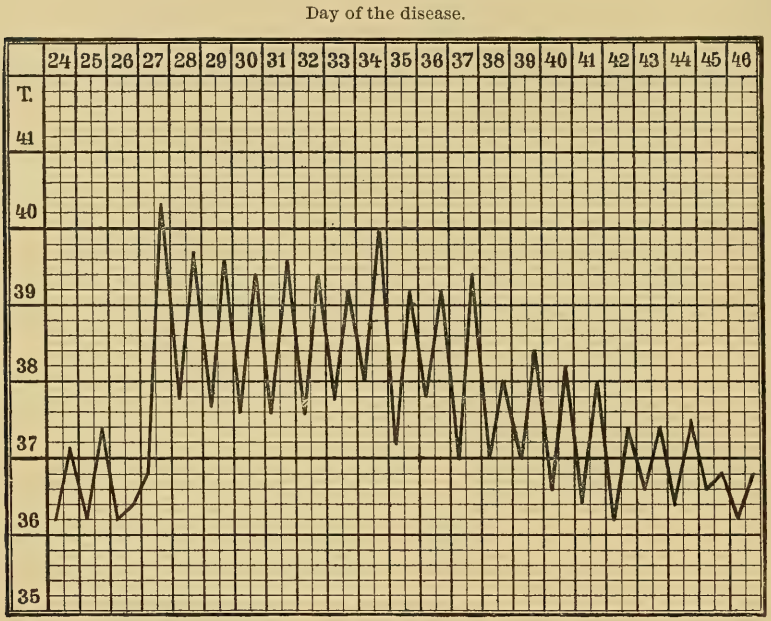

FIG. 39.

even of especially serious import. In addition to the increased frequency, the pulse during the relapse is also characterized by great variability. Even on slight physical or mental exertion it may be beyond computation, and in adults may reach 130 or 140. This instability of the pulse makes itself appreciable, as has been seen, as early as the period of incubation of the relapse. An instructive illustration of the character of the pulse in this period and during the febrile period is afforded by Fig. 35.

Dicrotism of the pulse is definitely not so frequently observed during the relapse as during the primary attack. It quite generally fails to appear even in those cases in which it was previously exceedingly well

marked. When the manifestation occurs at all, it takes place in the course of the severe, protracted relapse having an especially prolonged fastigium. In such cases symptoms of cardiac weakness also become apparent, which otherwise are not common. Irregularity of the pulse also is comparatively rare. It likewise occurs almost exclusively in the most severe relapses. Slowing of the pulse, which is so common in robust young men during the primary attack, I have never observed in relapses, even in such individuals.

The behavior of the roseolæ in the relapse is most important, especially from a diagnostic standpoint. Their appearance may be actually decisive in diagnosis, especially when doubt exists whether the reascent of the fever may not be attributed to severe complications,

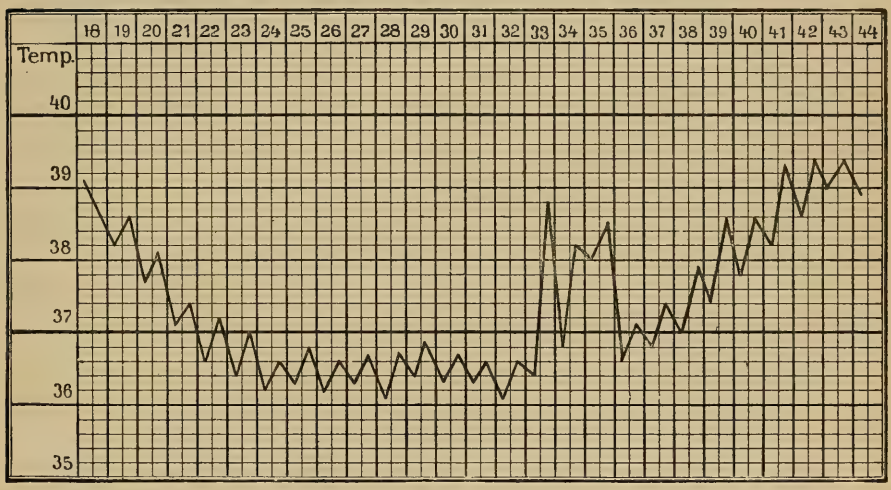

FIG. 40.

as, for instance, septic states or miliary tuberculosis. In general, their development during a relapse is quite usual—in my experience scarcely less common than during the primary attack. In 290 cases of relapse examined with regard to this point, I found roseolæ doubtful or absent in 23.7 per cent. It is true that, as with regard to so many conditions in cases of typhoid fever, the peculiarities of individual epidemics must be taken into consideration in this connection also. I have myself observed periods in which the roseolæ were even more frequent than has just been mentioned, and, in addition, were also remarkably profuse; and others in which they were distinctly less common and less abundant. Their number and extent in the individual case are generally somewhat smaller than in the primary attack; but, on the other hand,

the conditions observed during this period are repeated with remarkable frequency in the relapse. Only in greatly reduced, especially senile individuals, may the roseolæ be remarkably pale, small, and less elevated. In such cases individual roseolæ, it is true, may exceptionally become hemorrhagic, or actual petechiæ may appear, especially in the hypogastrium and the adjacent portions of the thighs. In accordance with the more rapid course of recrudescences and relapses in general, the roseolæ also appear somewhat earlier than in the primary attack. Mild and severe cases exhibit little difference in this regard. It is possible that in the severe protracted cases the eruption appears somewhat later. I have most frequently observed the roseolæ to appear during the relapse between the third and the fifth day; somewhat less commonly on the second or the sixth day; much less commonly at a later period. In only 2 instances have I observed roseolæ to appear on the tenth and the fourteenth days respectively.

I have analyzed about 300 cases of relapses with regard to this point. The first appearance of the roseolæ from the first to the third day was noted in 8.7 per cent.; from the fourth to the sixth day in 65.5 per cent.; on the seventh day in 14.5 per cent.; after the seventh day in 3 per cent.

The duration of the individual rose-spot was, in general, not shorter than in the primary attack. New eruptions and recrudescences of the exanthem also occurred in severe and protracted relapses just as commonly as in the primary attack.

Enlargement of the spleen, as has been mentioned, often does not subside completely after the primary subsidence of the temperature in cases in which relapses occur. It may even remain palpable during the entire interval, and, in connection with the peculiar character of the pulse and temperature previously described, may definitely suggest the impending relapse. Before basing conclusions upon the state of the spleen, however, one must have assured himself that previous enlargement of the organ, due to other causes, had not existed prior to the attack of typhoid fever.

More frequent than the persistence of splenic enlargement is its total disappearance in the interval between the primary attack and the relapse. The increase in size then again becomes demonstrable during the first days of the relapse, in general somewhat earlier than during the first attack—in my opinion, between the third and the sixth day. The cases are especially noteworthy, and of importance from the diagnostic standpoint, in which enlargement of the spleen had been entirely wanting during the primary febrile period, and became unequivocally demonstrable during the relapse.

I agree with Ziemssen,[1] who presents valuable statistics in support of his statement, that the enlargement of the spleen during the recrudescence and the relapse is rarely greater, but generally is less, than during the primary attack. Nevertheless, I have observed not a few cases in which enlargement of the spleen, appreciable during the primary attack only on percussion, became appreciable on palpation during the relapse. In this connection, it is true, the great emaciation and the relaxation of the abdominal walls, probably also the less marked meteorism during the relapse, may be of some importance.

The symptoms referable to the intestinal canal differ but little from those in the primary attack, and at most only in degree. The meteorism rarely attains marked intensity. The bowels are variable, as in the primary attack. At times there is diarrhea, with stools of characteristic color and consistence; and at other times, on the contrary, constipation; or one may alternate with the other. Anatomic examination—this statement is based upon the conditions found in 31 cases examined personally—discloses without exception, in addition to more or less recent cicatrices, or clean, almost healed ulcers, resulting from the primary attack, fresh medullary swelling of Peyer's patches and the solitary follicles, in part in process of sloughing or beginning ulceration. Not rarely, under such circumstances, in addition to cicatrized portions of a Peyer's patch, fresh infiltration of previously exempt portions of the same patch may be observed. In addition, there also occurs fresh swelling of the mesenteric glands.

No definite relation exists, obviously, between the extent and the intensity of the recent infiltration to those of the previous one. I have observed the new infiltration to be quite extensive in the presence of isolated cicatrices; and, conversely, have observed only isolated fresh swollen patches or follicles after very marked primary intestinal lesions. On the whole, however, the intestinal lesions of the relapse are distinctly less numerous, deep, and extensive than those of the primary attack. Undoubted relapses, associated with only recent catarrhal tumefaction of the mucous membrane and no alteration in the follicles, such as have been described especially by French investigators (Cornil), have, as yet, not occurred in my experience; but in the light of current conceptions the possibility of their occurrence is certainly not to be denied. In the majority of cases the fresh medullary swelling also occurs in those portions of the intestine preferably involved in the primary attack, in the midst of, or, more frequently, somewhat remote from, the primary

[1] *Würzburg. Jubil.-Gratul.-Schrift*, 1882, and *Deutsch. Arch. f. klin. Med.*, Bd. xxxiv.

lesions. It does, however, occur not at all rarely that portions of intestine affected previously in slight degree, if at all, become the seat of marked alterations during the relapse. Thus, for instance, I have observed in a case of "colon-typhoid" recent ulcers and swelling in the region of the ileocecal valve and the adjacent portions of the ileum, which previously were left almost intact; while in other instances, conversely, I have found ulceration of the follicles in the large intestine when the primary affection apparently involved almost only the lower portions of the small intestine.

The slighter development of the anatomic alterations in general explains also the circumstance that hemorrhage and perforative peritonitis are far less common during relapses and recrudescences than during the primary attack. While, for instance, in Hamburg we observed among a total of 3686 cases of typhoid fever, 153 cases—4.16 per cent.—with intestinal hemorrhage, this occurred in but 4 among 523 relapses—0.76 per cent.

With reference to the respiratory apparatus, little is to be said. In severe and protracted relapses bronchitis generally again develops. This, it is true, may be of alarming severity and extent in old and debilitated individuals, and may even lead to hypostatic congestion. The development of pneumonia and pleurisy is comparatively rare. This is applicable especially to true fibrinous pneumonia.

With regard to the nervous system also there is little of special importance to be mentioned. In moderate, short, and mild relapses the cases are in this respect often remarkably uncomplicated. In severe protracted relapses, especially those that, as appears to me, occur after a mild primary attack, the patients at times exhibit violent delirium, or they may soon fall into a state of sopor, and even of alarming coma. Focal lesions of the central nervous system or changes in the peripheral nerves, with corresponding sequels, are distinctly less commonly associated with relapses.

Course and Terminations of the Relapse.—While we have as yet been unable to distinguish any material difference between a recrudescence and a relapse with regard to the course of the fever and the changes in the viscera, such a difference undoubtedly exists with reference to the general course and termination. The true recrudescence exhibits more frequently than the relapse a severe clinical picture, even when the course of the fever is of the same duration and character in each. One almost gets the impression that the patient in the relapse, in contradistinction to the patient suffering from a recru-

descence, has already had an opportunity to recover during the afebrile interval and to fortify himself against the new attack.

Also, von Ziemssen emphasizes the severe course of recrudescences. He recorded severe symptoms in 50 per cent. of recrudescences, and observed as many as 15 per cent. terminate fatally. My own statistics are somewhat more favorable. Of 110 recrudescences, the course was severe and alarming in 40, while 11 per cent. terminated fatally.

Although the actual relapses with a highly febrile and protracted course may also exhibit a severe clinical picture, this is far less common, and the mortality is, on the whole, much lower, than in the recrudescences. Even in the severest epidemics the mortality probably scarcely ever exceeds 5 per cent.; 2.5 per cent., or at most 4 per cent., is probably the usual mortality.

In the epidemic at Hamburg the mortality during relapses was relatively high, namely, 4.9 per cent. (Among all fatal cases of typhoid fever, the proportion of those occurring during relapses was 0.7 per cent.) Our statistics at Leipsic exhibit a mortality of not quite 2 per cent.; those of Ziemssen, 2.8 per cent. Steinthal,[1] it is true, records 8.8 per cent. As this estimate, however, is based upon only 45 relapses, accidental influences are not excluded. The same is true of the unfavorable experiences of Murchison,[2] whose statements were based upon only 10 cases, and who, certainly without reason, considers that relapses, as a rule, are more severe than the primary attacks. Further, the severity of the relapse, and therefore also its mortality, vary, like so many other features of typhoid fever, undoubtedly not inconsiderably in accordance with temporal and local influences. Under all conditions, however, the mild cases are far more frequent than the severe, which, in general, may be estimated at from 10 to 15 per cent. We observed at Hamburg, among 496 relapses: Mild, 365—73.8 per cent.; moderately severe, 78—15.6 per cent.; severe, 53—10.6 per cent.

The duration, the height, and the character of the fever, as well as intercurrent local disorders, are especially of determining influence with regard to the character of the course and the termination. A special position with regard to prognosis is occupied by the protracted relapses attended with irregular, markedly remittent fever, as, both in adults and in children, they are at no time likely to give rise to serious concern.

It is an important question whether the character and the severity of the relapse depend upon those of the primary attack. Undoubtedly, as has been pointed out, it may be observed in many cases that the original character of the temperature-curve is reproduced in recrudescences and relapses; while this feature is less marked with regard to the remaining typhoid symptoms—the roseolæ, the enlargement of the spleen, and the diarrhea. With regard to the temperature-curve, it has been mentioned that if the curve exhibits an intermittent or remittent character during the primary attack this is

[1] *Deutsch. Arch. f. klin. Med.*, 1884, Bd. xxxiv. [2] *Loc. cit.*

likely to be repeated in the relapse or to become even more clearly marked (see Fig. 38). The character of the rise and of the decline of the temperature also frequently resembles that observed in the primary attack. This becomes especially conspicuous in the less frequent varieties; for instance, the ascent at a single stroke, or the critical decline. Only recently I observed a remarkable coincidence likewise with regard to the character of the curve at the height of the fever, in that a convalescent from a hyperpyretic attack of typhoid fever exhibited also during the relapse, lasting but a few days, evening temperatures of more than 41° C.

With regard, however, to the severity or the mildness of the course of the relapse, as compared with that of the primary attack, it must be considered as established that there is no rule. Thus, in the sequence of mild attacks—abortive, ambulatory, or afebrile typhoid fever—the most severe protracted relapses may occur. I believe, in agreement with a large number of writers (Ziemssen, Liebermeister, Jaccoud, Steinthal, Goth, and others), I may state that this is quite frequent.

The duration of the afebrile interval between the primary attack and the relapse appears to be without material influence upon the course of the latter. It is my impression, however, that relapses occurring especially late more frequently pursue a mild course. The duration of the relapse is, in the large majority of cases, from six to fifteen or twenty-one days. Periods of from twenty-two to twenty-five days are somewhat less common, and those of from twenty-six to forty days are observed only exceptionally. Relapses of more than forty days' duration I have observed in but 2 instances, one of forty-three and another of forty-five days.

Von Ziemssen noted that the duration in 101 relapses which he collected varied between four and thirty-five days. In the overwhelming majority (96) it varied between five and twenty-one days. The findings of Jaccoud, who noted the most frequent duration as from eight to twenty-one days, and our own statistics at Leipsic (Berg), where of 210 relapses, 182—86.6 per cent. —lasted from ten to twenty days, are quite similar. An analysis of the 523 cases of relapse observed in Hamburg in 1886–1887 discloses that likewise the great majority of cases, namely, 402—76.9 per cent.—lasted between five and twenty days.

Relapses of shorter duration, as, for instance, less than six days, are, however, by no means rare. If it be correctly assumed that recrudescences and relapses are really only repetitions of the primary attack, it is justifiable to conclude that inasmuch as mild and incomplete primary attacks may be observed, abortive and incomplete relapses also occur. The true nature of a portion of these is further disclosed by

renewed enlargement of the spleen and reappearance of roseolæ, in association with persistent elevation of temperature for only a few days. In other cases, with a reappearance of the fever for a short time after an afebrile interval of greater or less duration, the interpretation of a relapse, if roseolæ and splenic enlargement are wanting, is to be based only upon the possibility of excluding other febrile processes. That, on account of the inadequacy of our diagnostic means, great caution should be observed in this connection, and that in the individual case the diagnosis had better be left in doubt, need scarcely be emphasized. Transitory elevation of temperature, not dependent upon local disease, has, upon the suggestion of Biermer, been designated "after-fever." Some of the cases in which this occurs are certainly, by reason of their nature and development, to be included among relapses, so that it appears more appropriate for these, instead of employing the undistinctive expression of Biermer, to employ the designation shortest relapses or "abortive relapses."

In quite rare cases, after the fever had subsided and the patient had for days exhibited subnormal temperature, I have observed marked fluctuations in the temperature-curve with evening elevations, not, however, exceeding 37.5° C., associated with headache, malaise, restlessness, and even slight stupor, this condition lasting for from several days to a week. The simultaneous appearance of roseolæ, as well as the further circumstance that the enlargement of the spleen had not wholly disappeared after defervescence, but had rather increased somewhat during the period of relative temperature-elevation, justified me in considering these conditions also as relapses. It will be seen that the agreement between the various varieties of course of the primary attack and those of the relapse is so complete that one may even speak of "afebrile relapses."

The frequency of the occurrence of relapses appears, as has been mentioned, to vary considerably in accordance with temporal and local influences and in different epidemics. Probably the great diversity of statement among writers in this connection is dependent also upon differences in conception. If, as is not done in all statistics, the recrudescences are separated from the relapses, it will be found that the frequency of occurrence of the latter is, on the whole, in from 6 to 12 per cent. of all cases.

In Leipsic, we estimated the average of fourteen years, which, it is true, varied considerably among themselves, at 12 per cent.; while in Hamburg, in the year 1886–1887, 14.2 per cent. of relapses were observed—undoubtedly a high figure, in comparison with which the recrudescences in the strict

sense—1.8 per cent.—exhibited a great disproportion. The extremes that may be reached by various writers in accordance with the interpretation of the term relapse and with temporal and local differences will be shown by the following statement, which I have already had prepared in part in the dissertation of Schulz. Of relapses, there occurred, according to Lindwurm,[1] in Munich, 1.4 per cent.; Murchison,[2] in London, 3.0 per cent.; Biermer (Fleischel),[3] 3.3 per cent.; Beetz, Heimer (1874–1877),[4] 4.0 per cent.; Ebstein,[5] in Breslau, 4.3 per cent.; Eichhorst,[6] in Zurich (summer of 1884), 5.6 per cent.; Griessinger,[7] in Zurich, 6.0 per cent.; Gerhardt[8] (collection from reports of epidemics), 6.3 per cent.; Steinthal,[9] in Leipsic (1877–1881), 7.5 per cent.; Liebermeister,[10] in Basle (1867–1874), 8.6 per cent.; Goth,[11] in Kiel (1871–1885), 8.7 per cent.; Bäumler[12] (German Hospital of London), 10.9 per cent.; Bülau,[13] in Hamburg (1875), 11.4 per cent.; Butz,[14] in Munich (1878–1883), 12.5 per cent.; von Ziemssen,[15] in Munich (1878–1881), 13.0 per cent.; Freundlich,[16] in Freiburg, 14.0 per cent.; Weil,[17] in Heidelburg, 17.0 per cent.

Age and sex are not without influence upon the occurrence of relapses. With reference to age, it may be said that relapses undoubtedly occur more frequently in young persons than in the later years of life. This is exhibited with especial distinctness in the typhoid fever of childhood, and here, as we shall subsequently see, even extends to repeated relapses.

Analysis of 5302 cases at Hamburg and Leipsic disclosed 733 relapses—13.8 per cent. Among these, there occurred in adults 4687 cases, with 630 relapses—13.4 per cent.; in children, 615 cases, with 103 relapses—16.8 per cent.

The differences with regard to age appear more striking in a study of the statistics of Leipsic alone, which show 12.5 per cent. of relapses in adults and 19.1 per cent. in children.

The differences are less marked with regard to the influence of sex upon the frequency of relapses. With Griessinger and others, I am

[1] *Aerztl. Intelligenzbl.*, 1873, and Körber, *Inaug. Diss.*, Munich, 1874.

[2] *Loc. cit.* [3] *Inaug. Diss.*, Zurich, 1873.

[4] "Statistik der Typhusbewegung auf der med. Klinik des Herrn Prof. Ziemssen," *Deutsch. Arch. f. klin. Med.*, Bd. xvi., xvii., u. xxiii.

[5] *Die Recidive des Typhus*, Breslau, 1869.

[6] *Deutsch. Arch. f. klin. Med.*, Bd. xxxix., S. 297.

[7] *Loc. cit.*, S. 240.

[8] *Deutsch. Arch. f. klin. Med.*, 1873, Bd. xii., S. 8.

[9] *Ibid.*, 1884, Bd. xxxiv., S. 358, *Inaug. Diss.*

[10] *Loc. cit.*, p. 198. [11] *Loc. cit.*, p. 146.

[12] *Loc. cit.*, p. 397.

[13] *Deutsch. Arch. f. klin. Med.*, Bd. xviii., S. 107.

[14] "Statistik der Typhusbewegung auf der med. Klinik des Herrn Prof. Ziemssen von 1878–1883," *Ibid.*, Bd. xxxviii., S. 320.

[15] "Ueber de Typhusrecidive," *Ibid.*, Bd. xxxiv., S. 376.

[16] *Loc. cit.*, p. 324.

[17] *Zur Pathologie und Therapie des Abdominaltyphus*, 1885.

inclined to believe that females exhibit a slightly greater predisposition. At least, it can be said that if during an epidemic any difference

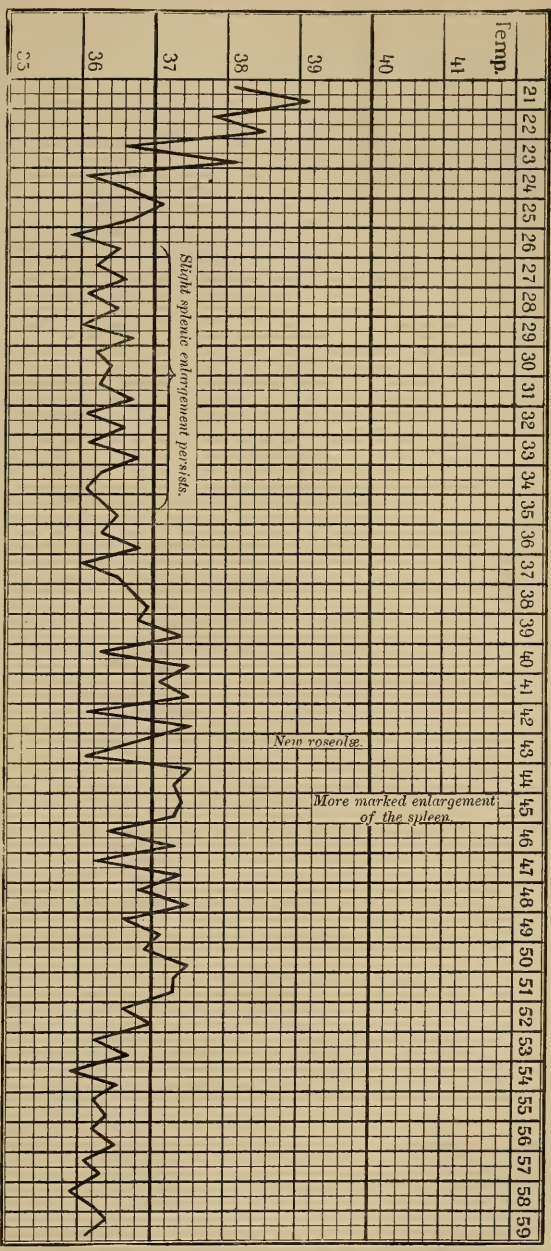

FIG. 41.—Temperature-chart from a case of typhoid fever of moderate severity without complication, lasting rather more than four weeks, in a woman, forty-two years old. Between the forty-second and the forty-fifth day of the disease new roseolæ appeared and renewed enlargement of the spleen occurred, with slight elevation and marked fluctuations in the temperature. "Afebrile relapse."

appears between the two sexes, the greater number usually appears in the latter.

In Hamburg the following figures were observed:

	Males.	Females.
1886	11.9	16.3
1887	13.3	15.9

Analysis of the Leipsic statistics exhibits similar results for a number of the years, but, on the whole, discloses no noteworthy differences.

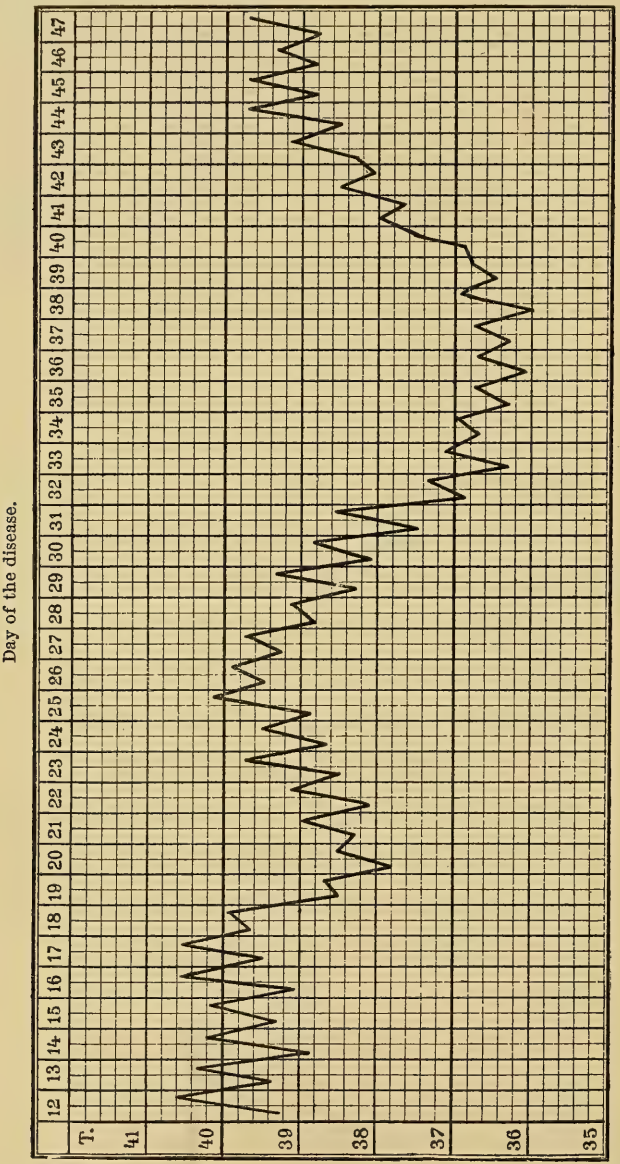

Fig. 42.

In most cases the disease terminates with a single recrudescence or a single relapse. Both may, however, be variously repeated. It may

happen that in one patient only recrudescences up to three occur, while another is attacked only by relapses. The occurrence of recrudescence and relapse in the same patient is not uncommon. Under such circumstances the recrudescence almost always occurs in the course of the primary period of defervescence; and then, after an afebrile period of varying length, one or several relapses occur (Fig. 42).

It is quite rare, and to my knowledge nowhere mentioned, that a recrudescence follows a protracted relapse—then generally moderately severe or severe—before the temperature has returned to the normal (Fig. 43). I lost such a patient at the height of such a recrudescence complicating a relapse, with symptoms of the most profound intoxication. Among the most frequent of the possibilities mentioned is the repeated relapse, there being generally but two, and rarely three. Four and five relapses are among the greatest exceptions. Under such circumstances every individual relapse should be most critically scrutinized.

Ziemssen found, among 108 cases of typhoid fever with relapse, only 6 in which this was repeated. In but 1 of these he believed himself justified, although not absolutely certain, in assuming the occurrence of three relapses. Among the 523 cases with relapse that we observed in the epidemic at Hamburg from 1886 to 1887, in 474—90.6 per cent.—there occurred but one relapse; two relapses in 44—8.4 per cent.; and in only 5 cases—0.9 per cent.—among this large number were three relapses observed. I have personally observed four relapses in each of 2 cases; and only recently I have seen a case in which, following upon a severe recrudescence, three relapses occurred, the shortest of which was three weeks in duration. I would further emphasize the fact that the proportion of 8.4 per cent. of cases in which two relapses occurred, as disclosed by the Hamburg statistics, exceeds that yielded by my previous and subsequent experience. I believe the occurrence of such cases to be, on the average, much less frequent—4 per cent. would probably represent the usual conditions.

With reference to the severity of repeated relapses, this appears to me to be generally slighter than that of the first relapse or of the recrudescence. The contrary, however, is not altogether rare. Thus, last year I saw in consultation a second extremely severe relapse of twenty-six days' duration occur nine days after the termination of the first mild relapse of only eleven days' duration; and also previously I had repeatedly encountered cases in which the second relapse exceeded the first in duration by a third and even by half. I have observed even the third relapse to be considerably more severe and more protracted than the two preceding ones.

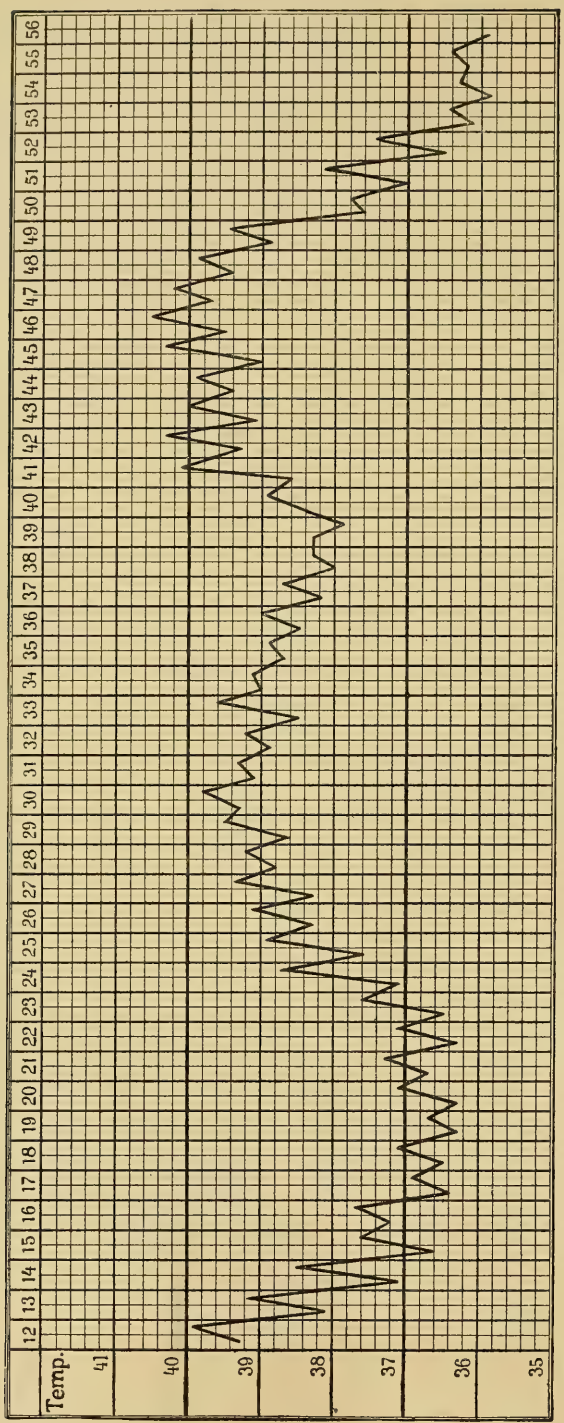

FIG. 43.—Temperature-chart from a case of typhoid fever in a servant-girl, sixteen years old. On the seventh day, after a mild primary attack of sixteen days' duration, a moderately severe relapse ensued, which was followed, before the completion of defervescence, by a recrudescence, attended with high temperature and severe general manifestations.

Von Ziemssen has made the following instructive tabulation of 4 cases of double relapse:

	Duration of the first relapse.	Duration of the second relapse.
First case	Three weeks.	Fourteen days.
Second case	Three weeks.	Fifteen days.
Third case	Eleven days.	Seventeen days.
Fourth case	Fourteen days.	Twenty-three days.

Just as the occurrence of the single relapse bears some relation to the age of the patient, so age also appears to play a *rôle* in repetitions of relapses and recrudescences. Here also young persons are distinctly more frequently attacked. Thus, at Hamburg, among 44 cases of double relapse, 12 occurred in children.

If, in conclusion, a few remarks be made concerning the mode of development of relapses and recrudescences, it should first be again mentioned that at the present day these are generally considered to be repetitions of the primary morbid process, dependent upon the infection responsible for this, and not the result of a new invasion by typhoid-bacilli. Also, no one doubts any longer that certain influences which were formerly considered as the cause of relapses play only the part of factors contributory to their development. This view must be adhered to in spite of certain hypercritical objections. Emotional disturbances, premature mental activity, and, among injurious physical influences, premature getting out of bed, and, above all, dietetic errors, must all be regarded in this light. That these are contributory factors, however, must be expressly emphasized, notwithstanding Murchison's views—to which Uhle and others agree—to the contrary, and even though we have as yet no knowledge concerning the mechanism of their unfavorable influence. It would be a source of great danger to the typhoid patient if this fundamental principle were neglected. I have also noticed relapses follow upon a number of other influences comparable to dietetic error. Thus, but a year ago, I observed such an occurrence after the institution of treatment for tapeworm.

The patient in question, a previously healthy house-servant forty-three years old, was brought to the clinic complaining of general malaise and anemia, the diagnosis of the fundamental trouble being indefinite. He appeared to be entirely free from fever, and exhibited for a time, notwithstanding increased pulse-frequency, persistent subnormal temperature (morning, 36° C.; evening, scarcely 36.5° C.). It could not be determined from the history whether fever had existed during the period prior to admission. As the pallid, considerably emaciated man lost over two pounds during eighteen days' residence in the hospital, in spite of careful nursing, the discovery of a Tænia mediocanellata was received as a welcome therapeutic indication. On the third day, after successful treatment for the tapeworm, the temperature began to rise, and there followed a febrile state of seventeen days' duration, which, from the character of the curve, enlarge-

ment of the spleen, roseolæ, thin stools, and diazo-reaction, proved to be typhoid. Undoubtedly, the patient came under observation during convalescence from an attack of ambulatory typhoid fever, and he suffered a relapse of the primary condition in consequence of the treatment instituted.

A question formerly earnestly and frequently discussed was whether antipyretic treatment of typhoid fever, especially that with cold baths, caused an increase in the frequency of relapses. Many physicians, even the most enthusiastic advocates of those methods, were unwilling to disregard the possibility of an unfavorable effect in this regard (Liebermeister, Biermer, Leyden, Goltdammer), while others (Leichtenstern, Vogl) expressed a contrary opinion. If the abundant literature upon the antipyretic method of treatment be studied with regard to this question, it will be found that in certain places and at certain times, under identically the same application of bath-treatment, the number of relapses exhibits the greatest variation. I have personally likewise observed such variable results at different times, when I employed antipyretics and baths more systematically than at present, that I am unable to convince myself that the methods in question exert any effect in causing relapses. The question, besides, no longer occupies the prominent position it formerly did, inasmuch as we have gained other therapeutic points of view.

CONVALESCENCE.

Accurate knowledge of the peculiarities of the period of convalescence, and accordingly of its careful supervision, is not less important than that of the earlier stages of the disease. In accordance with the extraordinary variability in the severity, the duration, and the symptomatology of the disease, the clinical picture of convalescence is also extremely variable. It is, besides, especially influenced by age, sex, constitution, complications, and relapses. In general, it may be stated that typhoid fever is one of those acute infectious diseases that most frequently either terminates fatally or, at the conclusion of convalescence, in complete restoration to health. Invalidism, sequels, and permanent defects are comparatively less common after it than after many other infectious diseases. Indeed, it cannot be denied that the statement often made by the laity that the general condition after recovery often becomes better and more flourishing than prior to the disease, particularly in young persons, is not without foundation.

GENERAL COURSE.

With the advent of convalescence, the beginning of which can be dated from the first day of persistent defervescence, the condition of the

patient is extremely variable, in accordance with the course of the antecedent attack and individual circumstances. In children and in previously healthy young adults the disease naturally is in general followed by slighter disturbances that are more rapidly recovered from than in older individuals or in those already debilitated in advance of the attack.

Under all circumstances, however, with the onset of convalescence from severe attacks of typhoid fever, the patients, of whatever age and constitution, exhibit considerable impairment of the general condition. Emaciation and **anemia** are most conspicuous. The symptoms of the anemia of convalescence, which often are most profound, are found on careful examination to be dependent especially upon **alterations in the number and character of the red blood-corpuscles** and upon variations in the percentage of hemoglobin. The red blood-corpuscles and hemoglobin, as in the earlier stages, usually pursue a parallel course also during convalescence, but not rarely their curves diverge. The reduction in hemoglobin and red blood-corpuscles, which is likely to be less in men and otherwise robust persons in general than in women and debilitated individuals, will have reached its maximum in the majority of cases, according to observations made at my clinic,[1] before the termination of the fever, subsequently to rise slowly again. Less commonly, the minimum percentage of hemoglobin remains unchanged for a certain time, during the first part of the afebrile stage, or the hemoglobin may undergo still further reduction. It is interesting that patients who have become markedly anemic, on the contrary, frequently exhibit immediately a steady and comparatively **rapid increase in the percentage of hemoglobin.** Thus, Kölner observed in a patient who had become particularly anemic an increase of 31 per cent. in the hemoglobin within six weeks, and in other patients, not at all rarely, an increase of from 10 to 15 per cent. in the course of a week. Especially in such cases of remarkably rapid reproduction, however, have we occasionally observed the occurrence of a stationary period or even a transitory diminution.

The not uncommon divergence in the relation of the red blood-corpuscles to the hemoglobin that has been mentioned is referable especially to the time and the circumstances of the greatest reduction in number. While in the majority of cases the number of red cells pursues a parallel course with the reduction in hemoglobin, it occasionally exhibits a still further progressive diminution extending into the afebrile period, when the hemoglobin has already begun to rise again. Even at a later stage,

[1] Kölner, *Inaug. Diss.*, *loc. cit.*, and *Arch. f. klin. Med.*, Bd. l. See also the extensive bibliographic references in this article.

a considerable diminution in number, which we have observed to reach half a million, and even more, sometimes occurs.

In all cases, even the moderately severe and mild cases, the restoration of the condition of the blood to that present before the attack takes place but slowly. Even after the lapse of seven weeks we have found that the normal number of red blood-cells and the corresponding percentage of hemoglobin have not been entirely regained. More or less marked deficiency in the regeneration of the blood was observed in almost all cases examined with reference to this point at a time at which they could be safely dismissed and considered able to return to work.

The emaciation of typhoid patients, which has been studied by Scharlau, Leyden, Botkin, and others, and subsequently with especial care by Kohlschütter[1] and Cohin,[2] is, in comparison with the duration of the disease and with the amount of weight lost in other acute infectious diseases, not so great as would be anticipated. It is naturally most marked in the cases of long duration and with high fever, but also after moderate and mild cases the loss of weight indicates the serious character of the recent infection and its deleterious influence upon the tissues.

All parts of the body apparently share in the emaciation—in what relation to one another has as yet not been sufficiently determined. The loss in weight is most manifest during the febrile period. The rapidity of this loss attains its maximum, in cases of normal or more protracted duration, at the end of the second, more frequently still in the course of the third, week; from that time on until complete defervescence it continues more slowly, not rarely in progressively lessening degree. After defervescence the bodily weight again increases, in general far more slowly than it declined; naturally, more rapidly, at times even with remarkable rapidity after mild attacks, and especially in children and in young, previously healthy individuals.

It is a most remarkable fact that has not been sufficiently dwelt upon, if at all, by even careful writers, that in a considerable number of cases, after complete defervescence, during the first, even during the second, with exceeding rarity during the third, week of convalescence, the loss of weight still progresses. This can be observed most frequently after severe, long-continued attacks; occasionally, however, also after short attacks of mild course. I have, under such circumstances, noted a loss of weight of as much as from 1.5 to 2 kilograms during the first

[1] *Volkmann's Sammlung inn. Med.*, No. 103.

[2] *Bull. gén. de thérap.*, May 15, 1887. My own observations are based upon the weekly weights of all my typhoid patients, the details upon the analysis of 92 cases at the Leipsic clinic, undertaken by my assistant, Dr. Hirsch.

week of convalescence. I am unable to give a satisfactory explanation for this phenomenon. Some of the evidence indicates that increased loss of water from the tissues plays some *rôle* in this connection. I have in a number of instances observed polyuria, increase in the specific gravity of the blood, and a relative increase in the number of red blood-corpuscles, in association therewith.

The loss in body-weight in the course of the fever appears to take place not abruptly, but uniformly, as Cohin, by the use of suitable apparatus, weighing the typhoid patient repeatedly for twelve days, has demonstrated. The average loss of weight a day in a mild, uncomplicated case was estimated by the same observer at 260 grams. Other writers, as, for instance, Botkin, observed it to reach 800 grams and above in severe cases.

The total weight which patients have lost at the beginning of convalescence is at times quite alarming. I have noted in an adult, after a severe, long-protracted attack, with various complications, a reduction of 41 per cent. in the original weight, and in mild and moderately severe cases I have seen even as great a loss as 10 and 19 per cent. respectively. It is worthy of note that in children I found the maximum loss of weight to be 9 per cent. These high figures may be contrasted with some extremely low figures collected from a large number of observations. Thus, in mild cases I have observed only from 1 to 1.1 per cent. loss of body-weight, and I have even seen severe cases in which the total loss was not more than from 1.5 to 3 per cent.

The conditions during convalescence in detail have been considered in various parts of this work. Thus, the behavior of the temperature during this period was fully considered on pages 140 and 141. It was shown that in almost all well-marked cases—and generally the more distinctly and the more protractedly, the severer the course—the body-temperature declined below the normal soon after defervescence, and gradually rose again, reaching the previous individual level only after days or weeks. It was seen, further, that during this period of subnormal temperature, assuming a condition of perfect quiet on the part of the patient, the daily fluctuations are slight, often less marked than in perfectly healthy individuals; but that they become extremely marked, however, in consequence of even slight physical or mental exertion. These peculiarities of the curve are generally so constant, and appear in so typical a manner after an attack of ordinary course, that they constitute important criteria in the recognition of convalescence. I have long been in the habit of considering convalescence after moderately severe and severe attacks not completely established until they appeared. Daily

experience teaches that when they are wanting relapses and complications are likely to occur.

The **pulse**, as has likewise been pointed out, is, in contrast to the temperature, rarely slowed at the beginning of the period of convalescence, and then probably only in special cases—most frequently is relatively slowed in elderly individuals, or, conversely, in especially vigorous men. Generally, it is slightly or moderately full and tense; after mild cases it is of normal frequency, and after severe attacks and in irritable individuals is of greater frequency—reaching in the neighborhood of 100 in the evening. Women and children frequently show a still higher rate. In addition, the pulse-frequency is extremely unstable, not only in the stage of subnormal temperature, but also often long after this. Up to the time of getting up, slight mental exertions or physical disturbances cause marked increase in the number of pulse-beats, this increase often rapidly disappearing again. This phenomenon may become especially striking and even actually alarming to the inexperienced physician and the friends, when the patient, by reason of his otherwise favorable condition, has been granted permission to get out of bed. Increase in the number of pulse-beats of, on an average, from 20 to 30, and persistence of the pulse-curve at this high level for some time—not rarely for as long as two weeks and more—is at this time quite customary; but it should be expressly stated that examination of the heart throughout the entire continuance of this condition discloses no special alteration.

The following two tracings may serve as characteristic instances of this character of the pulse and the temperature. Fig. 44 represents such a curve during convalescence. The case was that of a baker's apprentice, seventeen years old, who was free from fever after the twenty-eighth day of the disease, and exhibited, with a temperature-curve subsiding below the normal, also subnormal pulse-frequency, with moderate instability. Immediately after getting up there set in, without the temperature being influenced thereby, an unusual increase in the pulse-frequency, persisting for sixteen days. The heart at the same time remained completely unaffected both in size and action.

In the second case (Fig. 45) the first few days of convalescence still exhibit a subnormal temperature, with at first an increased pulse-frequency. With restoration of the body-temperature to the normal the number of pulse-beats then sinks somewhat, and fluctuates morning and evening between 80 and 85. Getting up on the forty-seventh day of the disease is again followed by excessive increase in pulse-frequency, with complete irregularity in its curve. This condition persists for three weeks without corresponding elevation of the body-temperature or other objective derangement of the heart, and then slowly gives way to the former normal conditions.

That such an unusual increase in pulse-frequency may constitute the beginning of a relapse may be again mentioned, principally for the purpose of introducing a curve that especially illustrates this point (Fig. 46).

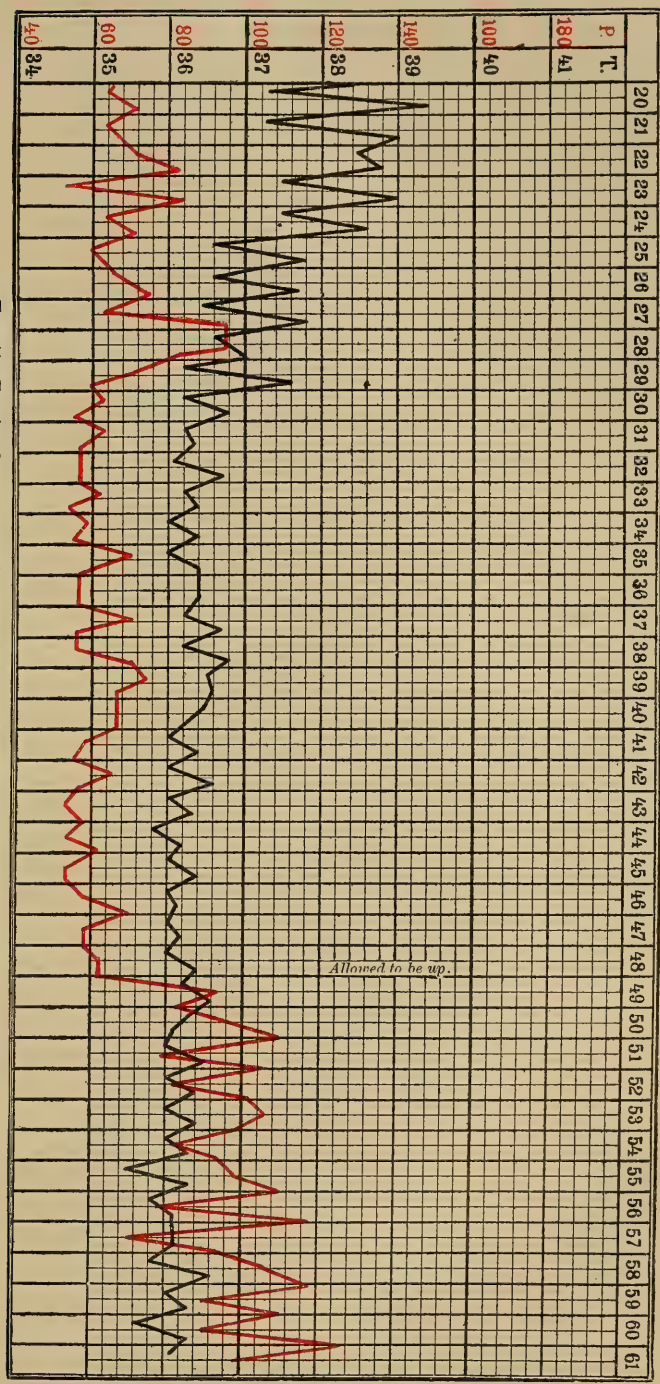

FIG. 44.—Tracing from a case of typhoid fever in a baker's apprentice, seventeen years old.

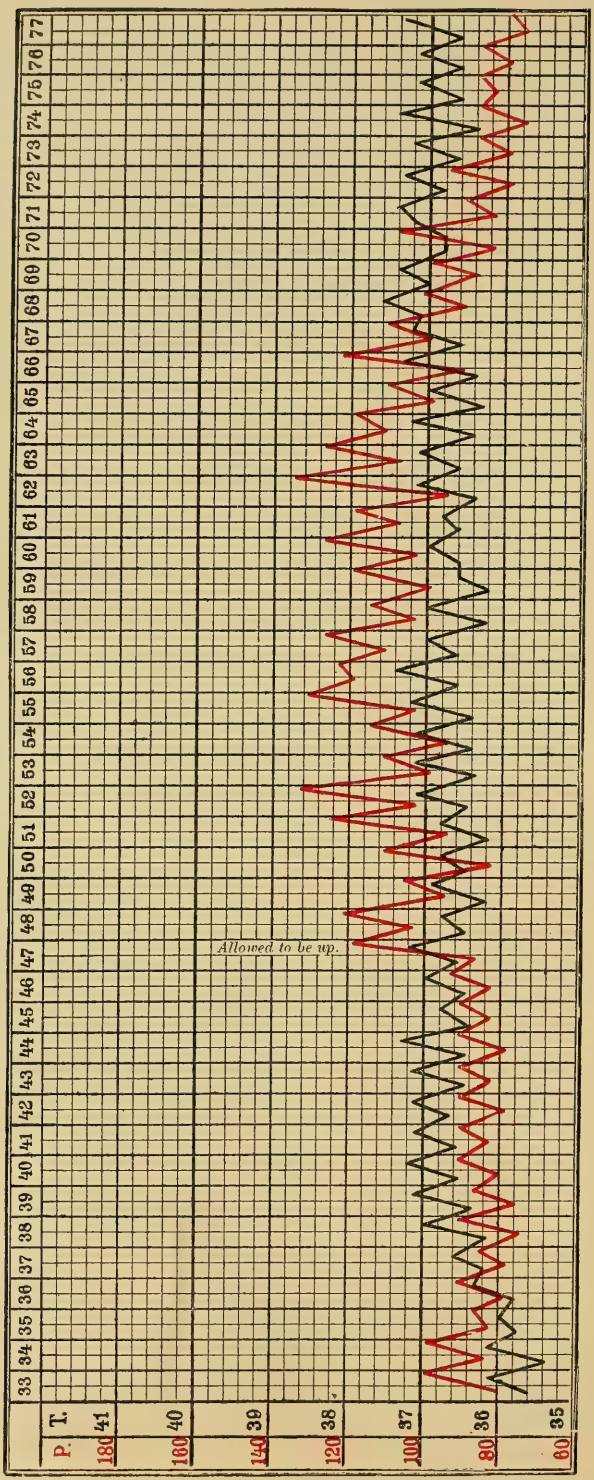
Day of the disease.
33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77
P.
T.
180 41
160 40
140 39
120 38
100 37
80 36
60 35
Allowed to be up.

FIG. 45.

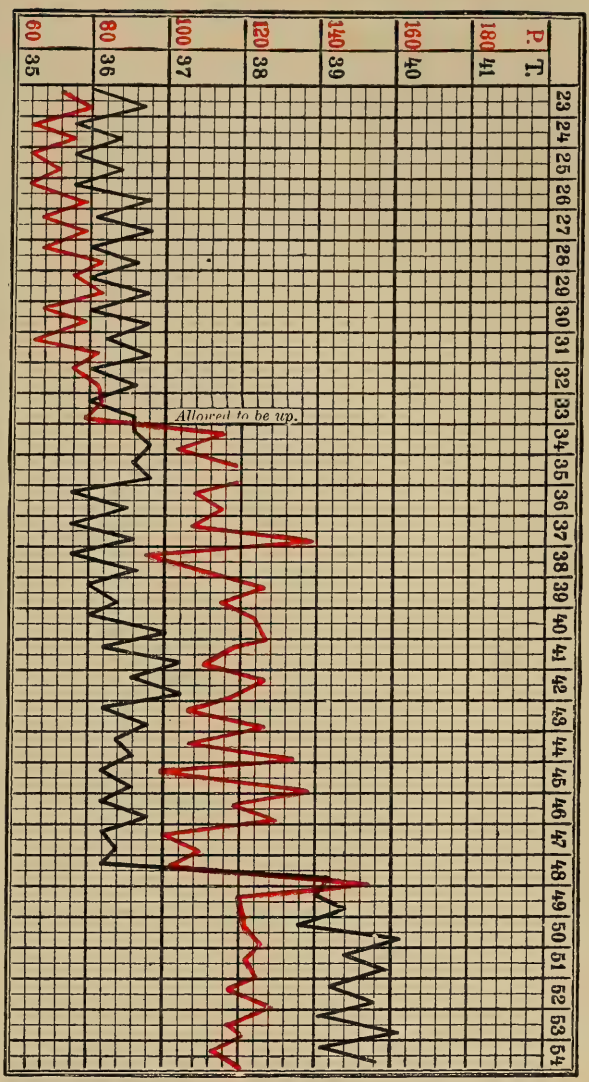

FIG. 46.—Temperature-chart from a case of typhoid fever of moderate severity, lasting twenty-one days, in a nurse, twenty-one years old. The patient arose on the seventeenth afebrile day. The temperature remained low for fourteen days, but was associated with an enormous increase in pulse-frequency. There then occurred a severe relapse of fourteen days' duration, with an abrupt onset.

CHANGES IN INDIVIDUAL ORGANS.

The **heart** only exceptionally exhibits alterations during convalescence. Now and again, undoubtedly much less commonly than during the febrile period, myocarditis, with dilatation and corresponding manifestations of cardiac weakness, occurs; generally, however, the termination is favorable. Endocarditis and pericarditis occur still more exceptionally. If they occur at all, they are almost always referable to mixed infection, especially to a complicating septicemia. A result of the conjoint influence of anemia and cardiac weakness, which is sometimes manifested

during the first portion of the stage of convalescence, is edema about the ankles and the legs, occurring especially in previously debilitated persons.

This is to be distinguished from that uncommon variety of dropsical swelling of the subcutaneous connective tissue, which is widely distributed over the entire body, and may even be associated with ascites. Griessinger [1] especially mentions the occurrence of this condition, and cites similar observations by Leudet. The cases are said to be but rarely attended with albuminuria, and may occur entirely without this phenomenon. Griessinger has no satisfactory explanation for them. Personally, I have not observed this symptom-complex except in association with coincident or shortly antecedent nephritis.

The **venous thromboses** previously described are encountered with relative frequency during convalescence, especially in the veins of the thigh and the deep veins of the calves. They are among those symptoms that often prolong convalescence unduly. Fortunately, they are rarely the source of fatal emboli. Arterial thrombosis with spontaneous gangrene, which is extremely rare, has likewise been previously considered (p. 167).

In the large majority of cases the condition of the **digestive organs** rapidly returns to the normal soon after defervescence. The lips and the tongue begin to clear even during defervescence, so that the tongue is but slightly coated during the first few days of convalescence, and then especially in the middle and posteriorly, while the margins and the tip are free from fur. After the tongue has become completely clear, it often for a considerable time appears thin, small and red, and remarkably smooth.

The appetite, which almost always returns with defervescence, often even previously, becomes the well-known voracious "appetite of convalescence," which may be a source of great difficulty for the friends and the physician, and readily of danger for a disobedient patient. Failure of the appetite to return is quite rare, and is worthy of special consideration. Except in previously ill and reduced individuals, this phenomenon is indicative of the latent persistence of earlier alterations or is a sign of impending complications. If associated with vomiting and persistence or recurrence of diarrhea, sluggish intestinal lesions must be thought of, as sequels of which intestinal hemorrhage and perforative peritonitis have been observed, even at a late period. Sometimes complete loss of appetite not amenable to any measure gives rise to the rare form of typhoid marasmus previously described, which persists until death finally occurs. In cases pursuing a regular and benign course, the typhoid diarrhea is likely to cease before deferves-

[1] *Loc. cit.*, S. 230.

cence is completed. As a rule, moderate constipation follows, which occasionally may be extremely obstinate, and then may be associated even with elevation of temperature.

In rare cases disorders on the part of the **liver** and the **biliary passages** make their appearance as late as the period of convalescence. They manifest themselves especially by tenderness over the region of the liver and the **gall-bladder,** and are in part probably attributable to inflammatory .conditions dependent upon the almost constant presence of typhoid-bacilli in the gall-bladder and large biliary passages of the patient (Gilbert and Girode,[1] Dupré,[2] Chiari,[3] Birch-Hirschfeld[4]) (see page 209).

In the light of these bacteriologic findings, the observations recently made by various writers of the occurrence of biliary colic during convalescence acquire special significance. After Bernheim had suggested the probability, Gilbert and Girode and Dupré demonstrated by illustrative cases that the presence of the typhoid-bacillus in the gall-bladder might be the direct cause for the formation of calculi. In this they were supported especially by Dufourt,[5] who presented an abundance of clinical evidence, and also by Milian[6] and Hanot.[7] Experimental proof for this has also been given by several observers (see p. 210).

From my own observations I agree absolutely with the opinion that the formation of **gall-stones** is by no means a rare occurrence in the period of convalescence, in spite of the most recent contradiction by Chauffard.[8] Naturally, the formation of gall-stones does not always make itself manifest as early as the period of convalescence. The first attack of colic often enough occurs only subsequently. That this may occur at a very remote period is shown by Hunner's[9] case, in which the attack occurred eighteen years after the attack of typhoid fever. The question as to whether cholecystitis and cholelithiasis may be induced by the action of typhoid-bacilli independently of any attack of typhoid fever has been raised by Cushing's[10] case in which, from the contents of the gall-bladder, a pure culture of typhoid-bacilli was obtained, and yet the patient gave no history of a previous attack of typhoid fever. It is noteworthy that, on obtaining a careful history of patients suffering from gall-stones, the fact of an antecedent attack of typhoid fever, a shorter or longer time previously, is encountered with remarkable frequency.

[1] *Compt. rend. de la soc. de biol.*, 1890 and 1893.
[2] *Gaz. des hôp.*, 1891.
[3] *Loc. cit.*
[4] *Loc. cit.*
[5] *Rev. de Méd.*, 1893.
[6] *Bull. de la soc. anat. de Paris*, Nov. 20, 1896.
[7] *Bull. méd.*, June 23, 1896.
[8] *Rev. de Méd.*, 1897.
[9] *Loc. cit.*
[10] *Johns Hopkins Hosp. Bull.*, vol. ix.

Among 42 cases treated for gall-stones at my clinic in recent years, there were 13, thus 30.9 per cent., in which there had been a previous attack of typhoid fever, and symptoms of cholelithiasis had appeared definitely only subsequently. Of these cases, the following 2 may be briefly described: A woman, thirty-six years old, was received in the clinic on August 21, 1891, on account of an attack of typhoid fever. After having been free from fever for almost four weeks, and in a state of perfect convalescence, she was suddenly seized with several attacks of biliary colic, succeeding one another at short intervals, which materially retarded recovery. The second case occurred in a woman, thirty-eight years old, who had, in May, 1890, passed through an attack of typhoid fever of five weeks' duration at the clinic. In the beginning of the following year an attack of biliary colic appeared for the first time, and thereafter was repeated several times. After she had been admitted to the hospital in March, 1894, on account of severe pain in the epigastrium, radiating toward the right half of the chest and the back, and associated with jaundice, several large gall-stones and a number of fragments were demonstrated in the stools.

Of 31 cases of cholecystitis associated with gall-stones treated at the Johns Hopkins Hospital, 10 gave a history of a previous attack of typhoid fever.

Also, in the vast majority of cases the condition in the respiratory organs, especially the **lungs,** returns to the normal toward the end of the febrile state or during the first period of convalescence. The bronchitis persists beyond the febrile stage almost solely in old or debilitated persons. Hypostatic congestion, however, if the patients recover, may persist into the first week of convalescence. Pneumonia is quite rare as a complication of convalescence, and pleurisy still more so. In greatly reduced individuals, with enfeeblement and dilatation of the heart, pulmonary infarction probably occurs exceptionally.

The relation of tuberculosis to convalescence is noteworthy. We have seen that old, previously latent tuberculous processes, or those giving rise to slight manifestations, may suddenly progress rapidly during convalescence; and also may give rise to new foci of disease in the form of caseous pneumonia or general miliary tuberculosis. Fortunately, it is rare for the residua and sequels of typhoid affections of the **larynx** to complicate convalescence, either in the form of simple ulceration of the mucous membrane or in that of perichondritic processes and necrosis of cartilage. Paralysis of the vocal cords has been exceptionally observed. As has been pointed out, most of the lesions of the larynx mentioned occur in the second half of the febrile period. It appears quite rare for them to develop as late as the period of convalescence.

The alterations and symptoms referable to the **nervous system,** likewise, generally improve rapidly during convalescence, in the great

majority of instances. Previously healthy, not hysteric or neurasthenic, persons acquire a peaceful, quite contented frame of mind soon after defervescence. At most, they distress themselves with desires with reference to food, which may not be fulfilled, and overestimate their functional ability, and in consequence are desirous of getting out of bed too early and of resuming their work. Women and debilitated persons remain gloomy, irritable, and even hypochondriacal during the first period. Children also are likely to be ill-tempered and lacrimose at first.

That mental disturbances, especially isolated delusions, may persist for a considerable time, and even far beyond the period of convalescence, has been previously pointed, out and illustrative instances have been cited. However, it should be noted that these disturbances persist from the febrile period far more frequently than they arise during convalescence.

Headache, which plays no inconsiderable *rôle* during the initial period of the attack of typhoid fever, is quite rare during convalescence. If the patient is not a person who for a long time preceding the attack had suffered habitually from headache, the appearance of this symptom during convalescence should be viewed with distrust. Not rarely complications are concealed behind it, as, for instance, meningeal inflammation secondary to middle-ear disease, sinus-thrombosis, and even cerebral abscess. Quite exceptionally following typhoid fever there may also be headache, continuing for years, or even throughout life, without demonstrable organic lesion.

Focal disease of the brain, persisting from the febrile period into convalescence, and even beyond it, may, of course, occur. In this connection monoplegia and hemiplegia, aphasic states, and multiple sclerosis should be borne in mind. Among the spinal affections and disorders of the peripheral nerves, ataxia and pseudo-ataxia, and the comparatively frequent distressing neuralgic disturbances, especially in the toes and the heels, should be borne in mind.

Among the organs of special sense, the ear almost solely plays any *rôle*. Affections of the middle ear, with perforation of the tympanic membrane and suppuration, may make the clinical picture of convalescence quite serious ; and, if life is preserved, may give rise to permanent impairment of hearing. As serious diseases of the eyes are far less common in the course of typhoid fever than are diseases of the auditory apparatus, so during convalescence are they but rarely likely to require the intervention of the physician. Photophobia during the first week

of convalescence in patients who are sensitive in other respects is comparatively the most frequent ocular symptom.

More frequent than nervous disorders during the period of convalescence are alterations in **muscles, bones,** and **joints.** In this connection the softening processes, the lacerations, and the hemorrhages into the substance of the muscles should be borne in mind. Attention has been called recently in a number of communications by surgeons to the typhoidal lesions of the bones and periosteum. I have repeatedly observed periostitis with secondary necrosis, as well as osteomyelitis, appear during convalescence, and prolong this unduly. Such lesions may eventually require operative intervention, sequestrotomy, and the like, and may give rise to even permanent impairment of function of the parts involved. Less common, but especially worthy of mention on account of their consequences, are inflammatory disorders of the joints arising during convalescence. Roser[1] had already called attention to such involvement of the hip-joint.

A more extended discussion of this subject will be found in the section on Pathology, p. 87.

Of alterations in the **urinary organs** there is not much to say. The polyuria of convalescents, which in itself is of little significance, and only with exceptional rarity constitutes the inception of diabetes insipidus, has been mentioned. Febrile albuminuria persists but rarely to the beginning of convalescence; the alterations in the urine caused by actual typhoid nephritis, however, may persist beyond the period of convalescence. Fortunately, it is an exceptional occurrence, especially in comparison with other acute infectious diseases, as, for instance, scarlet fever, diphtheria, and necrotic angina, for chronic nephritis to develop from the acute. When the lesions of the kidney actually persist beyond the period of convalescence, hope of their subsidence may still be entertained for months and even a year; and when subsidence does not take place within this time, a long-continued, but not violent, course may with probability be predicted.

In women vesical catarrh of slight virulence may occasionally occur toward the end of the febrile stage, or may first appear during convalescence. In men this is extremely rare, and then almost always as a result of careless employment of the catheter.

However, the typhoid-bacilli may persist in the urine for months and even for years and may induce a chronic form of cystitis (see p. 190).

With regard to the **genital functions,** it should be mentioned

[1] Helwig, *Inaug. Diss.*, Marburg, 1856; cited by Griessinger.

that pregnant women, after having successfully passed through the febrile stage, not rarely abort or are delivered prematurely during convalescence.

Menstruation returns in a most variable manner. In vigorous, robust women, but, unfortunately, sometimes also in already highly anemic ones, it occasionally returns soon after defervescence—in small amount, as a rule, for the first few times; occasionally, however, so profusely that the patient is thereby seriously injured and retarded in the progress toward recovery. In other cases, on the contrary, without special causes being discoverable therefor, menstruation long remains absent, even for many months beyond convalescence. Also, menstrual molimina previously not noticeable are considered by women, at times correctly, as a sequel of the attack of typhoid fever. Peri-uterine hematocele, described by Trousseau, and hematometra, which occurs rarely, with its often obstinate sequels, have been referred to (p. 196). Sometimes the residua of inflammation of the glands of Bartholin and decubital ulcers of the labia and the vulva cause much discomfort during convalescence.

In men, at the period of adolescence, erections again occur during early convalescence, and in addition not rarely distressing enervating pollutions. For some patients they constitute directly a disturbing complication at this time. Orchitis and epididymitis are, as is well known, quite rare, and then are generally affections of the last part of the febrile stage. Among 6 cases under my personal observation, 2 developed after defervescence.

The **skin** is generally dry at the beginning of convalescence, and when it has been indurated and thickened, particularly on the hands and the feet, it is desquamated at this time in shreds of greater or lesser size. On the trunk, and especially on the abdomen, branny desquamation of the epidermis often occurs if there has been an extensive sudaminal eruption during the febrile stage. This desquamation at times becomes so marked, particularly in children, that if the patients first come under observation during convalescence, serious doubt may arise as to the nature of the antecedent disease. Multiple furunculosis, which formerly constituted so distressing a disturbance of convalescence for patient and physician alike, is, fortunately, at the present day far less common than at the time when unnecessarily frequent and too cold baths were prescribed. Bed-sores also by no means play the same *rôle* as formerly. With regard to the condition of the hair and the nails during convalescence, reference may be made to pages 132 and 133.

THE DURATION OF CONVALESCENCE.

Convalescence, which begins with the close of the febrile period, cannot have its total duration accurately estimated, because definite criteria of its termination cannot be established. In general it may be considered as ended when the nutrition has been so far improved that the body-weight approximates its previous level, and the individual is free from complaints and is again capable of resuming his work. If the time included in this period be observed in a large number of cases, its length will be found to be extremely variable. An important *rôle* is played in this connection, naturally, by the severity of the antecedent disease, but age, sex, constitution, and complications are also of such importance that cases originally of mild course may be attended, in consequence of the influence of these factors, with extremely protracted convalescence. We may recall, in this connection, the course of typhoid fever in the aged, and the afebrile and slow forms. The probable duration is, naturally, beyond the range of estimation, in the presence of complications and sequels, as well as in cases attended with recrudescences and relapses. Apart, however, from individual conditions, extraneous circumstances still difficult of appreciation at the present day may in the course of certain epidemics cause convalescence in general to be protracted. If it be desired to express the duration of convalescence definitely in figures, a period of from two to three weeks, after well-marked, uncomplicated cases, may be considered as short and favorable. Scarcely less common, and quite usual after severe attacks, is a duration of from four to five weeks. In not a few cases convalescence may be protracted even beyond this period, and occasionally is of extraordinary duration, particularly in relapsing, slow, or marantic cases.

In Leipsic (Berg) the average duration of convalescence was: Up to twenty days, in 55 per cent. of all cases; twenty to forty days, in 39 per cent.; forty to sixty days and over, in 5.8 per cent.

An analysis of 3096 cases during the severe epidemic at Hamburg in 1886–1887 disclosed a duration of up to twenty days in 319 cases—10.3 per cent.; between twenty-one and forty days in 2447 cases—79 per cent.; between forty-one and sixty days in 211 cases—6.8 per cent.; sixty-one days and over in 119 cases—3.8 per cent.

THE TOTAL DURATION OF THE DISEASE.

It will be most appropriate at this place to make some additional remarks concerning the total duration of the disease, which, naturally, includes both that of the febrile period and that of convalescence. In the first place, some statements may be added with regard to the

duration of the febrile stage. It is incomparably more difficult to give an average figure for this stage in typhoid than in the acute infectious diseases that pursue a far more cyclic course, as, for instance, fibrinous pneumonia, typhus fever, relapsing fever, and the acute exanthemata. While in the latter the fever is confined to sharply defined time-limits, the febrile stage of typhoid fever is, as has been seen, of infinitely variable course and duration, from cases that become afebrile in the course of a few days, to those lasting many weeks. In addition, the proportionate frequency of the mildest cases, the moderately severe, the severest, and those of longest duration, is extremely variable at different times and in different places. The frequency of the mild and abortive cases is especially variable. This is not even proportional—as must again be especially emphasized—to the severity or the mildness of the character of the individual epidemic in other respects. Thus, I have encountered periods in which, in spite of a relatively large number of mild and abbreviated cases, the mortality was quite considerable, because the severe well-marked cases pursued an especially unfavorable course under the controlling influence of the predominating varieties of course and complications. If the indeterminate mild and abbreviated cases be left out of the count, and an attempt is made to determine the duration of the well-marked moderately severe and severe cases only, the average duration of the febrile period will be found to be from two and a half to five weeks, but this may be extended to six weeks and even beyond, even in the absence of complications.

It may be instructive to form an idea of the variable duration of all the cases in a single epidemic, the mild and the severe together. Thus, an analysis of the cases at Hamburg in the year 1886–1887 yielded the following results: The duration of the febrile period was observed to be up to twenty-one days in 2040 cases—57.1 per cent.; from twenty-two to thirty-three days in 1118 cases—31.3 per cent.; thirty-three days and over in 417 cases—11.6 per cent. In 9 instances the duration was more than sixty days, and the longest was seventy-five days.

With regard to the conditions responsible for the duration of the fever, as little is known as with regard to the circumstances responsible for the various forms in general. Even the general factors are but little known. The influence of age, however, is the most conspicuous of these factors. We have already seen that the febrile stage in children is in general shorter than that in adults, and that during childhood itself this is true of the early periods in greater degree than of the later. The course of the disease is especially prolonged after the fortieth year and in old age.

An examination of our statistics at Hamburg with regard to the duration

of the fever at the various periods of life (estimated with reference to the number of cases admitted at the various age-periods) yielded the following results:

Age.	Duration of febrile period.		
	Up to 21 days.	From 22 to 33 days.	33 days and over.
2 to 5 years	92.0	4.0	2.0
6 to 10 "	71.0	18.6	7.7
11 to 14 "	60.8	25.7	11.8
15 to 20 "	53.4	32.5	11.5
21 to 25 "	57.3	31.2	9.8
26 to 30 "	51.8	31.0	12.1
31 to 35 "	52.4	31.9	11.9
36 to 40 "	44.1	33.3	16.5
41 to 45 "	41.9	29.6	23.4

This table concludes with the forty-fifth year, as the number of cases admitted at later age-periods is naturally so small that they do not appear available for statistical purposes.

The difficulty of obtaining a general numerical idea as to the total duration of the disease—that is, from the beginning of the fever to the termination of convalescence—need not, in view of the foregoing, again be pointed out. Nevertheless, a few suggestive figures may be useful. For well-marked cases of typhoid fever I should consider the average duration from the beginning to the period of discharge and restoration of the capability for work as from five to ten weeks. Only the atypical and the milder cases run their course within a shorter period. Not a few cases, however, persist for a considerable time beyond the average period stated. I have observed extreme cases, which, nevertheless, terminated in complete recovery, last up to twenty weeks, exceptionally for a half-year, and even longer. In the latter cases, of course, the prolongation was dependent upon the influence of local lesions and upon recrudescences and relapses.

Of more than 3000 carefully studied cases in the epidemic at Hamburg, 72.5 per cent. had a total duration of from thirty-one to eighty days. The average duration of all the analyzed cases was fifty-five days.

FATAL TERMINATION. PROGNOSIS.

With regard to the prognosis of the non-fatal cases, abundant references have been made at many parts of this work, so that the following section will confine itself almost exclusively to the fatal termination and the related prognostic considerations. With regard to the frequency of a fatal termination in general, definite statistics are not readily attainable. Although a mortality of from 5 to 6 per cent., on the one hand, and of 30 or even 40 per cent., on the other hand, is mentioned, it may

be stated at the outset that such extremes are attributable to quite definite conditions. Leaving these groups of cases out of consideration, the general mortality is stated by the earlier classical writers to be between 18 and 20 per cent. According to modern experience, however, it is distinctly lower, namely, from 9 to 12 per cent., and at most, 14 per cent. Inquiry as to the causes for this reduction in mortality will show that it is due in part to improvement in special methods of treatment and in the general hygienic conditions, and possibly also to a reduction in the virulence of the disease, in favor of which is the evidence which is available with regard to the behavior of other infectious diseases in this respect. A more important influence, however, than these factors in reducing the present mortality resides in the perfection of diagnosis, so that a large number of cases previously not considered as typhoid fever, which unexceptionally terminate in recovery, are now recognized as examples of this disease. This circumstance is taken account of also by a number of earlier writers, who, in estimating the mortality, excluded the mild cases at the outset.

Thus, Griessinger deducts from 510 cases of typhoid fever 40 of mild, febricular character, and estimates the mortality of the remaining 470 at 18.8 per cent. Murchison arrives at approximately the same figures. He found among 2505 cases in the London Fever Hospital for the years 1848–1862 a mortality of 18.5 per cent. That his and Griessinger's results were the expression of the general mortality-rate in typhoid fever at that time is indicated by the result of an investigation of 18,612 collected cases (from London, Glasgow, Paris, Strassburg, and the French provinces) of the fifth, sixth, and the beginning of the seventh decade of the nineteenth century, which likewise yielded a mortality-rate of 18.52 per cent. The conditions at Vienna were remarkably more unfavorable during the same period. In the Vienna General Hospital there were observed between 1846 and 1861 21,189 cases of typhoid fever with 4708 deaths—22.2 per cent.

These figures may be compared with some of more recent date; there were treated in the Jakobsspital of Leipsic, from 1880 to 1893, 1626 cases of typhoid fever, of which 243—12.7 per cent.—terminated fatally. Earlier statistics by Uhle from the same hospital showed that 600 patients exhibited the average mortality at that time of 18.5 per cent. In the epidemic of 1886–1887 at Hamburg,[1] the mortality-rate was comparatively favorable. Of 10,823 patients throughout the entire city, 840 died—8.5 per cent. They were distributed throughout the two years as follows: 1886, 3948 cases, with 364 deaths—9.2 per cent.; 1887, 6875 cases, with 476 deaths—6.9 per cent.

Of the 3686 patients of this group treated in the hospital, the mortality was somewhat higher—362 (9.8 per cent.)—undoubtedly on account of the smaller number of mild cases. As compared with these, the statistics of Thüngel are interesting, who observed among 504 patients in the same hospital, between the years 1858 and 1861, 96 deaths—19 per cent. Finally, I would state further that a study of 3600 cases that I treated personally during the

[1] *Bericht des Hamburger Medicinalbureaus.*

period from 1877 to 1897 in various places (Berlin, Hamburg, Leipsic) exhibited a total mortality of 9.3 per cent.

During the ten years, 1889 to 1899, of 829 cases treated in the Johns Hopkins Hospital, 63 died—a mortality-rate of 7.5 per cent.

It has been pointed out that the figures given can be applicable only in a general way. They vary under diverse conditions, partly individual, partly general, not directly relating to the patient. It is well known that the mortality varies widely during different **epidemics** and **endemics,** just as the character and the peculiarities of the disease may exhibit great variations in detail at different times.

The extent to which **climate** and **season** are operative in this connection appears to be not yet sufficiently determined, although Murchison believed that from a study of the statistics of the London Fever Hospital he was able to make out a greater mortality from typhoid fever in the spring. **Geographic** and **racial differences** are insignificant in their influence upon the mortality. As typhoid fever is distributed over almost all parts of the world and countries, so its virulence appears to be everywhere approximately the same. Where distinct differences with regard to the mortality, particularly in an unfavorable direction, are apparent, these depend especially upon combinations with other severe morbid states of local origin. An illustration of this is afforded by malarial regions. Incomparably better known and more important than these general factors is the influence of personal conditions upon the mortality. It appears from previous statements that **age** is of greatest importance in this connection. The danger from the disease increases rapidly with advancing years. As early as after the fortieth, and particularly after the fiftieth, year the malignancy of the course is great, while it is undeniably least in children between the second and the tenth year. In the later years of childhood, and in the subsequent age-periods in adults, up to the middle of the fourth decade, the differences in the mortality and the rapidity of its increase with advancing years are less significant, but, on study of a large number of cases, they are, nevertheless, distinctly appreciable. Thus, for the periods from twenty-five to thirty years and from thirty to forty, the prognosis is distinctly more unfavorable than in the period from twelve to twenty-five years.

The figures of most writers agree with those given in the table on p. 385. Thus, Liebermeister, among 1743 cases, during 1865 to 1870, found a mortality of 30 per cent. for the age-periods above forty years; while in those below it was only 11.8 per cent. Uhle,[1] at the clinic of Wunderlich, observed death occur in more than half of the cases in patients above the age of forty years. Griessinger utilizes these facts for an interesting explana-

[1] *Arch. f. physiol. Heilk.*, 1859.

tion of certain striking differences in the mortality in different hospitals. While he lost 18.8 per cent. of his patients in Zurich, among whom those in the age-period above forty years numbered 12.9 per cent., Fiedler, in Dresden, with only 3.1 per cent. of the latter, had a mortality of only 13.1 per cent. The tracing (Fig. 47) is especially instructive, in which Fiedler[1]

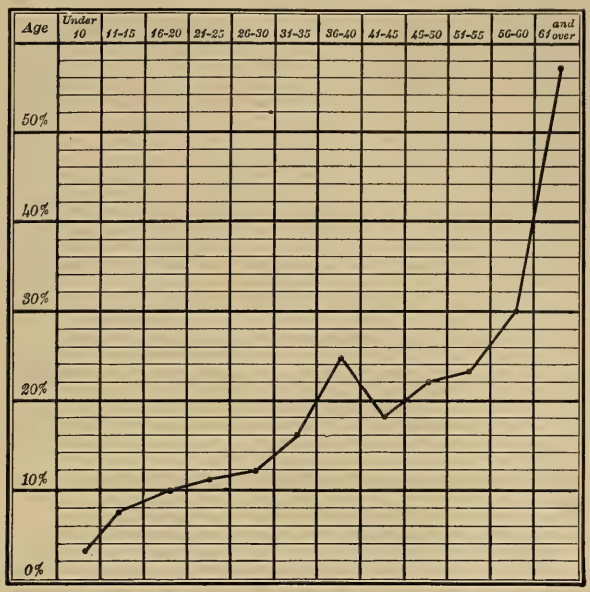

FIG. 47.

presents the percentage-relation of the deaths from typhoid fever to the total number of cases of typhoid fever, and their relation to age-periods, from the material of the Dresden City Hospital during thirty-four years (1850–1883).

The relation of age to the mortality is exhibited by the following table prepared from the Hamburg statistics for the years 1886–1887:

AGE.	Number of cases.	Deaths.	Percentage.
1 to 5 years	50	2	4.0
6 to 10 "	156	10	6.4
11 to 14 "	245	20	8.2
15 to 20 "	1100	96	8.7
21 to 25 "	992	77	7.7
26 to 30 "	602	74	12.3
31 to 35 "	269	31	11.5
36 to 40 "	127	19	14.9
41 to 45 "	81	15	18.5
46 to 50 "	26	7	26.9
51 to 55 "	13	3	23.0
56 to 60 "	8	3	37.3

The differences in prognosis dependent upon **sex** are, in contradistinction to those due to age, very slight. The little difference that is

[1] *Separatabdruck aus den Berichten der Gesellschaft f. Natur- und Heilkunde zu Dresden*, 1884. This valuable publication, which contains a large amount of carefully studied statistical data, is much too little known.

apparent in this connection is due in men rather to external and social conditions (occupation, mode of life, alcoholism); while in women the sexual functions are directly of influence, particularly pregnancy, parturition, and the puerperium. If an especially large number of women are accidentally received into a hospital in consequence of external conditions, these factors may be of considerable influence upon the mortality if the patients are largely at the period of adolescence. Under ordinary circumstances the differences in mortality between the two sexes are so slight that they can be almost entirely ignored. It is highly characteristic in this connection that, in the course of an epidemic of typhoid fever of considerable duration, the mortality among men may at times exceed that among women, and *vice versa*. Thus, at Hamburg in the year 1886 the mortality among men (8.5 per cent.) was greater than among women (3.5 per cent.); while in the year 1887 that among women (9.4 per cent.) slightly exceeded that among men (8.8 per cent.). It is not worth while to present here many statements of other writers. With a few exceptions they reach like results. Almost exactly the same mortality is shown, for instance, in the following table by Murchison, including 1820 cases of typhoid fever treated in the London Fever Hospital between the years 1848 and 1857:

	Admissions.	Deaths.	Percentage.
Males	905	160	17.68
Females	915	173	18.89
Total	1820	333	18.29

This table may be followed by one of Beetz, from the Munich medical clinic, including the cases of typhoid fever between the years 1874 and 1877, and exhibiting a marked preponderance of the mortality in men. Probably we have here an illustration of the influence of certain injurious habits of life in men (alcoholic excess, particularly of beer).

Munich.	Mortality—Percentage.		
	Males.	Females.	Total.
1874	8.4	4.7	6.7
1875	12.7	8.5	10.5
1877	13.0	7.5	9.9

Also, the **social position** and the **occupation** are not of so much significance with regard to the prognosis in typhoid fever as with regard to that in other infectious diseases, as, for instance, typhus fever. I believe that typhoid fever has as little relation to wealth and poverty as to special occupations. It is not even apparent that an indigent mode of life is, in itself, injurious. On the contrary, the mode of life of the

rich is almost more frequently to be taken into consideration as an injurious predisposing factor. Whether the occupations that favor infection with typhoid fever in somewhat greater degree (see Etiology) are to be considered more unfavorable also from the prognostic standpoint is exceedingly doubtful.

In certain superficial respects the well-to-do classes, it is true, appear to be somewhat more favorably situated. They are, in general, able to secure more careful nursing and attendance, and, above all, come under treatment early. The resulting advantages to the physician in his daily routine are in my experience also appreciable in the hospital, since here the prognosis of the cases which, by reason of unfavorable circumstances, are received exceedingly late, is generally far more grave than that of the cases admitted at an early stage. A not inconsiderable influence is exerted upon the prognosis by the **constitution** and the **condition of general health** present before the attack of typhoid fever. With regard to the constitution, the danger is from the outset least in young, muscular, spare persons, the so-called tough individuals; while, as has been mentioned, the prognosis must be made with great caution in the case of obese persons, even young ones, men as well as women. That, in addition, anemic and chlorotic persons are exposed to great danger; that in alcoholics, persons addicted to morphin, and those reduced by excesses in other directions, the outlook is unfavorable, need scarcely be emphasized. Among the excesses physical and mental overexertion are also to be included, as well as profound emotional disturbances, great grief, and anxiety. Among chronic diseases, gout, diabetes, heart disease, nephritis, chronic disease of the respiratory organs, particularly advanced tuberculosis, are to be considered as especially unfavorable.

TIME OF DEATH.

The early or late occurrence of death depends in the individual case especially upon the age and the constitution of the patient, upon the special form of the disease, upon the distribution of the typhoid process in the various organs, as well as upon the number and the character of the complications. Reference will be made later to a number of especially important points in this connection. It is, however, not without value to obtain general figures with regard to the time of the fatal termination. The largest number of deaths in average epidemics of ordinary character occurs between the second half of the second and the end of the fourth week. Death is much less common at an earlier period. It occurs even with distinctly greater frequency after the thirtieth than before the tenth day. It is noteworthy and in accordance with the

relative brevity of the course of the disease in children that the largest number of deaths in them occurs between the tenth and the twenty-first day. The special character of some epidemics is manifested by, in addition to other features, a remarkably early period for the occurrence of death. These epidemics are characterized by the frequent occurrence of profound intoxication or especially early intestinal hemorrhage. It is of practical importance to note that death may occur, and by no means rarely, long after the termination of the febrile stage. Marasmus, sluggish processes, and sequels play an important *rôle* in this connection. I have observed death occur as late as the one hundred and twentieth day.

Our Leipsic tables show a fatal termination in the eleventh week in 4 cases, and the Hamburg statistics show 26 cases—7.7 per cent.—in which death occurred after the fiftieth day. Both tables are herewith appended.

Death occurred at Leipsic in the first week of the disease in 6 cases—2.5 per cent.; second week, 37 cases—15.1 per cent.; third week, 63 cases—25.9 per cent.; fourth week, 51 cases—20.9 per cent.; fifth week, 22 cases—9 per cent.; sixth week, 20 cases—8.27 per cent.; seventh week, 9 cases—3.7 per cent.; eighth week, 7 cases—2.9 per cent.; ninth week, 5 cases—2.1 per cent.; tenth week, 2 cases—0.82 per cent.; eleventh week, 4 cases—1.6 per cent.

Death thus occurred between the second and the fourth week in 151 cases—62.1 per cent.

At Hamburg, among 362 cases of typhoid fever, death occurred between the sixth and the tenth day in 11 cases—3 per cent.; eleventh and the fifteenth day in 51 cases—14.1 per cent.; sixteenth and the twentieth day in 68 cases—16 per cent.; twenty-first and the twenty-fifth day in 46 cases—12.4 per cent.; twenty-sixth and the thirtieth day in 45 cases—12.4 per cent.; thirty-first and the fortieth day in 35 cases—11.4 per cent.; forty-first and the fiftieth day in 21 cases—5.8 per cent.; after the fiftieth day in 28 cases—7.7 per cent. From this it follows that in more than half of the cases—*i. e.*, 210 (58 per cent.)—death occurred between the eleventh and the thirtieth day.

According to most observers and my own experience, the prognosis of relapses is in general more favorable than that of primary attacks and of recrudescences. Of the cases of typhoid fever with relapse at Hamburg, I observed death in 4.9 per cent.

CAUSE OF DEATH.

The causes of death in detail have previously been somewhat discussed (see the chapters on Symptomatology and on Course and Termination). With regard to many points, therefore, reference must be made to them. Death results, on the whole, in one of three ways. In the first place, in consequence of the severity or the special character of the intoxication; next, in connection with unusual development and severe course of the peculiar localizations of the disease, especially in the intestine,

the respiratory organs, the nervous system, and the kidneys; and finally, in consequence of the seat and the severity of the actual complications.

The severity of the intoxication is probably the most important of the causes of death. From 30 to 50 per cent. of the deaths are, in my experience, to be attributed to it. In a larger sense the cases that pursue a fatal termination with the clinical picture of the hemorrhagic diathesis and of hyperpyrexia may also be included in this category. The profound toxic effects are exhibited especially and most conspicuously, and often simultaneously, by the central nervous system, the heart, and the vessels. Cases that are early attended with profound delirium or derangement of consciousness, in which coma, floccitation, subsultus tendinum, choreiform and spasmodic states early occur, are illustrative of the especial severity of the toxic action upon the central nervous system. Among such manifestations are often included also rigidity of the neck and the back and hyperesthesia. It may be noted, however, that these features may be early and marked also in cases that subsequently pursue a favorable course. On the other hand, they may be the symptoms of actual complicating meningitis.

Although, without doubt, constitution, sex, age, and individual circumstances occasion a variable susceptibility on the part of the central nervous system, it may be stated in general that the prognosis is the more unfavorable the more profound are the symptoms referable to the central nervous system, and the earlier they appear.

Liebermeister made an interesting analysis of his patients in the epidemic at Basle between 1865 and 1868 with reference to this point, and found that of those who exhibited no striking cerebral symptoms during the course of the disease, 3.5 per cent. died, while the mortality in those patients in whom only slight conditions of excitement, of short duration, or occurring only during the night, had existed, was 19.8 per cent. Of the cases with marked, furious, or with muttering delirium, 54 per cent. terminated fatally, while those attended with sopor and coma exhibited the enormous mortality of 70 per cent.

With regard to the effects of the toxins upon the circulatory organs, the disturbances that occur in these are also undoubtedly to be considered the more serious the earlier they occur and the more severe they are. They are usually included under the general designation cardiac weakness. It is certain, however, that in cases of typhoid fever and of other infectious diseases disorders of the vasomotors, as has been pointed out, play just as important a *rôle* as disorders in the activity of the myocardium itself. We are at present, it is true, not yet in a position to distinguish definitely one from the other, or to estimate the share each takes in their apparently frequent combinations.

The most important guide to the state of the circulatory organs is furnished, now as always, by a study of the pulse. Its frequency alone may be of considerable importance—less, it is true, in the case of women, children, and other nervous individuals, than in that of robust men or elderly persons of either sex. While in the former great frequency of pulse appearing early is common, and is of itself of little significance, it must, in strong young men or elderly persons, even by itself admonish the clinician to exercise great caution in prognosis. It may even be a matter of concern if in an apparently strong man the almost typical relative slowness of the pulse so generally present in the first half of the febrile stage remains absent. Diminution in the tension and alteration in the regularity of the pulse are naturally to be considered still more serious than increased frequency, and in this connection, as has been pointed out, more importance is to be attached to irregularity in force than to mere irregularity in rhythm. As a matter of course, these disturbances are all the more significant the earlier they appear, the longer they last, and the more positively it can be stated that they are not dependent upon probably transitory complications.

The extraordinary prognostic importance of the state of the circulation was especially appreciated by earlier physicians. With the introduction of thermometry, and the primary enthusiasm aroused by this new method, it was undeservedly pushed somewhat into the background. At the present day it has been restored to its proper position, and there is no doubt that for individual prognosis, on the whole, the state of the pulse affords better and safer guidance than that of the body-temperature.

The prognostic interpretation of the course of the temperature is distinctly more difficult, and is dependent upon the most varied possibilities and the most complex conditions. Although formerly decisive value was attached to the absolute height of the temperature, without adequate consideration of the general state, this is at the present day conceded to be but limited, and applicable only to rare conditions. Temperatures of 40° C. and above, especially in adults, if frequently repeated, or if a persistently high temperature-level is reached, may undoubtedly be considered serious. The prognosis is under some circumstances rendered unfavorable also by abnormally low temperatures. The collapse and pseudocollapse previously mentioned should be borne in mind, as well as the persistently low temperatures, such as occur in senile or in previously debilitated youthful individuals, and which become most marked in that dangerous variety of typhoid fever that pursues an afebrile, or even a subfebrile, course.

Further, prognostic conclusions based upon the temperature should not be formed after too short a period of observation or without consideration of the remaining circumstances. Indeed, the state of the body-temperature in cases of typhoid fever, as in some other infectious diseases, is as much dependent upon individual circumstances as is that of the nervous system and the circulatory organs. Every physician, and especially the family practitioner, has incontrovertible evidence of the fact that different individuals exhibit not only different febrile reactions to the same influences, but also varying degrees of resistance to these influences.

Presupposing all this, it is, nevertheless, useful, especially in the first part of the disease, to seek prognostic guidance from the state of the temperature. The height and the character of the curve are, in this connection, of equal importance. As Wunderlich and his pupils have pointed out, rapid elevation of the body-temperature in the initial stage, without or with but a suggestion of a step-like ascent, and a high temperature speedily reached and maintained for a considerable time without material morning remissions, are indicative of a severe course. Especially the hyperpyretic and fulminant cases are prone to begin with a rapid, uninterrupted elevation of temperature (Fig. 25, p. 289). On the other hand, it should not be forgotten that especially the abortive cases pursuing an unexpectedly rapid and favorable course at times set in in an almost identical manner.

While persistent high temperature with slight remissions is in general to be considered unfavorable, evening exacerbations of even considerable height permit of a favorable interpretation if they are associated with marked morning remissions, or even intermissions. It may be stated in general that the earlier, the more marked, and the longer the remissions, the more favorable may the course be expected to be. Naturally, remissions following a continued fever of considerable duration may be welcomed as an indication of the early advent of the stage of steep curves. All these circumstances, however, it may here be repeated, become more valuable from the prognostic standpoint, the more critically the condition of the body in general, and especially that of the pulse, is kept in view. If the pulse maintains a normal course, danger need not be feared, even in the presence of an apparently unfavorable course of the temperature. In the presence, however, of a suspicious state of the pulse, no course of the temperature, not even apparently the most favorable, is to be trusted. An important aid in the interpretation of the pulse and the temperature may be provided by the state of the lungs. Suspicious changes in the former must be

considered the more serious when extensive bronchitis appears early in previously healthy individuals, inasmuch as its severity, apart from its dependence upon the intensity of the toxic effect, is related especially to the impairment of cardiac activity. Still more distinctive in this connection, and sometimes evident even before the pulse has acquired a definitely serious character, is the early involvement by a rapidly progressive bronchitis of preferably the posterior and lower parts of the lungs. The prognosis is naturally most unfavorable with the onset of actual hypostatic congestion, simple or inflammatory.

Of the local typhoid disorders and the complications already repeatedly discussed, only the most important will be considered in this place, and then especially in regard to their prognostic importance. We shall consider first the state of the intestinal canal. The occurrence of meteorism is, from the prognostic point of view, of inestimable significance. Although its appearance is, in general, little to be desired, its presence in marked degree and its rapid development at the height of the disease in patients the regulation of whose diet has not been neglected must be considered as actually ominous. The meteorism is then almost the direct expression of the degree of toxic action upon the intestinal nervous system and the muscular layer. It should, in this connection, be expressly emphasized that the intensity of the meteorism is by no means in direct relation to the severity of the diarrhea, or even to the severity and the extent of the specific typhoid lesions of the intestine. Thus, I have observed the usual meteorism of the large intestine well marked in the absence of the slightest infiltration of the follicles.

That the frequency of the stools is no index of the degree and the extent of the medullary swelling of Peyer's patches and the solitary follicles has been previously emphasized. Nevertheless, cases with severe diarrhea of early onset and long duration are undoubtedly to be considered, in general, the more dangerous.

Of great importance in the prognosis, and among the most frequent causes of death, are two other manifestations on the part of the intestines, viz., peritonitis and intestinal hemorrhage. **Peritonitis** is, of the two, the less common but by far the more dangerous condition. In the nature of things, it is in the overwhelming majority of cases not circumscribed but diffuse, and therefore usually fatal.

Our Leipsic statistics show that among the fatal cases of typhoid fever death was due to peritonitis in 16.5 per cent. At Hamburg, where of 61 patients with peritonitis 51—83.6 per cent.—died, the proportion of these to the remaining fatal cases was 14 per cent., and if all cases of typhoid fever be taken into consideration, it was found that 1.4 per cent. of them terminated fatally from this accident. Although, as has been mentioned, the severity

of the typhoid intestinal lesions varies in accordance with temporal and local influences, the proportion of fatal cases from peritonitis to the remaining fatal cases of typhoid fever will, nevertheless, not usually fall below 8 per cent.

Among the 63 fatal cases of typhoid fever at the Johns Hopkins Hospital, 20 (31.74 per cent.) were associated with perforation and peritonitis. Therefore, of the entire 829 cases, 2.41 per cent. terminated fatally from this accident.

Although a much larger number of cases of typhoid fever are seized with **intestinal hemorrhage** than with peritonitis—this condition is likely to occur in from 3 to 5 and even up to 7 per cent. of all cases—this circumstance is, however, compensated for by the fact that even in the severest epidemics not more than from 20 to 30 per cent. of such cases terminate fatally; 40 per cent. would be the extreme limit. Moreover, it should be emphasized that at times the mortality from intestinal hemorrhage is remarkably low, and, in general, is far below 20 per cent. The variability of the conditions in this connection is shown by our Hamburg statistics for two consecutive years of virtually the same epidemic. While in the year 1886 20.9 per cent. of the cases with intestinal hemorrhage died, the proportion in 1887 was only 11.6 per cent. In spite of the much slighter danger from intestinal hemorrhage in the individual case, its much greater frequency puts it, nevertheless, in the front rank among the causes of death. I should estimate its mortality at about two-thirds of that of peritonitis.

Among the 829 cases of typhoid fever at the Johns Hopkins Hospital, hemorrhage from the bowels occurred in 50 (6.03 per cent.). Of these 50 cases, 5 (10 per cent.) died. Or, of all the cases of typhoid fever, 0.6 per cent. terminated fatally from this complication.

Scarcely less dangerous are the **diseases of the lungs,** especially the various forms of **pneumonia,** with their sequels—abscess, gangrene, etc. In severe epidemics from 10 to 15 per cent. of all deaths can be attributed to them. By reason of the imperfect development of the etiologic, and especially the bacteriologic, basis of the various forms of pneumonia, it has hitherto not been possible to reach definite views with regard to the prognostic significance of the individual varieties. In regard to the time of onset, the forms of pneumonia that develop late appear to be especially unfavorable, because, under such circumstances, hypostasis, antecedent extensive bronchitis, cardiac enfeeblement, and vasomotor disturbances exert an unfavorable influence; but also those cases that develop at an earlier period, particularly the initial cases progressing under the picture of the so-called "pneumotyphoid," may become quite dangerous. That age plays an important *rôle* in the prognosis of typhoid pneumonia scarcely requires special mention. While

in typhoid patients over forty or forty-five years of age the occurrence of pneumonia is probably always a fatal complication, the mortality from pneumonia in childhood is low. The favorable condition of the heart obviously increases the powers of resistance under these circumstances.

Pleurisy, which is much less common, is, apart from the presence of purulent and putrid effusions, by no means so unfavorable as pneumonia from the prognostic standpoint. Small and even considerable effusions subside without untoward consequences, even without the necessity for puncture. That patients suffering from chronic bronchitis, emphysema, or pulmonary tuberculosis before the onset of the typhoid fever are exposed to considerable danger is a matter of course. The relation of tuberculosis to the course of the attack of typhoid fever has been fully considered previously.

The condition of the **kidney** is also of great importance from the prognostic standpoint. Even the cases with simple febrile albuminuria are to be considered cautiously. This condition is indicative at least of feeble powers of resistance on the part of the body to the action of the toxins, and it is, in general, to be considered the graver the earlier it appears. The discovery of the excretion of albumin may be of especial significance in prognosis if it occurs at a time when the temperature is not particularly high, and when, also, the pulse exhibits no serious manifestations. Nephritis has a noteworthy influence upon the mortality, although it is not so important in this connection as the diseases of the intestines and the lungs. Although with regard to the frequency of its occurrence it occupies a position far behind the latter, it causes, on the other hand, a fatal issue in half of those attacked.

The unfavorable prognosis of so-called **nephrotyphoid** is generally recognized, but it is by some French investigators, however, exaggerated far beyond the actual degree. Of 605 fatal cases in Hamburg and Leipsic, 27—4.5 per cent.—were attributable to complicating nephritis. The uniformity of its occurrence in both sets of statistics is noteworthy: while of 243 fatal cases at Leipsic, death was due in 11—4.6 per cent.—to nephritis, among the 362 at Hamburg, nephritis was the immediate cause of death in 16—4.4 per cent. A ray of light in the gloomy prognosis of nephritis may be found in the fact that if it does not cause death, complete recovery generally follows. **Long-continued albuminuria** or transition into chronic nephritis is less common in connection with typhoid fever than with some other infectious diseases.

Although it has been necessary to emphasize the **influence of the**

toxin upon the heart and the vasomotors in general, the individual diseases of the myocardium, the pericardium, and the endocardium as causes of death are inconsiderable. The prognosis of typhoid myocarditis has already been pointed out as not so unfavorable as it might appear from the influence of the same condition in other infectious diseases, as, for instance, in diphtheria. Some significance is, nevertheless, to be attached to typhoid myocarditis in the explanation of cases of sudden death.

It is not worth while to discuss individually the remaining organs and systems with regard to their influence upon the mortality and the prognosis. They are rare or only occasional occurrences, and do not require special comment. The best idea of the conditions present in this connection will be afforded by the following tabular arrangement of the principal causes of death in 580 cases observed at Hamburg and Leipsic:

Causes of Death.	Hamburg.		Leipsic.	
	Number of cases.	Percentage.	Number of cases.	Percentage.
Severity of the infection	186	51.4	89	42.4
Intestinal perforation, peritonitis	51	14.1	40	19.0
Intestinal hemorrhage	24	6.6	19	9.0
Pneumonia	56	15.5	24	11.4
Nephritis	16	4.3	11	5.2
Hemorrhagic diathesis	. .	. .	5	2.3
Pyemia, septicemia	2	0.5	8	3.8
Erysipelas	4	1.1		
Decubitus	. .	. .	2	0.9
Multiple abscesses	. .	. .	1	0.5
Noma	1	0.3		
Ulcerative laryngitis, necrosis of cartilage, and sequels	4	1.1	1	0.4
Pulmonary edema	3	0.8		
Serofibrinous exudative pleurisy	3	0.8		
Empyema of the pleura	3	0.8		
Pyopneumothorax	1	0.3		
Pulmonary tuberculosis and miliary tuberculosis	3	0.8	3	1.4
Pulmonary embolism	1	0.3	2	0.9
Fatty heart (myocarditis?)	2	0.5	1	0.4
Endocarditis	1	0.3	1	0.4
Delirium tremens	3	0.8		
Meningeal hemorrhage	1	0.3		
Purulent meningitis with caries of the temporal bone	1	0.3		
Diphtheria	1	0.3	1	0.4
Abortion and premature labor	. .	. .	4	1.9
Pyosalpinx, perforative peritonitis	. .	. .	1	0.4
Total	367		213	

With regard to the **manner in which death occurs**, it is scarcely worth speaking in detail. From what has been previously said, it will appear that it is most frequently preceded by symptoms of the most profound intoxication, with paralysis of the heart and the nervous system, and these are not much different in cases of typhoid

fever than in other acute infectious diseases. At later periods of the disease the fatal termination is generally attended with symptoms of exhaustion and of marasmus, or those of complications. Each of the fatal local disorders naturally impresses with its particular stamp the manner in which death occurs.

SUDDEN DEATH.

In concluding this chapter, only the cases of sudden death in the course of typhoid fever will be considered somewhat more in detail. These include the cases that remain indelibly fixed in the memory of the physician, in which, quite unexpectedly, during convalescence of apparently satisfactory progress, there occur suddenly, like a lightning-stroke or after a short interval, the alarming symptoms to which the patient succumbs.

As with so many striking clinical features which are especially impressed upon the memory of the physician, and are therefore more frequently described and mentioned in statistics, so, with regard to the cases of sudden death, an impression has unconsciously been gained that they are far more frequent than they really are. On the contrary, I consider their occurrence as actually infrequent, and believe, in addition, that it can often be prevented if in the later stages of the disease, particularly the period of convalescence, the patients are carefully watched, and are kept at rest physically and mentally, and are not permitted to get out of bed too soon. This statement implies that the cases of sudden death are likely to occur especially in the period of defervescence, and even still more frequently in that of convalescence. The unfortunate occurrence is incomparably less common at the height of the disease, and it has been observed only exceptionally in the first week.

It would be a mistake to believe that cases of sudden death occur with preference in persons who already are especially debilitated by reason of constitution, age, previous disease, severe, protracted course of the attack, or complication. On the contrary, robust youthful individuals are attacked quite as often, almost still more frequently, even after attacks of the disease of moderately severe or even mild course. This indicates that in this connection antecedent predisposition or the severity of the disease itself is of less influence than certain more or less unanticipated alterations that appear in the course or after the termination of the disease.

Most frequently the cases of sudden death occur under the following conditions: The patient, apparently previously well, but still languid

and weak, or with complaint of transient palpitation of the heart, exhibiting a rather small, unstable, and frequent pulse, suddenly, in or out of bed, generally while engaged in some physical effort—sitting up to take food, or for examination or defecation, or indulging in short walks contrary to the instructions of the physician—becomes pale and collapses, falls back, and dies within a few minutes. If the physician soon reaches the patient, he will generally still be able to notice somewhat stertorous breathing, while the pulse is already imperceptible and the heart-sounds are scarcely audible. The impression is gained that the patient has succumbed to actual heart-failure, to which cerebral anemia, as one of the manifestations of profound blood-change, has contributed its share. To this the layman gives expression by attributing death to cardiac failure.

The occurrence of sudden death in cases of typhoid fever has for a long time been emphasized in the literature (Chomel, Louis,[1] Murchison[2]). The condition has been more thoroughly studied recently by Hayem,[3] Bussard,[4] and Huchard[5]; in Germany, soon afterward, by Leyden[6] and his pupil, Hiller,[7] in an especially noteworthy communication. The question was further elucidated by the investigations of Romberg[8] upon typhoid myocarditis in my clinic. These more recent publications have shown that inflammatory alterations of the myocardium play the most important *rôle* in this connection, while the earlier investigators assumed only fatty degeneration with atony, dilatation, and friability of the myocardium.

Among the French writers certain differences have arisen recently in that some believe that sudden death occurs especially or exclusively from cardiac failure, while Huchard, Bussard, and in part also Dieulafoy,[9] consider cerebral anemia as the more important cause. I believe that we have to do here with an unpromising controversy, and that both factors are inseparably necessary for a full explanation of the cases in question. I have personally, when I have been able to watch my patients carefully, particularly in the hospital, observed only a few cases

[1] *Loc. cit.*

[2] *Jour. of Med. Sci.*, March, 1867, cited by Hiller. It is interesting and indicative of the rarity of the event that Murchison, with his acute powers of observation, does not even mention the cases of sudden death in his well-known book.

[3] *Loc. cit.* [4] Cited by Virchow-Hirsch, *Jahresbericht*, 1876, Bd. ii.

[5] *Union méd.*, 1877.

[6] In his publication upon the cardiac affections of diphtheria, *Zeit. f. klin. Med.*, 1883, Bd. iv.

[7] *Charité-Annalen*, 1883. This paper contains also additional bibliographic references and statistical data. [8] *Loc. cit.*

[9] *Gaz. hebd.*, 1877, Nos. 20 and 22.

of sudden death, undoubtedly because I permit my convalescents to get up comparatively late, and exercise particular care with anemic patients who present suspicious activity of the heart.

Of my few cases, two may be described briefly here: A healthy, vigorous merchant, twenty-two years old, after having served in the army the first nine months of his term of a year, was attacked during the last period of his service. He continued to drag himself about for the first week, but during the following week was nursed in the lazaretto, and subsequently at home. In the fourth week he was free from fever, had a good appetite, and was in a contented frame of mind, so that the patient and his friends considered it pedantic that I forbade his getting up after twelve afebrile days had passed. My prohibition was based upon the fact that the patient, in spite of subnormal temperature, still continued to exhibit a soft, now and again intermittent, pulse of more than 80, and at the same time, with clear but faint heart-sounds, exhibited the signs of slight dilatation of the myocardium. On the fourteenth day of convalescence the nurse, retained by my direction, on returning to the room after an absence of scarcely ten minutes, found the patient lying in front of the bed, unconscious and pulseless; and before she was able to summon assistance the patient was dead. Apparently, the patient had, contrary to instructions, got out of bed for the purpose of urinating. Post-mortem examination was not permitted.

The second case is especially noteworthy, because I was present when death occurred. The patient was a woman, thirty-one years old, who, after a moderately severe attack of typhoid fever of four weeks' duration, without complications, had been free from fever for five days. The pulse ranged from 90 to 100 in the morning, up to 112 in the evening, was moderately full, tense, and regular, but still quite variable in frequency, so that during speaking or on slight movements after eating, at times also without extraneous cause, the frequency was increased from 10 to 30 beats a minute. The area of cardiac dulness was apparently normal; the sounds were dull and faint; no murmur was audible. I had examined the patient at the morning visit and had found nothing wrong, and at her request had even enlarged the diet. After I had got a distance of three beds away I was recalled. The patient had sat up and had reached for a letter which had been received the evening before, and which we subsequently found to be of an exciting character, had suddenly become pale, and had fallen back upon the pillow unconscious. Scarcely a minute elapsed before I saw the patient again, but her features were already relaxed, the pupils were dilated and fixed, the pulse was no longer perceptible, and, after a few stertorous breaths, death had taken place without complaint or sound. Post-mortem examination disclosed numerous recent cicatrices in the lower portion of the ileum and the adjacent portion of the large intestine. The brain and the lungs exhibited no peculiarities. The heart was moderately dilated and relaxed. The myocardium was yellowish gray in color, friable, and brittle. Microscopic examination disclosed fatty degeneration and segmentation of the muscular fibres, with partial obliteration of the transverse striation. The case was observed at a time when thorough microscopic investigation of typhoid myocarditis was not made, but I have no doubt that the condition was of this character.

In addition to myocarditic paralysis of the heart and cerebral anemia as a cause of sudden death, pulmonary embolism undoubtedly also plays

an important *rôle.* The emboli are derived in part from the cerebral sinuses (Griessinger) and the peripheral veins, particularly those of the extremities, and partly from the right side of the heart. Marvaud[1] undoubtedly goes too far in attributing the majority of all cases of sudden death to cardiac thrombosis. The reports of his own autopsies show that in addition to thrombosis there was present profound degeneration of the myocardium.

Much less common than pulmonary embolism as a cause of sudden death is embolism of the cerebral arteries. I have previously mentioned a case of my own (basilar artery). Hemorrhage into the substance of the brain and the meninges is not more common. It occurs in cases of the hemorrhagic variety, as well as now and then in alcoholic patients.

The view maintained by a few French investigators, that death may result in consequence of sudden peculiar intensification of the typhoid intoxication, is for the present without firm support. Nothing, also, of a definite character has as yet been demonstrated for other toxic conditions, as, for instance, uremia causing apoplexy. The view of Dieulafoy,[2] that death may be caused by reflex spasm in the structures innervated from the medulla oblongata, particularly by the pneumogastric nerve, excited by the diseased intestine, is based essentially upon the fact that in the clinical observations upon which this view is based local alterations of an explanatory character were not found. The theory has, so far as I know, remained without supporters, and has been restricted and altered by its promulgator in a later communication.[3]

[1] *Arch. gén. de med.*, Aug. and Sept., 1880.

[2] *Thèse*, Paris, 1869; Virchow's *Jahresbericht*, 1869, Bd. ii. [3] *Loc. cit.*

III. DIAGNOSIS.

THE ideal method of diagnosis of typhoid fever would be the demonstration with readiness, rapidity, and certainty of its cause, the bacillus of Eberth, during every period of the disease. Unfortunately, this most natural method is not yet available in a degree at all approaching perfection. Questions have at times even been raised as to the possibility of distinguishing the typhoid-bacillus from other organisms (colon-bacillus group) resembling it morphologically and biologically. But to-day we know that it has definite and peculiar characteristics which distinguish it from all other organisms. Foremost among these special features is its specific reaction to the blood and the body-fluids of typhoid patients and immune animals. These present methods of distinguishing this organism, however, while relatively simple for the experienced bacteriologist, present considerable difficulties for the practitioner. But aside from the identification, it is not an entirely easy task to isolate the organism directly from the patient or his secretions. The methods are constantly being simplified, however, and, where means are available, cultures from the urine, feces, rose-spots, and especially the blood, are frequently of the greatest aid in diagnosis. Later work with newer methods has shown the presence of typhoid-bacilli in the circulating blood in 70 to 80 per cent. of the cases, frequently quite early in the disease; and it is to be hoped that further improvements in methods may make the demonstration of its constant presence possible, and make the method readily available for clinical purposes.

The method of serum-diagnosis made possible by the labors of Pfeiffer, Gruber, and Widal has been shown by a large number of reports and by its almost universal use at present to be of great aid in diagnosis, even though, on account of the very frequently delayed appearance of the reaction, it has not proved to be of quite so much diagnostic value as was at first hoped.

But however valuable these methods of bacteriologic diagnosis may be in certain cases, it must be emphasized that at present observation at the bedside still retains the first place in diagnosis. It would be a serious blow to the further development of our clinical knowledge if the former methods should displace careful general and visceral examination. But just as little as exploratory puncture or even exploratory

celiotomy is likely to restrict thorough clinical investigation, so little also is it probable that the bacteriologic method will ever be the exclusive one in the diagnosis of infectious diseases.

There are, however, certain cases in which the most skilful and painstaking clinical study alone cannot make a certain diagnosis, but which may often be definitely decided by bacteriologic methods. The routine use of laboratory methods whenever possible cannot, therefore, be too strongly urged if an accurate and certain diagnosis is to be made in all cases. They do not and cannot take the place of careful clinical observation, but must be regarded simply as aids and accessory factors in arriving at diagnostic conclusions.

CLINICAL INVESTIGATION.

In accordance with the foregoing point of view we place clinical investigation in advance of the bacteriologic methods. Although we have no knowledge as yet of any clinical sign of typhoid fever, which is in itself conclusive from the diagnostic standpoint, there are, nevertheless, a number of symptoms that, grouped in accordance with the manner and time of their appearance, their sequence, and their association, may admit of almost complete diagnostic certainty.

The diagnosis of typhoid fever is by no means difficult if a case pursuing a typical course can be observed at the outset and for a considerable time; and if, in addition, one is informed with regard to the remote and the immediate circumstances attending its development. The situation becomes far more difficult, however, if, in the absence of knowledge of the antecedent conditions, a decision must be reached at once or after a short period of observation, and if the case is seen only at a later stage or if the attack is an abbreviated one or one pursuing a wholly atypical course.

It is particularly noteworthy and always to be kept in mind that the so-called typhoid state—that symptom-complex that formerly occupied the most prominent position with regard to the recognition of the disease—has lost more and more of its diagnostic significance, and that at the present day it is recognized to have been an obstacle to diagnostic progress in the past. At the present day it can only be said that an individual presenting the typhoid state has been for some time and in severe degree exposed to the influence (of the toxins) of an acute infectious disease; whether, however, this is typhoid fever or some acute disease, as, for instance, typhus fever, septicemia, meningitis, or miliary tuberculosis, is a question for further careful consideration.

The most important features, especially with regard to typhoid fever,

to be taken into consideration in this connection are the character of the febrile course, particularly the character of the temperature- and pulse-curves and their relations to each other, the acute enlargement of the spleen, the appearance of a peculiar roseolous eruption, and the character of the stools. Next in importance are bronchitis and pulmonary hypostasis, the state of the blood, especially of the leukocytes, and the demonstration of the diazo-reaction.

With regard to **the course of the temperature,** the character of its ascent, in the well-known step-like manner, as a result of which the height of the fever and the beginning of the fastigium are reached in the course of three or four, at most five, days, may be of great weight in the differential diagnosis. Scarcely any other infectious disease to be taken into consideration exhibits this mode of onset. It is true that the contrary condition—rapid, uninterrupted elevation of the temperature—does not, as has already been seen, exclude typhoid fever, although it is far more frequently observed in connection with other infectious diseases or with incomplete abbreviated cases of typhoid fever. If one hears Wunderlich's rules declared schematic by members of the younger generation, they should be made to understand that he was less familiar with the afebrile and the incomplete varieties of the disease, with regard to their course and frequency, than we are at the present day, and that he was correct, now as then, if his conclusions are applied to the moderate and the severe complete cases.

That the fastigium, with its peculiar temperature-course of continued fever or remittent continued fever, and particularly its duration, may be decisive in diagnosis need be but again mentioned at this point, as this subject has been discussed in previous chapters. The mode of defervescence, in the form of the characteristic steep curves, may also here be referred to. In addition, it should be pointed out that when the disease pursues a mild course and at a certain age, especially in childhood, very early remissions and intermissions in the temperature-curve should arouse suspicion of typhoid fever; however, this is true also of several other diseases which in other respects enter into consideration in the differential diagnosis. The subnormal temperature, which almost constantly and for a considerable time follows defervescence, is also to be borne in mind in this connection. Although in itself it indicates only recovery from a severe debilitating infectious disease, in no other disease does it appear so constantly and is so persistent as in cases of typhoid fever. That the temperature-curve may be irregular, variable, and wholly uncharacteristic in the various incomplete forms of the disease has likewise been fully pointed out previously.

The **character of the pulse** is noteworthy on account of its slowness, especially in youthful, vigorous males. Its remarkable slowness in comparison to the height of the temperature does not occur anywhere nearly so often in any other disease to be taken into consideration from the standpoint of differential diagnosis. Even the slowing of the pulse attending basilar meningitis is readily to be distinguished from that of typhoid fever by the time and the mode of its appearance.

The **dicrotism of the pulse** is also of diagnostic significance. It is much more common in cases of typhoid fever than in all the other infectious diseases taken together; it occurs in typhoid fever especially in persons in the bloom of youth, in later childhood, and even in older individuals who have not too marked changes in the walls of the arteries. If both phenomena, slowing and dicrotism, are observed together, this fact may materially strengthen the diagnosis, even in differentiation from basilar meningitis, in which, in addition to slowing, dicrotism is scarcely ever observed.

The **state of the spleen** is of diagnostic value if its acute enlargement is observed to occur toward the end of the first or at the beginning of the second week, after the step-like ascent of the temperature-curve has taken place. In no other acute infectious disease is the occurrence of enlargement of the spleen, especially at the time stated, even approximately so frequent; and in none does this condition persist so long—into the third or the fourth week of the disease, and perhaps longer. It is comparatively rare for the enlargement of the spleen to appear before the beginning of the fever or during the very first days of the disease, and this distinguishes typhoid fever from typhus fever, and from the acute exanthemata, to which typhus is closely related, if these diseases should ever be attended with any enlargement of the spleen. The state of the spleen during relapses is also noteworthy. The persistence or the reappearance of its enlargement after the primary defervescence of the fever is indicative of an impending relapse, and aids in distinguishing it, if it develop, from febrile conditions of other origin.

Although the **typhoid stools** possess no quality that is peculiar to them, nevertheless their color, their watery character, with the resulting tendency to the formation of layers, the yellowish, disintegrating sediment, the crystals, the penetrating odor, together with the relative infrequency of the discharges, are often quite distinctive. It is true that the diarrhea is less constant than the enlargement of the spleen. It has already been seen that scarcely one-third of all cases exhibit thin stools for a considerable time, while not a few, on the contrary, are even attended with persistent constipation.

Diagnostic significance is to be attached also to the occurrence of **meteorism,** which likewise is by no means so frequent as some believe. It is true that it is scarcely dependent directly upon, or stands in any other relation to, the ulcerated state of the bowel; but, on the other hand, it is, as has already been pointed out, merely a result of the influence of the toxin upon the intestinal wall. As it may develop in a similar manner, although less commonly, in the course of other acute infectious diseases, especially pyemic processes and general miliary tuberculosis, it may at times even increase the difficulty of diagnosis.

The most significant, almost specific, manifestation is the **roseolous exanthem.** Only with extreme rarity and only in a few other diseases do eruptions occur that can scarcely be distinguished from the typhoid roseolæ even by an expert. Personally, this has occurred to me exceptionally in cases of acute miliary tuberculosis, and it is reported also by reliable writers with regard to cerebrospinal meningitis and trichinosis. In addition, the roseolous eruption is among the principal signs of typhoid fever, almost the most frequent—by far more constant than the altered state of the bowels, perhaps even than of the enlargement of the spleen, and at any rate is in general more readily and more certainly recognizable than the latter. If, in addition, the time of the first appearance and that of the disappearance of the roseolæ, their appearance in crops, their characteristic distribution upon the body, and the short duration of the individual efflorescence be taken into consideration, they may be considered as one of the most valuable signs of typhoid fever, and all the more so as their occurrence and the degree of their development are not proportionate to the severity or the mildness of the cases; so that, especially in the atypical cases difficult of diagnosis, a distinctive criterion is at times thus afforded.

Crystalline miliaria, although one of the most frequent cutaneous lesions of typhoid fever, is far less significant from the diagnostic standpoint than the roseolæ. The circumstance that it appears relatively much later than the latter, and with distinctly greater frequency in severe and otherwise typical cases, explains this fact. In addition, it occurs by far much more frequently in other diseases. I have observed it rather commonly, especially in acute septic states, typhus fever, and miliary tuberculosis.

The negative *rôle* taken by **herpetic eruptions** is worthy of mention at this place. Almost all experienced writers are in agreement that facial herpes occurs so rarely in typhoid fever, even in the first febrile period, that its appearance in the initial stage of an infectious

disease of doubtful character is against its being typhoid. Especially certain diseases that are often to be most carefully considered in the differential diagnosis of typhoid fever in the initial stage—viz., pneumonia, cerebrospinal meningitis, typhus fever, malaria, and others—are, however, characterized by the frequency with which herpes occurs.

The diagnostic significance of **typhoid bronchitis** is not inconsiderable, and upon this I place emphasis, in contradistinction to other writers. Although it presents nothing characteristic as an individual symptom and attends all other possible infectious diseases, and some even in special degree, it may be a valuable sign in the not infrequent cases in which, although the existence of a febrile disease has been determined, other symptoms distinctive either of typhoid fever or of some other infectious disease have not yet been recognized. The occurrence of diffuse bronchitis at the end of the first or the beginning of the second week, in spite of the absence of other pronounced symptoms, indicates the presence of a severe infectious process; and under such circumstances the probability that it is typhoid fever is most likely.

Among the symptoms that have recently been recognized to possess diagnostic significance **the diazo-reaction** may next be considered. It has been seen that it occurs almost always in cases of typhoid fever in children, and in adults also in the vast majority of cases, and generally, in addition, early; and even in relapses, after having previously disappeared, it is likely to reappear. Unfortunately, the reaction is present almost as constantly in cases of acute tuberculosis, particularly miliary tuberculosis, pneumonia, certain acute exanthemata, malaria, and typhus fever, so that it acquires decisive significance with relative rarity.

More important is the **state of the white blood-corpuscles** in typhoid fever (see p. 172). Soon after the beginning of the fever, and progressively from this time on, there occurs an often considerable reduction in the number of white blood-corpuscles; this does not occur in a number of other diseases important in differential diagnosis, but in which, on the contrary, a more or less marked leukocytosis is the rule (p. 172). Also, the relative increase which occurs in the large mononuclear forms is occasionally of diagnostic aid.

When all the symptoms previously considered, especially the characteristic course of the fever-curve and the pulse-curve, the peculiar stools, the enlargement of the spleen, roseolæ, and bronchitis, coexist, or even if only some of these develop coincidently, the diagnosis is generally easy and certain. If, however, only one of these symptoms be present,

and then in an uncharacteristic manner, the establishment of the diagnosis will generally require a longer period of observation, and, above all, will demand repeated, thorough examinations directed to the exclusion of other forms of disease. In not a few cases in which the cardinal symptoms of typhoid fever do not appear or are indefinite, careful comprehensive investigation may provide the basis for a comparatively certain diagnosis by exclusion.

Not rarely in cases of obscure diagnosis some sudden occurrence tears away the veil and renders clear the existence of typhoid fever. Among such conditions are, especially, **intestinal hemorrhage,** which occurs at a certain period of the disease, **perforative peritonitis,** and combinations of both. **Epistaxis** may also at times be considered indicative of existing typhoid fever; at least, it is far less likely to occur in connection with a number of other infectious diseases, which are, especially in the initial stage, to be taken into consideration from the differential diagnostic standpoint. It should, however, be borne in mind that it is likewise quite frequent in cases of miliary tuberculosis and meningitic conditions.

Nervous impairment of hearing, occurring at the height of the fever, and **inflammation of the middle ear,** developing somewhat later, if with certainty preceded only by catarrhal or slight erosive affections of the pharynx, are of value from a diagnostic standpoint. Conversely, a number of individual symptoms are more or less opposed to the presence of typhoid fever. Among these **coryza** and **conjunctivitis** especially may be named, and **jaundice,** which, in spite of the frequent anatomic involvement of the larger biliary passages, develops with extreme rarity. It is noteworthy, further, that the occurrence of **profuse** or **persistent sweating** at the height of the fever is strongly opposed to the existence of typhoid fever.

Not less than the absence of characteristic individual symptoms, the variability in the course of typhoid fever may give rise to difficulty in diagnosis, and the more so, naturally, the less clear the history and the shorter the period of observation. Thus, the fortunately rare, rapidly fatal, fulminant or hyperpyretic cases, especially if the history is not suggestive of typhoid fever, and if, with exception of enlargement of the spleen, no striking symptom has developed, readily fail of recognition during life. In the true hyperpyretic cases especial difficulty is at times created by the mode of onset—with a chill—and the abrupt, not step-like, ascent of the temperature to a level that is not at all expected in the course of typhoid fever, and least during the first week.

Another form of disease, of opposite character from the prognostic

standpoint, the abortive form, exhibits a resemblance to the preceding in some respects, namely, a similar ascent of the temperature at a single bound, at times after antecedent chill, then a short, highly febrile course, terminating in recovery with a critical decline, not rarely without the development of roseolæ, intestinal symptoms, or even appreciable enlargement of the spleen. Some of the cases of this character are considered as instances of central pneumonia, or even of ephemera, unless the prevalence of an epidemic of typhoid fever or the simultaneous occurrence of other cases which are well-marked leads in the right direction. That also the remaining atypical varieties, the true mild and mildest cases of typhoid fever, may be a source of great difficulty will be obvious from the previous description of their course. Not less obscure may the protracted, otherwise mild cases prove, especially if attended with remittent, intermittent, or irregular temperature-curves.

Scarcely recognizable at times are ambulatory and afebrile cases of typhoid fever. Error in diagnosis in a number of cases may be due to the fact that thorough examination was not made, or that this was not suggested by reason of extraneous circumstances. In some cases roseolæ and enlargement of the spleen, which occur also in afebrile cases, and are scarcely less common in ambulatory cases than in others, would otherwise have pointed in the right direction. I have already mentioned that in apparently mild cases, in which the patients walk to the physician's office or to the hospital, one is occasionally surprised by such a discovery.

In comparison with the varieties mentioned, the well-marked hemorrhagic cases are much less to be taken into consideration from the diagnostic standpoint. Fortunately rare in themselves, they generally exhibit the characteristic symptoms of typhoid fever at the beginning. When, however, the case comes under observation shortly before the fatal termination, with an indefinite history, it will be wise to do no more than make the diagnosis of an infectious disease that has become hemorrhagic, but to refer its explanation to the prevailing type of epidemic.

It should not be forgotten that occasionally a complication of typhoid fever with ulcerative endocarditis and secondary multiple emboli of the skin may give rise to confusion with the true hemorrhagic form; and, as has occurred, that essential septicemic ulcerative endocarditis, if attended with profound toxic effects upon the central nervous system, may be confounded with typhoid fever.

It has already been seen how difficult the diagnosis may become if **certain typhoid disorders of the viscera** or **actual compli-**

cations dominate the picture of the disease from the outset, if it sets in directly with the local manifestations alone, while the remaining symptoms distinctive of typhoid fever make their appearance later. We may mention at this point the nephrotyphoid, pneumotyphoid, and pleurotyphoid, which have already been fully described. Far more frequent than these varieties, and therefore quite noteworthy, is meningotyphoid, which I was the first to study carefully. When it is present, the diagnosis may be rendered all the more difficult from the fact that in large cities isolated cases of typhoid fever and cerebrospinal meningitis almost always occur side by side. It is also noteworthy that in house endemics of typhoid fever occasionally all the cases set in with meningitic symptoms.

The condition of typhoid perityphlitis previously mentioned may also give rise to error in diagnosis and serious injury to the patient, especially when it develops without antecedent characteristic diarrhea, or as occurs at times even after obstinate constipation. The condition becomes almost beyond the possibility of diagnosis when the appendicitis develops in the course of the mildest form or of an ambulatory attack of typhoid fever, and the patients, after the symptoms have in large part subsided and are free from fever, are admitted into the hospital as "convalescents from appendicitis." Under such circumstances a relapse of the typhoid fever in a well-characterized form occasionally first brings the desired explanation. In those cases in which the patients have been under observation before the development of the perityphlitis, the height and the character of the accompanying fever, as well as the circumstance that it persists far beyond the period of development of the inflammatory exudate, may lead to a correct diagnosis.

Finally, there may yet be taken into consideration in this connection certain **mixed infections** that may greatly increase the difficulty of recognizing typhoid fever as the underlying cause of the morbid condition in question. The most important is the septicemic variety of typhoid fever, as well as the combinations with malaria not rarely observed in Europe, the tropics, China, Japan, and North America.

General conditions, personal as well as those not related to the individual, also have a determining influence upon the diagnosis. The *rôle* of **age** in this connection is undoubted. The conditions for a correct diagnosis are relatively most favorable during the period of youth, including late childhood. In early childhood, and especially during infancy, the course of the disease may in many respects be so unusual that its recognition is thereby rendered difficult. It must likewise be borne in mind that the disease frequently pursues an abbreviated,

irregular, unusually mild course in children; while, on the other hand, their tendency to react with considerable fever to slight, scarcely appreciable influences should be remembered. Not less difficulty often attends the recognition of typhoid fever in advanced life, in consequence of the frequently uncharacteristic course of the fever, and especially on account of the almost or wholly afebrile cases. In addition, enlargement of the spleen and roseolæ are frequently distinctly less marked or entirely wanting in old age.

Almost in the same way as in the aged, cases modified by **chronic disease** and **constitutional abnormalities,** as well as by a vicious mode of life, may readily fail of recognition.

It need scarcely be pointed out that isolated cases of typhoid fever without demonstrable connection with antecedent or simultaneous cases, and especially the primary cases in a place, may be difficult of diagnosis; and that, conversely, the fact that typhoid fever is prevalent in a place may throw light upon a number of obscure cases of febrile disease.

Of great importance in the diagnosis naturally are the duration of the period of observation in a case and the period at which it first comes under observation. The most favorable stages in the latter connection are, doubtless, the end of the first and the second week, because the development and the combination of the most characteristic signs occur at this time. It is in the second week that the diagnosis is most frequently made at first sight. The diagnosis is generally quite difficult at the beginning of the first week. At this time one must be governed, by reason of almost constant absence of local symptoms, almost alone by the mode of onset and the course of the fever. It should be borne in mind, however, that even at this time enlargement of the spleen is occasionally demonstrable, and that, particularly during some epidemics, there appear not rarely during the first days of the fever, and even during the last days of the period of incubation, anginose symptoms that are peculiar to typhoid fever, and which may cause the inexperienced to confuse the condition with croup and diphtheria.

The diagnosis is generally easier during the stage of defervescence than during the first days of the disease. It will then usually be known that a febrile condition has preceded, or a portion thereof may be observed, and, besides, there are likely to be found residua of roseolæ, developed sudaminal, persistent enlargement of the spleen, bronchitis, hypostases, and, finally, the characteristic febrile course with the well-known steep curves. In patients who come under observation in the first period after defervescence, persistent subnormal

temperature with relatively great frequency and instability of the pulse is indicative of an antecedent severe febrile disease, and in none of all these is this symptom so frequent and so persistent as in typhoid fever. The importance of the diagnosis, especially after the termination of the actual disease, with regard to the diet and permission to get out of bed, need only be mentioned at this place. Reference may be made here again to the diagnostic significance of **relapses.** Every experienced physician will be able to recall cases in which relapses, by their regular typical course, cleared up, from the diagnostic standpoint, primary febrile states which pursued an irregular course or did not at all come under immediate observation.

SPECIAL DIFFERENTIAL DIAGNOSIS.

Having established guiding principles with regard to individual symptoms, symptom-groups, and general conditions, we may now consider some of the most important diseases which may be confounded with typhoid fever. Few of these are to be taken into consideration from the standpoint of differential diagnosis throughout the entire course of the disease, but most of them, according to their character and their manifestations, are to be considered only during certain stages.

Acute Miliary Tuberculosis.—Confusion of typhoid fever with acute miliary tuberculosis is especially frequent, and *vice versa.* The best diagnosticians have made mistakes in this connection, or have failed to reach a definite conclusion after weeks of observation, until finally the recovery of the patient proved the case to be one of typhoid fever, or post-mortem examination showed it to be one of miliary tuberculosis. The principal difficulty in the differential diagnosis resides in the fact that both diseases often exist for a considerable time without conspicuous local manifestations, while the disturbances in the general condition due to the action of toxins, the typhoid state, may be equally developed in both. Both diseases, after an equal duration, are attended with sopor, muttering delirium, floccitation, subsultus tendinum, and finally coma, and are preceded by headache, vertigo, languor, and often nosebleed.

It has been said that the course of the temperature is distinctive in each disease. This may be applicable to typical cases of typhoid fever. In protracted atypical cases, however, the temperature-curve, especially the markedly remittent or intermittent type, may greatly increase the difficulty of differentiation from miliary tuberculosis. Profuse persistent sweating during the febrile stage, especially with an intermittent

temperature-curve, is in favor of miliary tuberculosis and against typhoid fever. More important than the state of the temperature may be that of the pulse, inasmuch as its relative slowness, so frequently observed in cases of typhoid fever in youthful individuals, does not occur in cases of miliary tuberculosis, except in the presence of a combination with basilar meningitis, which is readily recognizable from other symptoms. Marked dicrotism of the pulse is also incomparably less common in cases of miliary tuberculosis.

The appearance of the patient may alone be of some importance to the trained observer. In the presence of miliary tuberculosis a peculiar slight, diffuse lividity exists at the height of the disease, which, in combination with the general pallor, gives rise to a characteristic appearance, especially of the face and the extremities. The state of the spleen also is noteworthy; its enlargement, beginning toward the end of the first week of the disease and progressing from this time to the end of the second week, is in favor of typhoid fever; while enlargement of the spleen is much less constant in the presence of miliary tuberculosis, and is even not rarely permanently absent. That small hyperemic papular spots, in general not distinguishable from roseolæ, may be present also in cases of miliary tuberculosis, though rarely and in small number, has been previously mentioned. A profusion of roseolæ of typical development and distribution is, however, distinctive of typhoid fever.

I am unable to agree unconditionally with the opinion that the absence or the presence of meteorism is distinctive. It is true, flattening or retraction of the abdomen is more frequent in cases of miliary tuberculosis, especially if the cerebral membranes are also involved; but, as has already been mentioned, typhoid fever also is quite commonly unattended with noteworthy meteorism either temporarily or permanently. If it be considered, in addition, that severe cases of miliary tuberculosis may also, precisely like severe cases of typhoid fever, be attended with marked distention of the abdomen, the diagnostic value of this symptom is further diminished.

With regard to the diagnostic significance of diarrhea, it should not be overlooked that thin stools may occur also in cases of miliary tuberculosis, especially when old intestinal ulceration is present; they may even be of a yellow color when the diet is predominantly liquid and of milk. Constipation or regularity in the action of the bowels is not distinctive one way or the other; while intestinal hemorrhage occurs almost solely in cases of typhoid fever.

The symptoms referable to the lungs may also increase rather than diminish the difficulty in differentiating the two diseases, particularly at

the beginning. Both are attended with a dry, short cough, with scanty, macroscopically wholly uncharacteristic expectoration, and in which, even in cases of miliary tuberculosis, tubercle-bacilli are found only exceptionally, and then are derived from older ulcerative foci. On physical examination, with a normal percussion-note, dry râles, sibilant and sonorous, are generally present in both diseases. If, however, an especially dense, fresh eruption of tubercles in the lungs occurs in a case of miliary tuberculosis, highly characteristic manifestations may result, namely, subjective dyspnea, with far more marked increase in respiratory frequency than occurs in cases of typhoid fever with a similar range of temperature, and, at the same time, acute pulmonary emphysema, an especially decisive objective sign, which has hitherto received far too little attention, and which has rendered me excellent service in many cases. This pulmonary emphysema never occurs, in my experience, as the result of typhoid bronchitis, while it is an almost natural, readily explicable result of the direct or indirect occlusion of the bronchioles by a uniform, dense, and recent eruption of tubercles.

The differential count of the leukocytes may be of considerable value in differentiating these two conditions, in both of which there is a decrease in the absolute number. But, while in typhoid fever there is usually a relative increase in the large mononuclears, in acute miliary tuberculosis this does not occur.

One examination, finally, should never be omitted in doubtful cases, namely, that of the eyeground for tubercles of the choroid. It is true, this decisive condition occurs, according to many writers and my own experience, only in the minority of cases, and its detection is often rendered more difficult from the fact that the nodules develop with a certain degree of preference at the periphery of the eyeground.

Further, it should always be borne in mind that typhoid fever may be complicated by miliary tuberculosis. It is true that this generally occurs during the later stages of the disease, and even during convalescence. In the latter event, even careful observers, especially at the beginning, will not always be secure against the possibility of mistaking this for a relapse.

Meningitis.—When acute miliary tuberculosis is attended with **basilar meningitis,** the diagnosis is thereby rendered rather easier than more difficult; the reasons for this need not be given in detail here. From the beginning, under such circumstances, the unusually severe headache, the obstinate vomiting, especially after the ingestion of food, are far more indicative of impending meningitis than of typhoid fever.

It need scarcely be repeated that in a doubtful case lumbar puncture often proves of the greatest value.

That **simple purulent meningitis,** originating from disease of the nose or of the middle ear, may now and again give rise to doubt and confusion need only be briefly mentioned. The conscientious physician will, apart from this, make an examination of the ears and of the nasopharynx in the case of every febrile, soporose patient, and in a suspicious case lumbar puncture should be performed.

With regard to **epidemic cerebrospinal meningitis,** and the possibility of confounding it with typhoid fever, I may refer to a previous chapter (pp. 269–274).

Cryptogenic Septicemia.—The differentiation of cryptogenic septicemia from typhoid fever may under some circumstances be quite difficult. The quite usual development of a typhoid state, the febrile course, which, precisely as in a case of typhoid fever, may exhibit the curve of a continued or a remittent fever, and the rarely absent enlargement of the spleen, are particularly confusing in this connection. Diffuse bronchitis also, quite similar to that of typhoid fever, is not rare. Diarrhea is almost as inconstant as in cases of typhoid fever. Frequently there is slight, at times even marked, jaundice, which will then be strongly indicative of septicemia. In these cases blood-cultures are often of decisive diagnostic value.

Other Septic Processes.—An answer to the question whether **puerperal septicemia** or typhoid fever is present may under some circumstances be attended with greater difficulty than would be believed. On one hand, especially when the history is indefinite, severe puerperal septicemia of typhoid course may be mistaken for actual typhoid fever; and, on the other hand, it should always be borne in mind that pregnant women attacked with typhoid fever quite generally suffer from abortion and premature labor. Under such circumstances it has repeatedly happened that the continuation of the typhoid disease was looked upon as septicemia in connection with supposed primary premature labor. I have personally observed cases in which the history and the clinical conditions were so obscure that only the appearance of distinct roseolæ, or even serum-diagnosis, cleared up the condition.

Ulcerative endocarditis, which has been mentioned repeatedly, and is to be considered among the septic processes, is also generally attended with symptoms of the typhoid state, and not at all rarely with recent enlargement of the spleen. Nevertheless, the embolic lesions of the skin that occur will not readily be confounded with the typhoid roseolæ, especially as other emboli, recognizable without difficulty,

generally occur in the retina, the brain, the kidneys, and the lungs. Naturally, the acute development of a cardiac affection, with debility, irregularity, and murmurs, will not readily be overlooked. The onset may occur when the heart was previously intact, or—and this renders recognition of the condition more difficult—it may complicate previous valvular lesions. The diagnosis will be facilitated if it be borne in mind that endocarditis (not septic) is extremely rare as a complication of typhoid fever, and that myocarditis also is by no means frequent; and that both occur, if at all, generally at the height or toward the end of severe cases—at a period, therefore, when it has generally been possible to make the diagnosis of typhoid fever with certainty.

In youthful persons **infectious osteomyelitis**—designated by French investigators (Chassaignac) especially as "typhe epiphysaire"—is not rarely the cause for error in diagnosis. In such persons, with an obscure febrile, typhoid symptom-complex, dependence should never be placed upon the absence of complaints referred to the extremities, but these should always be examined carefully for edema, livid redness, and circumscribed tenderness, especially the epiphyseal regions of the long medullated bones.

Intoxications.—Doubtless, intoxication from the ingestion of decomposed organic substances (meat, fish, mussels) and fluids (water, milk, etc.) contaminated by the products of putrefaction also gives rise to acute intestinal disorders with "typhoid" symptoms. The inhalation of putrid gases also appears to be capable of giving rise to diarrhea, with enlargement of the spleen, fever, and stupor, as is shown by many reports in the literature, among which are the well-known instances in England previously mentioned (p. 50), which at the time of their publication were exploited as supporting the pythogenic theory of typhoid fever (p. 20).

Malaria.—Malaria generally will give rise to difficulty in diagnosis only in those regions in which the cases present remittent or continued fever. Error may under such circumstances be made in either direction, inasmuch as, on the one hand, malarial processes may be mistaken for typhoid; and, on the other hand, fulminant typhoid fever may be mistaken for pernicious malaria. That rare cases of ambulatory typhoid fever with intermittent fever and chills may under certain conditions simulate malaria has already been mentioned. Examination of the blood for malarial parasites usually clears up the diagnosis without difficulty in these cases.

Influenza.—The confusion of influenza and typhoid fever is occasionally pardonable. The high fever, the prostration, and the stupor of

the patients, and other severe nervous general manifestations, may contribute to this end. It is important in this connection to obtain a history of the beginning of the disease. In cases of influenza the initial coryza, with which are soon associated laryngotracheitis and bronchitis, will not readily be overlooked. In cases of typhoid fever coryza is, as has been mentioned, an extremely rare condition, and affections of the larynx, as well as bronchial catarrh, generally do not make their appearance before the second week, or even later. Besides, enlargement of the spleen is usually wanting in cases of influenza, while the roseola, or an exanthem resembling it, is never observed.

The Acute Exanthemata.—Among the diseases that practically never give rise to difficulty in the differential diagnosis at the height of their development, but do so all the more frequently in the initial stage, are the acute exanthemata. Scarlet fever and variola particularly, and also measles during the primary fever, may be responsible for such error in young nervous individuals. Apart from the knowledge of the prevalence of the one or the other of the diseases in question, the local initial symptoms that are soon added to the ill-defined general febrile state will soon serve as a guide to the careful observer. With regard to measles, importance is to be attached to conjunctivitis with coryza and catarrh of the upper air-passages, and with regard to scarlet fever, to the distinctive angina; while in cases of small-pox, the characteristic sacral pain, as well as the initial exanthemata, particularly the scarlatiniform, in the triangles of the thighs and the upper arms, and the appearance of the variolous efflorescence upon the pharyngeal mucous membrane immediately afterward, at times almost simultaneously, will lead in the right direction. At a later period varioloid, with a scanty eruption accidentally confined to the trunk, may at most be a source of doubt. If it be borne in mind, however, that the variolous eruption almost unexceptionally appears first upon the face also in cases of varioloid, that constantly with its appearance, even in the severest cases, decline of temperature takes place, one will seldom be seriously embarrassed.

Typhus Fever.—The differential diagnosis may be far more difficult with regard to typhus fever. This is exhibited historically in the fact that the two diseases were not properly distinguished from each other up to the middle of the nineteenth century. Even at the present day the conditions are not very simple in countries and at times in which both diseases are constantly prevalent side by side, and it is precisely under such circumstances that early and accurate diagnosis is of importance with regard to the interests of the community. If a decision be

desired in the first few days of the disease, it may be almost impossible if, in addition to the febrile "typhoid" state, the distinctive cutaneous manifestations have not yet developed. It should, besides, always be noted—what the inexperienced readily overlook—that even in quite severe cases of typhus fever the development of the associated eruption may be extremely imperfect or almost completely absent. In the presence of a marked exanthem in connection with both diseases, the differentiation is easy for an experienced observer. The typhoid roseola is almost from the beginning slightly elevated, papular, and, throughout its entire duration, purely hyperemic, constantly circular, and sharply defined. On the other hand, the spots of typhus fever are less sharply limited and are ill defined; at first pale, the majority soon become hemorrhagic, so that they are then simple, not elevated, spots of from a dusky, coppery redness, only in part disappearing on pressure, to a dark livid color, which then distinctly exhibit their petechial character.

The diagnosis is facilitated by the fact that the spots of typhus fever appear earlier than the typhoid roseola—between the second and, at the latest, the fifth day of the disease—and they rapidly attain their definitive development singly and collectively at a single stroke, invariably without recrudescences, within from forty-eight to seventy-two hours. The differences in the distribution of the eruptions over the surface of the body in both diseases are also noteworthy. While in cases of typhus fever the trunk and the extremities are quite uniformly covered, in cases of typhoid fever only the parts of the extremities adjacent to the trunk are involved, and the remaining portions are involved in lesser degree the further removed they are from the trunk. In cases of typhus fever, when the exanthem is developed to any considerable degree, especially the forearms and the legs are preferably involved, and also the dorsum of the hands and the feet, so that I advise careful inspection of these parts when there is suspicion as to the presence of this disease. With regard to the face, there is a certain degree of agreement between the two diseases, in so far as in the vast majority of cases of typhus fever this also is likely to remain free from the exanthem. On the other hand, the face in the latter disease exhibits a number of other distinctive features. Even from the beginning it is diffusely red and turgid, the conjunctivæ are vividly injected, subsequently often ecchymotic, while, in addition, the face has a wild and startled expression, which is in marked contrast to the indifferent, dull expression of the typhoid patient.

Not less important than observation of the skin in the differentiation of the two diseases is the course of the fever. In contrast with

the familiar step-like ascent in cases of typhoid fever, the temperature in cases of typhus fever generally, after one or rarely several chills, rises rapidly to its height with slight interruption, so that within from twenty-four to thirty-six hours a level of from 40.5° to 41° C. is reached—a far higher level than in cases of typhoid fever at this time, or even in cases of not unduly excessive severity, throughout the entire fastigium. The further course of the fever also exhibits important differences that cannot be considered fully at this point. Its total duration does not exceed from fourteen to seventeen days even in the most severe cases of typhus fever. It generally terminates with a critical or a rapid, step-like decline. With the abrupt onset and the rapid ascent of the fever to a considerable height corresponds, in cases of typhus fever, also the far earlier appearance of the severe general manifestations, with the unusual prostration that compels the patient to take to his bed as early as the first or the second day. The other profound disturbances referable to the nervous system also appear much earlier than in cases of typhoid fever. As early as the first days furious delirium often occurs; and from the beginning of the second week, profound coma.

The pulse in all cases of typhus fever, without reference to age and sex, is exceedingly frequent from the beginning. In women and children it may be 120 and more during even the first days; also, in previously healthy young men a frequency of pulse is sometimes encountered at the beginning, such as is rarely observed at the height of the disease in cases of typhoid fever. Enlargement of the spleen is far less constant in cases of typhus than in those of typhoid fever. When it occurs, it develops earlier and it subsides more quickly. I have generally observed it to disappear during the middle of the second week, and rarely to persist beyond the period of defervescence. Meteorism develops only exceptionally in cases of typhus fever, while one must expect the occurrence of diarrhea at the height of the disease, and the stools, under the influence of the food administered, may even acquire an appearance similar to those in cases of typhoid fever. With regard to the diazo-reaction, there appears to be no difference between the two diseases. Also, in cases of typhus fever, which differs in this as in many other conditions from the acute exanthemata, the diazo-reaction is generally demonstrable at the beginning and at the height of the fever. It may be mentioned that the leukocytes are usually increased in number in this condition.

Relapsing Fever.—Confusion with relapsing fever is more likely to occur with regard to typhus fever than with regard to typhoid

fever. Only the early cases in an epidemic, and these only during the first few days, could cause doubt. Here and there, it is true, confusion of the second paroxysm of relapsing fever with a relapse of typhoid fever might arise, especially if the first paroxysm failed to come under clinical observation. Even in such a case the disease cannot readily be confounded with typhoid fever. Its onset with a chill, the unusually high temperature—up to 41° C. and above—reached within a short time, the critical decline at the end of seven days, rarely later, protect against error. Naturally, the demonstration of the spirilla of relapsing fever, if this be thought of in the earliest cases of an epidemic, and which, as is known, can be found during the entire febrile period, and even for one or two days beyond (Birch-Hirschfeld), will remove all doubt.

Secondary Syphilis.—The confusion of the eruptive stage of secondary syphilis with typhoid fever is more likely to arise at times than would be believed. The best observers have made mistakes in this connection when the exanthem of secondary syphilis has made its appearance with remittent fever, enlargement of the spleen, and, in irritable individuals, even with general nervous symptoms, stupor, etc.

Trichinosis may, in mild cases, with predominant gastro-enteritic symptoms, quite readily be confounded with irregular, moderately severe cases of typhoid fever. In the presence of severe trichinosis, the painful tumefaction and induration of the muscles, the flexor contractures of the extremities, the edema, especially of the face, will permit of a decision without difficulty. As a final resort, removal of a piece of muscle for diagnosis would be indicated.

Anthrax, if unattended with carbuncle or edema, in the form of intestinal mycosis, with the attendant symptoms of enteritis, intestinal hemorrhage, and the typhoid state, might exceptionally cause difficulty in diagnosis.

Acute glanders also is suggestive at first sight of typhoid fever if the patients exhibit remittent fever, a dry, fissured tongue, and fuliginous deposits upon the lips and the gums. Generally, however, the characteristic impetiginous or ecthymatous eruptions, multiple abscesses of the muscles, or specific ulcerative lesions of the mucous membranes will lead to a correct diagnosis.

The diagnostic relations of **pneumonia** and **pleurisy** to typhoid fever have been sufficiently discussed at various places. At this point it may only be mentioned that those rare cases of central pneumonia, or at least pneumonia beginning at the center of the lung, may at times give rise to confusion, and particularly if they are attended with stupor

and delirium, without pleuritic pain, and if, in consequence of impaired consciousness or debility, their nature is not disclosed by characteristic expectoration.

BACTERIOLOGIC DIAGNOSIS.

The expectation generally held, after the discovery of the typhoid-bacillus, that the diagnosis of the disease would be made by the demonstration of the organism in every case, which many thought would be a relatively simple procedure, has, in the original sense, scarcely been realized. On the contrary, it may be said that the difficulties attending the direct demonstration of the bacilli in the patient or his dejections are considerable, and in some cases at present unsurmountable.

Differentiation of Bacillus typhosus from Bacillus coli.—The differentiation of the typhoid bacillus isolated from the excreta of the patient, from suspicious fluids, articles of food, etc., from other micro-organisms, especially from those belonging to the colon-group, is still so difficult that even at the present day some observers—a very small number, it is true—still maintain the opinion that the two are identical.

As a matter of fact, the great morphologic and biologic resemblance between the two structures, especially with regard to their form and size, their motility, as dependent upon the presence of flagella, their negative response to Gram's method of staining, and their equally remarkable resistance to carbolic acid, which, when added to the nutritive medium in amounts up to 0.25 per cent., does not prevent their development, is a source of no small difficulty. In addition, a great difficulty in the isolation of the organism arises from the abundant presence of micro-organisms of the colon-group in the stools, and their tendency to invade all possible internal organs. Numerous points of difference believed to be reliable have been laid down as the result of many hundreds of investigations,[1] but not a few of these differences were very quickly shown to be inconstant.

The following are at present considered among the more valuable criteria: The flagella are said to be more numerous and longer in the typhoid-bacillus than in the micro-organisms of the colon-group; in the hanging drop, with suitable precautions, typhoid-bacilli are believed to be more active and to preserve their motility for a longer time. While the characteristics of the growth upon gelatin and agar exhibit slight, at times scarcely demonstrable, differences, the results of culture upon potatoes are frequently more characteristic (Gaffky). It was formerly stated that if one-half of a disk of boiled potato be inoculated with the typhoid-bacillus and the other half with the colon-bacillus, there will develop upon the latter, after a certain period of time, a dense, distinctly visible, at first yellowish, then grayish-brown, moist, glistening, smeary coating, while the growth of

[1] See Lösener, *Arbeiten aus dem Reichs-Gesundheitsamte*, Bd. xi., one of the most comprehensive critical papers upon the subject of the differentiation of the typhoid-bacillus.

the typhoid-bacillus upon the other half appears only as an extremely delicate, moist, almost transparent deposit, so thin that at times it can be lifted up with a needle only in the form of most delicate filaments, if at all. It is now known, however, that these differences may be minimized, or even entirely disappear, with certain varieties of colon-bacilli, and that they depend largely also upon the reaction of the potato, so that the test, therefore, is not of great use.

Some other cultural characteristics are undoubtedly to be considered as more trustworthy, especially the growth in litmus milk. While the colon-bacillus causes the milk to become rapidly and extremely acid and to undergo coagulation, the typhoid-bacillus does not cause coagulation of the milk and renders it only very faintly acid, even if it be kept in the thermostat for weeks. The glucose-test is not less valuable. If of two (best, hermetically sealed) fermentation-flasks containing grape-sugar-bouillon, the one is inoculated with the typhoid-bacillus and the other with the colon-bacillus, and both are exposed for twenty-four hours to a temperature of 27° C., active fermentation, with the evolution of gas, will develop in the latter, while this does not occur in the other flask. The fermentation-test becomes more striking if made with solid nutritive media. Of two glucose-agar or glucose-gelatin tubes, the one inoculated with the typhoid-bacillus remains unchanged, while the active evolution of gas induced in the other by the colon-bacillus elevates the gelatin from the bottom of the tube and causes rents and fissures to appear in the media.

In addition to the milk-test and the fermentation-test, the negative response to the indol-test, for which Kitasato[1] has described a most useful, simple method, appears to be quite reliable. In general, the colon-bacillus yields the reaction, while it is wanting with the typhoid-bacillus. But, since Peckham[2] has shown that by particular methods of cultivation the typhoid-bacillus may be made to produce indol, and, on the other hand, that unless the colon-bacillus be grown on an absolutely sugar-free medium the development of indol may be prevented, the method must be considered of questionable value, and is useful only when taken in connection with other features.

More important than any of these tests in the differentiation of the typhoid-bacillus is its specific reaction to the blood-serum of immune animals and of typhoid patients. The use of this method (which will be more fully discussed later in considering its application to diagnosis of the disease) as a means of bacteriologic differentiation we owe especially to Gruber and Durham, who appreciated its full value, and who worked out fully the conditions under which it may be applied. While doubt has been thrown on its value as a means of differentiation by several observers, who also demand the use of extremely high dilutions of the serum—even 1 : 100,000 and over—it may be said that when the serum, even in moderate dilutions, is controlled by observation of its action on known typhoid-bacilli, the test is quite constant and extremely valuable. It must be emphasized, however, that no one test is sufficient for the determination of the nature of an organism of this group, and that only when all the various characteristics and results of different tests are taken into consideration can a definite conclusion be reached. Unfortunately, numerous earlier statements with regard to the presence of the typhoid-bacillus in the living body and its excreta have been made without consideration of this rule, and are therefore valueless.

Attention should again be called to the possibility of the occurrence of

[1] *Centralbl. f. Bakt. u. Parasit.*, Bd. xiv., No. 22.

[2] *Jour. of Exp. Med.*, vol. ii.

diseases presenting the clinical picture of typhoid fever, but which, as demonstrated by blood-cultures and agglutination-test, are probably caused not by the typhoid-bacillus, but by closely related organisms, the so-called paracolon or paratyphoid-bacilli. Such bacilli have been described by Widal,[1] Gwyn,[2] Cushing,[3] and Schottmüller.[4] Other bacilli intermediate between the typhoid and colon groups are of the hog-cholera or Bacillus enteritidis (Gärtner) type. A careful comparative study of these intermediate forms has been made by Cushing.[5] The bacillus of dysentery, the so-called Shiga's bacillus, is also very closely related, morphologically and culturally, to the typhoid-bacillus; the exact relationship between the two organisms has, however, not been completely worked out.

Blood-cultures.—Up to within the past year, cultures from the circulating blood have been of little aid in diagnosis. As has been previously stated (p. 175), newer work with better methods has made possible the demonstration of the typhoid-bacilli in the circulating blood in 70 to 80 per cent. of all cases examined. Cole, working at the Johns Hopkins Hospital, has lately isolated the bacilli from 43 of 58 cases examined. In many of the cases the cultures were obtained early in the disease, before a positive Widal test had been obtained. In certain cases the culture alone established the diagnosis, which had previously been doubtful or even unsuspected. The method used is as follows:[6] The skin over the anterior surface of the patient's arm at the bend of the elbow is carefully sterilized. To obtain the blood, a syringe holding 8 to 10 c.c., and fitted with a small needle which will readily enter one of the superficial veins, is used. By using a small needle and entering the vein with one thrust little or no pain is caused. From 8 to 10 c.c. of blood are withdrawn and divided among five or six Erlenmeyer flasks, each containing 150 c.c. of bouillon. The flasks are then shaken and placed in the incubator, and after twenty-four hours, if cloudy, agar plates are made. Usually, the organisms in the bouillon are somewhat clumped, at least sluggishly motile, and so are not suitable for trying the serum-reaction. The diagnosis of Bacillus typhosus in each case should be decided only by typical growth on all media and by agglutination-test with known typhoid serum. Frequently, a fairly definite conclusion can be reached in thirty-six hours after obtaining the culture. If the bacilli grow out in the bouillon in twenty-four hours, they can be transferred at once to the various media, and from the slant agar, after six to eight hours, a suspension in bouillon can be made in which the serum-reaction can be tried.

[1] *La Semaine Méd.*, Aug. 4, 1897. [2] *Johns Hopkins Hosp. Bull.*, vol. ix.
[3] *Ibid.*, vol. xi.
[4] *Deutsch. med. Woch.*, Aug. 9, 1900; also, *Zeit. f. Hyg. u. Inf.*, Bd. xxxvi., H. 3.
[5] *Loc. cit.* [6] *Johns Hopkins Hosp. Bull.*, No. 124, vol. xii.

Although the method presents considerable technical difficulties, where the conditions are such, as in a hospital, that it may be employed, it is of undoubted aid in diagnosis.

Cultures from Rose-spots.—As previously stated (p. 175), cultures made from the rose-spots have shown the presence of the typhoid-bacillus in a majority of the cases. The procedure is not readily applicable as a means of diagnosis, however, on account of the discomfort to the patient, and also because, in the cases in which well-developed rose-spots are present, the diagnosis is usually already clear.

Also **puncture of the spleen** during life (Lucatello, Chantemesse and Widal, Redtenbacher, E. Neisser), which undoubtedly frequently yields positive results (p. 176), has lost all significance as a practically applicable method, as it exposes the patients directly to danger. That in some cases **lumbar puncture**—which is often indicated even therapeutically—may facilitate the diagnosis is entirely probable, and has been verified by illustrative cases.

Especial hope was attached from the outset to **examination of stools.** It was soon recognized that the typhoid-bacilli (see p. 32) usually leave the body of the patient in the stools, and that they are demonstrable in these generally from the beginning or the middle of the second week of the disease to the fourth and even the fifth week, less commonly into the period following defervescence. Their demonstration was from the outset attended with the greatest difficulty, on account of the immense number of other micro-organisms at the same time present, and especially those of the colon-group. Elsner[1] has introduced the use of a special medium for this purpose which has given good results in his hands, and has been warmly recommended by Brieger,[2] Lazarus,[3] and others; but, on the other hand, has been declared by others (Breuer,[4] Haedke[5]) as not entirely reliable. However this may be, the procedure requires the greatest skill, so that while in the hands of the trained observer it is applicable to the solution of certain problems, in its present form it has no future as a clinical method.

Elsner's method, briefly, is as follows: If 1 per cent. of iodin is added to sterilized potato-gelatin of definite acidity, and if plates are made after addition of the fecal matter to be examined, it is possible, by the addition of the iodin, to exclude from development all other micro-organisms but the colon-bacillus and the typhoid-bacillus. In addition, the latter develops distinctly more slowly and incompletely. While in the course of twenty-

[1] *Zeit. f. Hyg. u. Infektionsk.*, 1895, Bd. xxi.
[2] *Deutsch. med. Woch.*, 1895, No. 50.
[3] *Berlin. klin. Woch.*, 1895, No. 49.
[4] *Ibid.*, 1896, No. 47.
[5] *Deutsch. med. Woch.*, 1897, No. 2.

four hours nothing of the typhoid-bacillus can be seen with the naked eye and with low powers of the microscope, after the lapse of forty-eight hours it will be present together with the colon-bacillus, from which it is readily distinguishable upon the plate. In addition to the large, much more markedly granular, brown-colored colonies of the latter, those of the former appear as small, bright, glistening, extremely finely granular points, resembling drops of water.

Within the past few years other media and special methods have been introduced by numerous observers. The most promising of these methods are those of Piorkowski, Remy, and Hiss. Each of these methods has given good results in the hands of its author. Hiss, using his method, was able to isolate the typhoid-bacillus from 17 out of 21 cases in the febrile stage. It still remains to be seen whether the general routine application of these methods is practicable or not.

As previously stated (see pp. 34 and 190), typhoid-bacilli are found in the urine in about one-third of the cases examined. While their presence is rare before the third week, they may occur during the second week, or even the end of the first week, and so their isolation may be of definite diagnostic value. In making cultures, females should be catheterized under careful antiseptic precautions, and the urine so obtained should be plated at once. In males, the anterior urethra should be irrigated with antiseptic solutions, and the patient should then void into a sterile flask. In the determination of a bacillus obtained in the culture, great care should be taken against confounding the typhoid-bacillus with the colon-bacillus, to which cystitis is quite commonly due. Attention should again be called to the peculiar shimmer described by Horton-Smith which is seen when a test-tube filled with urine containing large numbers of bacilli is held up to the light and gently shaken. In this way the presence of the condition can often be predicted before cultures have been made.

METHODS OF SERUM-DIAGNOSIS.

Within the past few years an indirect method of bacteriologic diagnosis has been introduced which has proved to be of great value. While this method of serum-diagnosis, owing to the frequently delayed appearance of the reaction, has not been found to be of so great value as was at first hoped, it is, nevertheless, an exceedingly important factor in diagnosis. This method is based upon the fundamental investigations of R. Pfeiffer[1] and his pupils, originally undertaken in the study of the question of immunity. These investigators studied the action of the blood-serum of animals immunized to cholera and typhoid fever

[1] *Zeit. f. Hyg. u. Infektionsk.*, Bd. xix.

upon the respective pathogenic micro-organisms. They showed especially (Pfeiffer and Kolle[1]) that, exactly as in the case of cholera, the serum of animals immunized to typhoid fever, when placed in the abdominal cavity of a previously healthy experimental animal (guinea-pig), together with an amount of typhoid culture experimentally determined to be fatal, not alone protected this animal against the action of the bacilli, but also induced granular degeneration of the latter, and finally their complete solution.

The Pfeiffer Lysogenic Action of the Immune Serum.—After the Pfeiffer school had with certainty demonstrated this "lysogenic" action of the immune serum to be specific, it made the important advance of establishing the procedure, not alone as one important in its bearing on the question of immunity, but also as a most available method of differentiation of micro-organisms, particularly of the typhoid-bacillus from the members of the colon-group, which had hitherto been done by direct culture-methods only with much difficulty, and then not with certainty.

A further noteworthy advance in this direction consisted in the demonstration, inaugurated by earlier investigations of Pfeiffer and his pupils,[2] Metschnikoff,[3] Bordet,[4] and others, that the reaction of Pfeiffer, at first believed to occur only in the body of the living animal, could be obtained also under certain conditions in the test-tube.

The Method of Gruber.—The introduction of the method into practice was effected finally through the important labors of Gruber and his pupils,[5] who furnished evidence that, in the same way as the blood-serum of an immunized animal, that of a human being, after recovery from typhoid fever, brought together with a culture of typhoid-bacilli in a test-tube, soon renders the bacilli immobile and causes them to aggregate in the form of clumps and to be precipitated in the form of a flocculent sediment (agglutination). Pfeiffer and Kolle[6] had, independently of Gruber, obtained similar results.

In the historic consideration of the entire question, it is of importance that Gruber at once emphasized the fact that his method of agglutination established not alone the differentiation of the typhoid-bacillus from similar bacilli, but that it was, furthermore, capable of furnishing, directly from the blood-serum of a human being, proof of the previous existence of typhoid fever; thus, of making the diagnosis subsequently or of confirming it if already made clinically. Therefore to Gruber, and with him to his

[1] *Zeit. f. Hyg. u. Infektionsk.*, Bd. xxi. [2] Issaeff and Ivanoff, *Ibid.*, Bd. xvii.
[3] *Annales de l'Institut Pasteur*, 1895. [4] *Ibid.*, 1895.
[5] *Wien. klin. Woch.*, 1896, Nos. 11 and 12. (Gruber and) Durham, *Proceedings of the Royal Society*, January 3, 1896, vol. lix.
[6] *Deutsch. med. Woch.*, 1896, No. 12.

pupil, Grünbaum,[1] belongs the credit of having called attention to the diagnostic utility of serum-examination.

Although Gruber's method was at first only retrospective, it was elaborated by Widal[2] in so far as he furnished proof that the serum removed exhibited the same agglutinating influence, not alone after recovery from typhoid fever, but also in the beginning and at the height of the disease. Accordingly, it is possible to establish the existence of the disease directly by means of serum-diagnosis, not alone subsequently, but also during its progress.

After Widal's elaboration of the doctrine of Gruber had received abundant confirmation in France (Chantemesse, Dieulafoy, Lemoine, Achard, Catrin, Menetier, and Sinedey, Widal and his pupils), his statements led to the inception of a number of investigations also in Germany.[3] With slight differences in detail, these agreed with the results of Gruber and Widal and contributed materially to the further development and simplification of the method.

The Widal Serum-diagnosis.—The Widal serum-examination as generally practised at present, and as it has been serviceable also in my clinic in a large number of cases, is carried out in the following manner:

Blood-abstraction.—The blood is abstracted either directly from the median vein of the patient to be examined, by means of a sterilized hypodermic syringe or by the application of a cupping-glass after a number of incisions have been made into the skin. Smaller amounts of blood from the tip of the finger, or, better still, from the lobule of the ear, which are quickly sent to the laboratory in a sterile culture-tube of considerable size, are adequate in private practice. The blood obtained is introduced into a narrow test-tube, which is then placed obliquely for sedimentation. If this does not take place completely, so that the serum overlying the blood-clot still contains red blood-corpuscles, this will not interfere with the further investigation, as even dried

[1] *Sitzungsb. d. Wiesbadener Congress. f. inn. Med.*, April, 1896, and the *Lancet*, Sept. 19, 1896.

[2] *Sem. méd.*, 1896, No. 33. Compare also Widal's historic description, *Münch. med. Woch.*, 1897, No. 8. Reports of the remaining French investigations are contained in *Sem. méd.*, 1896, from August to November.

[3] Breuer, *Berlin. klin. Woch.*, 1896, Nos. 47 and 48. Stern, *Centralbl. f. inn. Med.*, 1896, No. 49, and 1897, No. 11. Haedke, *Deutsch. med. Woch.*, 1897, No. 2. C. Fränkel, *Deutsch. med. Woch.*, 1897, Nos. 3 and 16. Jez, *Wien. med. Woch.*, 1897, No. 3. Pick, *Wien. klin. Woch.*, 1897, No. 4. Kolle, *Deutsch. med. Woch.*, 1897, No. 9. Gruber, *Münch. med. Woch.*, 1897, No. 17. Levy and Gissler, *Münch. med. Woch.*, 1897, Nos. 50 and 51. Du Mesnil de Rochemont, *Münch. med. Woch.*, 1898, No. 5. E. Fränkel, *Ibid.*

blood retains its agglutinating power and may be employed in an emergency[1] (Widal, Stern and Förster, Johnston).

Macroscopic Method.—If some of the serum thus obtained is transferred by means of a platinum loop to several cubic centimeters of typhoid bouillon-culture, preferably not more than twelve hours old, in a narrow test-tube, and if the mixture be exposed to a temperature of 37° C., in the course of from three to seven hours the formation of flakes and fragments begins to take place in the previously uniformly turbid fluid, and these soon settle to the bottom. At the end of twenty-four hours this separation of the flocculi from the fluid will be completed, so that the bouillon overlying the crumbling yellowish sediment will have become entirely clear and have regained its original color. Microscopic examination discloses that the sediment consists solely of the degenerated and coherent bacilli.

For the beginner, this test becomes especially distinctive if, together with the inoculated culture, one is prepared to which serum has not been added, and which then, in consequence of the undisturbed and persisting active motility and uniform distribution of the bacilli, retains its primary turbidity.

Microscopic Method.—The macroscopic procedure is useful only as a preliminary test. It is more convenient and more certain to permit the process of agglutination to take place beneath the microscope, when the entire procedure, which takes place in the course of a few minutes, can be viewed in detail and directly. Widal employed this procedure, and in the hands of subsequent observers it has been greatly perfected.

The simplest mode of procedure consists in adding the serum to be tested to a bouillon-culture of from ten to not more than eighteen hours old, and studying the hanging drop. If the serum is derived from a typhoid patient, especially at the height of the febrile stage or a later period, and if a sufficient amount—about an equal part—of serum has been added, the bacilli will be seen immediately after the admixture to become immobile and to collect in clumps of varying size. While the entire field of vision remains uniformly occupied by the swarming bacilli in a control-preparation to which no serum has been added, that to which immune serum has been added exhibits large areas of the visual field that are clear, with the agglutinated clumps collected only in certain places.

[1] Naturally, as will appear from what follows, if dried blood is to be employed for purposes of exact determination, its amount should be measured before it is dried, and before being made use of it should be mixed with an accurately determined amount of physiologic salt solution.

For clinical purposes the microscopic procedure has entirely displaced the macroscopic, especially because it alone is capable of fulfilling the recognized necessary requirement, namely, the determination of the greatest degree of dilution of the serum that in a given case will lead to the occurrence of agglutination.

The Earliest Appearance of the Reaction.—In his earliest publications Widal stated that the agglutinating action of the serum of typhoid patients could be elicited as early as the end of the first week of the disease. Unfortunately, this statement has not been wholly confirmed. On the contrary, it was found with growing experience that the serum acquired that property only in the minority of cases before the termination of the first week, most frequently not until the second week (from the seventh to the tenth day), while rarely it was delayed beyond that time, even to later weeks (Stern, Kolle,[2] Blumenthal[3]). Complete absence of the reaction is one of the rarest exceptions. Among a large number of cases, in only two, which were shown by autopsy to be instances of typhoid fever, have I failed to observe an undoubted reaction. Nevertheless, it should be borne in mind that the absence of agglutination during the first, and even in the beginning of the second week, is not evidence against the existence of typhoid fever, and that in order to obtain reliable results the examination should be repeated also during the further course of the disease at definite intervals of not too great length.

Specificity of the Reaction.—Naturally, the question soon arose whether, as a matter of fact, the blood-serum of typhoid patients alone possessed the agglutinating influence on the typhoid-bacillus, and, if this be not the case exclusively, whether this property might not be possessed exceptionally and in lesser degree by serum from other patients suffering from other diseases. It was soon found that the reaction occurs even during health (Stern[4]) and in the presence of a number of diseases, apparently especially in acute infectious diseases, so that for a time the diagnostic value of the procedure appeared to be diminished by this fact. On further investigation, however, it was found that under these conditions the reaction takes place only when comparatively large quantities of the serum to be examined are added to the culture.

Since Widal's first publication thousands of examinations have been directed to this point, and all have yielded approximately like results. It has been found that the occurrence of agglutination with equal parts of

[1] *Centralbl. f. inn. Med.*, 1896, No. 49.
[2] *Deutsch. med. Woch.*, 1897, No. 9.
[3] *Ibid.*, 1897, No. 15.
[4] *Centralbl. f. inn. Med.*, 1896, No. 49.

serum and culture, even one of serum to ten of culture, is of itself not conclusive of typhoid fever; and further, that the development of the reaction with a dilution of one to twenty, even one to thirty and one to forty, may also occur under other conditions; while a positive reaction with a dilution of the serum beyond one to forty occurs almost exclusively in cases of typhoid fever.[1]

Gruber and Grünbaum[2] and Stern[3] were among the first to direct attention to this distinctively important aspect of the question; and, after them, especially Breuer, C. Fränkel, Du Mesnil, and Förster.[4] That also mixtures above 1 : 20 up to 1 : 40 are not certainly indicative of typhoid fever has been shown especially by van Ordt,[5] Kühnau,[6] Ziemke,[7] Scheffer,[8] and others. According to my own observations, such high dilutions of the serum are but rarely effective in the presence of other infectious diseases.

Stern[9] had previously published the exact results of examinations in 70 cases of other diseases, and subsequently, in conjunction with Sklower,[10] in 100 cases. Among the latter there were: 25 in which a response to 1 : 10 was obtained; 10 in which a response to 1 : 20 was obtained; 2 in which a response to 1 : 30 was obtained; 1 in which a response to 1 : 40 was obtained.

Diagnostic Significance of the Quantitative Relations of Serum and Culture.—From the foregoing the important conclusion can be drawn that the diagnostic utility of the Gruber-Widal reaction is dependent, above all things, upon a careful consideration of the quantitative relations. The smaller the amount of serum necessary for the development of the reaction, the more certain is the diagnosis.

Thus it has been found, on further study of the condition, that at times the reaction may be obtained with almost incredibly high dilu-

[1] The methods for the exact preparation and the quantitative determination of the mixture of serum and culture cannot be fully described here, but they must be learned practically. The directions are carefully stated by A. Fränkel, *Berlin. klin. Woch.*, 1897, No. 11, and by Stern, *Centralbl. f. inn. Med.*, 1896, No. 49. The latter obtained especially delicate results, which, however, are not necessary for clinical purposes, with the aid of the capillary pipet of Gowers. It may be mentioned here that quite accurate results, quite sufficiently so for clinical purposes, may be obtained by the use of small glass capillary pipets, manufactured by drawing out small pieces of ordinary glass tubing in the flame. One or more drops of the serum are dropped from one of these pipets into a dish, and then from the same pipet a sufficient number of drops of sterile water or salt solution are added to make a dilution of one-half the required degree. If, then, with the platinum loop one drop of this mixture be added to one drop of the bouillon-culture obtained with the same platinum loop, a quite accurate dilution is obtained. This method has been in use at the Johns Hopkins Hospital and has proved quite satisfactory. The other methods, as well as a complete discussion of the whole procedure and a review of the literature, have been given by Cabot in his book, "The Serum-diagnosis of Disease."

[2] *Loc. cit.* [3] *Loc. cit.* [4] *Zeit. f. Hyg. u. Infektionsk.*, 1897, Heft 3.
[5] *Münch. med. Woch.*, 1897, No. 5. [6] *Berlin. klin. Woch.*, 1897, No. 12.
[7] *Deutsch. med. Woch.*, 1897, No. 15. [8] *Berlin. klin. Woch.*, 1897, No. 11.
[9] *Loc. cit.* [10] *Diss.*, Leipsic, 1898.

tions—1 : 3000 or 5000, and in a case of Widal's, even 1 : 20,000. For clinical purposes such dilutions are wholly unnecessary. Generally, I confine myself to dilutions of from 1 : 60 to 1 : 100, and after abundant experience I have every reason to be satisfied therewith. Nevertheless, I have frequently seen the reaction occur with dilutions of from 1 : 400 to 1 : 600 and above, often even when the reaction occurs within a short time. The **time elapsing before the reaction occurs,** as just mentioned, is an equally important factor in the diagnostic employment of the reaction. The shorter the action of the serum, in order to obtain a complete reaction, the more certain is the diagnosis, even when low dilutions are employed.

As a result of the foregoing, the principle has in the course of time developed in the clinical application of the method of dispensing with higher dilutions and demanding instead proportionately greater rapidity in the onset of the reaction. If, as happens so frequently, cessation of motility and aggregation in clumps take place with lightning-like rapidity on addition of the serum, a diagnosis of typhoid fever may be made with great probability when dilutions of 1 : 30, often even with dilutions of 1 : 20, are employed. With dilutions of from 1 : 40 to 1 : 50 error will, according to my experience, rarely be committed. Should the reaction not occur at once with such dilutions, the observation should be continued for a longer time, and, with a view to greater certainty, with the further addition of serum (lesser degrees of dilution).

In his admirable paper upon the sources of **error in serum-diagnosis,** Stern[1] suggests a continuation of the observation for as long as two hours, with progressively increasing dilutions. Although this has yielded him important results, such a period of observation is, according to our experience, no longer necessary for clinical purposes, in view of the present methods and the skill usually possessed by the observers. In my clinic our observations do not, as a rule, extend beyond from fifteen to thirty minutes, and they are made, as seems to me quite sufficient, at room-temperature. That the procedure of Stern may be employed in cases in which a decision is of especial importance is a matter of course.

It seems quite important that some definite rule be made in regard to dilution and time limit which should keep in view the widest possible application of the method to clinical purposes and yet carefully guard against errors. For several years at the Johns Hopkins Hospital a standard of dilution of 1 : 50 and a maximum time limit of one hour have been employed and have given complete satisfaction. It is required that complete agglutination be obtained within these limits,

[1] *Berlin. klin. Woch.*, 1897, No. 11.

in order that the reaction be considered positive. While with these standards it quite commonly occurs that a positive reaction is not obtained until late in the disease, if, on the other hand, they were made any less rigid, experience has shown that occasionally a positive result would be obtained in cases not typhoid.

Among the sources of error in serum-diagnosis, the important observation should, in conclusion, be considered that the agglutinating action of the serum may persist for months and even years after recovery from the attack of typhoid fever (Lichtheim, C. Fränkel, Stern). As a result, it might happen that in the case of a patient not suffering from typhoid fever, but exhibiting fever from some other cause, the Gruber-Widal reaction occurring in consequence of an antecedent but not existent attack of typhoid fever might lead to error. The possible defence that the history would afford protection from such an error is invalidated by the fact that mild cases of typhoid fever which yield the reaction equally with severe cases, not rarely remain doubtful or wholly unrecognized.

Prognostic Significance.—Finally, an effort has been made to ascribe to the serum-reaction a prognostic, as well as a diagnostic, importance, inasmuch as Catrin [1] believed that he observed a direct relationship between the rapidity and the intensity of the Widal reaction and the severity of the individual case. This statement has already been contradicted by Stern, with whom I am disposed to agree as a result of personal experience.

[1] *Sem. méd.*, 1896, No. 62.

IV. THE PROPHYLAXIS OF THE DISEASE.

THE measures for the prevention of the disease may be divided into three main groups:

1. General, which are directed to the protection of the inhabitants of entire districts, cities, or less extensive collections of dwellings, against the disease; or, if it has developed, to prevent its dissemination.

2. Special individual measures, by means of which the immediate or mediate transmission of typhoid fever to those who come in contact with the patient, or even to remote distances, is prevented.

3. Preventive inoculation, by means of which an attempt is made to render the person inoculated immune to the disease.

For the principles underlying the following statements reference should be made to the chapter on Etiology, and particularly to the concluding sentences thereof (pp. 77, 78).

GENERAL MEASURES.

By reason of the ubiquity of typhoid fever, the persistence of its exciting agent, and the character and the activity of intercourse at the present day, the danger of the dissemination of the disease by the sick or by intermediary agents, especially infected articles—beverages, articles of food, linen, articles of clothing, etc.—cannot wholly be prevented. In almost all places of considerable size, even in those with the best sanitary administration, the disease, at least with regard to individual, undoubtedly in part imported, instances, never becomes wholly extinct. In view of the impossibility of preventing this, the principal effort of public sanitation should be directed, by means of intelligent and adequate measures, to the restriction of the preservation and dissemination of the exciting agent emanating from the patient.

REGULATIONS OF THE SEWAGE-CONDITIONS.

By far the most important general measure is the appropriate regulation of the sewage-conditions and the provision of a hygienically unobjectionable and abundant water-supply. That public attention should also be given to the maintenance of the greatest possible degree of salubrity of the dwellings and their surroundings, as well as hygienic supervision of the community in general, is a matter of course, and will be referred to in detail subsequently.

The removal of refuse from inhabited places has in view, in accordance with present conceptions bearing on the prevention of typhoid fever, the certain removal of the germs derived from typhoid patients, and thus their withdrawal from any direct or indirect influence upon healthy persons. In addition to the urine and the stools, refuse water especially is to be taken into consideration in this connection. Above all other things, care should be taken that none of these are permitted to remain in badly devised, pervious cesspools and dung-pits in the neighborhood of human habitations, or is conveyed to adjacent unused land or gains entrance into gutters, or even into water-ways which serve directly as a source of the water used by the community for drinking and for domestic purposes.

In accordance with the size and particular conditions of a city, the arrangements for the drainage may be variable. While this can generally be secured in large cities only by means of appropriate flush-sewers with irrigating fields, less commonly by conveyance into large water-courses, for smaller and the smallest cities the provision of a combination of removal and flushing systems (separation of the solid and liquid refuse matters and removal in various ways), or even the tun-system or the pit-system, will be entirely adequate.

WATER-SUPPLY.

Almost still more important, in combination with the system of sewage adapted to the local conditions, is the provision of an abundant supply of unobjectionable water. It has already been seen that water, in the various forms in which it is employed—as drinking-water, as an addition to articles of food and beverages, and as used for cleansing purposes on a large scale—constitutes by far the most common medium for the dissemination of the disease which needs to be taken into consideration. Of how little service even the best system of drainage and sewage and the resulting purification of the soil may be, when it is associated with an unsuitable and directly injurious water-supply, has been shown by the events at Hamburg previously mentioned (pp. 44, 45).

An important requirement of a really good water-service is an uninterrupted supply, in such abundance that if possible a distinction need not be made between drinking-water and less reliable water for domestic purposes. Apart from the fact that abundant opportunity for infection is afforded through water used for domestic purposes (cleansing, rinsing, washing, and bathing), the prevention of its use for drinking purposes appears practically entirely illusory. In the determination of the character of water from an epidemiologic standpoint, biologic examination is of great direct, and chemic examination of rather indirect,

significance. The latter furnishes the chemic basis for the suspicion of organic contamination, while by means of the former the presence of bacteria in general in the water is established, and even at times the demonstration of typhoid-bacilli can be directly made.

In order to provide an irreproachable supply of water for drinking and domestic purposes it will be necessary, in case it shall be obtained from wells, that the excavation shall be sufficiently deep, and that the walls, particularly in the upper portions, shall be rendered impervious to the entrance of infected water from the upper layers of the adjacent soil by means of suitable masonry and cementing.

The water derived from springs—of as deep a source as possible—should be conveyed through impervious tubes directly to the place where it is used with all practicable avoidance of contact with the external world. Especial care should be directed to the certainty of imperviousness of the conduits for spring-water, from the prophylactic standpoint, and naturally, also, in connection with epidemiologic investigations. Water that is primarily the best, if not adequately protected in the course of its distribution, may become a source of danger owing to contamination from its surroundings—pits, infected superficial layers of soil, direct communication with cesspools, admixture of rain-water and melted ice and snow, and all other possible sources of accidental contamination. The history of typhoid fever exhibits a large number of smaller and larger epidemics developed in this manner (pp. 42, 43).

When the water-supply of a place must be obtained from open waterways, rivers, brooks, or from seas and ponds, the water, before being admitted into the dwellings, should be, in its entirety, subjected to trustworthy processes of filtration that can be constantly controlled biologically and chemically. The introduction of unfiltered water into cities, with dependence upon subsequent sterilization in the houses, is absolutely untrustworthy, as numerous examples, especially again that of Hamburg, have shown. It has already been seen how uncertain and serious may become the question of house-filters, and how they not rarely are actually a cause for further pollution of the water. If the use of suspected water is absolutely not to be avoided, boiling and preservation in clean vessels should be practised. This applies not only to drinking-water, but to all water employed, particularly that used for rinsing, bathing, and washing. The use of artificial mineral waters in suspicious places and in times of epidemic will be serviceable only when there is certainty that they have been prepared from sterile water, and that thorough cleansing of the bottles has been practised. That the addition to infected water of tea, coffee, or alcoholic beverages in ordinary amount cannot materially improve matters has long been known. Typhoid-bacilli may retain their vitality even in ice, as has been pointed out, for a considerable length of time—a circumstance that is well calculated to enjoin caution in the employment of ice.

The degree to which the prevalence of typhoid fever may be lessened by proper drainage and a suitable water-supply was shown first by the experiences in England, to which were soon added those of France and Germany. In German cities that formerly suffered seriously from typhoid fever—for instance, Munich—the disease has at the

present day almost wholly disappeared. The enormous influence exerted especially by a good water-supply has been demonstrated in France by the experiences with regard to the mortality from typhoid fever in the army and in the civil population.[1] The most convincing example in Germany is furnished again by Hamburg (see p. 45).

FOOD AS A SOURCE OF INFECTION.

That, in addition to the water, most careful attention should be given especially to fluids employed as food will be evident from previous statements. The first place in this connection is occupied by milk, which, as numerous exact investigations have shown, may be a source of infection from intentional or accidental addition of infected water. Also, the articles of food derived from it—butter, cheese, whey, etc.—have properly received great attention recently from the prophylactic standpoint. How readily still other articles of food, especially if eaten in an uncooked state, such as fruit, salad, etc., may be infected by the contaminated hands of the dispenser, by rinsing and sprinkling with water containing germs, and by other manipulations, will require no further elaboration. Sanitary officers should, far more than they have done in the past, devote attention to the commercial pursuits involved in this connection, such as dairies, restaurants, fruit-stores, etc. To adopt prophylactic measures in this connection, and to inquire into details, appear to me far more important than the still quite customary fruitless examinations of soil and ground-water.

PROPHYLAXIS WITH RELATION TO THE INDIVIDUAL.

In this connection those measures should be considered through which the dissemination of the developed disease from the patients to those by whom they are surrounded, and from these to more remote persons, is to be prevented. The underlying principle of the measures in question may be expressed in two sentences:

1. The only infective agent consists in the typhoid-bacilli which are reproduced by the patient and are extruded especially with the stools and urine.

2. Residence in the immediate neighborhood of the patient, in the same house, or upon the same floor and soil, is, in itself, absolutely innocuous, even for predisposed persons, if it is possible to protect them from the ingestion of bacilli, which takes place by far the most frequently in contaminated food and beverages.

It therefore follows that patients are to be so taken care of and

[1] See Chantemesse, *Abdominaltyphus*, p. 737.

their discharges are to be so treated that they shall not be a source of injury to others. The patients should, so far as practicable, be removed from crowded dwellings and from surroundings that do not permit of satisfactory isolation from those about them, and they should be sent to the hospitals. Should they remain in private dwellings, a number of measures that would be matters of course in a hospital should be rigidly pursued, but with appropriate modifications.

Treatment at Home.—In treatment at home one of the essential principles consists in the **provision of nurses and assistants** sufficiently informed with regard to the character of the infection and its mode of prevention. Those who do not assist in the care of the patient are to be removed from his vicinity, or at most must be permitted to be present for short visits only, avoiding direct contact with the patient. The nurses and attendants must bear scrupulously in mind the fact that the poison contained in the discharges of the patient may for a considerable time adhere in an active state to all possible articles, from which it may be transmitted directly or be conveyed for great distances. It is not less important for them to know that patients with mild and ambulatory attacks, as well as healthy persons, may, under certain circumstances, act as the carriers and disseminators of the virus.

Of the more important details, **the arrangement of the sick-room** may especially be referred to. It should not be too small, should be susceptible of ventilation, and situated so that as much quiet as possible can be secured. Unnecessary articles should be removed, and this applies especially to rough woollen articles, counterpanes, carpets, and upholstered furniture. In addition to the sick-bed proper, a second bed, if possible, should be in readiness for change.

Disinfection of the Stools.—The dejections of the patient, especially the stools, are best received in porcelain bed-pans or glass vessels (which, in the hospital, should be reserved for this particular purpose). Before being thrown into the water-closet, thorough disinfection, preferably with milk of lime, should be practised.

This is to be preferred to all other disinfectants on account of its cheapness, certainty, ease of application, and convenience to the attendants and the family. In detail, care should be taken that the bottom of the bed-pan be covered with milk of lime before each evacuation, and that after the bowels have moved, the stool be thoroughly admixed with an equal amount of milk of lime. In hospitals provided with a good system of flushing and drainage the dejections thus treated may be thrown at once into the closet, while in private practice it is advisable to permit the admixture first to stand for an hour. In addition, rigorous supervision and disinfection of the closet itself are necessary. The seat, the basin, and the pipes should be treated daily with milk of lime, and similar care should be devoted to the

floor. When, instead of a flushing system, there is a tun-system or pit-system, disinfection of the contents of the pit is also necessary—the addition daily of from 100 to 150 grams of milk of lime for each individual being considered sufficient. That thorough rinsing and cleansing of bed-pans and glass vessels should be effected regularly, best with a solution of lysol, may be considered almost as a matter of course. In this connection attention should be given especially to the exterior of the vessel and its handle, contact with which might otherwise readily result in infection of the hands of the attendants. In addition to milk of lime, carbolic acid, and lysol, mercuric chlorid is also applicable, on account of the relatively small amount of mucus and albumin contained in the typhoid dejections.

The reliable action of milk of lime depends upon its proper preparation. It should be employed in as freshly prepared a state as possible—at any rate not after it is older than three days. It is best to prepare the necessary amount daily, the slaked lime being mixed with from two to four times the amount of water. It should then be preserved in closed vessels.[1]

In France disinfection with copper sulphate is much employed, especially upon the recommendation of Vincent.[2] The fecal discharges are mixed with an adequate amount of a 5 per cent. solution, to which, besides, 1 per cent. of sulphuric acid is added. In Germany the method has not, to my knowledge, been employed upon an extensive scale, and I have no personal experience with it.

Disinfection of the Urine.—In view of the great frequency with which typhoid-bacilli are found in the urine of typhoid patients, often in immense numbers (see p. 34), the extreme importance of careful disinfection of all such urine will be apparent. Gwyn[3] has made a careful experimental study with reference to the best methods by which this can be carried out. He concludes that milk of lime hardly deserves the name of a disinfectant in this connection. Carbolic acid is of use only in large amounts and strong solutions if a speedy result is wished. Formalin is an excellent disinfectant, but is too expensive. Bichlorid of mercury, chlorinated lime, and liquid chlorids are of real value, are rapid in their action, and are efficient in comparatively dilute solutions. He has found that for disinfection within five to fifteen minutes, one volume of urine would require one-twentieth to one-tenth of its volume of 1 : 1000 H_9Cl_2 solution.

In view of the excellent results obtained by the use of urotropin in cases of typhoid bacilluria, Richardson has advised the routine administration of this drug in the latter periods of the disease as a preventive

[1] For particulars with regard to disinfectants and methods of disinfection, reference may be made to an article by E. Pfuhl, *Zeit. f. Hyg. u. Infektionsk.*, Bd. vi., vii., xii.

[2] *Annales de l'Institut Pasteur*, 1895. [3] *Johns Hopkins Hosp. Rep.*, vol. viii.

and prophylactic measure. Probably 5-grain doses given three times a day are sufficient for this purpose. It should be mentioned, however, that several cases of hemoglobinuria following the continued use of this drug have been reported.

The **disinfection of the sputum** may be accomplished by the use of milk of lime or solutions of carbolic acid or lysol.

In addition to the secretions and excretions of the patient, the greatest attention should be given to many other things that come in contact with him. Thus, **wash-water and bathing-water** and also **remnants of food** from the typhoid patient should not be thrown away without previous disinfection with milk of lime. Careful attendants will of themselves see that the patient is provided with special plates, glasses, and eating utensils. Especially important is **disinfection of the bed-linen and the body-linen,** and any other articles of clothing used by the patient, as well as his napkins and handkerchiefs.

In order to avoid unnecessary throwing about and repeated manipulation, the articles in question are best kept in (not water-tight) sacks, and these in turn in porcelain, earthenware, or zinc vessels that can be closed and are partly filled with a 3 per cent. solution of carbolic acid. The linen thus not completely disinfected is first subjected to sterilization in hot steam or by boiling in soap-water, with addition of soda or petroleum (Gärtner), before being given to the laundress, and only then submitted to the remaining processes of washing.

At the termination of the disease the beds are to be thoroughly disinfected. Wooden bedsteads are carefully cleansed with a 5 per cent. solution of carbolic acid or lysol, while iron bedsteads are treated by steam sterilization. Mattresses, blankets, and pillows also are disinfected by steam. When steam-disinfection is not available, mattresses and pillows are emptied, and both covering and contents are disinfected by boiling. Valueless articles of bedding—straw-sacks, husk-pillows, etc.—had better be burned directly.

The **bodies of those dead of typhoid fever** are by no means so dangerous with regard to the dissemination of the disease as was formerly thought under the influence of the putrefactive theory. Cleansing and covering the buccal, nasal, and anal orifices with gauze dipped in milk of lime or carbolic solution would be likely to suffice, as a rule. If especial care is to be exercised, particularly in the matter of distant transportation, the body, without previous washing, should be enveloped in cloths saturated with carbolic solution or milk of lime.

Disinfection of the Sick-room.—That the bedroom should receive most careful attention during and after the attack is a matter of

course. After it has been vacated by the convalescent patient, the wall against which the bed stood should be rubbed down with bread, or, should its covering tolerate moisture, it should be treated with a 5 per cent. solution of carbolic acid and soap. Furniture used by the patient, especially the bedstead and chairs, and the floor, should be disinfected in the latter manner. If the floor is not painted, it will be better to employ milk of lime. The cracks between the boards should receive particular attention. The disinfection of rooms not occupied by the patient and kept from contact with his dejections is unnecessary. In private practice, especially under conditions amid which the methods of cleansing cannot be sufficiently depended upon, it is advisable, after emptying the room, to undertake, besides, disinfection with the vapor of formalin.

Especially important also in connection with prophylaxis is **the maintenance of cleanliness on the part of the patient himself,** of his skin in general, particularly about the mouth and the anus, and his hands. Particular attention should be directed especially to the latter. If this is not done, the patient may readily convey infectious material to various utensils, articles of food, etc., and thus become a source of danger not only for those immediately about him, but for others at a greater distance. The **attendants** must, for the same reason, devote the most scrupulous care to their hands. I am convinced that not a few cases of auto-infection and of dissemination are attributable to carelessness in this connection.

The disinfection of the hands should be practised according to the rules observed by surgeons, namely, thorough washing and brushing with soap and water, followed by prolonged immersion in mercuric-chlorid solution, giving proper attention to the nails and the space beneath them. In hospitals, in this connection, too careful supervision of the nurses, particularly those of short experience, cannot be exercised.

Further, **physicians and nurses** in attendance upon typhoid patients should be provided with clothing that can be washed, and at the end of their service, especially before going to their meals, they should change their clothing. In hospitals it is advisable, in case typhoid patients are cared for in the same ward as others, to provide but one nurse for their care, and to keep others, particularly those who are concerned in bringing the food, attending to the cleansing in general, and the care of the remainder, as strictly as possible apart from the typhoid patients. When typhoid fever occurs in boarding-schools, barracks, jails, and institutions in general, especially those containing young persons in considerable number, immediate isolation of the patients, preferably removal from the house, is necessary. Prophylactic

measures would, under such circumstances, be susceptible of application only with difficulty and uncertainty.

Preventive Inoculation.—In addition to the prophylactic measures above discussed, which aim especially at the prevention of the further spread and dissemination of the virus, there has lately been introduced a measure directed toward the production of an artificial immunity in the individual.

Following the work of Haffkine in vaccination against cholera, Wright, of Netley, has introduced a similar method of vaccination against typhoid. The material used is a bouillon-culture of Bacillus typhosus of high virulence, heated until all organisms are dead. The amount inoculated should "be such a quantity which, if injected alive, would be fatal to a 350 gm. guinea-pig." The inoculation is followed by local tenderness and congestion, faintness, possibly nausea, fever, and restlessness. Usually, all symptoms have disappeared after twenty-four hours. It is recommended that the procedure be repeated in two weeks. Following the injection there is an increase in the bactericidal power of the blood, and also a very marked increase in the agglutinating power, which may persist for at least two years, as in cases reported by Foulerton. This procedure has been tried on a large scale in India, and also in the South African war. Full statistics from South Africa are not yet available, but out of 1705 persons inoculated at Ladysmith, only 2 per cent. were attacked; whereas of 10,529 not inoculated, 14 per cent. were attacked, and of those inoculated the mortality was 0.46 per cent.; of those not inoculated the mortality was 3 per cent. On the whole, the experience so far is strongly in favor of inoculation. Such a method is naturally most applicable in the case of persons going into a district where the disease prevails, or in the case of armies or other large bodies of persons likely to be attacked by an epidemic of typhoid fever.

V. TREATMENT.

OBSERVATIONS ON SPECIFIC TREATMENT.

We are yet far removed from a specific treatment of typhoid fever, *i. e.*, a method capable of destroying its exciting causes, the typhoid-bacillus, in the human body and preventing its dissemination, or at least of neutralizing or attenuating the activity of its toxins, although a number of recent observations stimulate earnest investigation in this direction.

Serum-treatment.—If those of less experience believed that after Behring's ingenious discovery of the action of the diphtheria-serum the production and the application of a "typhoid serum" would also prove convenient and inexpensive, they reasoned without sufficient foundation. Conclusions by analogy and hopes based upon them are especially deceptive in the clinical and bacteriologic field, and the difficulty and the peculiarity of the conditions attending typhoid fever especially have recently been again demonstrated by investigations into the phenomenon of agglutination and its relations to immunity. Valuable preliminary investigations on the subject of serum-treatment have been made by Chantemesse and Widal,[1] and especially by Stern,[2] and these were followed by Hammerschlag [3] and von Jaksch,[4] with investigations into the therapeutic activity of the serum of convalescents from typhoid fever, as well as by Beumer and Peiper,[5] Klemperer and Levy,[6] with attempts to treat typhoid fever with injections of the serum of immunized animals (calf or dog).

Although these observations have disclosed a limited influence of the immune serum upon experimental typhoid intoxication, a therapeutic result with reference to typhoid fever has not as yet been made out, and this could scarcely be expected to be otherwise, in view of the entire difference of the experimental typhoid infection from typhoid fever in human beings. Hardly more than the innocuousness of such attempts has been demonstrated. The attempts of Rumpf[7] to treat typhoid fever with dead cultures of Bacillus pyocyaneus, based upon the therapeutic experiments of E. Fränkel with cultures of dead typhoid-bacilli, have received little imitation, and their results have not yet been confirmed.[8]

Even at an early period, when only indefinite conceptions existed as to the nature of the typhoid virus, certain methods of treatment were employed that may be considered among the specific. Among these may be included the early attempts to cause an increased number of

[1] *Ann. de l'Institut Pasteur*, 1892.
[2] *Deutsch. med. Woch.*, 1892; and *Zeit. f. Hyg. u. Infektionskrank.*, 1894, Bd. xvi.
[3] *Deutsch. med. Woch.*, 1893.
[4] Pollak, *Zeit. f. Heilk.*, 1897, reprint.
[5] *Zeit. f. klin. Med.*, 1895, Bd. xxviii.; and *Verhandl. d. XIII. Cong. f. inn. Med.*
[6] *Berlin. klin. Woch.*, 1895.
[7] *Deutsch. med. Woch.*, 1893, No. 41.
[8] Presser, *Zeit. f. Heilk.*, Bd. xvi.

stools by means of purgatives, and thus to effect elimination of the typhoid virus from the intestine. Closely related to these were certain methods of treatment that, going a step further, were directed toward neutralizing abnormal putrefactive processes in the intestine, which were considered as the essential feature. These represented the first attempts at **intestinal antisepsis.** In this category belong, undoubtedly, the treatment by **internal administration of chlorin-water,** formerly much practised, the transitory employment of **carbolic acid** and **benzoates,** and the **iodin-potassium-iodid treatment,** warmly recommended by Sauer and Magonty, and still defended in the year 1866 by Willebrand.[1] While these methods possess only historic interest at the present day, a method undoubtedly allied to them, namely, the treatment with **calomel,** still has ardent advocates among the most distinguished living physicians (Liebermeister, von Ziemssen).

Lesser,[2] and after him Schönlein, Traube, and Wunderlich, undoubtedly sought to obtain with the remedy not simply a purgative effect, but also a specific, locally curative, possibly also antitoxic, action upon the intestinal mucous membrane. It was believed that these effects were most manifest at the commencement of the disease, and were capable of inducing an abortive termination, or at least considerable mitigation of the intensity of the disease.

The method of employment still recommended by the advocates of the remedy places the greatest importance upon its administration at the earliest possible period of the disease, at all events before the end of the ninth day. Only a small number of physicians believe that the remedy has proved useful also after the second week of the disease. Doses of 0.5 gram are administered at intervals of one or two hours, generally three or four in the twenty-four hours, at the beginning of the disease (Liebermeister). Liebermeister believes that treatment with calomel induces a marked mitigation in the intensity of the disease, while von Ziemssen, going somewhat further, attributes to the remedy an influence in diminishing the intensity of the whole infectious condition, and especially of the local intestinal symptoms. In view of the experience of these two trustworthy writers I am unwilling to advise against the employment of the method in suitable cases, but would emphatically state, with Bäumler and Weil, that I have been unable to convince myself of its abortive and abbreviating effect. What I have observed was an increase in the number and a greenish discoloration of the stools, often with transitory depression of the temperature, which, however,

[1] *Virchow's Archiv*, Bd. xxxiii.

[2] *Die Entzündung und Verschwärung der Schleimhaut des Darmkanales*, etc., Berlin, 1830.

could be considered as a result of the diarrhea itself, and not as a specific effect of the drug.

Undoubtedly, too little consideration has been given to the fact that the abortive course of cases of typhoid fever in which calomel has been administered at the outset might just as well be attributed to the nature of the case as to the treatment employed. The large number of cases of typhoid fever pursuing a mild and short course, even when the onset has been severe, as well as the fact that this number may at times be greatly increased without apparent cause, should be kept in mind, and especially it should not be forgotten that it is impossible in the first days of the disease to foresee the character of its subsequent course. That, however, the calomel treatment, even if included among disinfectant methods, is, like all others of its class, without sufficient theoretic foundation, will shortly be shown.

The earlier endeavors in the works of Rossbach[1] and Bouchard[2] with regard to systematic intestinal antisepsis have recently been taken up anew in accordance with modern views and methods. They aim at the introduction into the intestine of bactericidal remedies in amount and form capable of destroying the typhoid-bacilli in this situation, or at least of inhibiting their development and dissemination. Rossbach recommended for this purpose especially the employment of naphthalin; while Bouchard employed a series of remedies successively—in addition to naphthalin, α-naphthol and β-naphthol, iodoform, salol, calomel, and combinations of several of these remedies or in combination with others, as, for instance, naphthol with bismuth salicylate. The methods have hitherto received little imitation in Germany, while Bouchard in France has numerous, in part enthusiastic, disciples. I have personally made but few observations with the method of Rossbach, which has a frail foundation. I have not ventured to follow the more precise directions of Bouchard. His method requires as an introductory measure the administration of 15 grams of magnesium sulphate every third day, calomel in small doses for general antisepsis for four days, and, finally, daily doses of 4 grams of naphthol with 2 of bismuth salicylate.

It would take us too far to enter fully into the scientific aspects of the method of treatment in question. In this connection I would refer especially to the admirable investigation of Stern,[3] which led experimentally, practically and theoretically, to negative results. Also, Fürbringer,[4] who properly calls attention to the extraordinary variations in the number of bacteria present in the stools during health, was unable to convince himself that the introduction of antiseptic substances into the intestine was capable of effecting any difference greater than the physiologic one. An especially severe blow,

[1] *Verhandl. d. Cong. f. inn. Med.*, 1884.

[2] *Leçons sur les autintoxic*, Paris, 1887; and *Therapeutique des maladies infect. antisepsis*, Paris, 1889.

[3] *Volkmann's Sammlung klin. Vorträge*, N. F., No. 138; and *Zeit. f. Hyg. u. Infektionsk.*, 1892, Bd. xii.

[4] *Deutsch. med. Woch.*, 1887.

finally, was inflicted upon the doctrine of intestinal antisepsis by the recent observations of Fr. Müller,[1] who demonstrated conclusively its impracticability in healthy and diseased human beings with measures available at present. Even though it were assumed that there existed a procedure capable of injuring the pathogenic micro-organisms in greater degree and more permanently than their hosts, it would have little value on account of the relations of the typhoid-bacillus to the intestine and its contents, particularly in cases of typhoid fever. It is known that even at a time when the disease does not generally come under observation for treatment, even often when the clinician has as yet no knowledge of its existence, the bacilli have already passed from the intestines into the follicles, the mesenteric glands, and more distant organs, especially the spleen, where, naturally, they are no longer accessible to antiseptic remedies.

It is therefore justifiable for the present to assume a doubtful attitude toward the antiseptic method, and even one of skepticism with regard to the hope that it may in future prove more successful.

For the present, and probably for a long time, the successful treatment of typhoid fever will have to be pursued in some other direction. The principal factors in treatment are, therefore: (1) The general appropriate care and regulation of the condition of the patient, especially in a dietetic direction; (2) The treatment of a number of important manifestations and symptom-groups, of complications and other dangerous accidents, and, finally, that which is so important, supervision of the period of convalescence.

NURSING AND DIET.

Nursing.—The typhoid patient should, as a matter of course, be kept in bed throughout the entire duration of the febrile state, and beyond this into the period of convalescence. Although now and again ambulatory cases pursue a mild course, others, however, are attended with such profound manifestations and are so frequently followed by severe, even repeated, relapses and unusually protracted convalescence, that one cannot escape the impression of the highly injurious influence of an ambulatory course.

Patients whose circumstances offer no assurance of adequate care at home should promptly be sent to the hospital. The **management of a case in a private house** requires strict regulation of external conditions. Provision for the utmost physical and mental repose on the part of the patient, and order and discipline in the sick-room, are unconditional requirements. These can generally be attained only through well-trained nurses. When the care of the patient must exceptionally be placed in the hands of the immediate relatives, only a few

[1] *Verhandl. d. Cong. f. inn. Med.*, 1898.

of these should be entrusted with these duties, and these should, during the period of their activity, be separated from the other occupants of the house and from those employed in the household, particularly in the kitchen.

The sick-room should be as large as possible, situated in a quiet quarter, and easily ventilated. The best room in the house is just good enough. The temperature of the room should not be above 12° or 14° C. During favorable periods of the year the windows should be kept open day and night, and even in winter a thorough airing should be practised several times daily. In hospital practice, and whenever possible also in private practice, I have the patients during the summer lie for hours in the open air, with suitable protection from sun and rain. Glaring light, and also especial darkening of the sick-room, are to be avoided. Very unusual articles, decorations, figures, pictures, and the like, about which the phantasies and the delirium of the patient readily revolve, should be removed.

The **sick-bed**—making allowance as far as possible for the previous habits of the patient—should in any event not be too warm, and should be readily changed and rendered clean. Those severely ill should be promptly placed upon a water-bed. The sheets, which should be changed whenever soiled in the slightest degree, should not be too coarse in texture, and never wrinkled, on account of the danger of bed-sores. For the same reason immediate contact of waterproof sheets with the body should be avoided. While at the commencement of the disease quiet recumbency in the dorsal decubitus is the most natural and the most advantageous, at the height of the disease and toward the end of the febrile stage change of posture should be encouraged, and, especially for the prevention of pulmonary hypostasis, frequent alternation of the dorsal with the lateral decubitus. Evacuation of the bowels and the bladder should take place exclusively in the recumbent posture even into the period of convalescence. Also, when the bed is changed, the patient should not sit up, but always remain in the horizontal posture—preferably in another bed. Many a case of fatal collapse could have been avoided by the observance of these precautions.

That in maintaining strict **cleanliness of the body** attention to the dorsal, sacral, and anal regions plays a special *rôle* is a matter of course. Neglect in this respect, in conjunction with defective conditions of the bed, leads to the development of bed-sores, which are but rarely dependent upon the nature of the disease, but almost always upon deficiencies in nursing. Especial consideration should be given to the mouth, the lips, and the teeth of the patient. Frequent, thorough

cleansing, especially after the ingestion of food, frequent moistening of the lips, and the frequent proffering of small quantities of fluid, are indispensable. A well-nursed patient may only temporarily exhibit dry tongue and lips, and never a fuliginous deposit. In women great care should from the outset be given to the hair, which should be combed, under some circumstances cut short, or preferably be worn in a net.

Diet.—With regard to few **points in connection with typhoid fever** is there at the present day such satisfactory agreement as with regard to the dietetic management, of which the principles can be considered as fully established. The problem presented to the physician and demanding tact and discrimination consists in adapting these principles to the needs of the individual case. In general, the difficulties and peculiarities in the nourishment of typhoid patients are to be looked for in two directions: in the conditions attending the infective or the febrile state, and in those associated with the local changes induced by the typhoid process, particularly in the intestine.

The manifestations of the toxic action, particularly the febrile condition, are attended with profound metabolic disturbances, among which the active destruction of the body-proteid plays an important *rôle*. It is the most important problem in dietetic treatment to shield the proteids from this destructive process as far as possible by the administration of carbohydrates and energy-sustaining food. It must, furthermore, be taken into consideration that direct replacement of the disintegrating proteids through the food is possible only in a wholly inadequate manner, on account of the febrile derangement in digestive activity.

Naturally, the body nutrition is greatly disturbed in many other directions also, especially with regard to carbohydrates and fats. It should be borne in mind that, in addition to the production of hydrochloric acid in the stomach, the functions of the salivary glands, and probably those of the pancreas, are seriously impaired, and also the secretion and the constitution of the bile are altered, conditions that demand careful selection and preparation of the food, all the more since peristalsis and absorption appear to be also invariably impaired.

A further especially important peculiarity of typhoid fever with regard to the dietetic management is its long duration as compared with other infectious diseases. The nutritive disturbances resulting from the morbid process as a result attain an especially high grade. Their augmentation is progressive with the continuance of the disease; and this naturally increases materially the difficulties of treatment, and

should lead the physician to adjust his therapeutic measures systematically from the beginning.

Among the considerations arising out of the local alterations, those dependent upon the specific intestinal lesions preponderate over all others. The physician cannot make it sufficiently clear for himself in this connection that the intestinal symptoms clinically stand in no direct relation to the distribution and the severity of the anatomic lesions, and that every case, even apparently the mildest, may be attended with extensive and profound intestinal ulceration.

Fortunately, it is entirely possible at the present day to make perfect allowance for the local conditions without returning to the position, long abandoned, of a water-soup and hunger-diet. Owing to the insight of English physicians, under the guidance of Graves,[1] to whose support especially Murchison[2] energetically devoted himself, the following principle is recognized at the present day: We can and must fully nourish our typhoid patients from the outset; we should thereby endeavor to replace the disintegrating proteids, or attempt at least to limit the destruction, by means of energy-producing substances, carbohydrates, fats, gelatinous substances, and, finally, also alcohol.

In accordance with the general and local peculiarities of the disease already mentioned, however, throughout the entire duration of the febrile state, and for a certain period beyond this time, all articles of food should be given only in a fluid, readily digestible, and easily absorbable form. From the same point of view, care should be taken that nourishment is given frequently, in severe cases by day and by night, always in small amounts, at intervals of two or three hours, and that also somnolent patients should be induced by the attendants to take food regularly. On the other hand, especially in private practice, overfeeding of the patient should be cautioned against, and it should be made clear from the outset to the overzealous friends that the physician cannot hope during the febrile stage to make good entirely the loss, but that, by reason of the rest of the patient in bed and the otherwise diminished physical and psychic expenditure of energy, this is of little significance, and that the loss can subsequently be readily regained.

In some patients anorexia, even actual repugnance for the food hitherto administered, makes its appearance at the height of the febrile

[1] *Clinical Lectures on the Practice of Medicine*, second edition, Dublin, 1848. This work contains the famous statement often quoted: "If you should be in doubt as to an epitaph to be placed upon my grave, take this: 'He fed fevers.'"

[2] *The Typhoid Diseases*, German translation by von Zülzer, Berlin, 1867, p. 234.

state, in a larger number during the second period of the disease. The experienced physician will counteract these morbid manifestations not by unnecessary strictness, but by appropriate individual selection and variation. A febrile typhoid patient is not a subject for pedantic training. Under such circumstances the wisest will yield, and this the physician should be.

Drinks.—Even more frequently than derangement of appetite, complaint is made during the febrile period of thirst, and in somnolent patients an effort will be made on the part of the friends to quench the parched condition by administration of fluids. In contrast to previous views, these desires may be unconditionally acceded to, naturally with a consideration of individual peculiarities. Especially cold beverages, provided they were well borne during health, and even the addition to them of ice, need not be restricted. The best drink for typhoid patients is ordinary, good, clear water. Also certain natural mineral waters, as those of Selters, Giesshübel, Bilin, and others, may be permitted; while artificial waters should be forbidden, on account of the excessive amount of carbon dioxid they contain.

When the patients express an especial desire for, and the intestinal symptoms do not contra-indicate their use, fruit-juices, such as syrup of raspberry, lemon-juice, and orange-juice, may also be added to the water. Some physicians prescribe almond-milk, which, however, is tolerated by only a few patients for any length of time. Still better borne than these things is addition to water of red or white wine, and also cognac or sherry. For individuals with an irritable intestinal canal, weak cold tea has invariably answered admirably in my hands. I am not fond of prescribing albumin-water or gum-water, or of bread-infusion or mucilaginous drinks. By means of these the appetite of the patient is spoiled for actual nourishment, and in addition the keeping of the mouth clean is thereby rendered unnecessarily difficult.

Among actual articles of food, the first place should be given to **milk.** Theoretically, this appears undoubtedly to be the most rational form of nourishment for febrile patients, inasmuch as it represents the ideal combination of proteid, fats, carbohydrates, and salts in a liquid form. Especially the fats, which are so important for febrile patients, and utilized with so much difficulty, are most finely divided in milk, and are in the form of an extremely permanent emulsion, and are thereby rendered as easily assimilable as possible. Although some physicians, accordingly, advocate an almost exclusively milk-diet in cases of typhoid fever, it may be objected that not many patients care for it for any length of time, and a still larger number do not bear it.

The patients then complain of pressure in the epigastrium, a sense of fulness or of abdominal tension, and of pyrosis and eructation, and the stools

contain slightly altered, coarse coagula of milk in undesirable amount. Most frequently the administration of milk is prevented by the fact that it gives rise to the formation in the stomach of febrile patients of firm, lumpy coagula, which are with difficulty digested by reason of the diminution in hydrochloric acid present. This can at times be avoided by administering only boiled milk, the coagula of which are softer and smaller. Dilution with ordinary water, mineral water, or lime-water, also, may be of service in this connection. It is particularly advantageous often to add mucilaginous substances to the milk, such as oatmeal, tapioca, arrow-root, and similar articles. Some patients tolerate the addition of salt or cognac to the milk to improve the taste. Others are grateful for permission to take the milk in the form of kephyr. Under such circumstances, it is true, the considerable amount of carbon dioxid present should be borne in mind. At times the administration of buttermilk serves a useful purpose. Although it must be considered as less valuable on account of the absence of fat, it is easily digestible for the reason that in consequence of the mechanical influences to which it is subjected in the making of butter, the casein it contains is in an especially fine state of division. For patients who bear milk very well, the addition of cream may be permitted. To some patients the administration of milk in a frozen state is most agreeable. Such ice-cream is prepared by freezing, in a shallow vessel or by means of a cold-mixture, milk which has been condensed in a vacuum, and to which has been added a small amount of sugar, and for those who care for it, cinnamon, vanilla, or the like.

A not less important *rôle* is played by the administration of **carbohydrates** in the form of mucilaginous soups, which may be given alone or together with other nutrient or stimulating articles, especially with bouillon or proteids.

In order to render tolerable for some time the **mucilaginous soups** which are so necessary, the physician must have a wide range of formulæ. Among all the substances to be taken into consideration in this connection, oatmeal has the greatest nutritive value, on account of the relatively large amount of fat and proteid it contains. Unfortunately, it often early excites the distaste of the patient. Under such circumstances it should be alternated with rice, wheat, green corn, maize, tapioca, palm sago, and the like. I would further recommend especially the addition to soups of aleuronat flour, which, as is well known, contains 80 per cent. of proteids, is soluble in water and is not coagulated by heating, and which is admirably borne by almost all patients. In the case of children and young adults, success is often had with artificial food (Nestlé's, Kufecke's, and others). Some patients like the addition of white or red wine, instead of bouillon, to the broth. In the later stages of the disease—as the stage of steep curves and that of defervescence—certain other additions may be made, such as legumins or Hartenstein's leguminose.

Among the nutrient and stimulant articles, **meat-broth** prepared at home is by far the most to be recommended, and in preparing this it should be noted that the meat of full-grown animals (cow and ox) contains a larger amount of extractives, and that of veal and young fowl a smaller amount.

In the care of sensitive patients the presence of fat in bouillon should be

avoided as fully as possible, and this may be sufficiently effected by permitting it to cool, and, before heating it again, skimming off the coagulated layer of fat on the surface. It is still more advisable in such cases to prepare the meat-broth by adding hot water or mucilage to a definite amount of "bottle bouillon." The best mode of preparation, especially if the presence of gelatin also be desired at the same time, consists in boiling over the water-bath, for from two to four hours, equal parts of veal or beef, without the addition of water. The juice, expressed through a cloth, which at times is quite clear, may be used in the manner described, as an addition to milk or taken cold in the form of jelly.

A large number of artificial products have been placed upon the market for the preparation and for increasing the concentration of bouillon. A number of these are free from objection; however, some are quite expensive, and at any rate they offer no advantage over the bouillon prepared at home. Of the most approved of these there may be mentioned Liebig's extract of beef, Brand's essence of beef, and Valentine's meat-juice. Closely related to them are the so-called meat-peptones, which actually possess but little nutritive value, and only the influence of the extractives and the salts contained are to be taken into consideration.

In addition to carbohydrates, the **gelatinous substances,** which in Germany have been again restored to favor by Senator, may be mentioned as an admirable means of shielding the body-proteids.

The jelly is best prepared from calves' feet; but under some circumstances it may also be made from good varieties of commercial gelatin. It may be administered in the form of an addition to soup, in the form of the "bottle bouillon" already mentioned, or, what is especially refreshing to many patients, in the form of wine-jelly or fruit-jelly. Fastidious patients will be grateful if the gelatinous addition to soup be made in the form of crab-jelly or oyster-jelly.

Some reserve should be exercised in the administration of actual **proteid nourishment** in cases of typhoid fever during the febrile stage. Solid meat-food of any kind should be strictly forbidden. Also, **eggs** should be given only with caution, in especial form, and should never be urged upon the patient. They are generally permitted to be taken raw, and only the yolk stirred in soups. In addition, the yolk may be given beaten up with bouillon or wine, particularly port or sherry. Eggs admixed with milk are much more difficult of digestion.

In Osler's clinic at the Johns Hopkins Hospital, egg-albumin is very freely given to typhoid patients, usually in the form of albumin-water. In preparing this the albumin is thoroughly shaken with ice and a small amount of water, and is then strained, and flavored with lemon, sherry, or brandy.

Von Ziemssen especially recommends meat-albumin in the form of recently expressed **beef-juice,** which has been incorporated into the German Pharmacopeia. This contains 6 per cent. of dry proteid (Voit and Bauer),

and apparently is quite easily digestible. It is well borne by many patients as an addition to soup, and by others alone in a liquid or frozen state. For sensitive patients the addition of peppermint is a good corrective. When the patients object to the turbid, bloody appearance, the fluid may be administered in a green glass.

Of **artificial proteid foods**, a clear, thick juice, made intensely red by admixture with hemoglobin, and designated puro, has recently been recommended, which, according to the statement of the manufacturer, contains 20 per cent. of proteid, but the value of which still requires clinical investigation. Occasionally, the meat-preparation of Leube-Rosenthal may be valuable. Of the meat-peptones, of which Kemmerich's and Denayer's may be mentioned, I rarely make use. The physician is, of late, frequently importuned by the friends of the patient, who often have become fanatics on the question of nourishment, to use still other of the modern proteid preparations. Nutrose, somatose, and eucasin are those most commonly mentioned. Somatose is a readily soluble mixture of proteids prepared from meat, and almost free from peptone. Nutrose and eucasin are similar preparations made from milk. These powdered, readily soluble substances may, by reason of their almost total tastelessness, be highly serviceable when added in amounts of a teaspoonful to soups and beverages, particularly to patients who have a repugnance to the use of eggs.

In spite of all theoretic objections, **alcoholic beverages** are still indispensable to the practitioner in the treatment of typhoid fever, as well as in the treatment of acute febrile diseases in general. It would be superfluous at the present day to discuss former objections with regard to the influence of alcohol in increasing the fever. Von Ziemssen, Jürgensen, and Liebermeister have permanently disposed of this prejudice. Although the theoretic explanation is difficult, practically the stimulating influence of alcohol upon the circulation and respiration is established beyond doubt. In addition, it is useful for conserving waste and generating energy. I should not be willing to treat typhoid patients at all in certain stages and conditions without alcoholics. The employment of alcohol naturally requires strict discrimination in every case. In children it is to be avoided altogether, or to be employed only temporarily as a last resort. In severe cases in adults I permit from the outset small quantities of spirituous drinks to be taken regularly, undiluted or diluted, keeping in mind the constitution and previous habits of the patient, gradually increasing the amount with the rise of the fever. Care should be taken, apart from alcoholics, not to give large doses at the beginning, in order not to jeopardize the possibility of effective increase in times of necessity.

It is best to employ wine and strong spirits. Exceptionally, beer may be used, and then preferably those varieties that are rich in hops, are well fermented, and rich in alcohol, and they should be given only in small amounts. Among wines, the red Bordeaux, Burgundy, and old Rhine red wines (Assmannshausen and the like) are in general to be preferred in view of

the intestinal alterations; also, white Rhine wines of some age are usually well borne. Some patients bear southern wines—sherry, port, Madeira, and Tokay—also some Italian and Greek varieties. They may be administered undiluted or mixed with natural Selters water or cold tea. Undiluted, these wines, which contain from 12 to 17 per cent. of alcohol, are employed in the presence of progressive weakness and conditions of collapse; and in their stead, or alternating with them, also champagne, care being taken in this connection to avoid the dishonestly prepared, less valuable varieties so common at the present day. While ordinary white and red wines contain from 7 to 8 per cent. of alcohol, good brands of champagne contain from 10 to 10.5 per cent. If there be any reason to employ the stronger alcoholics, cognac, rum, and arac may be administered in tea or black coffee. A convenient mode of administering cognac, by means of which the dose can be well regulated, is in the form of the well-known Stokes mixture. This is especially available also for persons who do not tolerate alcohol well; in addition, the contained eggs appear to be easily digestible. The formula employed at my clinic consists of strong cognac 50, yolk of egg 1, syrup of cinnamon 20, distilled water, sufficient to make 150.

DIET DURING THE PERIOD OF DEFERVESCENCE AND THE STAGE OF CONVALESCENCE.

It has already been seen that in many patients the appetite begins to return during the stage of steep curves, and almost always and in still greater degree after defervescence. The desires of the patient should be restrained at this time on account of the still precarious state of the intestinal canal. On the other hand, one should not be altogether too timid, as, if the restriction in diet be too long continued, convalescence and the resumption of functional activity may be unduly deferred. Even during the stage of steep curves, especially if meteorism be not present or antecedent symptoms of peritonitic irritation or hemorrhage does not admonish especial caution, I permit the addition of soup to be taken in considerable amount, or the carbohydrate articles of food to be eaten, even in the form of a thin pap. Instead of eggs, sweetbread or brain passed through a fine sieve may be added to soups. These articles must suffice, with as much variation as possible, until the **end of the first afebrile week.**

From the **sixth or the seventh afebrile day** I permit the first solid food, beginning with some zwieback or cakes, especially pastry prepared from aleuronat, soaked in milk, tea, or cocoa. Then a soft-boiled egg may be permitted, and finely scraped raw fillet or salmon or a mixture of the two.

The meat is scraped with a silver spoon upon a porcelain dish, and for the first days additionally passed through a fine sieve.

If all these are well borne, roast young fowl, squab, chicken, or

partridge may be given, at first in the form of purée added to soup; then, finely divided, without fat sauce. At the same time or soon afterward, mashed potatoes or well-stirred rice, and, with the meat, some crust of roll or toast, may also be permitted. These articles may soon be followed by light fish, especially trout, boiled in salt water. After this, scraped, slightly overdone fillet may be given, and all these are followed at the end of the second or at the beginning of the **third afebrile week** by broiled lean, tender pieces of meat, veal or mutton cutlet, and fillet of beefsteak, young game, hare, or deer.

In the course of the third week resort may be had to light vegetables, asparagus-tips, spinach, purée of green peas, carrots, artichokes, and the like. During the **second and third weeks of convalescence** it is necessary to administer food at least five times daily; something should be proffered the patient even during the night, if he is awake, such as milk, cakes, and the like. In addition, all sorts of trifles should be given the patient during this period between the principal meals—at first, wine or meat jelly; if reduced, caviar or oysters; the patient will be grateful also for apple-sauce or other forms of stewed fruit that are not too sweet. Uncooked fruits, however, should be withheld for a long time.

The dietetic regulations previously mentioned will naturally serve only as a general guide for the solicitous physician, from which he will arrange a dietary in accordance with the patient and the character and the stage of the disease. While we must require strict obedience from patients and assistants with regard to the diet, their instructions should be given in a clear and well-defined manner. During the critical periods of the disease it is wise, in order that no difference of opinion may arise between the patient and the nurse and the family, that the daily instructions with regard to diet be given in detail in writing.

The mode of treatment described in the foregoing is often designated "expectant," but without propriety. It has been seen that the attitude of the physician is anything but expectant; but that, on the contrary, he is fully and most responsibly occupied with carrying out the treatment. One must go even further and say that for the mild, moderately severe, and even for a number of severe, uncomplicated cases, particularly in previously healthy individuals, the dietetic treatment and careful supervision otherwise render superfluous every other measure. Further therapeutic intervention will be necessary only if the course of the attack be severe or unusual, or in the presence of alarming conditions with reference to certain systems or organs, whether representing peculiar localizations of the typhoid process or actual complications. Particular attention has always been given to the fever in this

connection, and the last thirty years especially have witnessed the assumption of first place, practically and theoretically, of the methods of treatment comprehended under the designation antipyretic.

THE SO-CALLED ANTIPYRETIC METHODS OF TREATMENT.

Earlier and Present-day Methods.—Even at the present day there is still abundant reason for giving especial attention to antipyretic methods of treatment, but the present standpoint afforded by the recent results of etiologic investigation is quite different from the former one. The symptom-complex designated fever may be considered in the main as an expression of the action of the typhoid toxin upon the tissues and metabolism. The sole rational method of treatment for fever would, accordingly, consist in neutralizing the vital manifestations of the bacilli, and particularly the toxic effects to which they give rise. As is well known, we are still far from this goal.

Although for a long time one of the most conspicuous symptoms of the fever, the elevation of body-temperature was looked upon as the most deleterious, and therefore the most worthy of attack, and by some is still so considered at the present day, this view is no longer tenable in the light of current conceptions regarding the nature and mechanism of the infectious processes. Our present treatment is directed, on the whole, toward rendering the effects of the toxins, which, as has been noted, cannot be entirely prevented, so far as possible, innocuous for the patient, and toward sustaining his powers of resistance until the infectious process has spontaneously exhausted itself. Although at present much less importance is attached to direct control of the elevation of temperature than formerly was the case, we do not go so far as to ignore this entirely, nor do we consider it as the *vis medicatrix naturæ*, and therefore not to be interfered with, as, owing to the revival of old theories, is believed at the present day. On the contrary, it must be admitted that unusually high temperature, especially if maintained for a long time and at a uniform level, may in itself be attended with serious evils, viz., acceleration of respiration and pulse, and probably also increase in proteid disintegration and in the oxidation-processes in general. However, in cases of typhoid fever this is practically to be taken into consideration in far less degree than in connection with some other infectious diseases; because in cases of otherwise severe typhoid fever, even during the fastigium, the elevation of the body-temperature is in general confined within moderate limits.

Although we are thus unable to share the view of those who judge of the febrile process principally from the state of the ther-

mometer, and as a routine procedure aim at reduction of the temperature, we still believe, nevertheless, that measures directed to the relief of the symptom-complex as a whole, and thereby to the relief of a number of disturbances whose marked development and prolonged duration may become a source of danger to the patient, are often indicated and often constitute an important part of the treatment. The disturbances present are especially those resulting from the action of the toxins upon the central nervous system, and consist in the consequent states of sopor, coma, delirium, and profound involvement of the most vital cerebral centers, especially those of respiration and circulation, and upon which also certain disorders of the digestive organs, of the urinary secretions, and of the functions of the muscles, are intimately dependent. That by correcting the functional disturbances of the systems and organs in question the body may be rendered more resistant to external morbid influences—that is, to the development of complications—and that at the same time, apart from the immediate indications, provision may be made for the future is a further object of the antipyretic method of treatment.

From the foregoing it follows that the limits of the antipyretic methods of treatment are at the present day in many directions more extensive, and in others less so: more extensive in so far as we do not attempt to attack a single symptom, but an entire group of severe consequences of the intoxication, and this method of treatment is therefore thought to be indicated not only when the temperature reaches a high level, but also when, as so often happens, the intoxication is most manifest with a low body-temperature, or when it is scarcely elevated at all; less extensive in so far as the indication for antipyretic treatment is no longer looked for in a perfunctory manner in every elevation of body-temperature above a certain degree, but principally in profound disturbances of the central nervous system, the circulation, and the respiration, in consequence of which the larger number of mild and moderately severe cases are not subjected to antipyretic treatment.

With these qualifications the antipyretic methods of treatment may now be discussed. Hydrotherapy may be looked upon as its most efficient and most important form, while the employment of the so-called antipyretic medicaments are much less used and esteemed.

HYDROTHERAPY.

Historic.—As with the main principles of dietetic management, we are mainly indebted to English physicians for the principles of hydrotherapy also. It was first employed systematically in typhoid diseases toward the end of

the eighteenth century by the Liverpool physician, James Currie.[1] He used water, principally in the form of cold douches, at from 5° to 10° C., giving them generally twice daily, beginning at an early period of the disease. He was soon imitated by many physicians in all countries, so that in the third edition of his book he was able to report numerous confirmations of his success in his mode of procedure. Undoubtedly, Currie's statistics apply both to typhus and to typhoid fever, which at that time could not be thoroughly differentiated.

From Currie's douches, which, were for a long time adhered to in France as almost the sole method by the most distinguished physicians (Recambier, Trousseau, Chomel, and Guenneau de Mussy), there developed gradually the method of treatment with cold baths. In combination with the douches, and also variously modified in other respects, they were employed extensively in Germany in the first two decades of the nineteenth century, and soon became so highly esteemed that one of the most enthusiastic advocates of hydrotherapy, E. Horn,[2] designated it as the only useful method in the treatment of typhoid fever. Nevertheless, the procedure was not generally adopted. Although still practised by some (von Gietl, Niemeyer, Traube, Armitage, Graves), it gradually became displaced by certain medicinal methods—antipyretic and antiputrefactive. In Germany it was revived by E. Brand,[3] of Stettin. To him belongs the credit of having developed and applied the procedure methodically, and thereby of having given the stimulus for a new, permanent, and successful movement. As the leaders in this who based their clinical experiments and observations upon the prevailing conception of the typhoid process and of the *rôle* played by elevation of temperature in fever, Jürgensen,[4] Liebermeister and Hagenbach,[5] Ziemssen and Immermann[6] should be mentioned. In France, Glénard (1873), of Lyons, introduced the method into practice, and after him especially Fereol and Reynau; then Renoy, Tripier and Bouveret,[7] and others. The method soon became popular also in the remaining countries of the continent of Europe, and also in England and America.

Various Methods of Employment.—The methods of applying water are extremely diverse. Often some modes have been defended with great persistency as alone useful. In addition to the early

[1] *Medical Reports on the Effects of Water as a Remedy for Fever*, etc., London, 1797. German translation by Michaelis, Leipsic, 1801. Compare the historic description of the development of the method in England and France in Murchison's book, from which most subsequent writers have taken their data.

[2] *Erfahrungen über die Heilung des ansteckenden Nerven- und Lazarethfiebers*, Berlin, 1814.

[3] *Die Hydrotherapie des Typhus*, Stettin, 1861. *Zur Hydrotherapie des Typhus*, Stettin, 1862. *Die Heilung des Typhus*, Berlin, 1868.

[4] *Klin. Studien über die Behandlung des Abdominaltyphus mittelst des kalten Wassers*, Leipsic, 1866.

[5] *Beobachtungen und Versuche über die Anwendung des kalten Wassers bei fieberhaften Krankheiten*, Leipsic, 1868.

[6] *Die Kaltwasserbehandlung des Typhusabdominalis*, Leipsic, 1870.

[7] *La fièvre typhoïde traitée par les bains froids*, Paris, 1890. This careful article is based upon a large number of cases, and constitutes the best description of the development and the present status of the question in France.

douches of Currie, at the present day spongings, frictions with cold water, or, as is almost universally customary in France and in England, with vinegar-water, are practised; further, wet packs of varying temperature and duration, partial refrigeration by means of affusions, the use of water-bags filled with cold water, ice, or even cold mixtures, half-baths with frictions or douches (as were recommended by Brand in his first publication), and, finally, full baths of most varied kind.

Treatment by Baths.—Full baths are at the present day by far most commonly used; while the other methods are mostly employed as auxiliary measures or as partial substitutes when baths cannot be used on account of individual or extraneous reasons. At first, under the profound influence of the labors of Brand and his successors, and in consequence of overestimation of the significance of febrile elevation of temperature, cold baths were preferably given at temperatures as low as from 6° to 10° C., and these were warmly advocated at Wiesbaden [1] as late as 1882. In order, so far as possible, to avoid the supposedly deleterious overheating of the blood and the tissues, a bath thus became necessary whenever the temperature reached a certain level—generally above 39° or 39.5° C.—so that the patient not rarely received from ten to fifteen cold baths in the course of twenty-four hours. It was entirely overlooked in this connection that rest and equanimity are not less important therapeutic factors, which cannot be disregarded with impunity.

Most physicians have at the present day returned to less radical methods. Personally, I still employ very cold baths only exceptionally. In general I content myself with lukewarm baths, and with especial preference for those that are gradually, and then usually but moderately, cooled, such as von Ziemssen has introduced into practice. If one does not yet know the patients with regard to their susceptibility to hydrotherapeutic measures, they are first placed in a full bath at a temperature of from 31° to 34° C. Perhaps the first, but generally the second, bath may be cooled to 27° or 25° C. by the gradual addition of cold water. The use of water at a temperature below 22° C. is rarely indicated. The baths are at first of from ten to fifteen minutes' duration, and subsequently are extended up to twenty and even thirty minutes, the latter especially when the shorter duration yields only slight and not persistent effects upon the central nervous system, the pulse, and the respiration. In cases in robust young individuals, if stupor and confusion are marked, cold spongings or cold douches to the head and back are associated with the bath. These may be practised several times in the course of the same bath, or but once, shortly before its termination, in accordance

[1] *Cong. f. inn. Med.*

with the character of the case. In the cases also in which the douche is not employed, it is advantageous to cover the head of the patient with an ice-bag or with a cold cloth. It is, however, unnecessary and superfluous to have the patient, while in the bath, drink cold water abundantly, in order, as it were, to cool additionally the interior of the body.

Certain details should be strictly followed in the practical application of the bath. The patient should never get into or out of the bath unassisted, even if the tub be placed at the side of the bed. He must always be lifted and carried by the attendants. The bath-water should cover the chest, almost to the neck, and the well-supported patient should remain quiet. On the other hand, he is gently rubbed persistently and the water is constantly kept in movement. Debilitated individuals may take small quantities of alcohol—tea with cognac, port wine, or, with advantage, Stokes's mixture—before and during the course of the bath. After the bath all patients should receive such stimulants. At the conclusion of the bath the patient should be dried, always in the recumbent posture, upon an alternate bed, and delicate patients should be dried beneath a woollen blanket. They should then be kept in bed, suitably but not too heavily covered, and the utmost quiet about them should be maintained. It is agreeable and advantageous to some patients, as von Ziemssen especially advised, not to be dried at once, but to be permitted to lie quietly and to sleep, and to have their clothing changed only subsequently on awaking.

In private practice the tub is kept in the room constantly, at the side of the bed of the patient, while in the hospital it is generally portable, or often the patient in bed is moved into the bath-room. The practice of permitting the water to stand for days in the tub, and of using it for several days in succession after warming it by the addition of amounts of hot water, is a practice that should be strongly condemned. This would make it impossible to secure the necessary cleanliness on the part of the patient, and would certainly give rise not rarely to infectious diseases of the skin—furunculosis and phlegmon. In addition, the danger to the attendants from such infected water is by no means to be underestimated.

Indications and Counterindications.—The repetition of the bath is governed less by the range of the body-temperature than by the symptoms referable to the central nervous system, the pulse, and the respiration. Most physicians at the present day endeavor to avoid extreme reductions in temperature by means of the bath. From the use of the kind described, the simple lukewarm baths, or the Ziemssen gradually cooled bath, the reduction generally does not exceed one or two degrees. In general this may be considered as quite sufficient. Even in severe cases and at the height of the disease, from two to at most four baths in the course of twenty-four hours will generally be sufficient. The lukewarm bath (from 25° to 30° C.), of long duration—up to twenty-four hours—has been warmly recommended by Ries. His views have been accepted by Affanassief and Manassein, as well as

by Unverricht. Recently, they have been highly praised also by Eichhorst, and they are therefore worthy of further trial, on account of the wide experience and the reliability of this writer. Cases of severe onset, with symptoms of intense persistent intoxication, should from the outset be subjected to the bath-treatment, which should be governed strictly by the indications present in the individual case, and be conjoined with the auxiliary hydriatic measures previously mentioned. Under such circumstances the bath-treatment cannot be replaced by any other measure, and its omission or inadequate employment is to be considered a serious mistake. The conditions are different with regard to the mild and moderately severe cases. These may not require the bath-treatment; diet, rest, and the systematic regulation of the remaining conditions are here generally quite sufficient. Should exacerbations occur or intercurrent severe symptoms arise, baths should be given also in these cases at varying intervals, in accordance with the existing circumstances.

In all cases of typhoid fever, further, I have given daily one, possibly two, cool or tepid spongings, which are refreshing and exert a favorable influence upon the nervous system. In moderate and severe cases an ice-bag is kept constantly applied to the head throughout the febrile period. When the pulse-frequency is high, it is well also to apply an ice-bag over the heart. Marked intestinal symptoms, especially meteorism, demand the application of affusions to the abdomen. If bronchitis be severe, moist packs applied to the thorax and changed not too frequently are of great advantage.

Of the remaining hydrotherapeutic measures, to which, however, the principal advocates of such measures attach slight antipyretic value, I make little use; among these cold packs are most to be recommended. For many patients these are, however, troublesome, and especially exhausting if, as is recommended in order to insure their efficacy, they are repeated every hour or two, and if, in addition, cold water is used. I dispense entirely with the application of cold secured by filling the water-cushions with cold water, ice, or even cold mixtures.

Whereas caution has been several times advised in the employment of vigorous bathing-procedures, especially very cold and frequently repeated full baths, there are also certain absolute and relative contra-indications to even milder methods of procedure. Every form of bathing-treatment is strictly forbidden on the appearance of the first sign of intestinal hemorrhage, as well as on the appearance of even the slightest degree of peritonitic irritation. The method is also dangerous in patients with weakness of the heart, especially that resulting from

recent myocarditis, endocarditis, or pericarditis. Also, persons with arteriosclerosis or incompletely compensated valvular lesions of some standing are to be excluded from the bath-treatment. Pleuritic effusions of considerable amount likewise constitute a rigid contra-indication, while in the case of dry pleurisy and pneumonia this method is contra-indicated only if they are associated with weakness of the heart. Phlebitis also constitutes a contra-indication to the bath-treatment. Diffuse bronchitis or a tendency to hypostasis of the lungs is considered in my clinic as a special indication for the bath-treatment. In cases presenting severe laryngeal lesions it is best to omit the bath-treatment. Suppurative inflammation of the middle ear, with perforation of the tympanic membrane, demands great care to prevent the entrance of bath-water. Much caution should be exercised in bathing persons who have previously been ill, especially those having tuberculosis or bronchiectasis with a tendency to hemorrhages or in the presence of marked emphysema.

Old age also may constitute a contra-indication. The baths are generally not well borne by persons above the age of fifty years; even of those persons between forty and fifty, only a small number are favorable subjects for this treatment. In children the bath-treatment is in general less commonly indicated, both on account of the usually mild course of the disease, and particularly by reason of the greater powers of resistance on the part of the nervous system and of the heart. Children generally pass quietly and safely through an attack of typhoid fever without any active treatment. Should hydrotherapeutic measures be indicated by special conditions, particularly those involving the nervous system, such as restlessness, somnolence, or coma, lukewarm baths, with gradual reduction in temperature, and douches, in accordance with the conditions present, will almost solely be appropriate. Children bear very cold baths even worse than adults.

Certain physiologic states of the body, especially the puerperium, lactation, and menstruation, do not constitute absolute contra-indications. With regard to the constitution, chlorotic and, in general, anemic, debilitated individuals are usually to be spared forcible measures. Great care should be observed in the case of obese persons. They commonly bear hydriatic treatment poorly. Even in youthful persons of this character, particularly in "blooming, thriving" young women, unfortunate experiences are not rarely encountered. Such individuals exhibit a tendency to weakness of the heart, which becomes manifest unexpectedly and in an alarming degree, especially after frequent cool baths. The great tendency to cardiac weakness often

renders the baths dangerous also for alcoholics. That there are also previously apparently healthy persons who, when attacked with typhoid fever, do not bear the baths well and become markedly languid and exhausted in consequence, is a noteworthy fact. Of the several varieties of typhoid fever, only the rare hemorrhagic variety really demands care with regard to hydriatic measures.

ANTIPYRETIC MEDICAMENTS.

The Value and Action of Antipyretic Drugs.—Antipyretic drugs, which, even at the height of the bath-treatment, were considered by the majority of physicians as less important than the latter, to-day, in spite of their almost daily increasing number and often warm endorsement, play a minor *rôle.* The nature of their influence upon the elevation of temperature is still in dispute, and apparently is not the same for the different remedies.[1] Evidently, none of them exerts a specific influence upon the morbid process, and therefore the antipyretic effect is not at all comparable to that of quinin in the presence of malaria. A favorable influence upon the central nervous system, the pulse, and the respiration, which is considered as an especially important result of the bath-treatment, is scarcely demonstrable following the use of the antipyretic drugs, with a few exceptions. The majority, on the contrary, in full doses, give rise to markedly depressing or directly injurious secondary effects.

To the simple reduction in temperature, which all these agents usually bring about in marked degree, the earlier significance is by no means attached at the present day, as has been seen. The custom, still far too common, of administering antipyretics in a routine manner whenever the temperature reaches a certain level, and thus, of course, frequently, is to be condemned. The extreme efforts to maintain the temperature at a low level for a considerable time, or constantly "afebrile," as it is designated, by the administration of salicylic acid, kairin, thallin, and the like, are actually dangerous, and, fortunately, have been almost entirely abandoned.

Personally, I make incomparably far less use of antipyretic drugs than of baths. From year to year I have gradually given up the former more and more, and the large majority of my patients leave the hospital without having received any of these drugs. I can make this statement with a clear conscience, as my experiences during the last ten years, compared with those during the period in which I prescribed

[1] Compare the discussion upon antipyresis, *Cong. f. inn. Med.*, 1885; and *Internat. Cong. z. Kopenhagen.*

these remedies more freely, are not any less favorable than the latter. If at the present time I still occasionally administer an antipyretic drug, this is done preferably in the so-called hyperpyretic cases, and then especially when the baths cannot, for extraneous or individual reasons, be employed. I restrict myself, however, in this connection to a few remedies, of which I know that with very slight or no injurious secondary effects, they exert, in addition to the reduction in temperature, also some influence upon the typhoid state.

I do not use salicylic acid or sodium salicylate. Although they reduce the body-temperature markedly and certainly, they have neither an abbreviating nor any other favorable influence upon the course of the disease. They may, in fact, not rarely be actually dangerous, in so far as they may cause collapse in persons presenting not entirely normal cardiac conditions. In Germany, accordingly, the use of the preparations of salicylic acid has apparently been abandoned by most physicians; while in France, under the influence of Guenneau de Mussy, Jaccoud, and Vulpian, these preparations are still employed.

Kairin also has properly been almost abandoned. Its administration is likewise almost unexceptionally followed by marked depression of the body-temperature, but generally with most unpleasant, often actually alarming, secondary manifestations: cyanosis with cold sweats, cardiac weakness, and occasionally profound disturbance of breathing. The action of thallin appears to resemble that of kairin, but is attended with less serious secondary manifestations. In the opinion of competent authority, however, the entire effect is less marked and less persistent.

I would admonish also against the use of antifebrin. Although it is markedly antipyretic (three or four times more so than antipyrin), its administration may be followed by quite unanticipated and dangerous secondary manifestations, even when it is given only in small doses. Undoubtedly, even death may be attributable to its administration. The secondary manifestations in question consist in chilliness, cyanosis, and especially irregularity and feebleness of the action of the heart. Certain older remedies, particularly veratrin and digitalis, play no *rôle* whatever as antipyretics at the present day.

Together with most physicians,[1] I employ almost only quinin, antipyrin, and phenacetin. Contrary to a number of others, of these I still prefer **quinin.**[2] With a proper administration—this must naturally be learned—it has almost as certain an effect as the other two, and generally a more permanent effect; while such secondary dis-

[1] See, for instance, von Ziemssen, *Behandlung des Typhus;* Penzoldt u. Stintzing, *Hand. d. Therap.*, Bd. i.

[2] See Liebermeister, "Ueber die antipyretische Wirkung des Chinin," *Deutsch. Arch. f. klin. Med.*, 1867, Bd. iii. "Antipyretische Heilmethoden," *Ziemssen's Hand. d. Therap.*, Bd. i. "Typhus abdominalis," *Ziemssen's Hand. d. spec. Path. u. Therap.*, Bd. i. The well-known investigations of Liebermeister are still at the present day sufficient justification for the employment of the remedy. Even previously, Broca (1840), in France, and W. Vogt (1859) and Wachsmuth (1863) had made investigations concerning quinin, without, however, having cleared up the situation.

turbances as may be present are far less disagreeable and almost free from danger. The ringing in the ears, so distressing to other patients, makes little impression upon the typhoid patient, on account of his state of stupor. Vomiting is by no means so frequent as it is often said to be, and, what is most important, the remedy is the least dangerous of all these antipyretic drugs, even when the heart is in an unstable condition.

The dose for an adult is from 1 to 1.5 grams. Rarely, I give as much as 2 grams, and scarcely ever more. The administration should take place, as Liebermeister recommends, not at the height of the temperature-elevation, but some time earlier, in order to counteract this so far as possible. As the action of quinin generally becomes distinctly apparent only in the course of two or three hours, the drug should be administered at least this period in advance of the expected maximum temperature. The decline in body-temperature generally reaches the lowest level, on the average, from eight to twelve hours after the ingestion of the quinin. If the temperature then begins to rise again, it does not, in many cases, reach the previous level, even in the course of an additional twenty-four hours. It is noteworthy that the remedy should be administered at once in full dose, or in a few smaller doses at intervals of not longer than from one-quarter to one-half an hour. Smaller doses extended over a longer period of time are inefficient for antipyretic purposes (Liebermeister). The remedy is best administered internally in starch-capsules, followed by one or two tablespoonfuls of a mixture of hydrochloric acid. Should administration by the stomach be followed by vomiting, the remedy may readily be given by enema.

The antipyretic effect of **antipyrin** is more rapid and more marked. In my experience, however, it causes vomiting more frequently, and, what is most serious, heart-weakness not rarely occurs, unless great care is observed in its administration. First prepared by Knorr and introduced into therapeutics by Filehne, it is at the present time probably the most commonly employed antipyretic. It is best administered, as Liebermeister first suggested for quinin, and then also recommended for antipyrin, during the afebrile period, in order that its effects may be utilized in preventing the daily exacerbation. Like quinin, its use is followed, not only by a reduction in the body-temperature, but not rarely also by improvement in the mental state and by a certain feeling of well-being. The dose is from 2 to 5 grams.

When first administered, it is advisable not to give the entire dose at once, but in two equal parts, with an interval of an hour between them. In patients in whom there is any misgiving as to the condition of the heart, it is well to administer at first only from 1 to 1.5 grams, and thereafter hourly a dose of from 0.75 to 1 gram. The remedy, if badly borne by the stomach, may be administered by enema, and, by reason of its ready solubility, even subcutaneously.

Phenacetin, which has a similar effect to antipyrin, and is employed in half the dose, is advisable in some cases. It is better

borne by some patients than is antipyrin. In its administration also the condition of the pulse should receive careful attention.

With **lactophenin** (dose, from 0.5 to 1 gram), which has been recommended by von Jaksch,[1] and which has been credited by this observer and also by Immermann with exerting an especially favorable influence upon the general condition and with exhibiting no serious secondary effects, I have as yet not had sufficient experience, by reason of the slight use that I make of antipyretic drugs. Recently, also Eichhorst[2] has warmly praised the remedy on account of its action upon the nervous system, particularly its sedative influence upon excited, sleepless patients.

TREATMENT OF THE DISORDERS OF INDIVIDUAL ORGANS AND SYSTEMS.

The treatment of the **disorders of the circulatory organs** has already been referred to frequently. In this connection the symptoms due to impairment of cardiac and of vasomotor activity are especially to be taken into consideration. How successfully these are counteracted by the bath-treatment and how little of a favorable character is, on the other hand, to be expected from antipyretic drugs, which, on the contrary, may often be a source of injury, has likewise been sufficiently emphasized.

Should progressive enfeeblement of the circulation make itself manifest, in spite of intelligently employed bathing-treatment, further systematic intervention may be of great, and, under some circumstances, of life-saving, value. The first place should be taken by the employment of alcoholics. Beginning with small quantities of mild alcoholic agents, the dose and the strength are gradually increased in proportion to the increase of the collapse. It may in this connection be kept in mind that febrile patients bear distinctly larger amounts of alcohol than those in a state of health. Strong wines, old Rhine wine or Burgundy, Hungarian wine, port wine, and sherry are mostly used. Mulled wine and champagne, also cognac in strong coffee or tea or in the form of Stokes's mixture, are especially efficient. Patients who swallow badly or exhibit a distaste for alcohol may take cognac, under some conditions with ethereal tincture of valerian, in the form of an enema (cognac, 20; ethereal tincture of valerian, 5; yolk of egg, 1; mucilage of gum arabic, 20; water, sufficient to make 150; to be given in two or three parts by enema).

Among stimulating drugs I employ preferably caffein (internally

[1] *Prag. med. Woch.*, 1894, No. 11.

[2] *Lehrbuch*, new edition.

and subcutaneously), and, above all, camphor, which is generally most useful. Its internal administration, however, is disagreeable to the patient and is useless. I therefore employ the remedy almost solely subcutaneously. The official (10 per cent.) camphorated oil or a stronger solution may be used for this purpose. The following stronger solution is employed at my clinic: triturated camphor, 2; sulphuric ether, 3; olive oil, 7.[1] In accordance with the gravity of the situation, one or two hypodermic syringefuls of this solution may be given every hour or two, and even more frequently. I have never observed serious secondary effects from its use. Probably, in some cases, the method contributes in considerable measure to the successful outcome. Of the subcutaneous administration of pure ether I rarely make any use. Its effect is distinctly less certain and persistent than that of camphor. In addition, the injections are quite painful, and not rarely give rise to necrosis at the point of puncture. Musk has largely gone out of use, and it appears to me that not much has been lost in consequence.

At times, especially in hyperpyretic cases, an ice-bag applied over the heart renders good service. In a number of elderly or otherwise decrepit individuals, warmth to the precordium, preferably applied by means of Leiter's tubes, may be of service. Should the extremities become cold, the application of bandages and hot bottles should not be neglected.

Digestive Organs.—The care of the mouth and the nasopharyngeal cavity has already been considered. A number of infectious disorders of the larynx, the bronchi, and the lungs may in this way be averted. That artificial teeth should be removed throughout the entire febrile period, especially in the case of deeply stuporous patients, is a matter of course. The development of thrush should be attacked vigorously on its first appearance. In the presence of parotitis, which frequently subsides without the occurrence of suppuration, cold cloths or an ice-bag may be applied. Should suppuration prove inevitable, hot poultices should be applied, and then free incisions be made as early as possible.

The intestinal symptoms are generally a source of especial anxiety. For the diarrhea, which generally is not attended with marked frequency of bowel-movement in cases of typhoid fever, intervention should be undertaken only if the stools are unusually numerous and attended with peristaltic unrest, colicky pain, and tenesmus—the last occurring more commonly in cases of colotyphoid. In some cases it is

[1] The addition of the ether is intended only for the purpose of making the mixture more limpid, and therefore more available for injection.

then advisable to withhold milk and eggs and to administer only small quantities of mucilaginous soups or cocoa, and, in addition, under certain circumstances, some port or red wine. As a beverage, weak cold tea is much to be preferred to the gum-water or albumin-water customarily employed. An ice-bag upon the abdomen, often highly praised in this connection, is rarely well borne. Tepid affusion is best. Poultices may be permitted only under special conditions, as they increase the danger of the occurrence of intestinal hemorrhage.

Of drugs, if dietetic measures do not suffice, I employ opium almost solely, giving it in frequent small doses, in part by the mouth, in part in the form of suppositories, employing the latter particularly when it is thought that the colon and the cecum are especially involved. Little aid is to be expected from astringents. Conversely, persistent constipation, which is by no means uncommon, may require intervention. Contrary to the custom of a number of other clinicians who are less strict, I never employ laxatives under such circumstances—not even castor oil or calomel, which are in great favor. Simple enemata of water suffice, as a rule.

Marked **meteorism** in patients whose dietary has not be neglected is almost always the expression of profound intoxication. Under such conditions tepid, gradually cooled full baths are especially indicated, and in the intervals moist affusions or an ice-bag should be applied to the abdomen. Should these measures afford no relief, not much dependence can be placed upon others. I have observed scarcely any good from the use of oil of turpentine, externally or internally, in spite of its frequent recommendation by early practitioners. The highly praised high introduction of a rectal tube also will be successful in only a minority of cases. At best, I have been able to evacuate gas through it only when the meteorism was confined principally to the large intestine. When especially the small intestine is greatly distended, not much will be accomplished with the tube. Direct puncture of the intestine with a fine needle, which has received recommendation from various sources, is dangerous on account of the liability of peritonitis. At any rate, by reason of the marked paresis of the intestinal tube, almost always present, and the considerable loss of elasticity in the overdistended abdominal wall, no gas will escape through the needle, for obvious physical reasons.

In the presence of **intestinal hemorrhage,** and even upon the slightest indication thereof, absolute rest in the dorsal decubitus is necessary, and the abdomen should be covered with an ice-bag or a coil of cold water. The patient should for a time refrain from the ingestion of

all food. At most, bits of ice or cold tea in spoonful doses may be given. If the hemorrhage is slight, or on the cessation of more copious hemorrhage, a spoonful of cold milk, or a corresponding amount of mucilaginous soup, may be given every two or three hours. Control of intestinal peristalsis should be provided for by means of opium, in frequent, even heroic, doses, by the mouth or the rectum. In the presence of general restlessness, one should not hesitate to administer a subcutaneous injection of morphin.

The drugs recommended as direct hemostatics are less trustworthy. Some employ, with good results, it is stated, subdermal injections of ergotin. Nothing is to be expected from internal styptics or astringents, especially the much-recommended solution of ferric chlorid. They may, on the contrary, be directly dangerous, from the fact that at times they excite vomiting. When the patients become feebler, it is wise not to resort to the use of strong stimulants too early. Moderate collapse, if intelligently controlled, may be favorable to thrombosis of the bleeding vessel. In the presence of considerable cardiac weakness following profuse hemorrhage, these considerations may naturally be ignored. Under such circumstances the treatment already described for collapse will be indicated. In some especially alarming cases I have observed good results follow the subcutaneous or intravenous infusion of sodium chlorid, and even from transfusion of blood.

The use of calcium chlorid in large doses (2 grams every three or four hours), and the subcutaneous injection of a 2 per cent. solution of gelatin in order to increase the coagulability of the blood and so favor thrombosis in the bleeding vessel, have been lately tried at the Johns Hopkins Hospital, in some cases apparently with good results.

Intestinal Perforation. — Recently, surgery has undertaken intervention in these cases, resulting in the saving of life. The first attempts, in the presence of perforative peritonitis complicating typhoid fever, to open the abdominal cavity, to search for the site of perforation directly, and to close it, and then to make a thorough toilet of the peritoneum, are due to Mikulicz[1] and Lücke.[2] They have been followed by a large number of surgeons, some of whom, especially courageous, have even earnestly recommended resection of the perforated portion of the intestine.

[1] *Volkmann's Sammlung klin. Vorträge*, No. 262.

[2] *Deutsch. Zeit. f. Chir.*, 1887, Bd. xxv.; and *Verhandl. d. deutschen Gesellschaft f. Chir.*, 1889. A complete bibliography bearing upon the procedure in question is given by Geselewitzsch and Wannack, *Mittheil. aus den Grenzgebieten d. Med. u. Chir.*, Bd. ii., H. 1 u. 2, S. 32, *et seq.*

The details and methods of operating more recently employed are fully considered in the writings of the surgeons referred to on pages 234, 235.

In view of the excellent results obtained by the use of this procedure during the past few years, and since the chances for success from operation are far greater the earlier it is undertaken, it is of the utmost importance that the condition be recognized early; and with increase of skill in early diagnosis will undoubtedly come an appreciable reduction in the mortality from this accident. The attending physician should have the possibility of perforation constantly in mind, and with the onset of the first suspicious symptoms a most careful examination should be made. All feeding should be stopped at once, all forms of bath-treatment should be discontinued, absolute rest should be maintained, and the patient should be watched with the greatest care until all possibility of the existence of a perforation has passed. (In regard to early diagnosis, see p. 234.) The use of opium in these cases is justifiable only after the diagnosis has been made and operation decided upon. As soon as perforation is believed to have occurred, immediate surgical intervention is demanded. The results of this procedure (p. 235) fully warrant its application wherever conditions are such as to render laparotomy for any other condition justifiable. The introduction of the use of local cocain-anesthesia in these cases by Cushing has been a distinct advance, in that it has made the operation possible in many cases in which the administration of a general anesthetic would of itself be a source of considerable danger.

Even in cases in which the perforation has not been recognized early and general peritonitis is present, hope must not be lost. No case is so desperate, unless actually moribund, as to be without some hope in the hands of a good surgeon.

Cholecystitis.—The question of surgical treatment has been considered by the authors quoted on pages 209, 210. Undoubtedly, many of these cases recover without such interference. However, this is not true of a majority of the cases. Of 44 cases of typhoidal infection of the gall-bladder accompanying or following typhoid fever, collected by Keen,[1] 30 resulted in perforation. Of these 30 cases, 4 were operated upon, and of these, 3 recovered; while of the remaining 26 not operated upon, all died. There can therefore be little question as to the advisability of operation as soon as perforation is diagnosed. As to operation, in cases of cholecystitis with marked distention, before perforation, the opinion of Keen[2] may be quoted: "I am decidedly of the opinion that

[1] *Loc. cit.*

[2] Camac, *Johns Hopkins Hosp. Rep.*, vol. viii.

in distention of the gall-bladder prompt surgical interference is the best. It is far better to prevent perforation than to remedy it after it has occurred."

Operation in these cases, also under local cocain-anesthesia, has been done by Cushing and by Mitchell.

Suppurative cholecystitis and cholelithiasis following typhoid fever should, of course, receive surgical treatment.

The **diseases of the respiratory organs** may require therapeutic intervention. Marked degrees of nose-bleed are worthy of attention on account of the already reduced condition of the patient from other causes. A number of deaths have resulted from the circumstance that the patients, stuporous or sleeping profoundly, especially if the nasal orifice has been tamponed, have lost an immense amount of blood into the nasopharyngeal cavity and have swallowed it, in consequence of which the hemorrhage does not promptly come to the knowledge of the attendants. I have made it a rule in severe, obstinate cases of epistaxis to apply tampons not alone from the front, but also from behind.

The treatment of the typhoid lesions of the larynx has already given rise to an extensive literature.[1] It treats especially of the indications for and the performance of tracheotomy, with which, in severe cases, there should be no delay. The operation, however, has also its dark side, especially in cases of typhoid fever, inasmuch as in them, far more than in those free from fever, it favors the development of pneumonia, both by aspiration and by retention of secretion.

One must always be prepared for the development of abscess of the thyroid gland, on account of its gravity, but, fortunately, it is not frequent. It soon gives rise to attacks of suffocation, and it should therefore be incised as early as possible.

By far the best treatment for typhoid bronchitis is that with baths, cold friction, and moist applications. I scarcely ever use the so-called expectorants—ipecacuanha, senega, etc. When importance is attached to the use of drugs, the administration of liq. ammon. anis. is least injurious. Should symptoms of cardiac weakness be added to those of bronchitis, measures directed especially to the prevention of pulmonary hypostasis are indicated. Under such circumstances frequent change of position should be brought about, and an endeavor should be made to improve the enfeebled cardiac activity. In some cases the application of dry cups over the region of the lower lobes renders good service.

[1] See the references on page 239 and the following pages of this work, especially the exhaustive work of Lüning there mentioned (p. 243).

The treatment of **disorders of the nervous system** is, as has already been pointed out, likewise one of the principal uses of hydrotherapy. A number of drugs also (quinin, antipyrin, phenacetin, and lactophenin) appear to render valuable service in this connection. In addition to the general antipyretic treatment, special measures and modifications of hydrotherapeutic methods may become necessary. Severe headache during the first period of the disease should be relieved by means of the ice-bag, Leiter's coils, or by placing the head upon water-cushions kept constantly cool. Under such circumstances a dose of antipyrin or phenacetin also often yields the best results.

At a later period of the disease the sensitive states of the nervous system and the depressive states—coma, sopor, stupor with cataleptic symptoms—often require special treatment. The depressive conditions, when they attain a considerable degree of severity, should be controlled by means of cold douches in the tepid bath, and, in particularly robust persons and when the attack pursues a hyperpyretic course, even by means of quite cold full baths. A useful adjunct under such conditions consists at times in the enemata of valerian and cognac previously mentioned. In the presence of marked irritative states—delirium, attempts at flight, and sleeplessness—protracted, simple tepid or gradually cooled von Ziemssen baths are indicated. Cold douches and similar measures rarely do good under such circumstances. Greatly debilitated individuals may be treated advantageously with tepid wet-packs in place of the baths, but in order to secure the necessary rest for the patient the packs should be changed infrequently. If restlessness be particularly marked, one should not hesitate to give moderate doses of morphin; they never do harm, and they help to protect the brain from exhaustion. In drunkards, alcohol should be given generously, in addition to morphin.

Of the **organs of special sense,** the ear particularly should be given consideration. In profoundly stuporous patients frequent examination is necessary, even though they make no complaint. Should inflammation of the middle ear develop, the early performance of paracentesis of the tympanic membrane is recommended by most aurists.

External Integument.—With the present system of nursing, the occurrence of bed-sores, even in severe, protracted cases, is exceptional. Profoundly ill patients should, from the beginning of the second week, be placed upon a water-bed, as von Ziemssen and Immermann first recommended. If this be combined with the strictest cleanliness and appropriate bath-treatment, bed-sores can almost certainly be avoided. Placing the patient upon air-cushions likewise is usually sufficient.

Air-cushions and water-cushions should always be covered with a sheet free from folds and of not too coarse texture. They should never be unduly filled—in general, only to such a degree as not to rise above the level of the remainder of the bed when the patient lies upon them. I have water-cushions filled only with tepid water; the use of cold water is unnecessary and disagreeable to most patients.

If a typhoid patient presents a bed-sore when he comes under observation, or if such a condition cannot be prevented, in spite of the utmost care, it should be treated in accordance with the rules of antisepsis. The application of plasters, formerly practised, is to be rejected, on account of the danger of retention of the secretions of the wound. Dressings with borated or other antiseptic ointments are most suitable. The fortunately extremely rare cases of very extensive, multiple, and progressive bed-sores, attended with general nutritional disturbances, can at times be favorably influenced by treatment in a permanent water-bath.

The treatment of erysipelas, furuncles, and phlegmons should be carried out in accordance with general rules.

With reference to **typhoid affections of the kidneys**, it need only be remarked that they do not contraindicate mild bath-treatment, while under such circumstances certain antipyretic drugs, particularly salicylates, are strictly to be avoided. That the bladder should be frequently examined in the case of profoundly stuporous typhoid patients, and if necessary catheterized, cannot be too deeply impressed upon the young physician. When bacilli are present in the urine, as demonstrated by cultures or shown by the microscope, urotropin should be given in 10-grain doses.

With regard to the treatment of **especial varieties of typhoid fever** some statements have already been made. The hyperpyretic variety requires especially keeping the patient in a cool state, frequent cool baths, and not rarely antipyretics, among which I prefer quinin. In the varieties attended with septic manifestations I have at times observed good results from the use of frequent, fairly large doses of antipyrin. The so-called hemorrhagic variety has as yet proved little amenable to treatment. The use of calcium chlorid and the subcutaneous injection of gelatin solution should be tried. The highly lauded employment of ergot and the acids is worthy of little confidence. The conditions present consist in profound disturbances, which, so long as they are not understood etiologically, are not accessible therapeutically. That mixed forms of typhoid fever and malaria demand energetic treatment with quinin need scarcely be specially emphasized.

TREATMENT OF RECRUDESCENCES AND RELAPSES.

We have already learned to appreciate the serious prognosis of true recrudescences. Their treatment is the same as that of the severe typhoid state in general, with especial consideration for the circumstance that the patients, already greatly reduced in consequence of the antecedent period of disease, are predisposed to cardiac weakness, pulmonary hypostasis, and states of profound nervous exhaustion. Only the mildest hydrotherapeutic measures can be employed. Cold full baths, douches, and the like are entirely to be avoided. The most important consideration under these circumstances is suitable nourishment and abundant administration of stimulants, especially alcohol. The relapses, which, on the contrary, are of favorable prognosis, require treatment only when they are abnormally protracted or when a severe, long-continued relapse, following a mild, at times ambulatory, primary attack, constitutes actually the principal part of the entire disease. Under such circumstances, naturally, the rules already laid down for the primary attack are applicable.

Whether relapses can be prevented when their imminence is to be feared on account of the persistence of enlargement of the spleen and of the diazo-reaction into the afebrile period, as well as the relation between the pulse and the temperature previously mentioned, is doubted by many. I believe with von Ziemssen that this is possible at times by appropriate treatment with quinin. Under such circumstances I do not, however, administer single large doses, but smaller—from 0.25 to 0.5 gram—four times daily, and occasionally even more frequently. The same treatment has been serviceable also in cases in which, with or without persistence of enlargement of the spleen, the temperature-curve acquires a wholly irregular character, and with normal or subnormal daily temperature exhibits moderate elevation toward evening. I believe that I have, by means of treatment with quinin, materially shortened the duration of a number of such cases, which experience had shown might be prolonged indefinitely.

TREATMENT OF CONVALESCENCE.

A principal point in the treatment of convalescence, attention to the **nutrition,** has already been referred to (p. 451). Not less closely than this should also the general **physical and mental condition** of the patient be watched. He should not be permitted to get out of bed too soon; and it is well, both for the patient and for the friends, from the outset to name the much-longed-for day rather too far in

advance. Even after mild attacks convalescents should not be permitted to get out of bed earlier than two weeks after definite defervescence. After severe attacks this goal will scarcely be reached before the lapse of four weeks. Complications often require rest in bed for even much longer periods. The patient and the friends should be clearly instructed that the course of convalescence is not less dependent upon strict obedience than is that of the previous stages.

In bed the convalescents should remain as quiet as possible and avoid sitting up too long, particularly in the first part of the afebrile period (collapse). With regard to the mental state, they should, so long as possible, be kept away from severe, particularly technical, reading, while light, indifferent literature may be read to them. Visits also should be restricted during convalescence, and only such persons admitted as do not excite the patient and do not encourage him to participate actively in the entertainment. How injurious such visits may be is shown in hospitals by the temperature-curves of convalescents on the official visiting days. It is a useful and a welcome substitute for much that is forbidden to bring the convalescent in bed into the open air, if the weather is favorable.

When, after convalescence has been completed, the **usual activities** may be resumed cannot be determined in general, but must be decided according to the individual case. The nature of the attack that has been passed through, the character of the occupation, the constitution, and other external social conditions play the decisive *rôle* in this connection.

Persons in favorable pecuniary circumstances may be recommended to take a long holiday before resumption of work. For this purpose it is best to select a moderate mountainous elevation or a mild seaside resort. Considerable altitudes (above 1000 meters) or rigorous sea-baths, particularly in the German Sea, are in general to be interdicted. In winter a residence in the South, in Southern Tirol, at the upper Italian lakes, or the Riviera is appropriate. The Isle of Wight is also, under certain circumstances, a suitable resort for recuperation. Those of moderate means should, at least after severe attacks of typhoid fever, spend some time in the country. The efforts that are becoming more and more evident to provide for the less well-to-do classes by the erection of sanatoria in the country are to be cordially welcomed.

TYPHUS FEVER.

TYPHUS FEVER.

TYPHUS FEVER is an acute infectious disease, the hitherto undiscovered cause of which reproduces itself exclusively in the body of the individual affected. The disease originates and spreads only by contact either directly with the patient, or indirectly with a third person or with an inanimate object infected with the germs of the disease.

Being exceedingly contagious, it is, therefore, usually epidemic. Occasionally, when the external or personal circumstances of the population make it difficult for the contagium to obtain a foothold, or when the proper prophylactic measures have been carried out in good season, it may be endemic or sporadic. Typhus fever[1] has no connection whatever with typhoid fever.[2] It belongs, in fact, to another group of infectious diseases, the acute exanthemata, which it resembles in the extraordinary ease with which it is transmitted by direct contact from one individual to another, by its self-limited course, by the rare occurrence of relapses, by the peculiar character of the temperature-curve, and by the fact that the characteristic eruption appears at once instead of in successive crops.

HISTORIC.

The plan of this work does not include a detailed description of the history and geographic distribution of typhus fever. These subjects have been carefully treated by a number of authors, especially Murchison and August Hirsch, and their description is so complete that later writers have done little more than quote from their works without adding anything of their own.

Typhus fever is one of the diseases that were probably known to antiquity. It is possible that even Hippocrates[3] encountered the

[1] The synonyms for typhus fever are: Spotted typhus, exanthematic typhus, typhus contagiosus, febris pestilens, febris putrida, febris petechialis, morbus pulicaris, typhus carcerum (jail fever), febris bellica, febris castrensis (camp fever), febris nautica (ship fever), ship typhus, hunger typhus, and febris Hungarica (Hungarian fever).

[2] The term typhus, as well as other names by which it is known, such as spotted typhus, exanthematic typhus, petechial typhus, etc., came into vogue at a time when the disease was imperfectly understood, and should therefore be discarded.

[3] *De morb. popul.*, lib. ii., iii.

disease, and some investigators claim to have found passages that seem to refer to it in the writings of Aëtius, Rhazes, and Avicenna.

The earliest unmistakable reports date from the middle ages, and are by many authors ascribed to Jacobus de Partibus (1463) and the German, Agricola. Before that date, and for some time afterward, the disease was confounded with certain epidemic infectious diseases, especially the plague. Thus, the "plague" (pest) which originated in Cyprus in the years 1505–28 and ravaged almost the whole of Italy was undoubtedly typhus fever; this is probably true also of the disease called *morbus Hungaricus*, which raged in the army of Charles the Fifth during the siege of Metz, in the year 1552. The appearance of the disease in Italy at that time found a historian in Frascatorius, to whom is due the credit for the first lucid description of typhus, positively distinguishing it from other diseases, especially the plague. He called it *morbus lenticularis.*

Hildenbrand believes that a number of other diseases designated as the plague (pest) in the sixteenth and seventeenth centuries were undoubtedly epidemics of typhus fever—as, for instance, the plague in Hungary in 1556—febris Hungarica or pannonica; the plague in Meissen in 1574; the plague in Denmark (1613–52); and the plague in Leyden in 1669. Numerous other epidemics of later times—as, for instance, the "*Faulfieber*," reported by Hasenöhrl, that raged in and about Vienna in the years 1757 and 1759, and the epidemic of "*Faulfieber*" that spread over all the German provinces in 1771 and 1772—are with reason regarded by the same authority as *contagious typhus.*

In every century typhus fever has followed in the wake of armies. During the thirty years' war it claimed more victims than did the weapons of the contestants. It was the terror of the Napoleonic campaigns, and decimated the French army, already demoralized physically and morally by the terrible retreat from Moscow.

After the campaigns of 1793 and 1794 the scourge visited the whole of Germany. In 1796 and 1797 it broke out again, and after the great campaigns of the year 1805, it became epidemic throughout Gallicia, Hungary, and the Austrian crown-lands. The writings of Rennebaum, Schäfer, Hecker, Rasori, Larrey, Hufeland, Horn, and especially the famous monograph of Hildenbrand, which to-day stands as a pattern of epidemiology, refer to the above-mentioned epidemics of the end of the eighteenth and the beginning of the nineteenth century.

After 1830 the disease abated on the European continent, notably in Germany, while in Ireland and England, where the disease has always been prevalent, it continued unabated and occasionally broke

out in extensive epidemics. From 1816 to 1818 the disease raged throughout England and Ireland. In Ireland alone an eighth part of the entire population was affected, and in Dublin as many as a third of the inhabitants were attacked. Over 40,000 deaths were recorded.

The years 1826 and 1828 again witnessed severe epidemics in both countries. In the thirties Ireland suffered most, and in the beginning of the following decade Scotland chiefly was attacked. In 1846, the year of famine, an unusually severe epidemic broke out in Ireland, and this was carried to England, where it reached its highest point in 1847, and continued until the end of the following year. It is a fact that seems incredible that during that time more than 1,000,000 cases of typhus occurred in England, and more than 300,000 in Ireland (Murchison).

During these two decades the opinion that typhus had been permanently superseded by typhoid fever gradually gained ground in Germany. This illusion was dispelled by the epidemics of 1847 and 1848. Upper Silesia in 1847 was the first to suffer a severe outbreak of the disease. To Virchow we owe a classic description of the epidemiologic and social conditions of that period.

The later wars of the nineteenth century, like the campaigns of the first Napoleon, were characterized by the appearance of the scourge. During the Crimean war it decimated both the French and the English armies, especially the former, as even at that time hygienic measures were far better understood and carried out in the English camp. From the Crimea the disease was carried into France, where, as in Germany, the people had up to that time supposed that they were secure from the disease.

The Italian campaign of 1861 and the Turko-Russian war of 1878 contributed a number of victims. Judging from Michaeli's description, the sanitary conditions in the Russian army must have been appalling, and far worse even than during the Crimean war. According to this author, of 200,000 patients, at least 50 per cent. were attacked by typhus fever, and half of those attacked succumbed to the disease. During this epidemic the surgeons were the worst sufferers, the mortality among them reaching 60 per cent.

During the Franco-Prussian war, on the other hand, the armies remained entirely free from typhus, thus affording a striking proof that the disease is caused not so much by the massing and mobilization of large numbers of men, as by their continued presence in regions where the disease is either endemic or happens to be raging at the time.

In France, where the disease has never taken a firm foothold, its recent appearance again destroyed the illusion that French soil was not favorable to its development. In 1893 an epidemic broke out in Lille. The disease was carried to the prisons of Paris, whence it spread to the city and surroundings.

After the epidemics of 1847 and 1848, typhus fever continued to linger in certain regions of Germany until the beginning of the eighties. Since that time it has become endemic in Upper Silesia, and in 1867 it established itself in Eastern and Western Prussia. The disease is fed constantly from the neighboring Polish provinces of Russia, and at intervals it invades Germany, travelling in a direction from east to west, and spreading over the entire country. It is to be observed, however, that the intensity and distribution of the disease constantly diminish in the same direction, and it is only in the eastern portions of Germany, particularly in the frontier districts, that large endemic or epidemic outbreaks occur. When, in the years 1867 and 1868, the disease was carried into Eastern and Western Prussia by vagabonds, it swelled to enormous epidemics. Thus, in the district of Gumbinnen alone 4000 cases were reported (Guttstadt). During the period from 1875 to 1882 the eastern provinces and parts of Central Germany were visited by a severe outbreak of typhus fever; and during the five years from 1877 to 1882 Guttstadt reported 10,600 cases admitted to the Prussian hospitals.

In all the more extensive epidemics, Berlin and the larger cities of Northeastern and Southeastern Germany, such as Königsberg, Stettin, Danzig, Breslau, etc., were invaded to a greater or less extent. In every case the approach of the disease was from the east, and, fortunately, it never succeeded in obtaining a permanent foothold. In Berlin particularly, after 1870, the disease appeared almost every year, coming usually from Eastern and Western Prussia and Pomerania, the first stopping-place of the epidemic on its march from east to west. It spread among the class of inhabitants by whom it is usually carried—that is, vagabonds and persons out of work and without shelter. Charitable institutions, prisons, and the lowest variety of inns, known as "pens" (Pennen), were the chief foci of the disease. The better part of the population, those who possess a permanent domicile, were attacked only to a very slight extent, and these cases could almost always be traced to direct contact with typhus patients.

During the period from 1876 to 1879 I was superintendent of the Berlin pest-house, the lazaretto in Moabit, and there enjoyed abundant opportunity for studying the disease. I have the reports of 677 cases

dating from that time. Later I saw a few sporadic cases in Hamburg and Leipsic, brought by emigrants from Poland and Russia. The following description of the disease is based on a study of these epidemics and of a number of sporadic cases, occurring chiefly in my private practice, that were of especial importance from the standpoint of differential diagnosis.

ETIOLOGY.

ORIGIN AND MODE OF TRANSMISSION OF THE CONTAGIUM.

TYPHUS FEVER is one of the most contagious diseases known to medicine. It originates and spreads to predisposed individuals solely by the direct or indirect transmission of the specific contagium, developing in the body of the patient. The mode of transmission and entrance of the contagium into the body, although not as yet accurately known, is undoubtedly in all essentials similar to that which obtains in the acute exanthemata—small-pox, scarlet fever, measles, etc.

The possibility of the contagium of typhus fever originating outside and independently of the body of the patient is no more conceivable than is the spontaneous production of typhoid fever.

Long ago, at a time when a non-specific origin of typhus fever was considered possible and even usual, the contagiousness of the disease in the modern sense was upheld by a few physicians, notably by Budd, who was far in advance of his time. His teachings, however, were not able to dispel entirely the theory of miasmatic origin, which survived until a very much later date. Murchison himself, who acknowledged that the essential points in the disease are the specificity of the poison and its reproduction in the body of the patient, devotes some space to the possibility of an independent, spontaneous origin, a theory that even Griessinger, with all his acumen, does not quite venture to discard. He believes that in rare cases, especially when the disease breaks out in isolated places, as on shipboard, in prisons, etc., in the absence of typhus patients, "recourse must be had to the obscure realms of the miasma."

Long after Griessinger, Jaccoud [1] maintained that spontaneous production was possible and occurred not infrequently.

In quite recent times Kelsch again showed a leaning toward the same theory, believing that certain innocuous germs in the body may, under suitable external conditions, assume a great specific virulence.

Owing to the extreme facility with which the disease is carried from individual to individual, sporadic cases of typhus fever are very rare. The disease is almost always endemic or distinctly epidemic, and under unusually favorable conditions, especially when large numbers of men are massed together in social or military destitution, the number of individuals attacked is rarely equalled or exceeded by any of the other

[1] *Gaz. Heb.*, 1875; and *Patol. int.*, 1877.

infectious diseases. The most extensive epidemics are observed when the disease is carried from a country where it is endemic into a district usually free from the disease, and which therefore does not possess any immunity; or, conversely, when large numbers of predisposed individuals travel from such regions to countries where the disease is endemic, as occurs in emigration or during war.

GEOGRAPHIC.

In regard to the endemic distribution and permanence of typhus fever, England and Ireland occupy the first place among the countries of Europe. The disease never dies out completely in these countries, where it is the predominant form of "typhoid" disease. The disease is occasionally carried from the shores of Ireland and England to neighboring countries, particularly to countries with which England maintains an active commercial intercourse, and that are usually free from the disease and from the conditions that favor its becoming endemic. Such countries are Sweden and Norway, Belgium, Holland, North America, and, to some extent, France, whither, during this century, the disease has frequently been carried from other countries as well, notably from Russia.

With the exception of a few districts in the Southeast, such as Upper Silesia, Germany is usually quite free from the disease. When an outbreak occurs, it is almost always derived from the eastern countries, especially Russia, in many parts of which, particularly in the Baltic and Polish provinces, unfortunately for Germany, the disease is endemic.

In Hungary, Turkey, and the adjoining Oriental countries the disease apparently never becomes quite extinct.

Various parts of Italy have been visited repeatedly by obstinate epidemics of typhus fever. It has appeared in Piemont, Tuscany, Naples and its surroundings, Sicily, and Sardinia. In the two last-named islands the disease seems never to disappear entirely.

Spain and Portugal, owing to their geographic position, are relatively free from the disease, although mild outbreaks have occurred, the last one in Portugal in 1880.

In Africa the disease has been observed chiefly in the maritime portions that carry on an active trade with Europe. In Algiers, where it appeared for the first time in the early sixties of the last century, it seems to have become endemic.

Persia and China are never free from its unwelcome presence, the

misery and squalor of the inhabitants furnishing abundant opportunity for the occurrence of the disease.

India appears to be relatively free. Murchison could not determine to his entire satisfaction whether the reports that he collected from that country really referred to typhus fever or not; the reports of more recent times are also equally unsatisfactory.

THE NATURE AND MODE OF ACTION OF THE TYPHUS FEVER CONTAGIUM.

The foregoing remarks on the geography and history of the disease will suffice to show the enormous differences between typhus and typhoid as regards origin and spread. Whereas typhoid fever is found in almost all the countries of the earth, and is nowhere distinctly endemic, this quality of endemicity is peculiarly characteristic of typhus fever; and whereas, owing to the nature and mode of spread of its contagium, typhoid fever gives rise to severe epidemics only under very special circumstances, and occurs almost always sporadically or in circumscribed areas, the fugaciousness of the typhus poison and the ease with which it is transported through the air by inanimate carriers lead to rapid and widespread distribution of the disease when, in a given case, it is carried into a non-infected country whose inhabitants are predisposed to it by imperfect development, starvation, or the miseries of war.

Bacteriology.—Although, as has been remarked, we are quite certain that the contagium of typhus fever is a specific poison, elaborated solely within the body of the patient, and therefore undoubtedly referable to pathogenic micro-organisms, and although a great deal of careful investigation has been devoted to the subject, we are still in the dark as to its precise nature. Not one of the many micro-organisms brought forward up to the present time has gained complete recognition. In this respect the producer of typhus fever closely resembles that of the acute exanthemata, which, as will be shown more and more clearly in these pages, exhibit a very close similarity to typhus fever, both in their etiology and in their clinical features. Their exciting causes, like the cause of typhus fever, have obstinately resisted our present methods of bacteriologic research, and they accordingly form a special group among the acute infectious diseases, the etiology of which appears to require some entirely new and hitherto unknown methods of investigation.

The theory of the chemic nature of the poison of typhus fever is at the present time interesting for historic reasons only. Curiously enough, the supporters of the theory of a gaseous, ammoniacal nature of the "typhus

contagium" (Liebig and others) sought their strongest argument in the peculiar mode of origin and spread of the disease. Much interest attaches to a chapter in Griessinger's classic work, which stands as an example of incisive scientific reasoning, in which, after a careful analysis of all the etiologic factors, he refutes the theory of the gaseous nature of the contagium and declares it—the contagium—to be corpuscular and dust-like in character.

In regard to the various theories advanced as to the microparasitic nature of the typhus contagium, we shall pass over the isolated experiments of the first investigators and restrict ourselves to the more important of the newer contributions, which even the authors themselves do not always consider quite convincing.

In 1888 Moreau and Cochez[1] described a bacillus resembling the Eberth bacillus, which they isolated from the blood and urine of patients and which they regarded as the probable cause of typhus fever.

A year later Hlava's[2] work on the poison of typhus fever, based on material obtained from the Prague epidemic of 1888, aroused great interest among medical men. Hlava examined 45 cadavers and obtained from about two-thirds of them a peculiar streptobacillus, which he was able to find in the living subject also, although, it is true, not with the same constancy. The micro-organism was found only in the blood and could not be isolated from the organs. Hlava himself is very guarded in his statements as to the specificity of his micro-organism, and soon afterward it was disputed by other investigators (Cornil, Babes, and others).

In 1892 an important paper was published by Lewaschew,[3] who found minute, very refractive, coccus-like corpuscles in the blood of typhus patients, especially in that derived from the spleen. These were found in fewer numbers in other portions of the circulation—for instance, in blood taken from the tip of the finger. Some of these corpuscles were provided with flagella that could be stained by Löffler's method, like the flagella of the Eberth bacillus. He also found free flagella without any apparent connection with cocci. These Spirochetæ exanthematica, as he called them, Lewaschew regarded as various forms belonging to the same organism and indicating different stages of their life-history and development, and he was strongly inclined to accept them as the cause of typhus fever.

Soon afterward Thoinot and Calmette[4] declared that Hlava's micro-organism was only a secondary phenomenon without any etiologic significance, and brought forward a new cause of the disease. This they described as a flagellate, and in some cases ameboid, organism, which they claim to have found in the splenic blood of 5 living subjects, and in 1 case from the pulmonary blood after death.

Dubief and Brühl[5] described a small diplococcus provided with a capsule, which they claimed to have found in the blood, but especially in the

[1] "Contribut. à l'étude du typh. exanth.," *Gaz. hebd.*, 1888, No. 28.

[2] "Etude sur le typh. exanth.," *Arch. Bohème de méd.*, 1889, T. iii., 1, and *Centralbl. f. Bakt.*, 1890.

[3] "Ueber die Mikro-organismen des Flecktyphus," *Deutsch. med. Woch.*, 1892, No. 13. "Ueber die Mikroparasiten des Flecktyphus," *Ibid.*, No. 34.

[4] "Notes sur quelques examens de sang dans le typh. exanth.," *Annales de l'Institut Pasteur*, 1892, and *Traité de méd.*, by Charcot, Bouchard et Brissaux, T. ii., p. 9.

[5] "Contribution à l'étude anatomo-pathologique et baktériologique du typh. exanth.," *Arch. de méd. Expérim.*, 1894.

air-passages, in pulmonary foci, and in the sputum. These they said could easily be recognized when stained with methylene-blue. The micro-organisms were grown on various nutritive media, as agar, and yielded orange-yellow cultures. The authors also believe that they were able, by experimental inoculation of animals, to produce a condition resembling typhus fever.

Finally, it may be added that Mott[1] long ago described a variety of motile spirilla resembling Lewaschew's organisms in the blood of typhus fever patients, and, further, that Cheeseman claims to have discovered small non-motile bacilli with rounded extremities, occurring either in pairs or in short chains, which he says he was able to cultivate on blood-serum but not on gelatin, and which he called the Bacillus sanguinis typhi exanthematici. We thus have a veritable sample-card of bacteriologic findings, and it will be best for the present to reserve judgment. Quite recently, in fact, men (McOxney) have come forward declaring that the blood of typhus fever patients is free from specific micro-organisms. Kelsch's theory, that the cause of typhus fever is a micro-organism that is usually innocuous and becomes pathogenic only under special conditions, has already been referred to.

Nature, Persistence, and Mode of Dissemination of the Contagium.—It follows logically, from our ignorance of the precise nature of the *causa morbi*, that we are unable to say how and where it is produced in the body and what organs and tissues are particularly affected. For similar reasons the question as to the manner in which the poison leaves the body awaits future solution.

Most observers of the present day are of the opinion that the poison is contained chiefly in the exhalations of the patients—the expired air, the exhalations from the skin, etc.—and that it attaches itself to the dust contained in the surrounding atmosphere. Although the second part of this hypothesis tallies with the results of our experience, the first proposition should for the present be accepted with great caution.

The recent finding of Eberth bacilli in the rose-spots of typhoid fever (Neumann, Neufeld, Curschmann) strongly suggests the advisability, in future epidemics, of making similar examinations of the typhus fever rash with our improved bacteriologic methods. That the contagium is excreted in the feces and urine, as in other infectious diseases, seems doubtful in the case of typhus fever; certainly it has never been proved.

It is probable that for some time before and after, as well as during, the febrile period of typhus fever the contagium continues to reproduce itself in the immediate surroundings of the patient. During this time it undoubtedly attaches itself to the dust in the atmosphere, and is very easily transferred to inanimate objects handled by, or in the immediate neighborhood of, the patient, on which, under favorable circumstances, it maintains its virulence for some time. Among these objects are clothing, underwear, bed-clothes, curtains, carpets, upholstered furni-

[1] *Brit. Med. Jour.*, Dec., 1883.

ture, and, in fact, all objects with a rough, woolly surface. The fact that washerwomen, bedroom attendants, and those who are charged with the duty of disinfecting the infected articles are especially liable to be attacked by the disease in time of epidemic furnishes a strong proof of this, if additional proof were needed.

If such objects are protected against contact with air, particularly air in motion, the contagium clinging to them may maintain its vitality for many months, or even longer under especially favorable circumstances, and the disease may thus be carried to distant localities where it was not prevalent at the time and where it is not endemic. Such a transmission of the poison would furnish the most natural etiologic explanation of the well-known so-called spontaneous epidemics in prisons, on board ships, etc., which formerly afforded so favorite an argument in support of the non-specific origin of spotted fever. These facts also readily explain how the poison may linger in apartments inhabited by patients if the disinfection has not been properly attended to, as well as in cabs, railroad-cars, and other public conveyances. It should be remembered that healthy persons may, without becoming infected themselves, carry the poison in their clothes or in their hair, and in that way transmit it to individuals who are not immune. In the interest of the community this fact should be borne in mind by physicians, attendants, clergymen, friends of patients, and, in fact, by all persons who come in contact with them during times of epidemic.

There is a remarkable resemblance in all these conditions to those observed in the acute exanthemata—measles, scarlet fever, and small-pox. Owing to the great development of railroad and maritime transportation, spotted fever, like the acute exanthemata, has been carried even to distances that would formerly have been considered impossible for this disease to reach.

In Hamburg a furrier was attacked by the disease ten days after he had received a consignment of furs from an infected locality in Poland. He had not been absent from home for months; had not come into contact with any one suffering from the disease; and more than a year had elapsed since the last sporadic case of spotted fever had occurred in Hamburg. Fortunately, the patient was immediately isolated, and he was the only one among his immediate family and attendants who was infected. The disease was traced to the infected objects before they had been put on the market, so that they were immediately disinfected and the further spread of the disease prevented.

Transmission by Bodies Dead of Spotted Fever.—Even the cadavers of spotted fever patients may, under certain conditions, transmit the disease, although Murchison is, no doubt, disposed to exaggerate this danger, because he contracted his first attack of spotted fever in the dissecting-room. I do not think that the reproduction of

the poison in the cadaver is at all probable, and I believe that the infection takes place in very much the same way as in the case of inanimate objects on which the contagium has been deposited. In this connection it seems to me significant that the danger of infection is distinctly more marked in recent cadavers. Thus, while we never had a case of spotted fever among the physicians or servants during the epidemic in Moabit, although numerous autopsies were made in poorly ventilated rooms, one of my assistants and the dissecting-room attendant who performed an autopsy on a cadaver a few hours after death contracted the disease.

The Period of Greatest Danger of Infection.—At what period of the disease is the danger of infection greatest? Undoubtedly, at the beginning and at the height of the febrile stage. During the stage of defervescence, however, the danger of contagion is not inconsiderable. During convalescence, when the fever has disappeared permanently, there is probably no reproduction of the poison within the body, and contagion during this time occurs only by the transmission to predisposed persons of the poison that has been produced during the active period of the disease and been deposited on surrounding objects.

It is true that Perry and certain others consider the danger of contagion greatest during the period of convalescence; but I think this is an error that is due probably to a mistake in estimating the period of incubation.

For my part, I consider transmission possible during the period of incubation, and absolutely certain during the initial stage. The fact that during the latter period patients are able to go about or travel in cars may explain many cases in which the patients deny having come in contact with individuals affected with the disease.

In this connection I remember a very instructive case that I saw when a student. This occurred in one of my fellow-students, who became infected while attending a clinic on a typhus fever patient. He was one of three students from another department, who had spent an hour in a typhus fever patient's room at a time when the patient had as yet no fever, and complained only of slight general malaise, depression, and pain in the head and back; but none of the students had been in the room after that time. On the evening following their visit the patient was seized with a chill, this being followed by the usual initial rise in temperature. Eight days later one of the three students was taken with typhus fever. It was subsequently ascertained beyond a doubt that he had not returned to the house after that first visit and had not come in contact with any other patient; in fact, there had not been any other case of spotted fever in the town, all the others having been carefully isolated in the hospital.

The question whether or not the danger of infection varies in indi-

vidual patients or in certain forms of the disease is very difficult to decide. My own experience leads me to believe that it does not. Although Griessinger considers a severe case more dangerous than a milder one, we may venture to remind even this experienced author that it is never possible to estimate with sufficient accuracy the influence to be attributed to external favoring circumstances.

As to the claim that the severity of a given case is directly proportional to the severity of the case from which it is derived, I, for my part, must enter an objection. The intensity of the disease undoubtedly depends chiefly on the personal conditions of the individual attacked.

How and by what channels does the contagium find entrance to the body? I agree with the majority of observers in believing that in by far the greatest number of cases the poison that clings to infected objects in the immediate vicinity of the patient is carried through the air and enters the body through the organs of respiration. Entrance of the poison through the skin is also conceivable. The intestinal tract, which plays the most prominent *rôle* in the etiology of typhoid fever, appears to be of very secondary importance for the entrance of the typhus fever contagium. A very few authors (Netter) still maintain that direct contact with the patient is necessary for the transmission of the disease.

The question that has often been raised as to the **length of time necessary** to be spent in the neighborhood of the patient or the duration of the contact with inanimate carriers necessary to produce the infection has a purely theoretic interest. Given the necessary concentration of the poison and a fair degree of predisposition on the part of the individual, it appears certain that a very short time—even a few moments—may suffice to infect him, although it will be found difficult to procure reliable evidence on this point, especially during an epidemic.

I saw an instructive case of this kind, occurring in a furniture manufacturer, who was quite certain that he had not come in contact with any fever patients nor with any suspicious objects, and among whose employés there had not been any case of spotted fever. He had, however, interviewed a workman, who appeared to him to be ailing, promising him employment after he should have recovered his health. The interview did not last more than five minutes, and was held in his private office, which was very small and badly ventilated, the windows being closed. Two days afterward the workman was seized with typhus fever and admitted to the lazaretto at Moabit, where he had a typical, though mild, attack of the disease; while the manufacturer, whom I saw while acting as a consultant during his illness, contracted a very severe form of the disease on the seventh day after his interview with the workman.

Most patients give a history of having been exposed to infection repeatedly or continuously for a long time. The precise moment when the poison effects an entrance into the body is no doubt dependent on accidental individual or external conditions.

In general it may be said that the danger of infection increases with the frequency and duration of exposure and with the concentration of the poison. The latter stands in direct ratio to the number of patients, and in indirect ratio to the size and excellence of the ventilating facilities of the wards.

Reaction of the Poison to Chemical and Physical Agents.—The poison appears to be constantly reproduced in the body of the patient during the febrile period, and it unquestionably maintains its highest degree of virulence in his immediate vicinity, being intimately united to dust and other carriers of that kind. It does not appear to be easy to destroy the poison by chemical means. The simpler methods of disinfection formerly used, such as spraying the room with carbolic acid or chlorin water, are probably of very little value. The newer disinfectants that have recently been recommended, such as formalin, have not as yet been thoroughly tested. The disinfection of beds, linen, and other objects used about the patient's body with the above-named disinfectants is quite inadequate.

Physical agents, on the other hand, appear to be far more destructive to the poison than any chemical disinfectants known at the present time. High temperatures especially are of value in this respect. In Moabit, where many experiments with dry heat were made, the clothes and personal effects of the patients were rendered absolutely sterile by exposure to a temperature of 100° to 120° C. for one or two hours.

Of the effect of cold, very little is known, although Hildenbrand believes that very low temperatures have a distinctly destructive influence.

It is, of course, well known that epidemics are both more frequent and greater in extent during the winter than during the summer; this is due to the social conditions existing during the winter season.

It would appear that the poison is not carried a very great distance through the air. According to my experience, it is much less easily transported than that of variola, and possibly also than that of other acute exanthemata.

While in small-pox epidemics I have often seen cases in which the poison was wafted across a narrow street and carried to the inmates of a house on the opposite side, I have never seen infection carried in this way in Moabit, where we had often to fill one barracks with typhus

patients, and the adjoining one with patients suffering from surgical injuries. It is owing to this quality of the contagium—that of not being easily carried to a great distance—that, when an isolated case of typhus fever is admitted to a hospital by mistake or want of judgment, the disease does not spread beyond the patient's immediate neighbors, providing the wards are large and airy. The epidemic becomes general only when the number of typhus patients in the wards increases.

Ventilation has a marked influence on the contagium, the prophylactic importance of which cannot be too much emphasized. In large, well-ventilated wards that are not too crowded the virulence is much diminished, especially if the patients are kept in the open air, or if the doors and windows are left open.

I made some very instructive observations in this respect in the lazaretto at Moabit. During the summer months I kept our patients almost all day in the open air, which incidentally had a very good therapeutic effect, and in winter the windows were kept constantly open, the wards being kept well heated, however. Not a single physician and very few of the attendants were infected; of the latter, only those were infected who, contrary to my orders, had bathed the patients in the small, ill-ventilated bath-rooms, instead of in the spacious, well-ventilated ward.

So much for the general conditions that favor the origin and spread of the disease. The poison has always been found most virulent when large numbers of persons have been crowded together in improperly ventilated and ill-kept localities under bad hygienic conditions. Prisons, badly planned barracks, inns, and lodging-houses of the lowest kind, work-houses, ships, and defectively built hospitals are the chief foci of the disease. Hence it is that we have the various synonyms, lazaretto fever, ship fever, prison fever, camp fever, etc.

PREDISPOSING CONDITIONS.

PERSONAL CONDITIONS.

The predisposition to typhus fever appears to be universal, and is very strongly developed in most individuals.

Immunity.—Very few appear to be entirely immune by birth. The older authors, notably Hildenbrand, believed that the body could become accustomed to the poison, and in this way a certain grade of acquired immunity against the disease might be developed, as among attendants, physicians, and priests, who frequently work among patients during severe epidemics. I think this is very doubtful, and none of

the more recent authors, among whom I would count myself, appears to have had any favorable experience in this respect.

On the other hand, one attack of the disease confers an acquired immunity on the great majority of persons, lasting a long time—usually for the remainder of the individual's life. In this respect, also, typhus fever resembles the acute exanthemata, especially scarlet fever, measles, and variola. Whether the degree of immunity after an attack of typhus fever is as great as it is in these other diseases is a question on which there is a difference of opinion among the various authors. Griessinger and Murchison report cases of the same individual being attacked more than once. Griessinger does not seem to consider this a very rare occurrence, and Murchison acquired his experience from his own case, he having been attacked twice by the disease.

It has been reported that the same individual has been attacked twice even in the same epidemic.

I myself, however, am of the opinion that one attack of typhus fever confers almost as perfect an immunity for the remainder of the individual's life as does an attack of any of the exanthemata.

In consequence of such a belief, it has long been the custom everywhere in the beginning of an epidemic to employ attendants who have already had the disease. The wisdom of this procedure is proved by Murchison's experience in the London Fever Hospital. He says that he never saw an attendant attacked more than once.

Age and **sex** appear to exert a very subordinate influence on the susceptibility to typhus fever, as is shown whenever the entire population of a locality is exposed to the same channels of infection under identical external conditions. Not inconsiderable differences have, of course, been observed, some of which are easily explained, while for others the explanation has not as yet been found.

In many epidemics the male population is more generally attacked than the female; but when the conditions are carefully examined, it is found that the males, owing to their mode of life and occupation, are more frequently and more constantly exposed, both to the poison itself and to the various predisposing factors; and we accordingly find that whenever the disease is carried into localities that had before been free from infection, the cases are at first almost exclusively confined to the male population, but as the disease develops, and in the course of time gradually extends to the resident portion of the community, these differences gradually disappear. In countries where the disease is endemic and is not brought in by the floating population, it usually affects both sexes equally from the beginning.

The best proofs of this we find in England and Ireland, the classic homes of typhus fever. In the London Fever Hospital, during fourteen years, 3780 men and 3792 women were admitted. During the Irish epidemic of 1817–19 the number of women was even greater than that of the men, 32,144 males and 34,398 females being attacked by the disease.

If we compare this with the statistics obtained in Guttstat in Prussia, where typhus fever is endemic only in a limited sense, and is usually brought in from neighboring countries, we find that, during the years from 1881 to 1885, among a total of 3928 individuals attacked there were 2905 males and 1023 females.

The statistics that I obtained in Moabit strikingly illustrate what happens when the disease is not distinctly endemic and when stringent hygienic precautions are taken to prevent the floating population from infecting the permanent residents. During the years 1878 and 1879 we treated by far the greater number of all cases of typhus fever that occurred in Berlin, a total of 520; of these, 488 were males and only 32 females.

On the other hand, we have an interesting communication from Passauer, which proves that when the sexes are equally exposed to infection, they are equally susceptible. He tells of a wedding party that found a typhus patient in the house where the wedding was held, and that followed him to the grave a few days later. Of the members of the party, 19 were attacked —8 of them women.

I myself have observed similar cases. I remember, during the Berlin epidemic, in one of the meaner lodging-houses the proprietor, his wife, two barmaids, and a porter were attacked at the very outset of the epidemic.

As to the question of the influence of **age,** we must not place much reliance on mere numbers, but must take into consideration not only the variations in physical condition incident to age itself, but also the differences in social condition, mode of life, occupation, etc., peculiar to the different periods of life. If we examine the reports based on large numbers of patients in extensive epidemics, or the statistics of large hospitals in typhus fever regions, we find that the disease is not nearly so much confined to a certain period of life as are the other acute infectious diseases, especially typhoid fever. Every period of life will be found represented among the adults, including individuals over fifty years of age, in whom, as is well known, the predisposition to typhoid fever is diminished. In fact, the statistics in any large epidemic of considerable duration show that the percentage of individuals attacked in the later decades of life is quite as great, or even greater, than the percentage of all patients among the inhabitants.

Children are quite as liable to the disease as persons of advanced age, although older children appear to be more susceptible than younger ones. Infants at the breast are the least disposed. Among children, those between the ages of five and fourteen appear to be the ones most commonly attacked. From the first to the fifth year, just as in

typhoid fever, the susceptibility is diminished, although it is distinctly greater than in suckling infants. The degree of liability of children is seen when an epidemic breaks out in a locality where the disease has raged for some time among the adult population, a good many of whom are immune. Under such circumstances the morbidity among children, which usually ranges between 12 and 16 per cent., may increase enormously, as is shown by the Dorpat epidemic of 1866 and 1867. In this epidemic Behse found that 60 per cent. of those attacked were children.

The fact that among adults the prime of life and most productive period furnish unusually large numbers of cases is readily explained by external conditions. It is during this period that a man is most active in the struggle for existence, and is then, more than at any other time, exposed, both to the danger of infection and to predisposing factors.

For a further elucidation of the subject the following tables are added. The first table shows the distribution as to age of the 440 patients admitted to the lazaretto in Moabit in the year 1879:

Age.	Patients admitted.
Under 10	3
10 to 20	40
20 to 30	182
30 to 40	105
40 to 50	68
50 to 60	33
60 to 70	8
70 to 80	1
	440

If we compare this table with that of an equal number of typhoid fever cases similarly arranged according to age, we see at once that in typhus the latter periods of life are more strongly represented: almost one-third of the patients were over forty years of age, and 41 of 440 patients were between fifty and seventy.

A similar result is shown in the following table from the Guttstat statistics:

Age.	Patients admitted.
Under 15	433
15 to 40	3064
40 to 60	699
Over 60	89
Not ascertained	72

Murchison's statistics of 3456 cases treated in the London Fever Hospital possess an equally strong interest and are particularly instructive because they deal with a country where typhus fever is endemic.

Age.	Total number attacked.	Percentage.
Under 5	17	0.49
5 to 10	183	5.29
10 to 15	363	10.47
15 to 20	546	15.79
20 to 25	495	14.32
25 to 30	343	9.92
30 to 35	323	9.34
35 to 40	270	7.81
40 to 45	292	8.44
45 to 50	212	6.13
50 to 55	150	4.34
55 to 60	100	2.89
60 to 65	88	2.54
65 to 70	42	1.21
70 to 75	24	0.69
75 to 80	6	0.17
Over 80	2	0.06
	3456	

The proportion of children attacked is illustrated by the following figures collected by Gräzer and Lebert during the Breslau epidemic of 1869. Of a total of 1873 typhus fever patients, 271, or 14.57 per cent., were children, divided according to age as follows:

Age.	Number.
0 to 1	0
1 to 5	35
5 to 10	77
10 to 15	159
	271

The table shows a marked rise in the proportion with increasing age, and a similarity in the proportion shown by the various ages of childhood to that in typhoid fever—a similarity that disappears in the case of adults.

Again, suckling infants show a very slight disposition, as do also children under five years of age. From this period the liability increases with each year of life.

Certain physiologic conditions among women, such as **pregnancy,** the **puerperium,** and **lactation,** do not appear to have any particular influence on the liability to typhus fever, nor do they confer any immunity against the disease. This is an interesting point in the differential diagnosis from typhoid fever, against which these conditions appear to afford a certain protection. The influence of the disease on the fetus has not as yet been determined.

General Conditions.—The **general bodily health** and the **individual** and **social conditions of life** on which it depends play an important *rôle* in the etiology. Opinions on this point have not been modified to any extent by the experiences of later years.

It is a matter of general experience that the liability to typhus fever,

in itself so well marked and wide-spread, is increased by anything that exhausts the individual and lowers his bodily and mental tone. Want and poverty, hunger and worry, and other depressing circumstances have always been the most powerful allies of the disease.

Such conditions, of course, include unhygienic living and close crowding in filthy and ill-ventilated houses, subjects that have already been sufficiently discussed. We have seen what an important part they play in maintaining and augmenting the virulence of the contagium. Such unfavorable conditions are naturally most marked in times of general destitution and economic depression, during war and other great movements among the population.

In this respect typhus fever again presents a marked difference from typhoid fever, which is prone to attack young and vigorous individuals, and has comparatively little direct connection with overcrowding, insufficient ventilation, and pollution of the atmosphere.

A few investigators, especially in France, have expressed the opinion that the disease was not due so much to the mental and physical exhaustion induced by poverty and general misery as to the inevitable massing together of large numbers in small, badly ventilated houses, and the consequent increased danger of direct infection.

A glance at the conditions of the better classes will, however, suffice to refute this opinion. Although they live amid better surroundings and in more carefully ventilated houses, it is found that among them overexertion and exhaustion act as distinct predisposing factors. Physicians, attendants, officials, and clergymen are particularly likely to acquire the disease by contact with patients when they are weakened by long-continued labors during the height of an epidemic, their vital forces being exhausted by excessive work, worry, and loss of sleep.

Cases that furnish a striking proof of this statement can be found in almost all the epidemics. I recall the case of a young physician, in his thirty-second year, of powerful build and in prime condition, who worked through a severe epidemic of typhus fever lasting three months, during which time he spent almost all day and a good part of the night in ill-ventilated wards filled with typhus patients; but, nevertheless, he did not contract the disease. Some time later, after he had become much weakened by certain depressing experiences, loss of sleep, and nervous dyspepsia, he treated only a few patients in well-kept houses in a large city, contracted the disease within two weeks, and was brought to the verge of the grave.

Cases of this kind illustrate temporary variations in the liability of the same individual, and tend to show that the liability to the disease may suddenly become very great under certain conditions.

On the other hand, some facts can be cited to show that the susceptibility to the disease is diminished when the individual is in perfect

condition, although not in the same degree as it is increased by depressing bodily conditions.

In Hamburg I have frequently seen patients who had contracted the disease outside the city, and who, before coming to the hospital, had spent hours and even days in lodgings situated in narrow streets, without transmitting the disease to any of the native inhabitants. The only explanation for this that I can give is that even the poorer people in Hamburg earn comparatively good wages, and are, accordingly, fairly well fed, so that their bodies are generally in good condition.

It need hardly be said that **exhausting diseases** have the same effect as what the French call *la misère physiologique*. Among convalescents from other acute infectious diseases there is unquestionably a greater disposition to contract the disease and reproduce the *materia morbi*. In hospitals where the typhus patients are not sufficiently isolated, patients convalescing from other diseases are found to be particularly liable to the disease.

Chronic or Acute Diseases.—In the same way, a still existing chronic or subacute condition that has led to a marked disturbance of the nutrition will increase the liability to the disease. Individuals suffering from chronic or subacute gastro-intestinal catarrh and nervous dyspepsia appear to be particularly susceptible. Experienced physicians tell us how, during great epidemics, individuals who up to that time appeared to be comparatively immune, may be attacked if they become reduced by digestive disturbances and are then exposed to the infection. Patients suffering from chronic nervous diseases, especially when they are anemic or emaciated, also appear to be very easily infected.

Of the influence of circulatory and renal diseases, nothing appears to be known, nor have I any reliable observations to offer in this respect.

The relation of typhus fever to chronic pulmonary disease, especially to tuberculosis, has given rise to some differences of opinion. I cannot understand how some of the prominent older physicians, such as Hildenbrand, can speak of the relative immunity of such patients, and I must agree with Murchison in taking the opposite stand. Among my patients I had a large number whose apices were not entirely sound; and if it is admitted that tuberculosis not infrequently complicates or follows typhus fever, it cannot well be denied that at least a large proportion of these patients had a latent tuberculosis at the time they were infected with typhus.

Chronic intoxications, such as lead-poisoning, and particularly the abuse of alcohol, act as distinct predisposing factors.

The effect of the poison of typhus fever on patients suffering from

other acute infectious disease, especially during the febrile stage, has not as yet been discussed in the literature.

In regard to variola and typhoid fever, I think I have adduced strong proofs that they offer a marked resistance to the entrance of the germs of other acute infectious diseases, at least during the febrile stage, and that this immunity only diminishes with the beginning of defervescence and does not disappear until the fever has entirely subsided. But we know nothing of the behavior of typhus fever in this respect, except in connection with recurrent fever. Patients suffering from the latter disease are, according to my observation, as well as according to other authors, very susceptible even during the febrile stage.

I saw an instructive case of this kind during the epidemic of 1879 in the lazaretto at Moabit. It was that of a young man, twenty-three years of age, in whose blood the spirilla had been found on the last day of the third relapse. On the following day the patient had a severe chill and his temperature began to rise; the fever continued high, and on the fourth day a characteristic and very abundant typhus fever rash made its appearance. The attack was mild and very short, the fever having entirely disappeared on the eleventh day (see Fig. 57).

Needless to say, experiences such as these do not justify similar arguments in regard to other infectious diseases.

Occupation and **social conditions** can influence the liability to typhus fever only in so far as they determine the physical predisposing factors that have been referred to, or as they involve an unusual exposure to the infection. Both these conditions are present in the poorer classes. Among the better classes the question of exposure is, of course, more important than constitutional conditions, which are unfavorable only as the result of accident or occupation.

Some English authors claim for special occupations a certain degree of protection against typhus. They mention in this respect tanners, workers in fat, candlemakers, and butchers. In attributing their relative immunity to the fact that they are more or less constantly handling putrid material, Griessinger unconsciously inclines toward the miasmatic theory of typhus fever, which he has himself elsewhere refuted.

For my part I have seen as many cases of the disease among butchers as among other workmen. It is true that during our epidemic the individuals belonging to this trade were most of them vagabonds. But even if it should be found that butchers are less liable than other workmen, a fact which, as I have said, I do not consider proved, the most natural explanation is that they are unquestionably better nourished.

SEASON AND METEOROLOGIC CONDITIONS.

Among general etiologic factors the season and meteorologic conditions are to be mentioned. They exert very little influence on typhus fever, which, therefore, differs in this respect from other diseases. In fact, it would appear that the development and invasion of the inciting cause are in no wise modified by such external conditions.

It has been observed, however, that the disease is more prevalent during the colder season, most of the epidemics having reached their height in the early months of the year,—that is, in the latter half of the winter or the early spring,—and subsided again during the summer. But this can be explained in another way. During the cold season all the factors influencing individual disposition and transmission of the poison, such as want of employment, poverty, and overcrowding in badly ventilated houses, are much more active. With the coming of summer the poorer portion of the population naturally tends to scatter, work becomes more plentiful, and the conditions of life are accordingly improved.

It has always been observed in the larger cities, notably in Berlin, that the disease rapidly disappears among the wandering, houseless portion of the inhabitants as soon as they begin to sleep in the open air instead of seeking the shelter of "pens" and asylums.

GENERAL MANIFESTATIONS OF THE DISEASE.

Sporadic Cases.—Endemics and Epidemics.—The etiology of typhus fever is in many respects peculiar, and this alone lends to the disease a distinct character of its own, especially as regards its outbreak and the manner of its spread. A number of features that distinguish it sharply from typhoid fever and give to it a marked resemblance to the acute exanthemata could be mentioned. The development and extension of the disease depends chiefly on the following factors:

Individual predisposition, which is practically the same for both sexes and all ages; the immunity acquired by one attack, which in the case of most individuals persists throughout life; the great ease with which the poison is carried through the air; its virulence and persistence whenever ventilation is defective; and, finally, the fact that the disease is constantly present in but few countries of the earth and is only occasionally carried to others.

This explains why in countries where typhus fever is endemic, and the population is practically saturated with the poison of the disease, it is only relatively endemic or sporadic, becoming distinctly epidemic only when a large number of predisposed individuals have had time to

collect. It never fails to assume alarming proportions when it is carried to a region where it is not endemic and where the entire population is accordingly predisposed to it; or when, on the other hand, large numbers of predisposed individuals come into countries where the poison is constantly present, as occurs in time of war or in great migratory movements.

That the presence of the poison is an absolutely essential factor under such circumstances was shown by the Franco-Prussian war. Although the world has never seen the mobilization of greater masses of men than occurred at that time, typhus fever did not develop, while typhoid fever and dysentery, which have an entirely different etiology, claimed innumerable victims. The wide distribution of typhoid fever is one of its chief points of distinction from typhus fever. Thus, while typhoid fever occurs sporadically, or, at least, among a relatively small number of patients, and becomes epidemic only when the amount of the infective material is accidentally increased in rivers and water-systems, typhus fever is scarcely ever confined to single cases or house epidemics, and then only under special circumstances. It regularly assumes the form of a tremendous epidemic whenever the contagium invades a population that is not protected by constant exposure and that lives amid bad social and hygienic conditions.

Epitome.—Our discussion of the etiology may be epitomized in the following conclusions:

Although the cause of typhus fever has not as yet been determined, it is certain that the disease does not arise spontaneously, and that its development and distribution depend on the action of a specific cause that is produced only in the body of an individual affected with the disease, and that is transmitted by him either directly or indirectly to other predisposed individuals.

The disposition to the disease is universal. Other things being equal, all ages, excepting infancy, and both sexes are equally attacked.

The condition of the individual, especially a depraved state of nutrition and loss of vital energy due to the effects of poverty, hunger, and disease, exerts an enormous influence on the disposition. Typhus fever is the disease of poverty-stricken and suffering humanity, and it always follows in the wake of war and misery.

The great majority of individuals acquire immunity by one attack of the disease.

The way in which the germs leave the body of the individual in whom they are produced, and the port of entry by which they gain access to the body, are not known; it is probable that the respiratory

organs and the external skin play the most important *rôle* in this respect.

The germs of the disease are most plentiful in the immediate neighborhood of the patient, and they are carried by dust.

They attach themselves with great tenacity to the various objects that come into direct contact with the patient or that have been exposed to the surrounding air. In this way the disease may remain dormant for a long period of time and may be carried to distant places entirely free from the disease, circumstances that lend color to the former theory of spontaneous development.

Plenty of fresh air and good ventilation exert an undoubted influence in restricting the spread of the disease. Conversely, also, the vitality of the germs increases in direct proportion to overcrowding and inadequate ventilation.

The germs do not appear to be carried by liquid media, least of all by water; nor do they appear to reside in the soil or to have any especial relations with it, as was formerly erroneously believed of typhoid germs.

The sum total of etiologic factors easily explains the great ease with which the disease spreads and its peculiar tendency to appear in epidemics. It also explains why the disease, when imported into regions where it is not epidemic, first attacks the poorer portions of the population and spends its greatest force among them, and, if it spreads to the better classes at all, does so only in severe epidemics and when the disease is at its highest.

PATHOLOGY.

GENERAL FEATURES.

THE STAGE OF INCUBATION.

LIKE the other acute infectious diseases, typhus fever has a stage of incubation—that is to say, a period intervening between the effective inoculation of the patient and the true beginning of the disease.

In the great majority of cases the patients are entirely free from symptoms during this period. Only occasionally do they complain of indefinite symptoms, such as headache, vertigo, pain in the back, loss of appetite, fatigue, or depression. In a few instances coryza and conjunctival catarrh have been noticed. In the case of two individuals who became infected in the hospital, under my personal observation, there was very slight fever, with practically normal daily variations.

The length of the period of incubation varies, owing to some causes not as yet very well known. I agree with most authors in considering the usual duration to be from eight to twelve, at most fourteen, days; but a duration of from four to seven days has repeatedly been observed. On the other hand, an incubation stage of three weeks' duration should always be regarded with suspicion.

A few cases have been reported in the literature by reliable authors (Murchison, Gerhard), in which the incubation was said to have lasted only a day or but a few hours. The shortest period in my experience was four days. This was in a man, forty years of age, coming from a locality absolutely above suspicion, who had taken part in certain festivities at a public house where he had been a stranger. Four days later he was attacked by the first manifestation of the disease. Immediately after the festivities referred to, the innkeeper, his wife, one child, and several regular patrons of the place developed typhus fever and were admitted to the lazaretto.

The statements of some of the older writers (Hayarth, Barallier and Cheyne, Bankroft) in regard to cases in which the incubation period lasted from one and a half to six months are due unquestionably to errors of observation or diagnosis.

THE SUBSEQUENT COURSE OF THE DISEASE.

The subsequent course of the disease may best be described by giving the history of a severe, well-developed case in a healthy adult, ending in recovery.

Unlike typhoid fever, but similar to the acute exanthemata, spotted fever presents a remarkable uniformity in its chief manifestations, in its

duration, and in the course and mode of its termination. In all large epidemics not markedly modified by external conditions, especially social ones, the characteristic picture is the same in its main features. A comparison of the disease as we know it to-day with the descriptions of older authors shows that it has not changed in any essential particular in the course of time.

The onset of the disease is almost always abrupt. The fever is ushered in by one or two distinct chills, or, more rarely, by chilly sensations lasting for several hours or an entire day. This in most cases ends the true initial stage of the disease. In consequence of the sudden, violent onset and the rapid rise of temperature with chills, the patients are very much prostrated from the outset. Most of them are quite unable to work, and take to their beds on the first day; while even those who possess a great resistance usually give up on the second or third day; consequently, medical treatment is sought much earlier than is usually the case in typhoid fever.

The chill is either accompanied or followed immediately by nausea, vomiting, a sense of pressure in the epigastrium, and pain in the back, the patient from the very beginning lying passively in bed in the dorsal position. The face is feverish and red, presenting a peculiar edema; the conjunctivæ are usually very much congested, and secrete copiously. The mucous membrane of the nose and palate in many cases becomes boggy and reddened as early as the evening of the first day, and the patients complain of a feeling of dryness and scratching in the throat, or even of marked dysphagia. While the mind is usually clear except for a slight depression and apathy during the daytime, marked disturbances of the sensorium begin to show themselves toward evening or during the night. The patients begin to lose interest in their surroundings, easily drop the thread of a conversation, and, if left alone, have disturbing dreams and talk in their sleep.

After the chills and the nausea and vomiting have subsided the fever rapidly rises, and a dull, throbbing, sometimes violent and stabbing headache, vertigo, and tinnitus aurium become prominent symptoms. Some individuals suffer from violent pain in the sacral region and cannot rest easily in any position, while others complain of tearing and dragging pains along the large nerve-trunks, especially in the legs, or of hyperesthesia in the finger-tips, toes, and soles of the feet. Pain in the joints is rarely present.

The tongue is tremulous and dry, and before the end of the first twenty-four to thirty-six hours it has become covered with a dirty, yellowish-brown exudate. The dryness of the other mucous membranes

becomes more marked, the swelling of the pharynx and tonsils increases, and the patients complain bitterly of a raging thirst.

The appetite is altogether lost. The abdomen is neither swollen nor painful, excepting in the epigastric region, which in many patients is very sensitive to the touch. In the beginning and during the entire first week the bowels are usually constipated; rarely there is diarrhea. The spleen, *even at this period*, is found by percussion and palpation to be distinctly enlarged, a feature that is characteristic of the disease and forms a useful diagnostic point in the differentiation from typhoid fever.

The prostration increases so rapidly that most patients are barely able to sit up during the first days of the first week; but, notwithstanding their lassitude, they toss about restlessly in bed, unable day or night to obtain refreshing sleep.

The fever-curve differs from that of typhoid fever in that it rises rapidly on the first few days, reaching a considerable height and exhibiting slight daily variations, which do not, as a rule, exceed half a degree. It partakes of the character of a continued fever, or, more rarely, of a continued remittent fever, and early attains an evening temperature of 40° C., although in severe cases and irritable individuals it may reach from 40.5° to 41°. The temperature rarely falls below 39° in the morning.

With the rapid rise of temperature there is a corresponding rapid, uninterrupted rise in the frequency of the pulse. Even in vigorous men the pulse usually reaches 100 on the forenoon of the second day, and in the evening hours it rises to 110 or 120, while women and children show an even greater excitability in this respect. I have never seen, in the beginning of typhus fever, the disproportion between the pulse-rate and the temperature that is so valuable a diagnostic feature of typhoid fever, and that is so frequently observed in young men with typhoid.

The arteries in the beginning are soft and the pulse is normal in volume and tension. The dicrotism, characteristic of typhoid fever, is absent during the first days, and sometimes later, in by far the greater number of cases.

While the fever and other general disturbances are undergoing a rapid and uninterrupted rise, there appears, between the third and the fifth day, or occasionally before that time, a phenomenon that is most characteristic of the disease and often determines the diagnosis. This is the roseolous eruption. It appears at first in the form of pale-red, hyperemic patches, varying in size from that of a pin-head to that of a lentil, circular or oblong in shape, and having ill-defined edges.

When the rash develops uniformly, the patches appear first on the lower abdomen and on the chest and shoulders. Thence they spread at once over the back and extremities down to the dorsal surfaces of the hands and feet with such rapidity that the ultimate number of the patches is usually reached within from forty-eight to seventy-two hours. The palms of the hands and soles of the feet almost always escape, and by far in the greater number of cases the face as well, the last being simply very much reddened and swollen, and often assuming an absolutely uncanny expression on account of the reddening and hemorrhagic injection of the conjunctivæ.

Simultaneously with the eruption of the roseola, or, in irritable individuals, before it, a measle-like rash makes its appearance, affecting with predilection the extensor surfaces of the forearms, the legs, chest, and abdomen. This fades before the disappearance of the typical eruption and leaves no trace.

During this period of the disease, which is often designated the stadium exanthematicum, many patients present marked disturbances of consciousness, even during the daytime. Their movements become more abrupt, and they lose all interest in their surroundings. At first loud in their complaints, they become more and more subdued, and cease to complain of vertigo, headache, or backache.

The tongue now becomes covered with scales and is marked with fissures that bleed easily. If, as happens in some cases, the coating separates, the tongue appears unusually thin and pointed, and its surface shines as if it were lacquered. Meanwhile the catarrhal symptoms in the pharyngeal structures and in the larynx have increased. There is hoarseness or even aphonia; the presence of a short, dry cough shows that the bronchi are also involved. This is confirmed by auscultation, which reveals crepitant and subcrepitant râles over the entire extent of the lungs.

The complete development of the eruption usually marks the zenith of the disease. The fever by this time has reached its height and remains stationary for a varying period of time, the temperature-curve usually presenting the character of a continued remittent fever. The apathy and somnolence that marked the beginning of the disease are now often replaced by violent excitement. The patient is quite unconscious, and finds no rest by night or by day. Some talk, work, or gesticulate in their dreams, either reviewing former periods of their lives or imitating their usual occupations. Others become violently excited by visual or aural hallucinations. They imagine they are being pursued and threatened with personal violence; they cry out and defend

themselves; they jump out of bed and try to escape from their tortures by flight or by attacking their attendants. Typhus fever patients in this stage of the disease are incomparably more difficult to manage than any others, and the work in a well-filled ward is about as exciting and exhausting an experience as doctors or nurses are likely to meet with in the exercise of their profession.

During this time—usually on the second or third day after its appearance—the roseola eruption, which was at first a pure hyperemia, undergoes a peculiar transformation. A certain proportion of the spots, varying in number in different cases, assume a petechial type, small hemorrhages appearing in the center of the patches or spreading to the periphery and eventually occupying the entire site of the eruption. The roseolæ, which at first were pale and indistinct, now become more pronounced. They become copper-colored, with livid centers, or the entire spot may assume a dirty, bluish-red appearance. In the severest type of the disease most of the lesions undergo this transformation; and when, in addition, cutaneous or extensive subcutaneous hemorrhages make their appearance, the skin may assume a many-colored dusky appearance that is positively terrifying.

During the first half of the second week—sometimes a little earlier, sometimes a little later—the clinical picture, as a whole, has usually reached its highest development. The patients are at this time extremely weak and prostrated, absolutely apathetic, and cut off from the external world. The hearing is practically lost, the speech is mumbling and unintelligible, and the eyes are staring; with mouth wide open and hanging, tremulous jaw, the patient lies in bed picking at the bedclothes, with subsultus tendinum and carphology.

The wild gestures and the shouting, tossing, and struggling cease, and in their place we have a condition of stupor, or, in extreme cases, a true coma-vigil. All desire for food or drink is gone, swallowing is difficult, and the urine and feces are discharged involuntarily. At this time there is frequently diarrhea.

Meanwhile the fever still continues at its original height. The pulse is more frequent and much smaller and weaker; occasionally it may be intermittent and irregular. As a result of the long continuance of the hyperpyrexia and the further extension of the bronchitis, the respirations are accelerated, superficial, and labored. In grave cases an examination of the chest at this time will show either a simple hypostatic condition, a lobular pneumonia, or an extensive inflammatory hypostatic consolidation of one or both lower lobes.

Taken all together, the clinical picture is worse than anything that

can be imagined in acute infectious diseases. But recovery is possible, even when the disease has reached this extreme stage. Fortunately for the patients, it is a sharply self-limited affection that runs a certain course and from which recovery is possible even in the severest cases, providing the physician can manage to sustain his patient during the few days that must elapse between the time of severest intoxication and the crisis.

In moderately severe cases, and in severe, uncomplicated cases ending in recovery, the fever usually begins to fall between the tenth and the twelfth day of the disease. It may continue to the fourteenth day, but it rarely lasts longer than this. With the fall of temperature most of the other symptoms begin to subside. The temperature-curve up to this time maintains the character of a continued remittent fever. In a few cases there may occur, one or two days before the crisis, a so-called *pertubatio critica*, or very marked variation in the temperature, the nature of which will be discussed in detail in another place.

In the great majority of cases the fever falls by lysis, with a step-like curve, rather than by crisis, with a rapid, continuous defervescence. In other cases, however, the fall is so abrupt that the normal temperature is reached within forty-eight hours, or at most after three days. A defervescence lasting five days and over, with marked intermission or irregularity in the curve, is comparatively rare, and should suggest a careful examination for possible complications.

The beginning of defervescence is marked by an improvement in the pulse. At first soft, small, and of low tension, it decreases in frequency, as a rule, in direct proportion to the fall of the temperature, so that during the first afebrile days it registers between 80 and 100, but does not fall quite to the physiologic rate.

The return to the normal frequency is gradual. As late as the fourteenth day, or even later in very severe cases, there may be marked variations in the pulse-rate after the slightest physical or mental disturbance, which, under normal conditions, would have no effect. As in other acute infectious diseases, the period of defervescence is frequently followed by bradycardia, which may last for from several days to a week, the exact nature and cause of which have not been satisfactorily explained.

The enlargement of the spleen, which is not present in all cases, even in the beginning, subsides with the commencement of the second week, when it can no longer be determined by palpation. A persistence of the enlargement until the period of defervescence is so rare that it

suggests the presence of complications or of a splenic tumor due to some cause existing before the onset of typhus fever.

The characteristic skin-lesions subside after the disease has reached its highest point, and, with the exception of those patches that have undergone petechial change, do not persist until the period of defervescence. The petechial lesions usually undergo branny, rarely shreddy, desquamation, and, after the subsidence of the fever, they remain in small numbers as dirty-brown, livid, or yellowish-green spots.

The skin during the height of the febrile stage is hot and dry. As the fever begins to fall, however, it becomes moist, and in many cases, especially when the fever has fallen by crisis or rapid lysis, there is profuse sweating.

With the subsidence of the febrile symptoms the tongue regains its moisture, the coated patches clear up, and the excoriations and fissures heal. The voice gains in strength and resonance, and the hoarseness, when due simply to catarrh or erosions in the larynx, disappears; not infrequently, however, the laryngeal manifestations are quite severe and persist for some time or may even be incurable.

The disturbances in the digestive apparatus, particularly the diarrhea, which is quite frequently present during the second week, disappear with the subsidence of the fever. Most patients very soon show a good appetite, which, as will presently be seen, it is quite safe to gratify with a comparatively liberal diet.

If, as usually happens in uncomplicated cases, even before the fever has entirely disappeared, the evening rise of temperature becomes less marked and the patient gets a little uninterrupted sleep, he may in a surprisingly brief time recover from a disease that shortly before had been the cause of the greatest anxiety, not to say the despair, on the part of his attendants.

Barring complications and sequels, the duration of which cannot be foreseen, the end of defervescence is reached in the great majority of cases within from twelve to seventeen days, and the patient enters upon the period of convalescence. In not a few moderately severe, mild, and abortive forms of the disease the febrile period is ended much earlier. Cases that at the onset were quite severe may reach the stage of defervescence in from six to ten days; while the milder and abortive cases may terminate favorably as early as the third or the fifth day.

When death is caused simply by the severity of the disease—that is to say, by the toxic effect on the vital organs—it occurs usually in the middle or second half of the second week. A fatal termination before the ninth day, or as early as the fifth or sixth day, occurs only in the

most severe forms of the disease or in individuals with little resisting power. Very few uncomplicated, fatal cases last longer than the second week.

As in all infectious diseases, complications and sequels may prolong the morbid process indefinitely, and eventually lead to a lethal termination.

MORBID ANATOMY.

THE EXTERNAL FINDINGS.

With the exception of the not very numerous cases in which the skin of the cadaver shows pronounced traces of the characteristic eruption, little that is peculiar is found at the autopsy. The chief findings are such as are always observed in acute infectious diseases, and a diagnosis at the autopsy-table can at best only be made by exclusion.

Owing to the brief duration of the disease, typhus fever cadavers exhibit very little emaciation. Rigor mortis is often slight, and lasts but a short time. Livid spots appear early and in great profusion, and, as in many other infectious diseases (septic processes, typhoid fever), decomposition begins early, even in cool weather.

If death occurred while the eruption was present, greenish-yellow or livid, dimly outlined patches, interspersed with petechiæ and larger hemorrhagic areas, may still be seen. Branny desquamation of the epidermis may also be observed, particularly when, as frequently happens, sudamina were present.

Bed-sores are usually absent, being found only when the patient has died of complications and sequels lasting some time. In a few cases phlegmonous processes or circumscribed areas of cutaneous gangrene are present on the fingers, toes, ears, and tip of the nose.

The muscles, which, like the fat, are not diminished in volume, appear red and dry, and on section often have a dull sheen. Certain muscles, especially the recti and the muscles of the thigh, occasionally present ulcerations that, from the presence of fresh hemorrhages, are seen to have been produced during life. Under the microscope the muscles present the changes described by Zenker in typhoid fever: simple atrophy of the fasciculi, with granular and fatty degeneration; more rarely, waxy degeneration occurs, which, when present, is less extensive than in typhoid, thus possibly affording an explanation why the peculiar linear or macular changes producing the "fish-flesh" appearance so frequently found in typhoid fever cadavers are almost constantly absent in typhus fever.

The bones and joints do not appear to have been carefully investi-

gated in typhus fever, and I myself have no personal observations to offer on this point.

THE CHANGES IN THE RESPIRATORY ORGANS.

The respiratory organs frequently, if not regularly, present changes of various kinds.

The changes in the upper air-passages, which are so frequent and which in many epidemics extend to the deeper portions, have already been referred to in describing the general clinical picture.

Swelling, maceration, and congestion of the mucous membrane of the nose, pharynx, and larynx are among the typical findings. In addition to these, we often find superficial erosions of the mucous membrane and moderate inflammatory enlargement of the tonsils. On the other hand, diphtheric changes in the pharyngeal structures, with the production of deep ulcers, are distinctly more rare. In a few cases I have seen an extensive diphtheric membrane in the larynx, extending as far as the trachea and the larger bronchi.

In reports of many epidemics we find mention of extensive suppuration of the pharynx and of severe laryngeal affections, conditions practically absent in other epidemics (Griessinger, Murchison). My personal observations were of a very unfavorable character. In almost 4 per cent. of the cases coming to autopsy I found intense laryngeal disease, consisting in marked reddening and swelling of the mucous membrane, with edema and erosions or fissures, the last particularly on the posterior wall, on the epiglottis, and on the ventricular bands. Associated with these changes I observed repeatedly the presence of perichondritis, which in every instance was confined exclusively to the arytenoid cartilage. The condition appears to be generally unilateral, and it almost always leads to necrosis of the affected cartilage, which, being in immediate contact with the deeper layers, is constantly bathed by the pus contained in the pocket formed by the mucous membrane. Weichselbaum reports similar findings in connection with the purulent changes of the pharynx and larynx. Comparing these changes with those observed in the same parts in typhoid fever, one is struck by an extraordinary resemblance, pointing to similar causes in the two processes, which unquestionably are not specific. In the deeper air-passages the most constant findings consist in a catarrhal condition of the trachea and bronchi, involving usually their finest ramifications, a condition that should be regarded as part of the disease itself rather than as a complication. The mucous membrane is intensely red, and covered with a moderate amount of tenacious secretion; occasionally it is the seat of

hemorrhages, rarely large in extent, occurring particularly in cases where similar changes are found in other mucous and serous membranes. In 4 cadavers in which the laryngeal mucous membrane presented a diphtheric exudate the same condition was found throughout the entire bronchial tree, including its finest ramifications.

This diffuse bronchitis is closely related to the atelectasis and lobular pneumonia which are quite frequently found. Hypostatic congestion of the lower lobes was found in almost all the bodies examined. Occasionally there were found infarcts.

The frequency of lobar pneumonia varies in the different epidemics and in different localities. While Murchison and the older English writers regard it as a rare occurrence, and some of the prominent younger French physicians (Thoinot, Netter) do not even describe it, we in Berlin found lobar pneumonia of one or several lobes as the immediate cause of death in 15 per cent. of all our typhus fever cadavers. The infiltration was exceedingly dense, and the color on section was a grayish yellow or an unusually bright yellow, closely resembling the appearance generally seen in fibrinous pneumonia. It remains for later bacteriologic investigations to show whether the similarity in the appearances depends on a similarity of cause, in which case lobar pneumonia must be considered as a true complication.

We may mention in passing that pneumonias evidently similar in character have been in more recent times also observed in other localities (Krukenberg and Braunschweig, Hampelen and Riga).

A few authors note the transition of pneumonia into gangrene of the lungs, but I have never seen such a result follow the form of pneumonia just described. Murchison, Griessinger, and others do not appear to have seen many cases of gangrene. It is true that I have seen 5 cases of gangrene, but they were all due to perichondritis of the larynx, which was exceedingly prevalent in the epidemic of 1879, and was present in every one of the cases mentioned. In each instance the necrotic cartilage was immersed in a pocket of fetid pus that had perforated into the interior of the larynx, so that aspiration of the putrid materials must have been inevitable.

Except for the fibrinous pleurisy regularly present in pneumonia, few changes were observed in the pleura; the most frequent were ecchymoses and small circumscribed patches of fibrinous exudate. Serous exudates are very rare, while empyema and fetid effusions in connection with putrid changes in the lungs are somewhat more frequent.

THE CIRCULATORY ORGANS.

There is almost always unilateral dilatation of the heart. In cases where death occurs relatively early, the muscle is flabby, friable, dull, and of a yellowish red color, with occasionally reddish streaks and linear and punctate markings. We unquestionably have to deal with the form of infectious myocarditis that has recently been studied by the aid of modern microscopic technic in typhoid fever, scarlet fever, diphtheria, etc.

In some of the older reports of autopsies the endocardium is often described as dark red or livid in color. There is no doubt that such changes are due to post-mortem imbibition. True inflammatory processes in the endocardium, especially in the valves, are by common consent regarded as among the greatest curiosities in typhus fever. Pericarditis appears to be equally rare. I have never seen it.

The condition of the vascular system in typhus fever has not been the subject of much investigation. In the aorta and large arterial trunks I have found isolated, apparently recent, peculiar yellowish patches. It is uncertain whether the circumscribed cutaneous gangrene described in a former paragraph is due to vascular changes; and if it is, the character of these changes is unknown.

The blood in a typhus fever cadaver is darker and more fluid than normal. Coagulation is distinctly less marked, and in the majority of cases is not observed in the cavities of the heart.

These findings tally with the statements of older authors in regard to the character of the blood taken from the patient during life. These authors emphasize the diminished coagulability and the softness and solubility of the blood-clot, from which, however, they draw conclusions that we are not disposed to admit at the present time.

THE DIGESTIVE ORGANS.

In addition to the above-mentioned changes in the pharynx, we may include among the alterations at the entrance of the digestive tract occasional excoriations and fissures in the tongue, with maceration, hemorrhages, and even ulceration of the gums. Older authors speak of the noma-like degeneration of the mucous membrane of the mouth and cheeks. Nothing of this kind was noted in the more recent epidemics.

The esophagus is almost always intact, and the stomach exhibits no characteristic alterations. Occasionally small hemorrhages are found in the mucous membrane, and in rare cases lacerations (Virchow) that during life had caused an admixture of blood with the stomach-con-

tents. In addition to catarrhal phenomena, the intestinal mucous membrane not rarely presents ecchymoses; in other respects the intestinal canal is almost always normal. Infiltration or degeneration of Peyer's patches and the solitary follicles is never found, and the mesenteric glands are accordingly unchanged. Very occasionally I have observed slight prominence and softening of the follicles in the lower portion of the small intestine. The statements in the older literature in regard to the occurrence of intestinal ulcers, especially in the small intestine, betray an error in diagnosis. The cases were undoubtedly "ileotyphus" (typhoid fever), which, as we know in practice, was not properly distinguished from typhus fever until long after the difference between the two diseases had been firmly established on theoretic grounds.

When ecchymoses are present in the gastric and intestinal mucous membrane, they are usually also found on the peritoneum, which in all other respects is unchanged.

The liver does not, as a rule, present any variations other than those observed in acute infectious diseases generally, namely, marked enlargement, increased consistency, hyperemia, or distinct signs of cloudy swelling. A fatty liver, which is said to occur frequently (Krukenberg), is not, in my experience, a common occurrence.

THE SPLEEN.

The splenic changes are not so constant as they are in typhoid fever. When death occurs later in the disease than usual, the enlargement of the spleen is not infrequently absent; while, on the other hand, when death occurs between the eighth and the twelfth day or earlier, it is practically always present. The section in such cases presents a dull wine-red, or occasionally dark-red, color; the markings are completely blurred and the pulp is soft, sometimes even semifluid or almost fluid. Occasionally we find infarcts, which in extremely rare cases may lead to rupture (Jaquot).

Both the older and the more recent authors agree that the occurrence of splenic enlargement is much less frequent and the degree of enlargement is much less in typhus than in typhoid fever. One of the most radical statements on this point is that of Barallier (epidemic in the prison of Toulon), who found splenic enlargement in only one-third of a total of 166 cases. Gerhard found the enlargement present also in only one-third, while Murchison reports finding it in two-thirds of his autopsies. I myself investigated the spleen in 72 autopsies on typhus fever patients during the years 1878 and 1879. Taking 250 grams as the extreme for a normal spleen (Henly), I obtained the following results: Not enlarged in 22 cases; 250 to 300 grams in 15; 300 to 400 grams in 16; 400 to 500 grams in 10; 500 to 600 grams in 2; 600 to 700 grams in 3; above 700 grams in 1 case.

This shows that when enlargement was present at all, a moderate degree was the rule. The relation of the splenic enlargement to the duration of the disease in fatal cases has been referred to previously. It is illustrated in the following table of 63 of the foregoing cases, compiled by my assistant, Salomon:

Duration of the Disease.	Weight of the Spleen.						
	Normal.	To 300 grams.	To 400 grams.	To 500 grams.	To 600 grams.	To 700 grams.	To 800 grams.
7 days	1	. .	. .	. .	1	1	
8 "	. .	1					
9 "	1	1	1				
10 "	1	. .	1	. .	1	1	1
11 "	2	1	. .	1			
12 "		1	3	1			
13 "	2						
14 "							
Over 14 "	12	4	4	3			

THE GENITO-URINARY ORGANS.

The kidneys, as a rule, are moderately enlarged, hyperemic, and quite often in the condition of pronounced cloudy swelling. Acute nephritis, such as occurs in scarlet fever, is mentioned by most observers as a comparatively frequent complication.

In Moabit, in 1878 and 1879, we found, among 80 cadavers, 5 cases of pronounced recent parenchymatous nephritis. Three of these cases were described as hemorrhagic nephritis, as they presented hemorrhages in the kidney substance, in the mucous membrane of the pelvis, and in the upper portion of the ureters.

Nothing else peculiar to typhus fever was seen in the remaining portions of the genito-urinary tract and in the genitalia. Occasional changes in the endometrium, suggesting premature labor or abortion, seem to show that typhus fever, like most other infectious diseases, is very likely to interrupt pregnancy.

THE NERVOUS SYSTEM.

The nervous system in typhus fever has received little attention, notwithstanding the prominent part it plays in the symptomatology. Hyperemia of the surface of the brain, edematous infiltration and opacity of the pia mater, and an increase in the ventricular fluid, which, as a rule clear, may occasionally become hemorrhagic, are the most important changes noticed with any regularity. True meningitis appears to be very rare, or at least to occur only in certain epidemics. Personally, I have not met with a case of it at the autopsy-table. Hampelen, on the other hand, mentions 4 cases of purulent meningitis in the epidemic studied by him.

Meningeal hemorrhages are distinctly more frequent. Every one

acquainted with the morbid anatomy will recall a few cases of circumscribed meningeal hemorrhages, sometimes so extensive as to cover an entire hemisphere.

On the other hand, hemorrhages into the brain-substance are distinctly rare. The tissues of the brain are usually softer than normal and exude a serous fluid. The thickening and whitish opacity of the pia mater and of the dura, which is closely adherent to the cranium, and the increase in the Pacchionian bodies, are merely signs of chronic alcoholism, so frequent in typhus fever patients.

As to the spinal cord, a few authors have mentioned increase in the quantity of the spinal fluid. In regard to changes in the peripheral nervous system, nothing is known.

SYMPTOMATOLOGY.

Whereas the anatomic changes in typhus fever are quite indefinite and present so little that is characteristic that it is exceedingly difficult to make a diagnosis at the autopsy-table without an accurate knowledge of the patient's condition during life, the clinical course of the disease, at least in well-developed, severe or moderately severe cases, is so characteristic that it may be said to follow certain definite laws. Such unvarying regularity is found in but few other diseases, except possibly in the acute exanthemata. Although the cause of typhus fever, like that of the acute exanthemata, is still unknown to us, we may, nevertheless, assume the existence of a micro-organism, the effects of whose development and activity on the body of the individual attacked are so marked as far to outweigh in importance any of his constitutional or acquired peculiarities. Indeed, these effects are much more marked than is the case in many other infectious diseases, especially in typhoid fever. It is to this micro-organism that we attribute the regular mode of onset and ending of the disease, its well-defined duration, the regularity with which certain symptoms, especially the eruption, appear and disappear, and the peculiar character of the temperature-curve. The latter is of such vital importance in the diagnosis and prognosis of the disease that we accord it the first place in the following discussion.

THE TEMPERATURE.

This was first subjected to careful study by Wunderlich.[1] His results were later confirmed by Griessinger, Moers, and others. In the main, these original results obtained by Wunderlich still hold good at the present day.

[1] *Arch. f. physiol. Heilk.*, Bd. i., S. 177, and *Das Verhalten der Eigenwärme in Krankheiten*, Leipsic, 1870, 2. Aufl.

The Temperature in the Beginning and Later Stages.—The fever is ushered in by one, or possibly several, chills, more rarely by a vague sensation of chilliness, and the temperature rises rapidly, so that as early as the evening of the first day it may exceed 39°, and not rarely reaches 40°. After a moderate remission of not more than half a degree on the following morning, the temperature continues to rise steadily, and on the evening of the second day goes beyond the point reached on the preceding day, registering 40.5° and over. After another lapse of twenty-four hours, with a very slight morning remission, it reaches 41° and even higher. In most cases another rise is noted on the evening of the fourth day (compare Fig. 48). This rapid rise in the curve distinguishes typhus from typhoid fever. A gradual

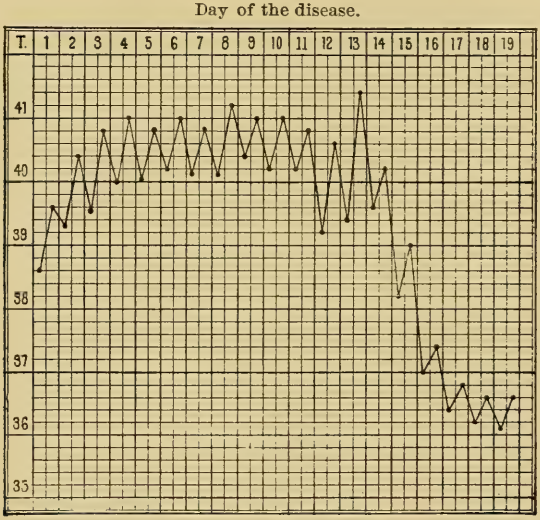

FIG. 48.—Severe case of typhus. Typical fever-curve (in part diagrammatic).

rise in the temperature to its highest point, such as occurs in the latter disease, would be a great exception, and cases of typhus are quite frequent in which the highest point is reached at the end of thirty-six, twenty-four, or even in a very few hours (compare Fig. 57). During the second half of the first week the curve persists at the same height, with moderate morning remissions not exceeding 0.5°, or it continues to rise slowly until the eighth day, so that in severe cases the thermometer at this period may register 41° or over. The behavior of the curve during the first week of the disease is so very peculiar as to be of the highest diagnostic value. While, on the one hand, it rules out typhoid fever, the diagnosis of any other of the exanthemata is equally improbable, as in none of these diseases, much as they resemble typhus fever in other

respects, do we have the same rise and uniformity of the temperature during the first week of the disease (Fig. 48).

Most of the modern authors, evidently on Wunderlich's authority, mention the occasional occurrence of a characteristic drop in the temperature at the end of the first week, usually on the evening of the seventh day. They are inclined even to accord it some diagnostic value. There can be no question as to the fact, since it has been reported by a goodly number of reliable observers, but it is probable that the phenomenon does not appear with the same frequency in every epidemic. Of the 440 cases in my hospital analyzed by Salomon, this temporary fall in the temperature was noticed in only 3 cases (Fig. 49).

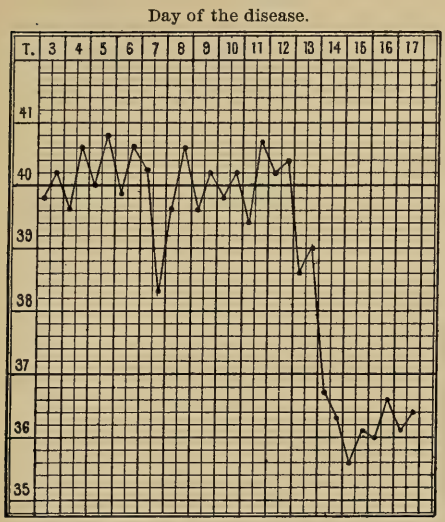

FIG. 49.—Peddler, eighteen years old. Moderately severe case of typhus fever. Remission on the evening of the seventh day of the disease.

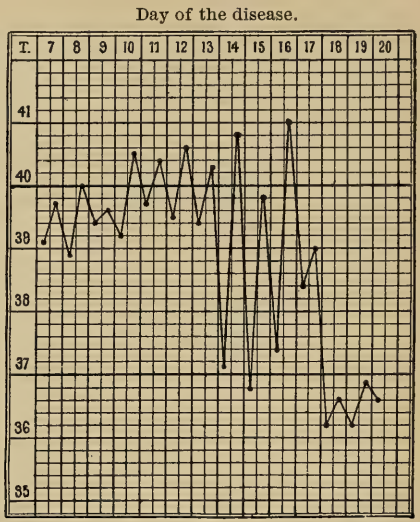

FIG. 50.—Apprentice, seventeen years old. Moderately severe course. Marked precritical variations in the curve.

A few clinicians (Lebert) attach some value to the observation that even in severe cases the temperature-curve presents marked irregularities as early as the last days of the first week, affecting particularly the daily variations. This is, I believe, true of the milder cases; but when the disease runs its full course and the case is a grave one, the phenomenon, in my experience, does not occur. On the contrary, the fever, which is of a continued remittent type in such cases, usually persists at the same height until the first days of the second week, or there is a perceptible remission during the morning hours, while the evening temperature remains constantly high.

After the tenth and eleventh days of the disease, sometimes as early

as the ninth, a marked evening remission begins to appear (compare Figs. 48 and 61), and the curve becomes distinctly more irregular, often showing marked intermissions. In the severest cases, where the prognosis is very bad, the fever continues high even during the last days of the (second) week, and occasionally rises to great heights. In such cases the ominous phenomenon of *calor mordax* is particularly marked.

The beginning of defervescence in severe and moderately severe cases ending in recovery is noted at the end of the second, or, rarely, during the first days of the third, week. I observed it most frequently between the twelfth and the fifteenth, and exceptionally on the sixteenth or the seventeenth, day of the disease. The permanent subsidence of the temperature that follows in the great majority of cases is occasionally preceded by a period of from twenty-four to thirty-six hours (compare Fig. 50), during which there are marked variations in the curve, with severe and very alarming disturbances in the patient's general condition. Not infrequently there is an extreme rise of temperature, to the height of 41° or even 42°, followed within from twelve to eighteen hours by a fall below the temperature of the preceding morning (compare Figs. 48 and 61), whereupon the final fall by crisis or lysis usually occurs without any further interruption. The older authors have described this by the expressive term *perturbatio critica* (Fig. 51).

A contrary (precritical fall) behavior of the curve is a distinctly rarer occurrence. Immediately preceding the permanent subsidence of the fever, the temperature suddenly falls to the normal or below it, and within twelve hours or less returns to or a little beyond its former height. This so-called "pseudocrisis" is immediately followed by the final fall in the curve (Fig. 52).

The Period of Defervescence.—The temperature-course during the stage of defervescence strikingly recalls what occurs during the initial stage. The abruptness and rapidity with which the fever rises are usually paralleled by the completeness with which the temperature falls to or below the normal within a few hours or days. It is not at all a rare occurrence for the temperature to fall at one drop, usually during the night, from a considerable height—40° and above—to 37° or even less (Fig. 53). More frequently this fall is interrupted by a temporary rise in the curve, the temperature at first sinking to 38.5° or 38°, and then, toward evening, mounting 1° or 1.5° before its final return to the normal, where it then persists practically without interruption.

With almost equal frequency, instead of this single interruption, the fall of the temperature may present a step-like curve extending

over from three to four days (compare Fig. 61), while an even more gradual ending of the curve by distinct lysis is much rarer (Fig. 54)

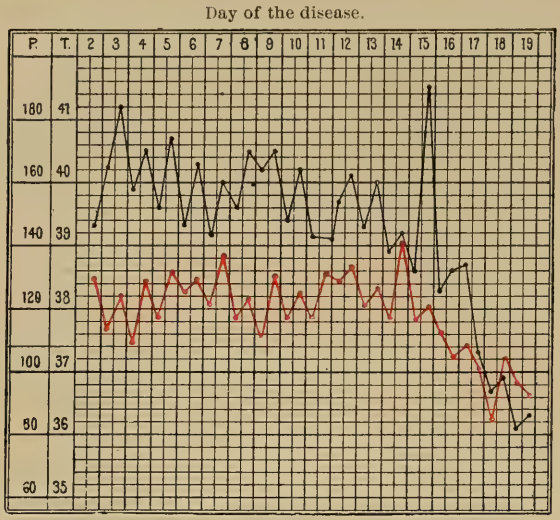

FIG. 51.—Woman, thirty-three years old. Very severe, uncomplicated case with great cardiac weakness. Marked precritical rise in the temperature.

The tendency to marked intermission during the period of defervescence, which is almost typical of typhoid fever, is very slight in

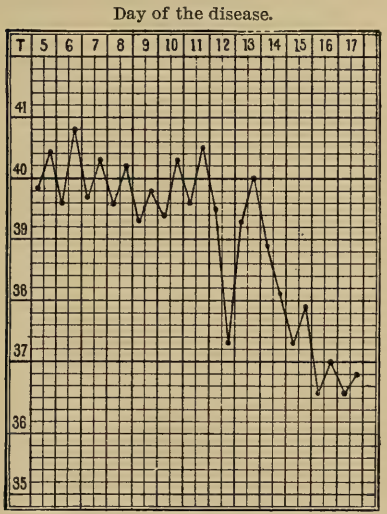

FIG. 52.—Man, thirty-one years old. Severe case of typhus fever. Pseudocrisis on the twelfth day of the disease.

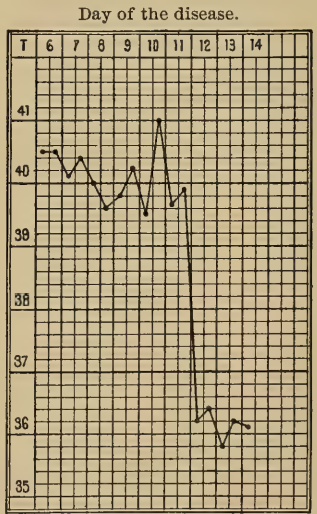

FIG. 53.—Man, nineteen years old. Moderately severe case of short duration. Distinct fall by crisis, preceded by a pronounced precritical rise.

typhus fever. As we have seen, we find only occasional cases (compare Fig. 50) in which the final subsidence of the fever is preceded by a

period lasting two or three days, during which there are considerable variations in the curve, with low morning and very high evening tem-

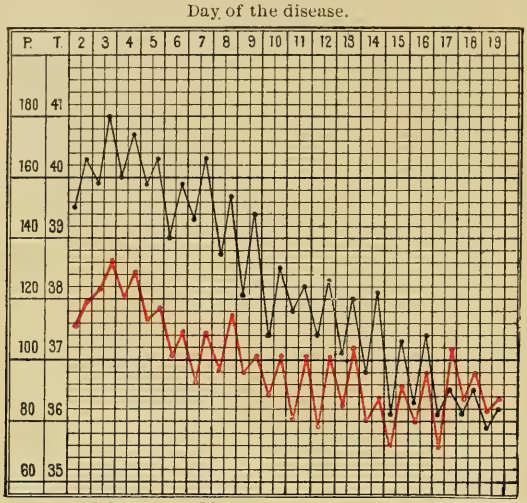

FIG. 54.—Foreman, twenty-eight years old. Onset severe; subsequent course mild and short, with a very protracted period of defervescence.

peratures. This phenomenon has received special attention from Rosenstein, who appears to have observed it frequently.

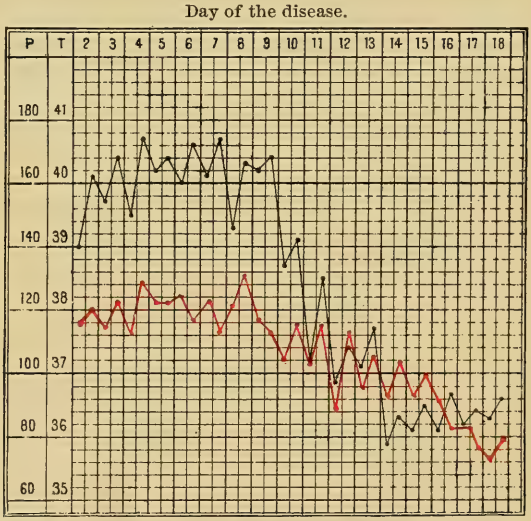

FIG. 55.—Woman, twenty-seven years old. Severe course during the first week; very short duration. Beginning of defervescence on the ninth day of the disease.

Temperature Variations in Different Forms of the Disease.—In severe and moderately severe cases the febrile period, as has previously been stated, usually ends between the fifteenth and the

twentieth day. Sometimes, though rarely, uncomplicated cases remain febrile until the beginning or even the end of the fourth week.

Cases that begin to recover before the end of the second week belong to the milder forms of the disease. The lessening of the duration affects chiefly the fastigium, during which the temperature may be quite high. Cases are not at all rare in which there is an evening temperature of 40° or even 41° C., persisting until the end of the first week, with a morning temperature of not much lower than 40° (Fig. 55). Others, again, present marked remissions and intermissions of the curve during the very first days, but even in such cases the evening temperature rises to a higher point than is commonly observed during the first week of typhoid fever.

The initial stage also is frequently abridged in the milder cases—

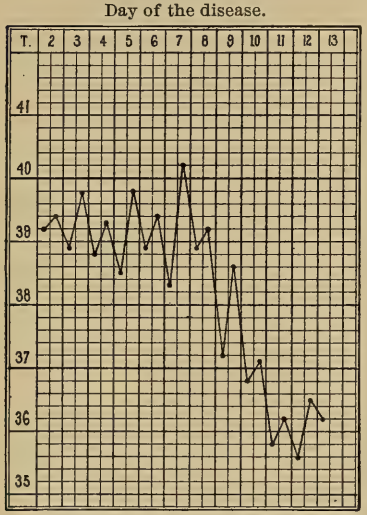

FIG. 56.—Waiter, eighteen years old. Mild case with relatively low temperature. Precritical rise.

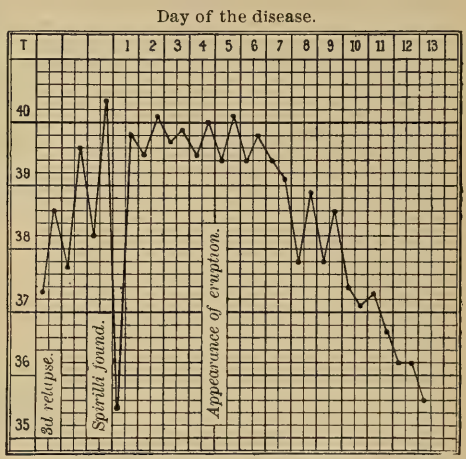

FIG. 57.—Man, twenty-three years old. Mild case of typhus fever following immediately upon an attack of recurrent fever. Abrupt rise of the temperature without remission, and gradual, step-like defervescence.

more frequently, perhaps, than in the severe ones. The fever may attain its height in from twenty-four to thirty-six hours, either at one bound or with a single interruption. Among the cases that have come under my observation during the first days I have never observed a gradual rise of the fever followed by an abortive course. On the other hand, the period of defervescence is more often protracted in mild cases than it is in severe ones, in which the course of the disease is not abridged. In such mild cases I have often observed a gradual, step-like fall of the temperature, covering from five to eight days, down to or

even below the normal (Fig. 57). The daily variations are usually comparatively slight. A termination of the fever by crisis, lasting not more than from twelve to eighteen hours, appears, on the other hand, to be no more frequent in mild than in severe cases.

Very mild or distinct abortive forms of typhoid fever have not as yet received very careful study. My own observations, especially in regard to the course of the temperature, are incomplete. The accompanying illustration (Fig. 58)—the history of the case will be given later—shows that the temperature may reach a considerable height after a rapid initial rise. Cases with very low temperatures, or practically afebrile, such as the typhoid fever expert is so familiar with, I have

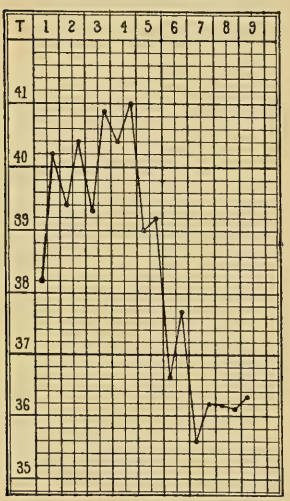

FIG. 58.—Woman, thirty-one years old. Abortive case of typhus fever with severe onset.

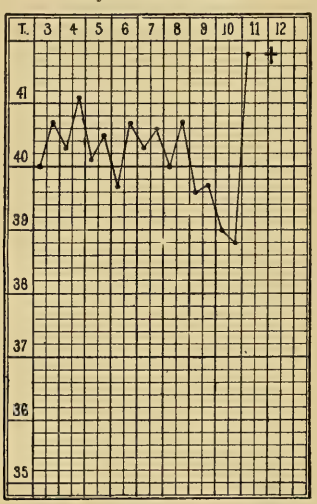

FIG. 59.—Laborer, forty-two years old. Excessively high temperature immediately preceding death.

rarely observed in typhus fever, but I would not care to affirm that they are in reality rarer than in typhoid fever.

In those fatal cases in which the patient succumbs to the severity of the intoxication and not to complications, the temperature-curve is usually shorter than in the severe ones ending in recovery. The great majority of such cases are characterized by violent onset and chill and an unusually high temperature from the very beginning, with slight morning remissions. Death usually occurs between the ninth and the twelfth day—rarely as late as the sixteenth day. A perceptible preagonic rise in the temperature is a common phenomenon (Fig. 59). In one of my cases the thermometer registered 42.2° C., and Wunderlich

reports a case in which the temperature was 43°. I was frequently able to determine a marked rise in the rectal temperature after death.

Of the causes that determine a preagonic rise of temperature we know nothing, nor can we give any more definite information in regard to those cases in which death was immediately preceded by a rapid fall of temperature far below the normal. The accompanying illustration shows a terminal temperature of 33° C. (Fig. 60).

In isolated cases, preferably, as it would appear, in individuals reduced by want and illness, this ominous fall in the temperature lasts several days. The pulse gradually diminishes in tension and becomes so rapid that it cannot be counted. The patients become cyanotic, and the temperature steadily falls until life finally ebbs away in almost imperceptible degrees. The occurrence of marked intermittent variations in the curve preceding a lethal termination, of which Wunderlich gives an illustration, did not come within my experience.

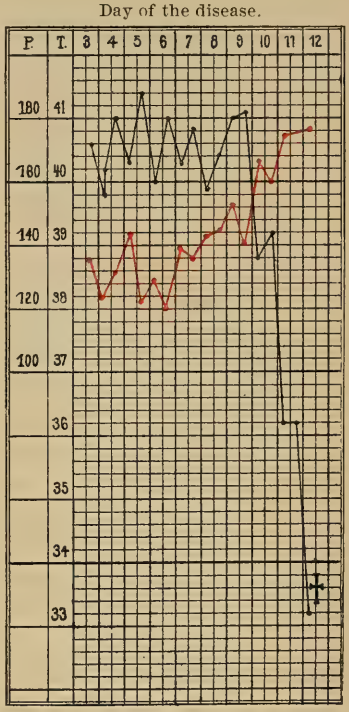

FIG. 60.—Vagabond, twenty-three years old. Alcoholic.

Sweating in Typhus.—This description of the behavior of the temperature may be properly concluded by a few remarks on the occurrence of sweats during typhus fever, a point that has been accorded undue prominence by the older authors belonging to the humoral school of pathology.

During the initial stage, and at the height of the fever, whether the case be mild or severe, the skin is almost always hot and dry. Only in very rare cases, where the initial rise of temperature is followed by a marked remission lasting several days, is sweating occasionally observed.

During the fall by crisis the skin is usually more or less moist; rarely, there may be profuse sweating. The occurrence of the latter is distinctly more common in lethal cases about the time of the ominous fall in the temperature.

The offensive or even specific odor of the perspiration mentioned by older authors I have never been able to observe, perhaps because the

Day of the disease.

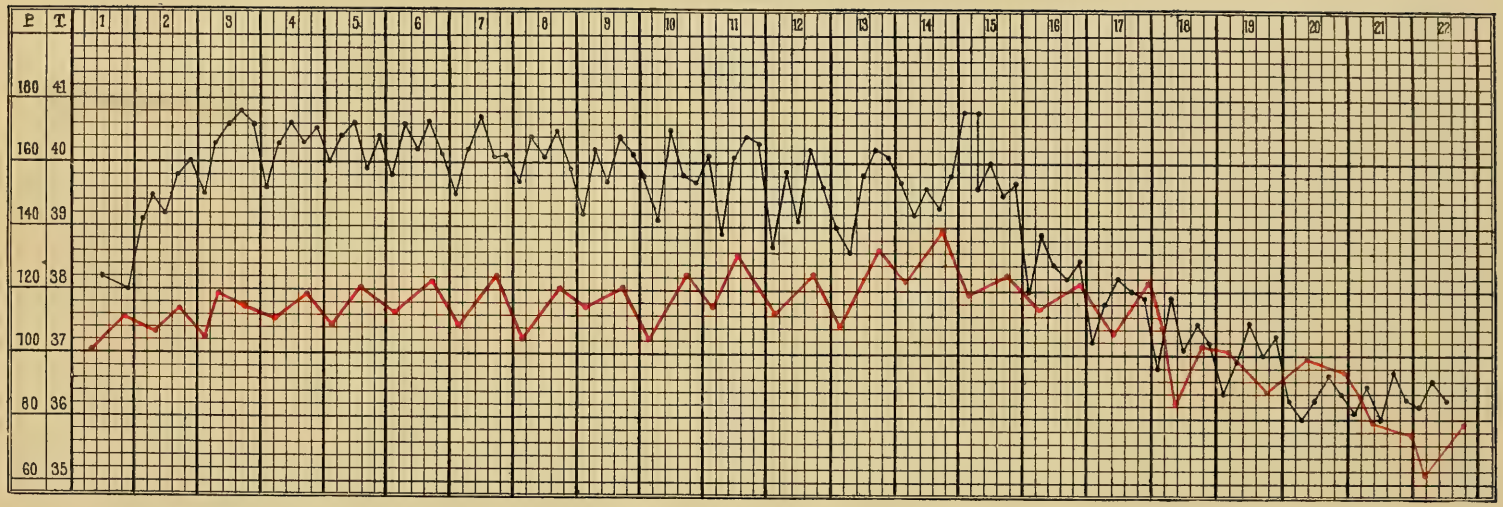

FIG. 61.—Man, thirty-four years old, in perfect health before the attack. Typical pulse and temperature for a severe, uncomplicated case of typhus fever.

ventilation in the barracks at Moabit was carried out with such painstaking care as is rarely possible under other conditions.

ALTERATIONS IN THE CIRCULATORY ORGANS.

The changes in the circulatory organs, especially the cardiac changes in acute infectious disease, have recently been studied, especially by my students, Krehl, Romberg, and Pässler, with such signal results that it becomes a matter of the utmost importance that in future epidemics our newest acquirements in this direction should be tested by a careful examination of the behavior of the heart in typhus fever. As cardiac dilatation and certain marked alterations in the heart-muscle are usually observed in the cadaver (see the section on Pathologic Anatomy), so also there occur clinically such early and marked effects of the toxins on the heart, and probably on the vasomotor nerves, as occur in few other infectious diseases.

The Pulse.—From a prognostic point of view, therefore, the condition of the pulse from the very beginning of the disease is quite as important as, if not more so than, that of the temperature or even of the nervous system.

Even during the initial stage, in severe and moderately severe cases, and usually also in milder cases, the pulse attains a considerable frequency, and this occurs among vigorous young men as well as among women and children and older individuals (compare Fig. 61).

In women the pulse-rate after thirty-six hours often reaches 110, with slight morning remissions, which are less marked, however, than commonly occurs in typhoid fever. In children the pulse-rate is considerably higher, and even in vigorous young men an evening pulse-rate of from 110 to 120, with a morning fall to 90 or 100, is observed as early as the third day.

In severe cases ending in recovery the pulse-rate persists at the same height during the first week, with even smaller daily remissions than were present at first. Usually, at the end of the first week an additional rise in the frequency occurs.

Except in cases with a very bad prognosis, the volume and tension of the pulse are usually good during the first week. Toward the end of the week the pulse is likely to become soft and more compressible.

The occurrence of dicrotism, so common in typhoid fever, I find to be by no means frequent, and my experience in this respect agrees with the observations of reliable authors (Griessinger, Murchison, and others). It was present in 5.9 per cent. of all my cases. In more than half

of the cases it appeared during the height of the disease and persisted for some time; in the remainder it lasted only from two to three days, occurring principally during the period of defervescence. I do not remember ever to have observed the phenomenon either during the initial stage or during the first days of the first week.

During the second week in severe cases, even in such as end in recovery, the rate continues high and the pulse becomes smaller and weaker, sometimes intermittent, so that in some cases for days it can be felt and counted only with great difficulty. Absence of the apex-beat on palpation, increase of the area of cardiac dulness to the right and left, and muffled heart-sounds, point to acute dilatation following intense infectious changes in the myocardium. Marked cyanosis of the face, hands, and feet at this time is a very unfavorable symptom. It occurs usually in alcoholics, in sufferers from chronic disease, or in those who have just recovered from some acute affection, and almost all the patients in whom it is present die. However, I have known individuals who were well nourished and vigorous to recover in spite of this very grave symptom.

Whether the extreme cardiac weakness has any connection with the gangrene of the tip of the nose, ears, toes, and fingers which occurs in severe cases is an interesting question that still remains to be solved. It seems probable, however, that the gangrene depends in part on the specific changes in the vessel-wall, with thrombus-formation, etc., conditions that have been shown to play a part in the process in typhoid fever.

A retardation of the pulse-rate, particularly a low pulse-rate in proportion to the temperature, which is so characteristic of typhoid fever in previously healthy young men, I have observed only exceptionally in typhus fever, and then only in mild cases. Its occurrence in severe cases (Griessinger) I have never observed. During the period of defervescence, the pulse, which in severe cases has been weak and irregular, gradually gains in strength, and the pulse-rate begins to diminish (compare Fig. 61). If there has been marked cardiac weakness with dilatation, the pulse, after the normal or subnormal temperature has been reached, continues between 80 and 90 in the morning and reaches 100 in the evening, and is exceedingly unsteady, so that any trivial bodily or mental excitement is followed by a considerable temporary acceleration.

In other cases, marked by a moderately severe or mild course, the pulse-rate diminishes *pari passu* with the fall in the temperature, the physiologic pulse-rate being reached within twenty-four or thirty-six

hours in cases ending by crisis, and in from three to five days in those ending by lysis.

A renewed rise in the pulse-rate during the period of convalescence occurs only in those severe cases with marked cardiac involvement, when the patient has left his bed too early; or it may occur as a manifestation of some complicating condition. The pulse-rate during the period of convalescence occasionally falls to below the normal, as low as 50 or 48, and may remain at that point for from eight to fourteen days. The cause of this bradycardia has never been properly explained. It also occurs in other acute infectious diseases—diphtheria, typhoid fever, and scarlet fever—and has no ominous significance. It was known to the older authors (Barallier, Kennedy, Murchison, Griesinger).

The State of the Heart and Blood-vessels.—In typhus as in typhoid fever, the myocarditis in the great majority of cases appears to undergo complete involution. I cannot remember a single case in which there remained any chronic insufficiency of the heart-muscle if the integrity of the organ was established beyond a doubt before the beginning of the disease.

The same is true of valvular lesions, which neither I nor anyone else has ever observed as sequels of typhus fever. We may accordingly infer that acute endocarditis must be very rare. The same may be said of pericarditis. I never found any inflammatory deposits or exudates at the autopsies, and only once or twice heard a temporary pericarditic friction.

Of the changes in the blood-vessels, the arteries, and veins, but little is known. As in all acute infectious diseases, the period of convalescence from typhus fever is marked by the occasional occurrence of so-called marantic thrombi in the veins, especially in the veins of the legs. They are most frequent in patients whose vital powers have been sapped by want or chronic disease, and in those who have suffered from a severe form of typhus fever.

Changes in the Blood.—The state of the blood in typhus fever has been repeatedly referred to in the sections on Morbid Anatomy and Etiology.

The records bequeathed to us by former observers in regard to the color and coagulability of the blood no longer possess the significance attributed to them by the older authors. Little as we have learned by microscopic examination in regard to the specific cause of the disease, a few valuable observations have been obtained in regard to the blood-corpuscles. While the shape and appearance of the red

corpuscles is unaffected in the main, their number is diminished in well-marked cases at the height of the disease, and the anemia persists during the period of convalescence. Corresponding to the oligocythemia we find a reduction in the hemoglobin during the latter days of the first and during the second week. Mey found this reduction to be from 10 to 15 per cent. in 6 cases that he examined.

On the other hand, the white blood-cells appear to be increased in number (Combemale). This appears to be a special feature of the disease, and it affords a very important aid in the differential diagnosis from typhoid fever, which, as is well known, is marked by a diminution rather than by an increase in the number of the leukocytes.

In those cases in which serum tests have been made, it has been found, as was to be expected, that the serum has no agglutinating effect on the bacillus of Eberth. This fact is of the greatest importance in differential diagnosis.

THE SPLEEN AND LYMPH-GLANDS.

The discrepancies in the statements of various authors in regard to the state of the spleen in typhus fever present a marked contrast to the uniformity of the observation in regard to the organ in typhoid fever.

While a few authors affirm that the spleen is always enlarged, others, as Oesterlen-Dorpat and the English writers, regard splenic enlargement as rare, or even as constantly absent, in typhus fever. The want of agreement on this point is so marked that it cannot be altogether explained by differences in the character of the disease due to local conditions or to different periods of the epidemic.

According to my own experience, enlargement of the spleen can be determined *clinically* much more frequently than at the autopsy table in the great majority of severe and moderately severe cases and in many milder ones, providing the examination can be made early enough. This difference between the clinical and anatomic findings points to the main reason why authors fail to agree; it is that they made their examinations at different stages of the disease. I have always observed enlargement of the spleen very early, distinctly earlier than in typhoid fever—as early as during the first febrile days, or even before the beginning of the initial stage. It does not, as a rule, persist until the beginning of defervescence, and for that reason has usually disappeared almost completely in fatal cases before the subject comes to the autopsy table. In several instances where the organ was at first perceptibly enlarged I failed to make it out with certainty after the beginning or

middle of the second week. Cases in which a perceptible enlargement persists beyond the period of defervescence are distinctly rare.

Occasionally, under conditions where it is absent in other acute infectious diseases, such as in individuals of advanced age and depraved bodily condition, I have found no perceptible enlargement of the spleen either at the beginning or during the entire course of the disease. In examining a typhus fever patient for enlargement of the spleen, the only reliable method—palpation—is rendered somewhat difficult by the fact that the enlargement rarely exceeds a moderate degree, and the consistence of the organ is, on the average, less than in other infectious diseases. Sensitiveness of the organ, whether passive or elicited by pressure, is comparatively rare.

Among 70 patients admitted during the first week of the disease, we failed utterly to make out enlargement of the spleen by palpation, and made out a doubtful enlargement by percussion in 17, while in the remaining cases the enlargement was made out usually between the third and the fifth day. In the case of a watchman who had become infected in the hospital, a large, soft, palpable spleen was made out at the first examination, immediately after the first chill. I have never had the opportunity to make an examination during the period of incubation. It is probable that a positive result would often be obtained at this time.

The external lymph-glands, like the mesenteric and bronchial glands (see Morbid Anatomy), are, so far as I could observe, almost always normal in uncomplicated cases. In a few of the larger epidemics—as, for instance, those of the Crimean war and of the Russian campaign against the Turks—inflammatory swelling of the axillary and sometimes of the inguinal lymph-glands appears to have been somewhat more common, and occasionally to have ended in suppuration.

CHANGES IN THE SKIN.

The nomenclature of typhus fever (typhus exanthematicus, typhus petechialis, spotted fever, febris puerpera epidemica, morbus pulicaris, morbus puncticularis, febris peticularis, etc.)[1] shows the importance attributed by physicians to the characteristic changes of the skin, from the earliest times when typhus was considered a subvariety of typhoid fever, to the present, when it is recognized as a distinct disease.

The Typhus Exanthem.—The rash is indeed sufficiently peculiar in the manner of its appearance and development, its character and distribution, to be counted among the few specific and diagnostically important phenomena of the disease.

The eruption, as we have seen, most frequently appears on the fourth

[1] See Murchison, who gives nineteen names of the disease, all of which refer to the skin-eruption.

or fifth day of the disease. It may appear on the sixth or seventh, or as early as the second day.

The time of its appearance varies in different localities and in different epidemics. In Berlin, in 1878, I found that the eruption appeared early—on the second, third, or fourth day; whereas, in the epidemic of 1879, the eruption occurred usually later—on the fourth, fifth, or as late as the seventh day. I subjoin a table from an article by my assistant, Salomon. In 39 cases during the epidemic of 1879, where the time of appearance could be accurately noted, it was found to be as follows:

Day of the disease.	Cases.	Day of the disease.	Cases.
Second	2	Seventh	5
Third	4	Eighth	2
Fourth	11	Ninth	1
Fifth	13	Tenth	0
Sixth	0	Eleventh	1
			39

Murchison gives the fourth day as the average time of appearance of the eruption, and expressly states that he rarely saw it appear later than the fifth day.

Cases in which the eruption is reported to have been delayed until the beginning of the second week, or even until the twelfth or the fourteenth day, must be accepted with great caution. That a very late appearance is possible is proved by the case in our table, that was distinguished by the appearance of the roseola on the eleventh day, without presenting any other peculiarity in the course of the disease.

With its first appearance the eruption comes out all at once in a single crop, so that the ultimate extent is usually complete within forty-eight hours. It is very rare, in my experience, that the duration of the eruption lasts longer than this. A second crop, or the disappearance of the earliest spots and the appearance of a new crop, is practically unknown, and we thus have an important diagnostic point differentiating the roseola of typhus from that of typhoid fever.

In regard to the topography of the eruption, the first spots in cases that I was able to observe from the beginning usually appeared on the lower abdomen and about the back and shoulders, and almost at the same time, but less thickly at first, the spots appeared on the chest and upper abdominal region. Very soon they appear on the extremities, while those on the trunk continue to increase in number. Not rarely the extremities are covered at the same time as the trunk. On the forearms the spots usually appear first on the flexor surfaces, and immediately afterward on the dorsal surfaces, down to the back of the hand. On the legs the eruption appears as far down as the dorsum of the foot, where it is often very conspicuous. In typical cases the eruption is least marked on the thigh, especially on the anterior surface.

This distribution of the eruption presents a marked difference from

that seen in typhoid fever, where the rose-spots become less abundant the farther the parts are removed from the trunk. Rose-spots on the forearms in typhoid are so rare as to be almost a curiosity, and I have never seen them as far down as the dorsum of the foot.

The face usually escapes, or at least is but sparingly attacked by the typhus eruption. A few spots may be found on the faces of women and children or individuals with fair, tender skin. On the other hand, the face is almost always flushed, especially in the beginning, and is often distinctly edematous.

The assertion that the rash of typhus differs from that of typhoid in the greater abundance of the lesions is true only in a general sense. It is quite true that, except in certain cases in which the eruption is particularly abundant on the trunk, the number of rose-spots in typhoid fever does not nearly equal that observed in many cases of typhus, where both the trunk and the extremities are so thickly covered that the name "spotted fever" appears to be entirely justifiable. On the other hand, there are not a few cases of typhus in which the eruption is very faintly developed and can be found only after a careful search, and between these two extremes we meet a number of gradations, both as regards the number and the distribution of the spots. There can be no doubt that cases occur also that, in analogy to similar conditions in the acute exanthemata, might be designated as *febris exanthematica sine exanthemate.* They must, however, be distinguished from cases in which the eruption, which may be fairly abundant, is completely obscured by dirt, pigmentation, parasitic eruptions, scratch-marks, etc.

As regards the development and special character of the eruption, three distinct stages may be observed in a fully developed case: The stage of simple hyperemia; the stage during which hemorrhagic changes begin; the stage of pronounced petechial appearance.

A fresh typhus fever spot appears as a pale-red macule, ranging in size from that of a pin-head to that of a lentil, rarely larger, with ill-defined outlines (Plate I., Fig. 1), which, as may be best determined by means of the glass pleximeter, disappears completely on pressure, and is therefore at first of a purely hyperemic nature. In young individuals with tender skin a few or a majority of the macules are at first slightly elevated. In contrast to the rose-spots of typhoid fever, which are always more or less papular, and retain that character as long as they are present, the serous infiltration in typhus fever, if present at all, is always much less pronounced and very evanescent.

The macular nature, the irregularity and indistinctness of the outlines, and the pale color of the spots combine to make it exceedingly

difficult to demonstrate the eruption during the first purely hyperemic stage. While a search for the rose-spots on dark skins is practically hopeless, it is difficult in an any case to recognize the eruption with certainty without proper illumination, a circumstance that causes the greatest trouble to hospital residents in admitting patients during the night.

Occasionally, the eruption stands out more prominently from its surroundings when seen at a slight distance than at close range.

In not a few cases the eruption does not develop beyond the first hyperemic stage, and, after persisting for several days or longer, disappears completely without leaving the slightest trace on the body of the convalescent, or on the cadaver if the case has terminated fatally.

In the great majority of cases the simple hyperemic stage soon passes away, and the spots become darker, of a coppery, dirty-red color, and do not disappear completely on pressure. They become somewhat paler when the pleximeter is applied, but the central portion still presents a dark-red or bluish discoloration, due to a deposition of blood-pigment (Plate I., 2). This deposition begins at the center and spreads to the periphery, so that the spots sometimes end by having a livid, bluish-red color and undergoing a true petechial transformation. If the spots are abundant and widely scattered over the body, the appearance of the patient becomes absolutely repulsive. Such cases are, however, exceptional. In most patients only a few spots undergo petechial transformation. The eruption presents such variations in the number of lesions, their degree of development, and the distribution over the body, that each case presents a different appearance.

In general, it may be said that the hemorrhagic spots are most numerous near the large folds in the skin—in the inguinal regions—and on the dorsal surfaces of the body; hence, these regions should be examined with particular care in cases in which the nature of the eruption is doubtful.

The rose-spots that have undergone hemorrhagic transformation must be distinguished from true petechiæ in the strict dermatologic sense of the word, for the latter appear as bluish-red spots due to direct hemorrhages into the skin, and are not preceded by a hyperemic stage. Such true petechiæ usually appear during the height or toward the end of the development of the rash. They are, however, according to my experience, comparatively rare. When present in small numbers, they are of no significance. When they are abundant the prognosis is bad, especially when they are combined with extensive hemorrhages into the skin and subcutaneous tissue and cyanosis of the face and

1

2

DESCRIPTION OF PLATES.

PLATE I.

1. Recent typhus fever spots of not more than twenty-four hours' standing, still in the hyperemic stage; taken from the abdomen of a man twenty-seven years of age, during an unusually severe attack from which he ultimately recovered. The rash appeared on the fourth day of the disease.

2. From the abdomen of the same patient. Beginning of the ninth day of the disease.

The rose-spots are now for the most part of a dark livid hue, a few of them rather more copper-colored, owing to hemorrhagic change.

Scattered among the rose-spots are a few recent petechiæ, and at one spot (in the lower right-hand portion) a more extensive cutaneous hemorrhage.

PLATE II.

3. Compare this with Plate I. Rose spots taken from the abdomen of a woman thirty-one years of age, suffering from *typhoid fever*. Twelfth day of the disease. The eruption is quite copious, and some of the lesions are well developed.

The three pictures were made by the author at the bedside, and have been faithfully reproduced.

extremities. Patients in whom this phenomenon is present as a rule present a horrifying spectacle on account of the hemorrhages into the conjunctivæ and the dark, livid appearance of the rose-spots. Such patients but rarely recover.

Occasionally, especially in alcoholic males in impaired physical condition, the legs and dorsal aspects of the feet are covered with numerous petechiæ, occupying the region of the hair-follicles or the hair-follicles themselves. This phenomenon has no more prognostic significance than the cachectic condition that is at the bottom of it.

It is a well-known fact that, in times of epidemic, patients suffering from any febrile condition and presenting small, circumscribed cutaneous hemorrhages, pyemic skin emboli, purpura, flea-bites, and the like, have been frequently sent to the hospitals as typhus fever patients by physicians of limited experience.

As in other acute exanthemata, especially variola, but not with the same frequency, the appearance of the eruption in typhus fever may be accompanied or immediately preceded by a diffuse macular, purely hyperemic redness of the skin, especially on the back, chest, and neck. This phenomenon is, however, very evanescent, and usually disappears by the end of the first day of the eruption.

In a few cases, especially in persons with a soft, white skin, I have seen the true eruption accompanied or immediately preceded by the appearance of a peculiar large macular, "measley" eruption, occupying chiefly the forearms and backs of the hands; this eruption rapidly disappears, and continues to recur for a short time at the same place.

The duration of the true typhus eruption and the duration of the individual stages appear to vary in the different epidemics and to some extent in different individuals. The average duration for severe and moderately severe cases may be given as from seven to ten days; traces of the hemorrhagic eruption, in the form of pale-brown or greenish-yellow spots, may, however, persist beyond that time and continue during convalescence.

The primary, purely hyperemic rose-spots last a very short time. If they fail to undergo hemorrhagic change, they usually disappear on the first or second, or, at the latest, on the third day. If the hemorrhagic change is only partial, the macules may not be visible after five or six days.

Like many other phenomena of the disease, the abundance and degree of development of the eruption depend, among other things, on the character of the epidemic. In some epidemics, according to reliable authors, they are of slight extent; whereas, on the other hand, epidemics

have been described that were distinguished by the unusual abundance and pronounced character of the cutaneous changes. Age does not, so far as I have observed, appear to affect the abundance of the eruption. Contrary to the experience of Murchison, Griessinger, Ebstein, Bese, and Wyss, I have seen the eruption quite as profuse in children as in adults, and Filatow[1] appears to have observed the same.

Judging from my own experience, there appears to be no distinct relation between the abundance of the eruption and the severity of the disease. I have seen the most severe fatal cases with little or no eruption, and, conversely, I have frequently observed the same condition in very mild cases. I am well aware that I am at variance in this view with that of Murchison, Griessinger, and many of the older authors (Rasori, Henderson, and Stuart).

In addition to the specific changes so far described, there are many other cutaneous phenomena that deserve notice.

Among the more important is the appearance of **miliaria crystallina** in the middle or at the end of the second week, from one to three days before the beginning of defervescence. The eruption is often very abundant on the chest and abdomen, and is more frequent in younger than in older individuals, rarely occurring after the forty-fifth year. The contents of the vesicles in all the cases examined by me were acid or neutral in reaction, never alkaline.

I observed miliaria crystallina in abundance in from 6 per cent. to 8 per cent. of my cases in the years 1878 and 1879. Other authors give a much higher percentage, while Murchison, on the other hand, states that the symptom is rare.

Whenever they were well developed, the sudamina were followed by distinct branny desquamation of the skin. This desquamation, however, is without doubt a very common occurrence during the period of convalescence, and follows the specific skin-eruption as well as miliaria crystallina. It affects the entire skin, including such portions as were not covered by the roseolous eruption—as, for instance, the face. In 2 cases during convalescence I saw a shedding of the epidermis in large scales, such as are usually seen in scarlet fever.

There is a marked variation in the statements of different authors in regard to the occurrence of **herpes facialis.** Jacquot saw it in one-fifth of his patients, while in other epidemics it was altogether absent (Hermann, Petersburg, 1874–75). I believe the absence of herpes facialis to be exceptional; it is certainly fairly frequent—much more frequent than in typhoid fever. In 1879 herpes facialis was present in

[1] *Vorlesungen über acute Infektionskrankheiten im Kindesalter*, Wien, 1897.

5.4 per cent. of our patients, and more frequently during the beginning of the disease than during the period of defervescence.

In a number of cases, during the second week of the disease, I saw a moderately severe **icterus,** without marked change in the color of the stools. These cases were all very grave, and most of them (4 out of 6) terminated fatally. At the autopsies no changes were found in the larger gall-passages or in the duodenum, but very marked cloudy swelling was present in the liver.

Cutaneous abscess and **furuncles** are not frequent. They were present in a few cases, were most abundant on the nates, and occasioned considerable annoyance to the patient during convalescence, which was prolonged on account of their presence.

Bed-sores occurred in a little over 3 per cent. of my cases. Disregarding cases that were much protracted by complications and sequels, the condition occurred during the true course of the disease only in very severe cases, but in these the sores appeared so rapidly and were so extensive as to suggest a severe trophic disturbance in addition to the ordinary pressure-effects. Occasionally, they were combined with abscesses and deep ulcerations undermining the subcutaneous cellular tissue, or even more or less extensive exfoliation of necrotic bone, involving the sacrum and coccyx and even the scapulæ.

In very severe cases, especially where there had been marked hemorrhagic changes in the eruption, slight irregularities in the bedding—wrinkles in the sheets, etc.—sufficed to produce bluish-black spots and stripes on the skin of the back and buttocks in a very short time, and these often formed the nucleus of extensive purulent tissue-necrosis.

Gangrene may be observed in typhus fever in certain portions of the skin not exposed to pressure, but far removed from the center of circulation. For obvious reasons this does not occur in the severest forms. Thus, I have seen gangrene of the tip of the nose and ear, and very frequently of the skin covering the toes. An entire toe may necrose and necessitate exarticulation. Seliger observed gangrene of the fingers. I myself have never seen it, and other authors note it as a curiosity.

Erysipelas, which in the older writings is mentioned as a frequent complication of typhus fever, has become very rare, owing to the favorable conditions prevailing in modern hospitals.

Noma and **hospital gangrene,** which are also mentioned in the literature, are of no more than a historic interest at the present day.

Certain reliable observers (Murchison, Lind, Gerhard) profess to have noticed a peculiar odor from the skin of typhus fever patients, as in the case of the other acute infectious diseases, especially the exanthemata.

The odor is described as musty or as "mousey," and is said to become very marked when the patients are closely crowded: this is quite to be expected. Whether it was due to the faultless ventilation I cannot say, but I never noticed any specific exhalation from our patients in the Moabit lazaretto.

THE NERVOUS SYSTEM AND ORGANS OF SPECIAL SENSE.

Disturbances of the nervous system are very marked from the beginning, and later they form the predominant feature in the clinical picture. They are so conspicuous that typhus, as well as typhoid, fever was, until after the middle of the eighteenth century, identified with "nerve-fever," or at least regarded as one of its subvarieties. Except in very mild cases of short duration, the symptoms referable to the nervous system during the entire febrile period, and in severe cases during the convalescent period as well, are far more marked and persistent than in any other acute infectious disease, not excepting typhoid fever.

The clinical phenomena do not in the least tally with the organic changes found in the central nervous system by our present methods of research. These phenomena are, without a doubt, due much more to the effect of the toxin than to the rise in temperature itself, as was formerly believed, since, notwithstanding a rapid rise during the beginning of the disease, there are no corresponding nervous phenomena at this period. Quite often they are most severe during and after the period of defervescence, and any experienced practitioner will recall cases in which the temperature remained low throughout, and, nevertheless, there was marked delirium or coma-vigil.

In severe and moderately severe cases, the patients complain, on the very first day, of such great lassitude and general prostration that they immediately go to bed. None but the very mildest cases, and these only exceptionally, remain ambulatory cases throughout their entire course.

Headache.—Almost all the patients in the beginning complain of headache, which persists throughout the initial period until the appearance of the rash, and often becomes so intense as to mask all the other symptoms. The pain is referred to the vertex, frontal region, eyes, and, in a few cases, to the occiput, radiating down into the neck and shoulders. Combined with the headache there are frequently present vertigo, pain in the sacrum and limbs, and hyperesthesia of the finger-tips, toes, and soles of the feet, which many patients find particularly distressing.

Psychic Disturbances.—During the first day there is little or

no disturbance of consciousness even in severe cases; the patients are dull and lethargic, and, although restless, lie supine on their backs. In spite of the great prostration most of the patients cannot sleep day or night; if they do fall asleep, they are immediately roused from their slumbers by terrifying dreams. These consist sometimes in peculiar sensations recurring again and again, such as a sensation as of soaring, flying, or falling.

At this period the mental faculties, even in these very severe cases, are still well preserved. Although they are dull and disinclined to any mental or bodily activity, the patients still retain consciousness of their surroundings. When spoken to, they answer slowly and in broken phrases, but, on the whole, correctly. They evidently, however, experience some difficulty in collecting their thoughts, cannot readily comprehend long and complicated questions, and when they attempt to do so, their attention soon wanders, their thoughts drift into other channels, or they later complain of a marked increase of the pain in the head and eyes.

Toward evening and during the night dreams and hallucinations continue to haunt them, even though they are awake. A few are violently delirious, even at this early period.

It is only in the milder cases, however, and in moderately severe cases of very short duration, that the psychic disturbances are confined to these narrow limits throughout the course of the disease. During the second half of the first week most patients become more and more stupid and confused even during the day. As their mental condition becomes worse, the subjective symptoms, especially the headache and backache, subside, and by the end of the first or the beginning of the second week loss of consciousness is usually complete and permanent. With eyes half-shut, completely cut off from the external world, the patient lies either motionless in bed, sunk in a deep apathy and muttering to himself and picking at the bed-clothes with trembling hands, or else gesticulates wildly and cries out in his terror.

The patient's behavior during this stage depends on various external circumstances and on individual temperament. In some patients depression is most prominent, in others delirium, making its appearance in the evening and lasting the entire night, sometimes persisting in the daytime. In vigorous young individuals the delirium often partakes of the nature of violent mania. They rage and cry out, jump out of bed, and try to escape from their terrifying hallucinations. Sometimes they become intensely aggressive and try to injure their attendants, or they endanger their own lives by endeavoring to escape through the window, etc.

Suicidal attempts, some with disastrous result, have also been observed. Those who were in an impaired state of health before the beginning of the disease and old and decrepit patients present a quieter, more muttering form of delirium from the very beginning and during the entire febrile stage.

In most cases the delirium is based on one or more torturing hallucinations; in others there is a veritable flight of ideas, reducing the patient to the verge of exhaustion. The delusions are usually of a saddening, depressing, or agitating nature—delusions of death or disease affecting friends or relatives, of persecution and personal danger, sometimes under the most remarkable conditions, such as flying in a balloon, or being in an open boat on the high seas, etc. In other cases the hallucinations are connected with persons or objects in the patient's immediate vicinity. These hallucinations may assume the most fantastic and terrifying forms, or, what seems to me more frequent, they may refer to former events in the patient's life, to his occupation, to some fixed habit, or to his vices and passions. In a considerable number of cases the condition, as is quite frequently proved by the history, is a simple exacerbation of febrile and alcoholic delusions.

A large ward full of typhus fever patients offers the greatest imaginable contrasts, and the confusion arising from this wild medley of feverish groans and delirious ravings is enough to shake the nerves of the steadiest physician; it has been known to scatter the less responsible attendants in panic-stricken flight.

Almost every author tells of peculiar and often very remarkable hallucinations. Murchison, Hildenbrand, and Guneau de Mussy described their own very interesting psychic conditions as they recalled them after recovery. One of my patients, a lawyer, of a naturally vivacious temperament, exhibited during the fever so violent an antipathy toward his attendant that the man's life was in danger. After his recovery he remembered distinctly the details of the terrifying apparition, and described how the man sometimes appeared to have enormously long arms and legs or else inflated himself to frightful proportions, or sat by his bed without any head. The apparition was so frightful at one time as to induce him to attack the monster with a knife, as he himself afterward remembered. Another one of my patients, an old sailor, imagined himself for days together in a crow's-nest during a violent storm, surrounded by huge black birds. In many patients the hallucinations are exceedingly monotonous and repeat themselves day after day. We had a scissors-grinder in the ward who for days and days would repeat, "Have ye anything to grind?" and a coachman who was continually urging on his horses and found constant occupation in repairing his evidently much dilapidated vehicle. Another of my patients, who after his recovery turned out to be a clerk with hysteric tendencies and given to onanism, imagined himself dead and translated to the higher regions, whence he could look down on his dead body and witness the prep-

arations for his own funeral. During this time he lay in a muttering delirium alternating with cataleptic rigidity. Delusions of death and of being buried alive have also been described by other authors.

The onset and duration of the delirious stage, like the expressions of the delirium itself, are, of course, subject to many variations. In comparatively rare cases, as we have seen, the delirium appears during the first days of the disease, and in such cases the prognosis is bad. I remember one case in which, with a rapid rise of temperature, furious delirium declared itself before the end of twenty-four hours; this case ended fatally on the eighth day.

Much more frequently the delirium appears late in the middle or second half of the second week, or it may in rare cases, as observed once or twice by myself, be delayed until a day or two before the beginning of defervescence. As a rule, the restlessness reaches its highest degree toward the end of the first or the beginning of the second week. After that the patients become quieter, the insomnia, which up to this time had been almost constant, begins to yield, and one of the most delightful events at this time, indicating a marked change for the better, is a long and restful sleep.

Other patients, again, who are suffering from a very severe form of the disease, lose their restlessness only to sink into deep and lasting coma, which in the great majority of cases ends in death after a few days or sometimes even after twenty-four hours, but which, after persisting several days, may end in recovery, as I myself have seen in several cases.

Coma.—The form of stupor known as coma-vigil is of the worst possible prognostic significance. The patient is pale, cyanotic, with haggard features and hanging jaw, eyes wide open and staring into space; usually, he is absolutely impervious to external influences, although sometimes the sensorium is only moderately involved. The external skin is cool and covered with a cold perspiration, while the temperature in the rectum may be subnormal or even febrile. The extremities are icy cold and cyanotic, the skin covering the toes and fingers often is wrinkled, and the limbs are either flexed and motionless or in a constant tremor resembling subsultus tendinum with carphology. The tremor sometimes reaches so intense a degree as almost to warrant being called a convulsion. Whether the edema of the pia found at the autopsy has anything to do with it is a question that is still open for investigation. Add to this that the respirations for days may be invisible, that the pulse cannot be felt, and that the heart-sounds are barely audible, and it can readily be understood, especially

if the extremities are free from tremor, that the transition from such very faint manifestations of life to actual death often occurs almost imperceptibly.

Sensory Disturbances.—For obvious reasons but little is known regarding the disturbances of sensation during the disease, especially during the febrile stage.

The distressing symptoms of the first stage, such as pains in the toes, fingers, and thighs, radiating to the popliteal space, which subside during the period of stupor and coma, often reappear as consciousness is re-established, and continue to annoy many patients up to the time of convalescence.

Severe neuralgic pains in certain nerve-tracts occasionally appear during the time of defervescence. These neuralgic pains are quite common, but fortunately subside after a comparatively short time without any special treatment. The nerves of the lower extremities, especially those of the feet and toes, are attacked with predilection; but I have also known the sciatic nerve to be affected. The distribution of the brachial plexus is more rarely attacked. Whether or not it is a mere accident I am unable to say, but as regards the trigeminus, I saw only supra-orbital neuralgia, and but 6 cases of that, in my experience in Moabit in 1878 and 1879.

Anesthesia confined to approximately the same regions as the neuralgia, though more rare, has been observed also. The attacks of anesthesia are likely to last longer than those of neuralgia. I have known anesthesia of an area on the thigh as large as the palm of the hand to persist for three months after recovery, and a similar one in the distribution of the ulnar nerve to persist two months after recovery.

Motor Disturbances.—Among general motor disturbances we may mention a more or less extensive tremor, which is almost always present at the height of the disease in severe and moderately severe cases. Most frequently, it is confined to the forearms and hands; at other times it affects the trunk and the four extremities equally, and in such a degree as to suggest to the observer genuine convulsive or choreic contractions, and this may possibly account for the fact that some authors have reported general convulsions and St. Vitus' dance as occasional complications of typhus fever. It is worth noting that any external motion when the patient is conscious or semiconscious, or any change in the delusion when the patient is comatose, is followed by marked aggravation of the tremor, just as in the case of a true intention-tremor.

In many patients the muscular unrest assumes the character of sub-

sultus tendinum with carphology. All these convulsive phenomena are much more common and more violent during the height of a typhus fever attack than they are in typhoid fever.

True general and partial convulsions are comparatively rare. If they occur at all, they do so in young, excitable individuals or in alcoholics, usually in the middle or toward the end of the second week of the disease, and they are, as a rule, of bad prognostic significance. The patients may pass away in a convulsive attack or they may live for a few days afterward, during which they remain in deep coma, with or without a return of the convulsions. Although these attacks present the general picture of eclampsia, and are often accompanied by albuminuria and nephritis, it has not as yet been satisfactorily determined whether they are to be regarded as uremic in character. I have seen violent convulsions in 2 cases, one of which was entirely free from albuminuria, and the other showed but very small amounts of albumin in the urine.

Partial convulsions are distinctly more rare. The best marked case that I have seen was one in a writer, nineteen years of age, in whom the convulsions were confined to the right lower half of the face and the right upper arm; this case terminated favorably.

Tetanus and conditions resembling trismus are occasionally mentioned in the literature. They have not come under my personal observation.

On the other hand, I have seen tonic contractures in individual muscle groups, as, for instance, in the flexors of the forearm, keeping the hand convulsively clenched for days at a time, and once in the form of obstinate contraction of the left biceps, causing forced flexion of the forearm on the arm.

A few of the patients under my observation were much depressed during their period of convalescence by repeated daily attacks of painful cramps in various muscles and muscle groups following sudden movements in these parts. The muscles chiefly affected were those of the calf of the leg, individual muscles of the back and abdomen, and the muscles of the forearm. One patient would be attacked by cramps in various parts of the body at the same time, following such slight movements that for days together he did not dare to move. These cramps had no prognostic significance and disappeared after the patient recovered.

Distinct cataleptic conditions, which for convenience are referred to at this point, are not frequent, although a more or less pronounced tendency to cataleptic rigidity is not at all rare. It has been observed chiefly during the height or in the second half of the febrile stage,

rarely earlier, and is usually associated with stupor or coma-vigil. As these conditions often make the clinical picture appear much worse than it is, it is important for the practitioner to become thoroughly familiar with them.

Palsies referable to anatomic alterations are rare—certainly not more common than in typhoid fever or in small-pox and other acute exanthemata.

Hemiplegia has been described in various epidemics (Gourvier, Hampeln). One case of the kind was observed among our patients in the epidemic of 1879. They appear to be dependent, as shown by some of the autopsies, on hemorrhages into the meninges or into the substance of the brain, more rarely on embolism or thrombosis of the larger arteries of the cerebrum, and Hampeln described one case of thrombosis of the left middle cerebral artery.

Associated with these conditions we find palsies of single extremities combined often with disturbances of sensation—anesthesia, paresthesia, etc. One case of partial paralysis of the entire right leg (during the epidemic of 1878), which at first was combined with hyperesthesia and later with formication, and which during the period of convalescence developed into a well-marked monoplegia, I am now inclined to regard as a neuritis, as I find, by reference to my notes, that it was later followed by pronounced muscular atrophy. It would be both interesting and profitable to examine by modern methods such cases of monoplegia in future epidemics, to see whether the majority are not due to neuritis.

Meningitis.—Inflammation of the cerebral and spinal meninges occurs with varying frequency in the different periods and epidemics. The most experienced physicians (Murchison, Peacock, Jenner, Jaquot, Barallier) absolutely deny the occurrence of meningitis in typhus fever. Möering[1] also, during the Crimean epidemic, was unable to discover any inflammation or suppuration in the meninges of 200 cases, even though a careful microscopic examination was made. Hampeln, nevertheless, reports 4 fatal cases of purulent meningitis out of a total of 726 patients in the epidemic of Riga.

DISTURBANCES OF THE SPECIAL SENSES.

Eye Disturbances.—The eyes, as we have seen, are almost always involved to a slight degree, there being a marked injection and an increased secretion of the conjunctivæ. This conjunctival catarrh, which very much resembles that which occurs in measles, in some instances appears during the stage of incubation, associated with coryza. With the beginning of

[1] Quoted by Murchison.

the febrile period in the great majority of cases the catarrh becomes so marked as to be of considerable diagnostic importance, since this stage presents so little else that is characteristic. In severe cases, in which the patients lie with eyes open or half-open and the conjunctival reflex is very inactive, the condition not rarely leads to the formation of superficial corneal ulcers. The deeper layers of the cornea but rarely become diseased, although I have myself seen one case of extensive parenchymatous keratitis, and in very severe epidemics instances have been reported of necrotic keratitis with perforation of the cornea, and even panophthalmitis, conditions that, fortunately, did not occur in any of my cases. These conditions appear to be confined to forms of the disease in which coma-vigil is a prominent feature.

Hemorrhages into the conjunctivæ are quite common in severe cases, especially in alcoholic subjects. When both eyes are affected and the hemorrhage is extensive, the patient's appearance is absolutely uncanny, although the process is of no special significance to the eye itself.

From the beginning of the disease the pupils present nothing characteristic, but later, especially in severe cases, they often become markedly contracted, and when the contraction is extreme, the appearance of the face in persons with light-colored irides becomes quite peculiar. How this phenomenon is produced is not known, although, obviously, it cannot be the result of accident.

In regard to the changes of the refractive media and of the eye-ground, we have very little definite knowledge. It is true that we find mention of the occurrence of vitreous opacities, choroiditis, iritis, and optic nerve atrophy in special text-books, but in these, unfortunately, the distinction between typhus and typhoid fever is not always sufficiently clear. The muscles of the eyeball are rarely involved. In 2 cases I saw strabismus develop in the course of the febrile stage, and disappear after recovery was established. Other authors have mentioned spasms of the individual muscles of the eye and of the levator palpebrum, followed by ptosis.

Disturbances of the Hearing.—In contradistinction to what is observed in typhoid fever, interference with the sense of hearing due to the toxic effect on the auditory center in the brain or on the auditory nerve appears to be rare in typhus fever. My own experience compels me to contradict Lebert's statement that the hearing becomes affected toward the end of the first or at the beginning of the second week.

As a rule, auditory disturbances do not make their appearance until the period of convalescence, when they become comparatively frequent.

They are usually due to swelling of the mucous membrane lining the Eustachian tubes, and to catarrh of the tympanum, ending sometimes in purulent otitis media with perforation of the tympanic membrane or even in inflammatory disease of the labyrinth. Occasionally, the condition goes on even to purulent infiltration of the mastoid cells with periostitic abscesses, necessitating surgical interference.

These morbid changes all depend on the hyperemia and swelling of the mucous membrane of the nose and nasopharynx that are peculiar to typhus fever, and develop during the first days of the disease.

According to my experience in Moabit, they usually end favorably. Most patients were entirely free from auditory disturbances when they were discharged.

These remarks on diseases of the ear are based principally on the investigations made by Hartmann[1] on my patients in Moabit in 1879. These investigations appear to be the most accurate and most complete that have appeared on this subject up to the present time.

Among 130 men whom he examined during the period of convalescence, Hartmann found aural diseases in 42, or 32.3 per cent. His table is as follows:

Accumulation of cerumen in the external auditory meatus	6
Swelling of the tubes with catarrh of the tympanic cavity	14
Acute inflammation of the tympanic cavity without perforation of the membrane	4
Acute inflammation with perforation of the tympanic membrane (6 cases were unilateral, 3 bilateral; 2 cases were complicated with periostitis of the mastoid process, 1 case with exuberant granules in the external auditory meatus)	9
Aggravation of tinnitus aurium and difficult hearing present before the disease	3
Recurrence of an old otorrhea	1
Tinnitus aurium without objective findings	2
Diseases of the labyrinth	3
	42

Nothing definite is known of any deeper **alterations in the nose** than the typical catarrhal affection already mentioned.

The occurrence of epistaxis during the first stage of the disease, and even before the beginning of the fever, is worth noting.

CHANGES IN THE RESPIRATORY ORGANS.

The various parts of the respiratory tract all participate in the morbid process of typhus fever.

The catarrh that affects the nose and nasopharynx spreads uninterruptedly to the larynx, trachea, and to the coarser, as well as the finer, ramifications of the bronchi.

This catarrh of the respiratory tract, especially the bronchitis, is to be regarded not as a complication, but as a peculiar manifestation of

[1] *Zeitschr. f. Ohrenh.*, Bd. viii., H. 3.

typhus fever. It can generally be discerned during the very first days of the disease, reaches its greatest intensity and widest distribution throughout the bronchial tree during the height of the morbid process, and begins to subside with the commencement of defervescence.

Tracheobronchitis.—The inflammation of the trachea and bronchi is accompanied from the very beginning by frequent cough, with but slight expectoration. In fact, the cough is accompanied by very slight expectoration during the entire disease. This irritative cough is particularly distressing during the early stages, on account of the acute aggravation of the headache that it occasions.

I have seen slight traces of blood in the scanty, glairy expectoration following severe paroxysms of coughing, although not a trace of any tuberculosis was present even then or later. The presence of a trace of blood is readily accounted for when one remembers the extraordinary swelling, maceration, and intense reddening of the respiratory mucous membrane so often observed at the autopsy.

The atelectatic conditions—lobular pneumonia and hypostatic congestions of the lower lobe—are undoubtedly dependent on the catarrh of the finer bronchioles and the cardiac weakness that is present in all severe cases. Hypostatic congestion usually begins to develop between the tenth and fourteenth days of the disease, at the time of greatest prostration—rarely earlier or later—and, as in all acute infectious diseases, it is of exceedingly unfavorable prognostic significance. As I have mentioned in a former section, it is never absent in the cadavers of typhus fever patients.

The older authors lay great stress on the occurrence of diphtheric affections of the respiratory tract both in the nose and nasopharynx and down to the finest ramification of the bronchi. They occur especially in severe and extensive epidemics.

We observed this condition in 5 cases in 1878 and 1879, and in all the result was fatal. In 3 of the cases tracheotomy was performed, but the patients succumbed, as the process had extended into the most minute ramifications of the bronchi. Whether these deposits are mere diphtheric membranes in the anatomic sense, or whether they are to be referred to the Klebs-Löffler bacillus, is a question for future investigators to decide.

Among other severe and important diseases of the respiratory tract those affecting the larynx deserve particular mention, as they afford the best explanation for the varying frequency of certain morbid phenomena in different epidemics and the different periods.

Murchison, with his wide experience and the extensive literature at his disposal, does not appear to have investigated this subject very

thoroughly. He only mentions in passing the occurrence of erysipelatous disease of the larynx. According to my own experience, the character of the individual epidemic plays an important part in this matter. While in 1878 we had scarcely any severe laryngeal infections, their number was absolutely terrifying in 1879.

Changes in the Larynx.—The laryngeal examination is, for obvious reasons, very difficult and cannot often be carried out. When it is possible, however, the cause of the hoarseness observed during the first week is found to be a simple catarrhal condition, redness and maceration of the ventricular bands, with discoloration of the vocal cords and marked swelling of the mucous membrane covering the arytenoid cartilages. Slight erosions are also occasionally perceptible. These changes usually disappear completely, and the voice during convalescence, while weak, is perfectly clear or at most very slightly hoarse.

In a certain number of cases, on the other hand, the initial stages are followed by more profound alterations in the larynx, which, either in themselves or from the consequences that follow in the remaining portions of the respiratory tract, may be of the gravest significance.

These more severe changes become manifest during the height or toward the end of the febrile period, and appear to take their origin in erosions and fissures of the posterior laryngeal wall.

These defects are due directly to the drying-out of the already macerated and partially disintegrated mucous membrane, caused by the constant mouth-breathing of the patients, who at this stage lie in a semi-conscious condition with mouth wide open.

These fissures occur principally on the posterior wall, which faces the interior of the larynx, and develop into extensive ulcers that spread usually to one side, and, as the ulcerative process becomes deeper, attack the cartilages of the larynx, particularly the arytenoid. The mucous membrane covering the latter swells and forms a smooth, bluish-red, roundish tumor covered by a whitish exudate, which in the form of an edema spreads to the neighboring portions and the entire entrance to the larynx, and may seriously endanger the patient's life by asphyxia. The patient being usually in a very low condition, quite unconscious, incapable of self-control, and so weak that the remaining flicker of life cannot resist even the slightest degree of dyspnea, this danger is very great, and it is of great importance to bear it constantly in mind. Hence, in any severe case the earliest appearance of cyanosis or any other symptoms of interference with respiration must be carefully looked for, and tracheotomy be performed without undue delay.

In not a few cases perichondritis leads to necrosis of the cartilage, and occasionally even to complete separation of the cartilage from its attachments, so that it lies free in the small pus-cavity, and if, as I myself once observed, perforation takes place, the cartilage may be expelled when the patient coughs.

If death is avoided in such cases by timely interference, the period of defervescence is usually extraordinarily prolonged. As a rule, the patients are voiceless for the remainder of their lives; and sometimes stenosis of the larynx remains, which requires a long and tedious course of treatment or forces the patient to wear a cannula permanently.

In 16—that is, 4 per cent.—of our cases treated in the Moabit lazaretto in 1879 there occurred severe laryngeal affections. This does not include a still greater number of patients who developed hoarseness and complete aphonia at the height of the disease, but in whom the voice was restored after they recovered. In 4 cases tracheotomy became necessary on account of perichondritis of one of the arytenoid cartilages and resulting edema of the larynx. Three of these recovered, but had to wear the cannula so long as they were under my observation; in the fourth case, operative interference came too late.

Perichondritic abscesses are undoubtedly the direct cause of many severe pulmonary and pleuritic complications, particularly certain forms of lobular and lobar pneumonia ending in gangrene or gangrenous pleurisy. They are produced by aspiration of septic masses from the abscesses, which, as we have seen, tend to rupture into the interior of the larynx after a certain time.

I do not mean to say that all cases of gangrene of the lungs and empyema are referable to purulent affections of the larynx, for there is no doubt that putrid inflammations of the pulmonary tissues may be produced in ways other than by aspiration. I do maintain, however, that infection from the larynx plays a very much more important part than has hitherto been supposed or reported in the literature.

During the epidemic of 1879 we observed 6 cases of gangrenous disease of the lungs accompanying perichondritic abscess. Five of these occurred in the right lower lobe, which, owing to its shape and the course of its principal bronchus, appears to be much more accessible to aspirated material than its fellow of the left side.

Five of these cases ended fatally—the total number of deaths was 93; the sixth, in which there was a small circumscribed gangrenous focus in the lower lobe of the right lung, finally ended in recovery after a prolonged illness, and after the laryngeal affection had been cured.

Diseases of the Lung Parenchyma and the Pleura.—Among the most frequent pulmonary diseases in typhus fever, in addition to the atelectasis and hypostatic congestion that have already

been referred to, is a form of fibrinous pneumonia that cannot be distinguished microscopically from the ordinary forms. No bacteriologic examination has so far been made.

It develops in the second week of the disease, rarely earlier, and, as the patients at this time are usually in a stuporous or comatose condition, there are no marked symptoms. Occasionally, an increase in the respiratory rate or a rise of temperature points to its occurrence. Rusty sputum or, in fact, expectoration of any kind, is often absent. Only frequent and careful examinations of the patient will therefore insure the detection of this complication. I am inclined to doubt that the marbled and almost whitish appearance of the infiltrated portions of the lung, pointed out by Salomon, are due to any peculiar pathologic alteration. They are more naturally explained by the general anemia that is usually present.

Fibrinous pneumonia in typhus fever varies, as regards the frequency of its occurrence, according to time and place. On the whole, it appears to be distinctly more frequent than in typhoid fever, and runs a decidedly more severe course. In 1879 we had to report fibrinous pneumonia as the immediate cause of death in 14 cases, or 15 per cent. of all fatal cases; but 3 cases in which this diagnosis was made ended in recovery.

Inflammation of the pleura is also distinctly more frequent than in typhoid fever. It is apt to follow lobular and lobar pneumonia, and especially purulent pneumonia, and leads to purulent and putrid effusions, so that operations for empyema are quite often required.

The pleuritic affections, like pneumonia, are quite likely to be overlooked. The patients often do not complain of pain in the side, and pleuritic friction is frequently absent, partly, no doubt, on account of the peculiar soft consistence of the fibrinous exudate, and partly also on account of the limited respiratory movements.

Almost all authors agree in mentioning pulmonary tuberculosis or general miliary tuberculosis as an occasional complication of typhus fever. It may make its appearance during the height of the disease, or even during the later stages of convalescence.

From our present knowledge of the disease, it is certain that such cases are always due to a latent tuberculosis that has been lighted up again by the typhus fever.

Among the patients under my care in 1878 and 1879 there was 1 case of general miliary tuberculosis, 4 cases of fulminating (florid) pulmonary phthisis, and 1 case of chronic ulcerative infiltration of the lower lobe of the left lung, following immediately on an acute lobar fibrinous consolidation.

ALTERATIONS IN THE DIGESTIVE TRACT.

Digestive disturbances are of far less importance in typhus than in typhoid fever.

The absence of specific, regularly recurring alterations of the intestinal canal in typhus fever has already been pointed out in the section on Pathology. Accordingly, there is also an absence of pain in the region of the small intestine, and any noteworthy degree of tympanites is rarely observed. I believe that it occurred in only 1 per cent. of my cases.

Pain, localized in the right iliac region, with gurgling, never occurs in typhus fever.

As there is no constancy in the anatomic appearances of the intestinal canal, there is a corresponding absence of regularity or anything especially characteristic in the frequency of the stools.

As a rule, there is constipation during the first week, and not rarely during the entire period of the disease. Later on, especially at the height of the disease and during defervescence, diarrhea occasionally occurs. I believe that alcoholics are more disposed to diarrhea than other patients.

There is nothing characteristic about the appearance of the stools, even when they are semiliquid or quite thin. The statements of certain physicians that the stools resemble the characteristic pea-soup stools of typhoid fever, rest simply on superficial observations. When the diet consists principally of milk and broths, the stools may be yellowish-white in color, but they are never watery and free from mucus, there is no tendency to separate in layers, and the coarse granular sediment and sharp ammoniacal odor characteristic of typhoid fever are altogether wanting.

As hemorrhages into the gastric and intestinal mucous membrane have occasionally been observed at the autopsies of very severe cases, there is, of course, a possibility of blood appearing in the stool (Barallier, Tweedie, Frerichs, and others). Such cases must, however, be very exceptional, and the reports should be received with great caution. There is always a possibility that the blood is simply a concomitant symptom of a hemorrhagic diathesis, or a mere local hemorrhage from the rectum, or hemorrhoids, etc. The statements of some of the older authors in regard to the frequent occurrence of intestinal hemorrhage probably depend on an error of diagnosis between typhus and typhoid fever, since, as we know, the two diseases were not infrequently confused, as, for instance, in England and Ireland.

One of the cases observed in Moabit in 1879 well illustrates the necessity of great care in judging these hemorrhages.

A young man, several of whose relatives had been treated in the lazaretto for typhus fever, and who was admitted with typical symptoms of a severe attack of the disease, had a profuse hemorrhage on the ninth day of his illness that evidently came from some of the higher portions of the intestine. At the autopsy, the source of the hemorrhage was found in a duodenal ulcer that was evidently of long standing.

There is little of importance to say regarding other portions of the intestinal tract.

During the first day the tongue is thickly covered with a whitish or yellowish-brown exudate. As the patient becomes more and more apathetic and his mental condition more clouded, the tongue becomes leathery, dry, tremulous, covered with crusts and marked by fissures, or smooth and glazed (Obermeier). The gums and lips are also dry and covered with sordes. This dryness cannot be avoided altogether even with the best care during the height of the disease.

More rarely there is a scorbutic softening of the gums and other portions of the oral mucous membrane, with a tendency to hemorrhages.

The soft palate and the tonsils are at first of a deep-red color and macerated; later they become dirty yellow, dry, and covered with strands of tenacious mucus and dry crusts.

In a few epidemics and in rare cases diphtheric affections of the pharyngeal structures occur, followed by superficial or even deep ulcers. Personally, I have seen 3 cases of this kind; 2 of them ended fatally, and the third recovered after a much protracted convalescence.

CHANGES IN THE GENITO-URINARY ORGANS.

The changes in the **kidneys** and their secretion, so far as is known,[1] is practically the same as in other acute infectious diseases, especially in severe cases of the acute exanthemata.

From the very earliest days of the disease until past the height of the febrile period the urine is scant in quantity—that for twenty-four hours rarely exceeding from 1000 to 1200 c.c.—is high in specific gravity, and strongly acid, with an abundant sediment of uric acid and urates.

As the fever subsides, and during the period of convalescence, the urine is lighter in color, clear, and sometimes very abundant.

Griessinger, who also quotes Jenner and Finger as authorities, repeatedly saw, during the height of the fever, a temporary secretion

[1] The most careful work on this question has been done by Pribram and Robischek, Wyss, Rosenstein, and Lanceraux.

of large quantities of clear, pale urine. I myself have observed this several times, especially a short time before the beginning of defervescence. This phenomenon, which I have never observed in typhoid fever, is difficult to explain.

During the height of the disease the excretion of urea is often not increased, sometimes it is even diminished (Rosenstein, Lanceraux); while the excretion of uric acid is always distinctly increased.

Lanceraux, even when the patients were taking large quantities of milk, never obtained more than from 11.5 to 24 gm. of urea in twenty-four hours.

Rosenstein found that the secretion of urea was at first considerably increased; during the subsequent course of the fever it fell far below the physiologic daily amount, and during convalescence it again rose gradually. His findings show a remarkable agreement with those obtained by Barallier as early as 1861.

Others among the older authors (Parkes, Buchanan) speak of a continuous marked increase in the production of urea during the height of the disease. These discrepancies suggest the necessity of careful investigations, during future epidemics, with the improved methods that are now at our disposition.

The chlorids regularly undergo marked diminution, and sometimes reach a minimum during the febrile period. From the beginning of the second week it is often impossible to demonstrate them.

As we should expect from the frequency of cloudy swelling in the kidney during the height of the disease, as shown by numerous autopsies, there is usually a moderate febrile albuminuria in the febrile stage in severe and moderately severe cases. The albuminuria occasionally makes its appearance as early as the middle of the first week, more frequently toward the end of the first or beginning of the second week, and disappears with defervescence, or occasionally a few days before that period. Microscopic examination of the urine in such cases shows, in addition to crystalline sediments, only a few epithelial elements from the kidney and pelvis, and hyaline casts in moderate numbers.

Severer grades of **albuminuria,** lasting into the period of convalescence and accompanied by bloody urine and numerous renal epithelial cells and epithelial casts in addition to hyaline casts, indicate parenchymatous nephritis, a complication of unfavorable prognostic significance that fortunately is rare. In a few, but by no means all, cases it ends fatally with symptoms of uremia. Five cases in which we could demonstrate parenchymatous nephritis at the autopsy had been clinically quite free from uremic symptoms.

In young individuals, especially in children, albuminuria with abundant admixture of blood in the urine has been observed on the fourth or fifth day of the disease (Weiss), even before the appearance of the

eruption. The prognosis in such cases, which, as a rule, are complicated with pneumonia, is quite as bad as in similar conditions among adults.

If the patients survive the nephritis, they, as a rule, make a complete recovery after a variable period of time; recovery is undoubtedly much more frequent than in nephritis accompanying angina simplex, diphtheria, and scarlet fever.

It is worth noting that some recent observers, Vierordt among them, have obtained a positive diazo-reaction with a fair degree of regularity in their analyses of typhus urines, which is a point of similarity between typhus fever and typhoid fever and a number of the acute exanthemata.

Occasionally, the urine also gives Gerhard's ferric chlorid reaction. The occurrence of sugar in the urine, observed in several cases by Buchanan, has not, so far as I know, been confirmed by any other authority.

Bladder disturbances of any severity are not of frequent occurrence; and, although we repeatedly found hemorrhages into the mucous membrane at the autopsy, the condition had not produced any symptoms during life.

Retention of urine is very rare in men, but quite common in women, especially during the febrile stage. While we had to use the catheter on males in only 2 instances in the epidemic of 1879, a daily, or at least an occasional, resort to the catheter was necessary in almost all the female cases.

In regard to changes in the genital organs in typhus fever, our knowledge is very limited.

The Male Genital Organs.—Orchitis appears to be even more rare in typhus than in typhoid fever. I saw a single case of unilateral orchitis in a young man shortly before the crisis; it lasted ten days, and subsided without going on to suppuration. Most of the authors do not even mention orchitis.

The Female Genital Organs.—On the other hand, the disease appears to have a marked effect on the female genital organs, manifesting itself in a variety of ways. The effect on **menstruation** is similar to that observed in other acute infectious diseases.

The onset of the disease is quite frequently accompanied by premature menstrual flow. The flow is often more profuse than in health, and occasionally the hemorrhage is so severe as to have a marked weakening effect that shows itself in the subsequent course of the disease. If the disease occurs shortly after the last menstrual period, menstruation is almost always suspended during the entire duration of the attack. In mild cases the menstrual flow reappears soon after the period of

defervescence, and may even be increased in amount. After severe cases, on the other hand, its appearance may be delayed for some time.

Pregnant women do not appear to have any special predisposition to, nor does pregnancy afford any protection against, the disease.

The effect of the malady on pregnancy has been overestimated by many authors. Typhus, like typhoid, fever is not by any means so dangerous to a pregnant woman as is variola. A large percentage, if not half, of all pregnant women have the disease without suffering abortion or premature labor. This is true particularly in cases in which the disease makes its appearance during the later months of pregnancy, but even during the earlier months abortion is by no means a constant occurrence.

The English physicians, who have probably enjoyed the greatest experience in this respect, believe that typhus fever has a slighter effect on the course of pregnancy than has any other acute infectious disease. Wardell states that he has never seen an interruption of pregnancy during the course of typhus fever, although it must be admitted that his statement would carry greater weight if it were based on a larger number of cases.

Even when pregnancy is interrupted by the disease, the accident is not always followed by grave consequences. The greatest danger to the patient is that of severe hemorrhage. After studying a number of these cases one gets the impression, however, that the metrorrhagia is not a result of the expulsion of the fetus, but rather that the hemorrhage occurs because the disease has assumed a "hemorrhagic character."

VARIATIONS IN THE COURSE AND MANIFESTATIONS OF THE DISEASE.

The end of the febrile period in almost every case marks the end of the disease.

RELAPSES AND RECURRENCES.

Relapses and recurrences, so common in typhoid, are of the greatest rarity in typhus, another among the many points of resemblance between this disease and the acute exanthemata. Although some authors, among them Barallier, claim to have observed relapses frequently, they have failed to produce any positive proof for their statements, for it is absolutely necessary to exclude with certainty other complications or sequels as causes of the renewed fever, and to show that the rise in temperature was immediately followed by a second appearance of the characteristic rash.

Murchison himself never saw an undoubted case of relapse or recurrence, and Griessinger denies its recurrence absolutely. Jenner, Stewart, and, more

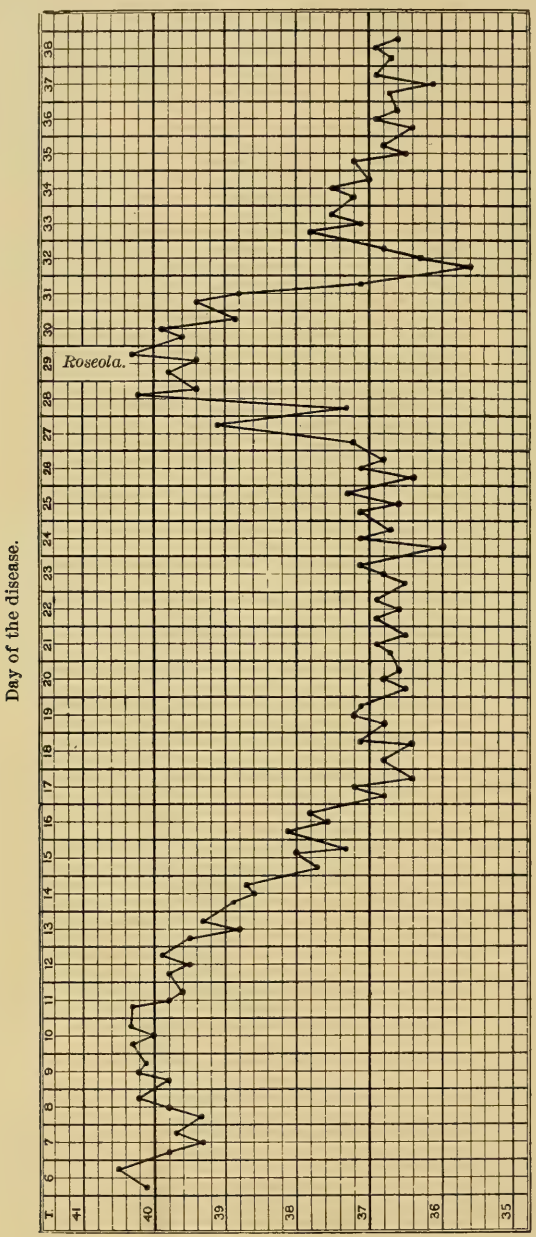

Fig. 62.—Laborer, twenty-six years old. Severe case of typhus fever, with relapse beginning on the tenth day of convalescence and lasting a short time.

recently, Thoinot, each saw 1 case, and even Buchanan (see Murchison) could not find more than 1 case of undoubted relapse to record among 5000 cases in the London Fever Hospital. I myself have 2 observations to

report that, I believe, are undoubted cases of relapse, but I will also add that I believe the cases to be anomalous, which is proved by the fact that

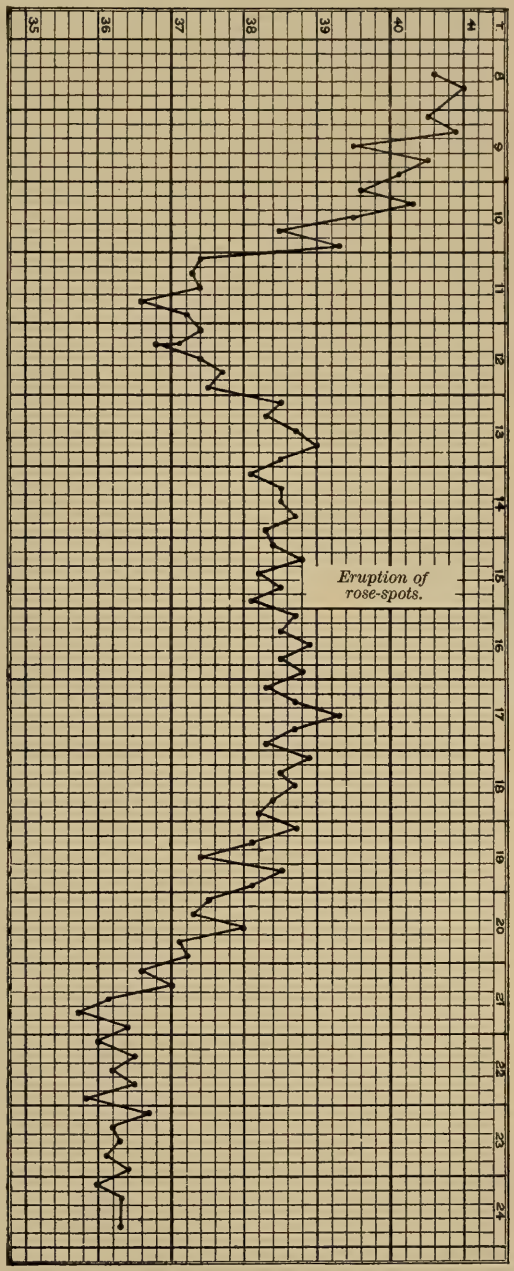

FIG. 63.—Male, twenty-five years old. Short but severe attack of typhus fever. Relapses with hemorrhagic nephritis within less than two days.

both of them occurred in 1878 among a very small number of patients, while in 1879 we failed to observe anything in the least resembling a relapse or a recurrence.

The first case was that of a laborer, twenty-six years of age, who, after a severe, uncomplicated case of typhus fever terminating by lysis, entered upon his convalescence on the seventeenth day. After this period he was free from fever, his temperature being usually subnormal. Eleven days later, the patient being still in bed because he was very weak and emaciated, he had another chill and the temperature rose rapidly. The spleen, which had not been enlarged before, was distinctly palpable and sensitive to pressure. On the third day of the disease there was a distinct, though scanty, eruption of rose-spots on the abdomen and chest, with a few spots on the extremities, including the dorsal surfaces of the feet, the rose-spots later in part undergoing a petechial transformation. On the fifth day the temperature fell by crisis (Fig. 62) and the patient began to mend, and this time his recovery, although protracted, was not again interrupted.

In the second case the most marked feature was the short duration of the afebrile period between the end of the primary attack and the beginning of the relapse, so that the case rather resembles what is usually described as a recurrence. The patient was a carpenter, twenty-five years of age. After an attack of typhus marked by extremely high temperature, the fever fell by lysis on the eleventh day (Fig. 63). The rash had disappeared except for a few dirty-brown and yellowish-green spots. Except for a marked catarrhal affection of the larynx no organic disease of any consequence had developed; albumin had never been found in the urine. During the night between the second and the third day after the subsidence of fever the patient had a chill and the temperature again began to rise, reaching 39° C. on the evening of that day. The temperature continued moderately high for the next few days, and then gradually began to fall by distinct lysis, the period of defervescence being completed by the ninth day. On the very first day of the second attack of fever albumin and blood, with hyaline and epithelial casts and casts covered with red blood-cells, made their appearance in the urine, and on the third day a very characteristic and moderately abundant eruption of rose-spots made its appearance. Splenic enlargement was not observed. After this the case ran an ordinary course. The symptoms of nephritis disappeared completely after four and one-half weeks.

VARIATIONS IN THE COURSE.

The course of typhus fever is subject to very wide variations, which at different times and on the strength of observations obtained in different epidemics have received a great variety of different names.

Older Nomenclature.—Thus, it was formerly the custom to apply various names to the disease, depending on the prominence of symptoms referable to definite groups of organs or to single organs.

The term *typhus nervosus* or *typhus ataxicus* was applied to cases with unusually severe nervous manifestations, such as delirium, coma, subsultus tendinum, and carphology.

When loss of strength with cardiac weakness and a tendency to collapse made its appearance early, the case was called *typhus ataxo-adynamicus*. *Typhus dysentericus* was diagnosed when diarrhea or true dysenteric symptoms formed a prominent feature, while the older

English and Irish physicians particularly were likely to speak of *typhus catarrhalis* when the mucous membranes of the air-passages early became involved and presented the most conspicuous symptoms.

These names, to which a large number that arose in a similar manner might be added, have little more than a historic interest at the present day. The appearances and manifestations of the disease are capable of an infinite number of combinations, and the number of clinical pictures is so varied that it can be neither justifiable nor useful to dignify individual forms by special names.

On the other hand, it is of much practical utility, not to say of absolute necessity, for a proper understanding of the disease to form a careful estimate of the differences in severity and duration, and use a nomenclature based on these differences.

We will first consider in this connection cases of mild degree, cases of short duration, and abortive cases, which in typhus fever, as in all acute infectious diseases, play a very important *rôle.*

The manifestations and the course of these forms are subject to remarkable variations, and the conditions on which they depend are even yet practically unknown. The frequency of their occurrence varies with the time and variety of the epidemic, and also may vary during different periods of the same epidemic. As the epidemic spends its force, a remarkable increase in the number of milder cases is often observed.

I think we are justified, in studying the reasons for this phenomenon, to assume a gradual decrease in the strength of the morbific agent as the epidemic progresses; or it may be assumed that after most of the individuals specially predisposed to the disease have been attacked, those who are less disposed to it also become affected. We cannot hope to gain a true understanding of these conditions until we learn more of the nature of the typhus fever poison, and until such general questions as predisposition and immunity have been further elucidated.

If we examine cases of short duration and cases of mild degree more carefully, we find that a short attack is by no means necessarily characterized by a mild course. A case may be mild from beginning to end, without being at all short in duration; and, conversely, cases of short, or even very short, duration not infrequently present a grave clinical picture, not only during the active course of the disease, but even until the beginning of defervescence.

Cases of Mild Degree, Well-marked Cases, and Cases of Short Duration.—As compared with the frequency of mild forms of typhoid fever with relatively low temperatures known as "gastric

fever" or "mucous fever," analogous cases of typhus fever are distinctly less common. Even such cases as end rapidly in recovery without any unusual complication or permanent injury to the health of the individual, sometimes, at least, run their course with high fever and correspondingly severe disturbances of the general condition. In any epidemic, however, cases will be observed in which the disease runs its course in the usual time—from fourteen to seventeen days, or even longer—without once manifesting an unusually high temperature.

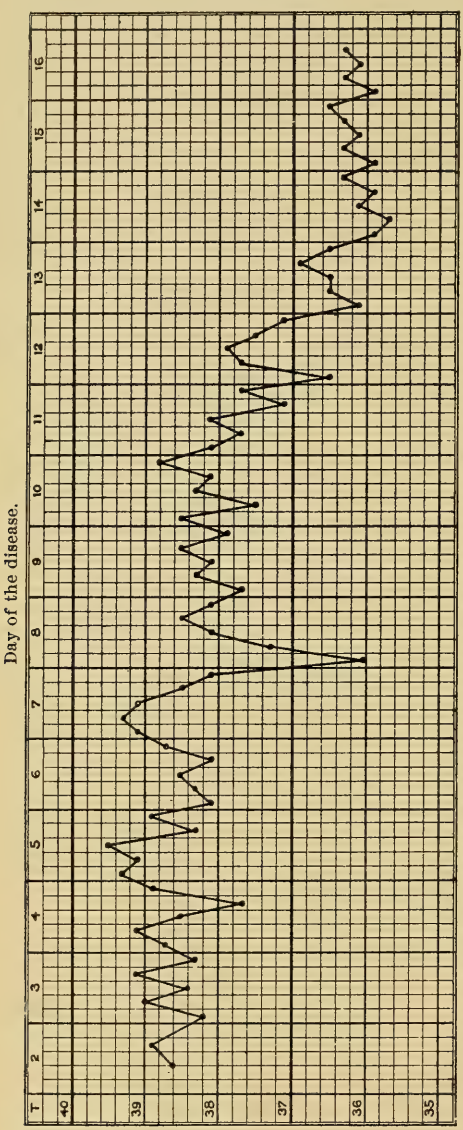

FIG. 64.—Merchant, twenty-two years old. Mild case of typhus with relatively low temperature.

These mild cases generally do not begin with a distinct chill. After a period during which the patient complains of chilly feelings, the temperature rises gradually, by successive steps, so that it may not reach its ultimate height before the fourth day of the disease. Accordingly, the initial symptoms—headache, backache, vomiting, etc.—are also less severe, and in many patients the mind remains clear even in the evening and during the night. The subsequent course of the fever is often irregular, with marked remissions and intermissions (Fig. 64), and the period of defervescence is often protracted. The pulse, particularly in men, is much less frequent than in the severe cases, and in women it usually remains of good volume and tension throughout.

I have an impression that splenic enlargement is less frequent in cases

of this kind, and that the rash also is, as a rule, less well marked. In a number of these cases catarrhal laryngitis and tracheobronchitis

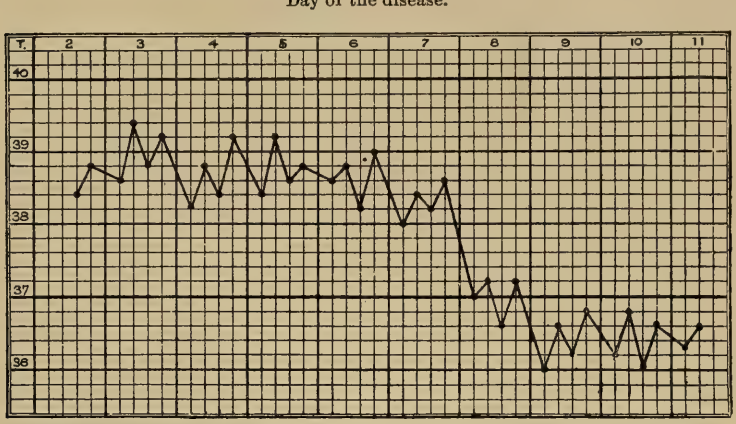

FIG. 65.—Strolling actor, aged forty-seven. Short and mild attack of typhus fever.

were both early and marked features, and formed the most conspicuous characteristics of the clinical picture.

In addition to these cases of "catarrhal typhus" I had occasion to observe 2 cases, characterized by a relatively low but protracted fever, lasting in 1 case as long as twenty-two days, in which symptoms of

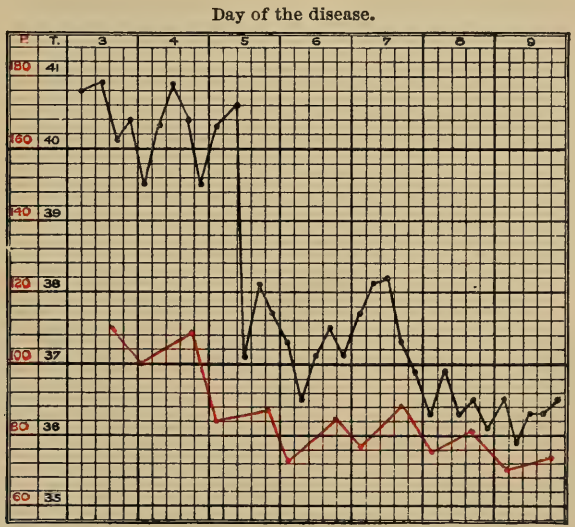

FIG. 66.—Baker, aged twenty-one. Abortive attack of typhus, ending by crisis.

hemorrhagic nephritis were at first very conspicuous, and vanished completely after the end of defervescence. In the case in which the fever

lasted twenty-two days the rash was so scanty and lasted so short a time that the diagnosis might have remained doubtful if the examination had been at all superficial.

We come next to the cases characterized by short duration and a mild course. The morbid phenomena in many of these cases are even milder than in the foregoing group. The splenic enlargement and the eruption are only very sparingly developed, and the disease ends within from five to eight days. This variety is illustrated in Fig. 65 (compare also Fig. 66).

These are the cases in which the characteristic clinical picture is often so disguised as to be quite unrecognizable. If they are the first ones during an epidemic, the diagnosis is practically impossible, and even during the height, or toward the end of the epidemic, the diagnosis will depend largely on the history and the determination of frequent or intimate relations with undoubted cases of typhus fever. I cannot agree with Griessinger and other authors who maintain that the rash, or at least the characteristic roseolous eruption, is constantly absent in these cases, which, by the older authors, were usually designated febricula. I have seen patients of this kind exhibit a well-marked and characteristic eruption which lasted even longer than the febrile period when the latter was very short.

Abortive Cases.—It will be well, for practical reasons, to make a distinction between the cases of "*febris exanthematica levis et levissima*" just described and those in which, after a severe onset and clinical course, defervescence makes its appearance unexpectedly early. The term "abortive typhus" may with propriety be applied to such cases.

In the cases of this class it happens more frequently than in those of "febris exanthematica levissima," although by no means constantly, that the highest temperature—after a violent initial chill—is reached within from twenty-four to thirty-six hours or even earlier. After this time the temperature usually persists for several days at its maximum, in the form of a continued fever or continued remittent fever; less frequently it is quite irregular. The temperature, which may be extremely high, then falls by distinct crisis (Fig. 66) lasting but a few hours, and remains normal.

The condition of the patient in these forms is often extremely alarming for several days or even until just before the beginning of defervescence; after initial phenomena of great violence the patients present marked hebetude, profound prostration, and even furious delirium. The condition of the spleen varies greatly. In some cases I have seen a marked enlargement; in others the organ was not swollen at all.

The rose-spots in abortive forms are, as a rule, few in number and last but a short time, although sometimes a number of them undergo petechial transformation or petechiæ may develop independently among the rose-spots. The eruption of large macules that has been referred to appears to be more common in abortive cases than in well-marked forms of the disease; and another point that seems to me worth noting is the frequent appearance of herpes facialis during the crisis.

Grave pulmonary complications, especially pneumonia, are rare in abortive typhus fever, although sometimes laryngitis and bronchitis, as occasionally occurs in cases of the "febris exanthematica levissima," form a prominent feature of the disease.

In a few cases I observed an unusually slow pulse of good volume

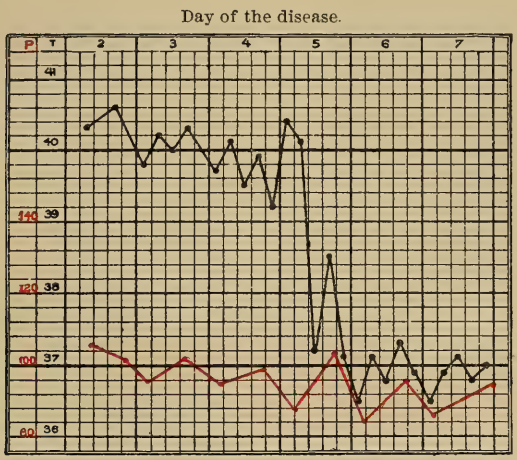

FIG. 67.—Tailor, aged nineteen. Abortive course. Slow pulse even during the febrile period.

and tension, sometimes not exceeding from 80 to 100 in the evening. This phenomenon in itself is a good prognostic sign, and justifies the hope that the course of the disease may be abortive (Figs. 66 and 67).

The condition of the kidneys in the abortive forms is usually good. Slight degrees of albuminuria may occur: marked excretion of albumin with blood I saw in only 1 case, and that was of rather long duration, so that it could hardly be called a distinctly abortive case. I give the temperature-chart of this case in Fig. 68, as it shows not only the course of the temperature, but also the occurrence and significance of a relatively slow pulse.

These cases, it need hardly be said, form the transition between abortive cases and those of moderate severity ending in recovery in which the duration is not abridged.

So far we have discussed cases in which, as we have seen, a diagnosis could be made with certainty, or at least with a fair degree of probability, especially if they were under observation for a sufficiently long time. In every epidemic, however, especially when it is at its height and

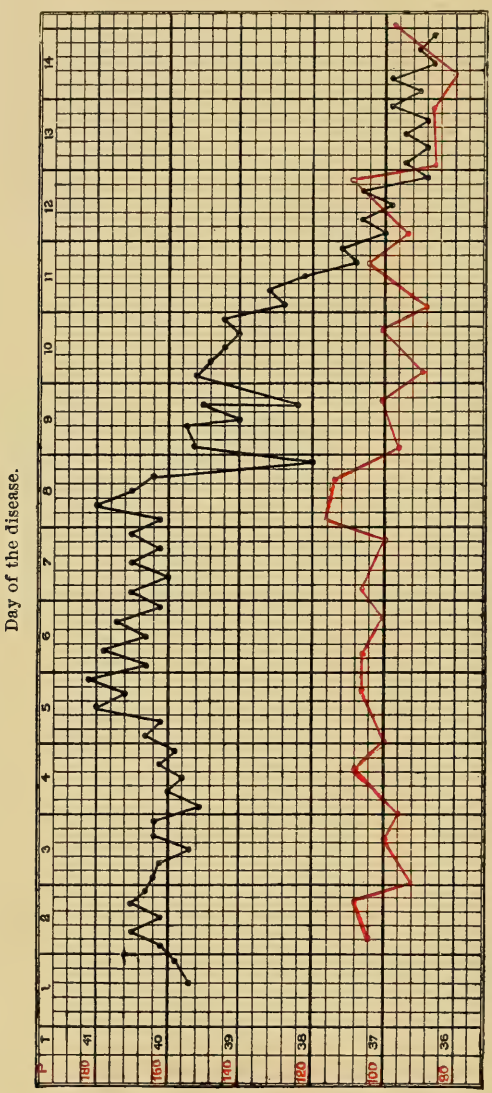

FIG. 68.—Butcher, aged twenty-four. Severe course with very high fever and hemorrhagic nephritis; beginning of defervescence on the eighth day. Good, moderately frequent pulse throughout the disease.

toward the end, cases occur that cannot be diagnosed with certainty and in which the interpretation will be greatly dependent on the point of view of the observer. In these cases the fever lasts but a short time and examination fails to disclose any positive signs of typhus, such as

the characteristic rash, although, at the same time, other diseases can be positively excluded, and the history shows that the individuals have had close relations with typhus fever patients.

Some of these cases might with perfect justice be called "*febris exanthematica sine exanthemate*," in imitation of analogous cases that occur in variola and scarlet fever.

This form is mentioned in the writings of other authors, especially the more recent ones, among whom I may name Rosenstein and Naunyn; the former claims to have observed it quite frequently.

Finally, we have a group of most perplexing cases, baffling all attempts at diagnosis. Individuals who have for a long time been exposed to the influences of the typhus fever poison develop a condition of general depression, loss of appetite, insomnia, pain in the head and limbs, ringing in the ears, bleeding at the nose, and irregular febrile disturbances lasting for days or even weeks, without ever exhibiting any pronounced symptoms of the disease. Physicians, ward attendants, and other persons whose duties bring them in contact with typhus fever patients are particularly prone to develop this condition, and it is a noteworthy fact that they usually recover very quickly as soon as they are removed from their unfavorable surroundings. Jaquot has described this condition, which he calls "*typhisation à petite dose*," a term that sufficiently describes his interpretation.

Ambulatory Cases.—In this connection the question comes up whether walking cases occur in typhus, as in typhoid, fever. Some of my own observations, I believe, point to the occurrence of such cases, if not with certainty, at least with a fair degree of probability, and among other authors I may quote Becher and Passauer,[1] in whose writings similar statements may be found.

The frequency of mild and very mild cases also appears to vary with the period and the individual epidemic. The fact that some authors do not mention them does not indicate that they did not occur, but rather that the clinical material was observed under peculiar circumstances.

It is worth noting that children appear to be more frequently attacked by this form of the disease than do adults (Griessinger, Wyss), and that the milder forms often become more prevalent among adults toward the end of the epidemic, particularly among individuals who, owing to favorable surroundings and good physical condition, may be assumed to possess a greater resistance to the poison.

It is difficult at this time to give any figures in regard to the frequency of cases of short duration. Among 347 cases in Moabit analyzed by my

[1] *Berlin. klin. Wochenschr.*, 1868.

assistant, Salomon, 24 were free from fever on from the seventh to the ninth day. It will be seen, therefore, that we failed to get the mildest and shortest cases, for the simple reason that they rarely enter the hospital, and are seen practically only in private practice. It is rather interesting that Murchison, who has given so careful a description of the disease, fails to say anything about this class of cases. His statistics in regard to the duration of the disease do not include any cases of less than one week's duration. Among 53 patients, he had 3 in whom the disease ended on the eighth or ninth day.

RELATIONS TO, AND COEXISTENCE WITH, OTHER DISEASES.

Acute Exanthemata.—The most interesting relation is that which exists between typhus fever and the acute exanthemata, to which it is so nearly related. It may be stated that typhus fever probably does not occur simultaneously with the acute exanthemata, although isolated instances of such occurrence are mentioned in the literature. The reports are not convincing, however, and the foregoing statement must hold good until more positive cases are reported.

Murchison, who does not himself appear to have met with the complication under discussion, gives Barallier and Buchanan as his authorities for the simultaneous occurrence of small-pox and typhus fever.

Barallier's statements cannot well be investigated, and Buchanan's case, the history of which Murchison quotes in full, unquestionably admits of more than one interpretation.

In regard to the coexistence of typhus and scarlet fever we also lack reliable information, and the statements in regard to the complication with measles are more than uncertain, because, as we have seen, both diseases during their initial stage present the symptoms of conjunctival and bronchial catarrh, and because the morbilliform rash of typhus fever is sometimes indistinguishable from a fugacious eruption of measles.

We must, however, clearly distinguish between actual coexistence and a rapid or even immediate succession of typhus fever and the acute exanthemata. That infection with one of the acute exanthemata may occur during convalescence or even toward the end of defervescence in typhus; and, conversely, that individuals recovering from scarlatina, measles, or variola, may, owing to some unfortunate accident, immediately contract typhus fever cannot be denied.

I may mention the case of a young man, eighteen years of age, in whom a well-marked rash, which for the most part immediately became petechial, developed while the skin was still undergoing the typical lamellar desquamation of scarlet fever. He had a severe attack of typhus fever which ended in recovery. Murchison, out of a total of 7 cases of typhus following immediately upon scarlet fever, twice saw the disease develop during the period of desquamation.

Other Acute Infectious Diseases.—A number of these are capable of being combined with typhus fever during the height of the febrile stage or toward the end, or during the beginning of convalescence.

This applies particularly to **pyemia** and **septic processes** caused by streptococci and staphylococci, especially erysipelas.

The occurrence of **fibrinous pneumonia,** due to the action of the Fränkel-Weichselbaum bacillus, during the febrile period of typhus fever has already been referred to as a distinctly frequent and very grave complication.

In this connection acute tuberculosis, especially **acute miliary tuberculosis,** is spoken of by all authorities. It may develop in any stage of typhus fever, but occurs most frequently toward the end of the febrile period or during convalescence. I have observed this complication 5 times. One case, occurring in a young woman twenty-three years of age, presented a typical picture of acute basilar meningitis, the first symptoms appearing toward the end of the second week of an attack of typhus fever with moderately severe onset.

The relation between typhus fever and **relapsing fever** is both interesting and important from a prognostic standpoint. That the diseases may coexist is beyond all doubt. It is probable that the stage of incubation of typhus fever may begin during the continuance of an existing relapsing fever; whereas, conversely, the spirillum of relapsing fever probably does not become pathogenic in the body of a typhus fever patient, or at least such an occurrence is extremely rare.

I have already given a brief account, with the temperature-curve (Fig. 57), of a case, observed in Moabit in 1879, of typhus immediately following an attack of relapsing fever. Similar complications of typhus and relapsing fever had been repeatedly observed before that time. Such cases are probably not rare when the two diseases are epidemic at the same time. The combination was not unknown to Griessinger; and Hermann [1] mentions not only the onset of typhus one to three weeks after an attack of relapsing fever, but also cases in which typhus fever appeared to follow directly upon the latter disease. Spitz [2] reports that in the Breslau typhus epidemic of 1879 several relapsing fever patients, after they had been in the hospital from three to five weeks without coming in contact with typhus fever cases, were attacked by the disease. One of these cases closely resembles ours in the absence of any interval between the end of the relapsing fever attack and the beginning of typhus. Seeliger [3] also reports 4 instances of typhus infection during an attack of relapsing fever, and 19 cases in which typhus declared itself a short time after the patient had recovered from relapsing fever.

[1] *Petersb. med. Wochenschr.*, 1876. [2] *Deutsch. Arch. f. klin. Med.*, Bd. xxvi.
[3] *Berlin. klin. Wochenschr.*, 1888, Nos. 51, 52.

That typhus and **typhoid fever** can exist together seems to me very improbable, or at least open to question. Unfortunately, many of the statements on this subject are of little value. Some of them date from a time when the two diseases were not carefully distinguished, while many others antedate the discovery and study of the Eberth bacillus.

I am equally disinclined to accept the numerous statements in regard to the coexistence of typhus fever and **diphtheria.** Diphtheric changes, in the simple anatomic sense, are, of course, known to every experienced observer, but it remains for bacteriologic investigations in future epidemics to show whether these changes ever depend on the Löffler bacillus, and can therefore be interpreted as diphtheric in the etiologic sense.

The coexistence of **dysentery** and typhus fever I consider very probable. I myself saw 2 cases in which dysenteric manifestations, with mucous and bloody stools and separation of the intestinal mucous membrane in shreds, formed prominent symptoms of the disease.

Murchison regards dysentery as a rare complication, occurring with any degree of frequency only in certain epidemics. Thus, during the Crimean war the two diseases existed side by side, and among the French soldiers, who lived amid unfavorable hygienic conditions, cases were observed in which the same individual was attacked by both diseases.

Acute articular rheumatism and typhus fever may be combined in the sense that the latter can be acquired during the existence of a polyarthritis. An instructive case in this respect is that of a man, thirty years of age, in the Charité Hospital, who became infected during the febrile stage of an acute articular rheumatism, and was admitted to the lazaretto in Moabit with a severe case of typhus, complicated by hemorrhagic nephritis.

The Relations between Typhus and Chronic Affections.—The relations between typhus and other diseases, especially chronic conditions, have been repeatedly referred to.

I do not believe that any disease affords a protection against typhus fever. On the contrary, not a few chronic conditions characterized by malnutrition and loss of strength seem to heighten the predisposition of the individual.

Among such conditions **chronic alcoholism** is especially to be mentioned. Not only are a great number of alcoholics found among the classes usually attacked by the disease, but it is a fact that such individuals are actually more prone to contract it.

The course of the disease assumes also a special character in alcoholic subjects; it is distinctly more severe and is more likely to terminate fatally than in persons free from the vice. There is no doubt that it largely explains the fact, determined by numerous statistics, that the mortality is lower in women than in men.

Some of the earliest and most marked manifestations of the disease in alcoholics are seen in the nervous system, in the heart, and in the kidneys. Grave disturbances of consciousness make their appearance during the very first days: violent, even furious, delirium, often followed by a transition into coma, particularly the ominous form of coma-vigil. Protracted cases are particularly likely to assume the form known as "ataxo-adynamic."

In chronic alcoholic subjects the pulse becomes alarmingly small very early in the disease, the tension diminishes, and the rate is greatly increased. There is but little doubt that this condition of the pulse is due quite as much to vasomotor paralysis as to weakness of the heart-muscle.

The kidneys in alcoholic patients regularly show early and severe involvement. In some cases the nephritis manifests itself merely by marked albuminuria and the presence of simple hyaline casts in the urine. Other cases present symptoms of the severest forms of hemorrhagic nephritis, and may terminate fatally at the end of the first or the beginning of the second week with pronounced symptoms of uremia.

That alcoholics are particularly liable to develop hypostatic congestion of the lungs follows logically from what has been said in regard to the action of the heart.

Cases with **chronic tuberculous disease of the lungs** also frequently occurred among the material under my observation. It may be said with certainty that persons suffering from this condition do not escape typhus fever.

The development of general miliary tuberculosis, or an acute local extension of the tuberculous process after typhus fever, has already been referred to. When this is not the case, and the local or general changes are not pronounced, the course of the typhus fever appears to be little influenced by the chronic tuberculosis.

THE EFFECT OF CONSTITUTION, AGE, AND SEX.

The effect of the **constitution**—that is to say, the general bodily condition at the time of infection—on the course of the disease has frequently been touched upon. It has been stated that weak, badly

nourished, debilitated individuals are particularly prone to be attacked, and we may add that such individuals, as a rule, show diminished powers of resistance. Vigorous, well-nourished individuals with normal hearts are better able to resist the effects of typhus fever, just as they better withstand all acute processes.

On the other hand, very corpulent persons, even when not alcoholic, withstand the disease badly, just as they do typhoid fever. The heart and the vasomotor system in these individuals seem to find especial difficulty in resisting the effects of the toxin.

Sex, *per se,* does not appear to have any marked influence on the course of the disease. It is true that in all epidemics the influence of sex shows itself to a marked degree in the circumstance that the severity of the disease and liability to death are distinctly greater in men than in women, but the cause of this lies in the fact that women are much less exposed to unfavorable external conditions; for, first, they are less constantly engaged in the struggle for existence; and secondly, they are not, as a rule, addicted to vice, especially that of alcoholism.

The differences in regard to **age** are distinctly less marked in typhus than in typhoid fever. This will be reverted to later in speaking of the prognosis. For the present I shall confine myself to a few remarks on the manifestations of the disease in infancy and old age.

Typhus Fever in Old Age.—The effect of old age makes itself felt as early as the fortieth year; after the fiftieth year it becomes so important a factor that almost half of such patients succumb to the disease.

Typhus fever in old age does not present a typical clinical picture, such as we see in senile typhoid. A considerable proportion of the large number of young invalids in a reduced state of health who are attacked by the disease have a comparatively low, irregular fever from the beginning of the attack. In older persons, on the other hand, very high temperatures are not, according to my experience, by any means uncommon. It may at least be said that older persons are less likely to have a high continuous or remittent continuous fever of long duration, and present rather an irregular temperature-curve with marked elevations and depressions.

On the other hand, in old people the disease exerts an early and pronounced influence on the circulatory and respiratory organs. During the first week of the disease, during even the first days, aged individuals present symptoms of failing circulation; the pulse is small, rapid, and of low tension; a morning pulse of 120 and an evening pulse of 140 are not at all uncommon.

As a direct consequence of the cardiac weakness and the constant occurrence of severe catarrh extending into the finer bronchioles, aged persons are prone to develop lobular pneumonia and simple or inflammatory hypostatic conditions in the lungs very early in the disease. Inflammatory diseases of the lungs form a characteristic feature of senile typhus.

The central nervous system in old persons early becomes involved to a very marked extent. Although the delirium is rarely violent or furious, but, rather, assumes a muttering form, hebetude is likely to show itself much earlier and become much more severe in old persons. As early as the middle, or toward the end, of the first week deep coma develops, with subsultus tendinum and carphology. The form known as "ataxo-adynamic" is particularly liable to occur in old persons, even when they are not alcoholic.

As regards the kidneys, I cannot say that I have met with more numerous or more marked cases of nephritis in senile patients than in young and vigorous ones.

On the other hand, diarrhea and dysenteric affections of the large intestine are distinctly more common in old age than in youth.

Owing, probably, to the atrophic condition of the skin, the typhus fever rash seems to appear somewhat later in old persons and to reach its complete development more slowly. On the other hand, hemorrhagic changes in the rash appear earlier and are prone to be more extensive. In the matter of amount of rash, I do not think there is any great difference between old age and other periods of life.

Typhus Fever in Childhood.—Although the disposition to typhus fever is not less in childhood than in later years, if we disregard the period of infancy, the actual number of cases among children is comparatively smaller than among adults. This is due to the fact that typhus fever is practically confined to the floating population and to those among the permanent residents who come into immediate contact with them, and that the number of children who come in contact with diseased persons is small in proportion to the total number of children in the community.

Of the course of typhus fever during childhood little is known. Even the better text-books on pediatrics present little more than general accounts closely resembling descriptions of the disease in adults. Henoch, who has enjoyed a wide experience, does not believe that there is any marked difference between the course of the disease in children and that observed in older persons.

One thing, however, is certain: the course of the disease in children

is usually more rapid and very much more favorable than in adults. In the great majority of cases the disease terminates between the eighth and the twelfth day. A duration of from fifteen to seventeen days, which is usual in severe and moderately severe cases among adults, is distinctly rare in childhood.

That the average course of the disease in childhood is mild is shown by the death-rate, which is from 5 per cent. to 7 per cent.; whereas in adults it is at least $2\frac{1}{2}$ or 3 times, and in old age 10 times, as great.

It is worthy of note that the severity of the disease shows marked variations in the different ages of childhood. The severest cases are found in very young children up to the fifth year; the mildest, in children between the tenth and fifteenth years, whereas children between the ages of five and ten years occupy an intermediate position in regard to the severity of the disease.

That children from five to fifteen years of age are much less severely attacked is partly due to the fact that the vital organs, especially the circulatory system and the central nervous system, possess greater powers of resistance to the toxins, and partly on account of the comparatively short duration of the disease and the greater rarity of complications.

Another factor in the low death-rate is the great preponderance of cases of very short duration, or absolutely abortive cases, in childhood. Severe forms of the disease, such as are observed in adults, especially the so-called fulminating forms combined with coma-vigil, are distinctly rare among children.

The beginning, the course, and the defervescence of the fever in well-marked cases do not present any marked differences from those observed in adults. The temperature-curve may, even in children, attain a considerable height—41° C. and over—and may, during the fastigium, assume the form of a continued or continued remittent fever.

The pulse is almost always extremely rapid, but usually retains a good tension. Alarming cardiac weakness occurs almost exclusively in children who are debilitated from the effects of other diseases or the miserable conditions amid which they live.

Although fatal paralytic symptoms are comparatively rare, irritative nervous phenomena occur more frequently and are more violent in children than in adults who had been healthy before being attacked by the disease. Children are more frequently attacked by convulsions during the rise or at the height of the fever, and the delirium, restlessness, and noisiness in severe cases among children are quite as marked as are the same symptoms observed in adults.

Conjunctivitis, laryngitis, and catarrhal bronchitis occur regularly and often assume alarming proportions in children. Lobular and lobar pneumonia are quite as common as in adults, but hypostatic consolidation is distinctly more rare.

The appearance of the typhus eruption is practically the same as in adults of youthful and middle age. In children, as in adults, the abundance of the rash unquestionably varies widely in different epidemics, and this is probably the reason that certain authors (Griessinger) regard the absence or scanty development of the eruption as particularly common among children. In the same way the different epidemics vary widely in regard to petechial transformation of the rose-spots, both in children and in adults, although the rare transformation of the purely macular rash into small papules or even circinate patches appears to be somewhat more frequent in children than in adults.

Cancrum oris, which claimed many victims among the children during epidemics of former times, has now become so rare that it may practically be passed over in silence.

Decubitus is distinctly less frequent in children than in adults.

DURATION OF THE DISEASE AND PERIOD OF CONVALESCENCE.

Having sufficiently discussed the abridged and abortive forms, I will now devote a few paragraphs to the question of the duration of well-marked cases ending in recovery—that is, the period between the beginning of the fever and the end of defervescence.

Duration.—The discrepancy among the statements of the older authors in regard to this is much greater than among those of the more modern ones, probably because many infectious diseases, especially typhoid and relapsing fever, were not properly distinguished from typhus fever.

The views of modern authors exhibit an astonishing unanimity. Almost all give as the average the shorter duration that has already been mentioned. For a well-marked case in an adult, the average duration may be regarded as from twelve to seventeen days; or, to be even more exact, I should say that the fourteenth day, according to my experience, most frequently marks the end of defervescence.

Cases in which the fever lasts longer than the eighteenth day are comparatively few in number, while an uncomplicated case in which the end of defervescence is delayed beyond the twenty-first day, in my experience, is distinctly exceptional.

This sharp limitation and the strictly cyclic course of the disease are the principal points of difference between typhus and typhoid fever.

Murchison calculated that in almost half of all the cases convalescence begins on the thirteenth or the fourteenth day, and in more than three-fourths of all cases between the thirteenth and sixteenth days. These numbers were obtained from an analysis of 53 uncomplicated cases. In the epidemic of 1879, in Moabit, we succeeded in determining the duration of the disease in 296 cases, and obtained the following instructive table:

Convalescence began after—

7	days in	1	case	14	days in	42	cases
8	"	7	cases	15	"	33	"
9	"	16	"	16	"	28	"
10	"	25	"	17	"	16	"
11	"	25	"	18	"	14	"
12	"	35	"	19	"	9	"
13	"	41	"	20	"	4	"
						296	"

Griessinger gives the duration of milder cases as from twelve to fourteen days—that of the majority of cases as from sixteen to twenty days. Jenner believed that uncomplicated cases run their course in from fourteen to twenty-two days at the most. Barallier calculated the average duration in 698 cases, and found it to be from ten to twenty-two days.

In uncomplicated cases **convalescence,** when not protracted by sequels, proceeds more rapidly than the severity of the clinical picture and the condition of the patients immediately after the end of defervescence would lead one to expect.

Condition of the Various Organs during Convalescence.—After a severe or moderately severe attack almost all patients, although they soon begin to feel quite comfortable, are pale, debilitated, and usually very much emaciated. A loss of from 10 to 15 pounds, which in a disease lasting only from two to three weeks cannot be regarded as inconsiderable, is not at all uncommon. In severe cases both I and other authors[1] have frequently observed, even during the first week after the disappearance of the fever, an additional loss of from $2\frac{1}{2}$ to 5 pounds, the cause of which we can at present merely surmise.

The greatest loss in weight occurs naturally during the height of the disease. In one of Rosenstein's cases a loss of 10 pounds occurred between the seventh and the fifteenth day of the disease. In another the same amount was lost in the course of four days. I myself have not infrequently seen a loss of from $7\frac{1}{2}$ to 12 pounds in the course of from five to seven days, and in one case a loss of $16\frac{1}{2}$ pounds between the eighth and the thirteenth day of the disease.

In a few cases, where the attack had been very severe and protracted and the patients were previously much reduced in health, I had occasion to observe hydremic conditions with edema over the smaller joints, although the urine was free from albumin.

[1] Herrmann, *Petersb. med. Wochenschr.*, 1876, No. 16.

During the first week after defervescence, sometimes as early as the third or fourth, and usually before the tenth day, my patients were, as a rule, allowed to get up, and, if convalescence was not interrupted, they were usually ready to be discharged and go back to work after three to four weeks.

This favorable course of convalescence, while partly due to the short duration of the disease, violent as it is, is unquestionably influenced to a large extent by the fact that the organs of digestion are so little involved in the morbid process. For this reason convalescents in this disease, more fortunate than those recovering from typhoid fever, can be permitted fully to satisfy their appetite, which returns before or during the period of defervescence.

In severe cases, even when the patients feel quite well, the pulse remains during the first or even the second week comparatively small, soft, rapid, and so extraordinarily sensitive to external conditions that the slightest provocation may induce a considerable although transitory rise in the frequency. On the other hand, in some very feeble patients I have seen a remarkable slowing of the pulse—in one case down to 40 beats a minute—accompanied by pronounced retardation. How this bradycardia, which is also observed in other infectious diseases—I need only mention typhoid fever and diphtheria—is produced I have been quite unable to determine.

The temperature usually falls below the physiologic level on the first afebrile day, and remains subnormal during the first, and often part of the second, week of convalescence. It may be extremely low: 35° or 36° C. in the morning, with a very slight evening rise, is not at all uncommon. After the second week the temperature-curve gradually returns to the normal.

Like the pulse, the temperature shows a marked instability during the first part of convalescence. Physical and mental disturbances, so slight as practically to be imperceptible to a healthy person, often bring about a sudden material rise lasting a short time, and the fever-curve becomes a faithful record of any little disturbances, such as errors in diet, etc.

Although the nervous system in well-marked cases regularly shows such severe implication, the disturbances, as a rule, subside very quickly. A persistence of the delirium, especially during the evening hours, beyond the time of defervescence is the most frequent of these persisting disturbances. I have seen delirium last in this way from three to four days, and even until the end of the first week of convalescence.

In the great majority of convalescents, however, the cerebral func-

tions are restored during the first days, often immediately after the disappearance of the fever. Individuals who continue to have delirium in the evening during the first few days usually exhibit during the daytime a certain weakness of mental activity, especially a loss of memory for former events. The patient's recollection of his illness is almost always very limited in severe or moderately severe cases. Most patients remember only the initial stage—that is, the days during which the fever begins to rise. They retain a lively recollection of the agonies of that period, and convalescents who have gone through an attack of relapsing or typhoid fever affirm that the initial symptoms in these diseases are not nearly so bad as they are in typhus fever. These initial symptoms appear to be comparable only to those of small-pox, judging from what I have learned from typhus convalescents who had formerly had the former disease.

On the other hand, the period of hyperpyrexia and of most intense symptoms leaves a blank in the minds of the majority of convalescents from a severe attack. A few of them may remember one or two particularly impressive events, such as baths, the visits of the doctor and his examinations, or attempts at flight that they may have made and the measures adopted to prevent their repetition. Others remember only the subjects of their early delirium and hallucinations, and of these they retain so lively a recollection that they continue to be troubled by them in their sleeping and waking moments, and even when they are fully conscious cannot quite rid themselves of the idea that there must have been some truth in them. When it is remembered that their hallucinations frequently have to do with most unusual and distressing situations and actions, it will not be difficult to understand that they may be a source of great distress and interfere seriously with convalescence.

True psychoses appear to be rare during convalescence. Mild melancholia and hallucinations are sometimes seen, and even mania has been observed. Among patients treated in Moabit in 1878 and 1879, 4 cases of mental disturbance occurred during convalescence. In 2 cases—1 in 1878 and the other 1 of the 3 that occurred in 1879—the disturbances immediately followed the end of defervescence. One case, that of a young girl with delusions of persecution, ended in recovery after eight days. In the case of 2 men, the psychosis made its appearance later: in 1 case toward the end of convalescence; in the other, after his discharge from the hospital. The former, who had to be sent to the insane asylum on account of violent mania, exhibited also severe auditory hallucinations that were undoubtedly due to the fact that he had had a bad otitis media with perforation of the tympanic membrane during the height of his illness.

Severe organic lesions of the central nervous system being, as has

been said, quite uncommon during the febrile period, were rarely met with in disturbances continuing during or even after convalescence. Isolated cases of paraplegia and hemiplegia have, however, been observed in every epidemic. No cases of the former have ever been carefully investigated either clinically or anatomically, and it is not even known which of them are to be attributed to spinal and which to neuritic disturbances. On the other hand, the morbid anatomy of the hemiplegias is much better known. They have been found to depend either on hemorrhages into the brain-substance or meninges, or on embolism and thrombosis.

Paralysis of individual muscles or groups of muscles, or of a single extremity, is quite as uncommon as hemiplegia. Of the muscles in the upper extremity, the deltoid appears to be most frequently attacked; on the trunk, the serratus magnus; and in the leg, the extensor muscles of the thigh. Whereas hemiplegia, being due to an organic lesion, is usually very slow to disappear or even remains incurable, palsies of individual muscles, as a rule, disappear much more quickly, showing that they are probably of a neuritic nature.

A much more common event than paralysis during convalescence is neuralgia, which is often very distressing, particularly the neuralgic pains in the toes and soles of the feet already referred to. They sometimes make their appearance during the latter part of the febrile period, and persist for a variable length of time during convalescence. Although I have seen them disappear by the end of the first week, I have also known them to last two or three weeks. Among the rarer forms of neuralgia I may mention neuralgia of the supra-orbital nerve, which appears to be more obstinate than the other forms that have been mentioned. One of our cases was still suffering from the condition at the time of his discharge. Mention may also be made of neuralgia in the distribution of the brachial plexus, which assumes a very severe form, although, fortunately, it occurs more rarely.

The nervous form of deafness usually disappears with the fever, but disturbances due to disease of the middle ear or other grave alterations are likely to be more obstinate and may end even in permanent deafness.

The changes in the respiratory organs, which so frequently form a disturbing factor in the course and duration of convalescence, have already been referred to, but we must once more consider in this connection the frequent occurrence of severe alterations in the larynx during many epidemics. Even after the fever has subsided they require the most careful and persistent treatment, in spite of which permanent aphonia and laryngeal stenosis cannot always be avoided.

Among the severe complications of convalescence should be mentioned the various purulent and necrotic pulmonary affections depending on purulent perichondritis. As has been stated in another place, they often lead to purulent effusions, and subject the patient to all the difficulties and dangers of an empyema operation.

The organs of digestion being but little involved during the height of the disease, there is but slight interference with convalescence to be expected from that quarter. I myself do not remember any case of this kind, but from the reports of several epidemics it appears that violent vomiting, occurring after the ingestion of food, has been observed during the first week after defervescence. However, as a number of these cases presented certain symptoms referable to the central nervous system, one cannot avoid the thought that the phenomenon may have been of central origin.

In a few instances patients were greatly troubled during convalescence by painful maceration of the gums associated with hemorrhages.

Inflammation of the salivary glands, developing during the febrile period and continuing during convalescence or arising after the end of the febrile period, occurs with variable frequency according to the period and individual epidemic. It usually takes the form of unilateral parotitis, or, in very rare cases, of which I have personally seen but one, inflammation of the sublingual glands. In very feeble patients I have met with suppuration of an entire salivary gland, with necrosis of the connective-tissue stroma.

Changes in the skin are a particularly fruitful source of disturbance during convalescence. Many patients continue to suffer for some time after defervescence from gangrene of the ears, fingers, toes, tip of the nose, and skin of the penis and scrotum, arising during the febrile period. In 2 instances during the epidemic of 1879 we were driven to perform exarticulation of gangrenous toes.

Noma and hospital gangrene have become so rare that they need scarcely be reckoned with during convalescence.

Decubitus, owing to the relatively short duration of the disease, is comparatively rare, and is practically seen only in the most severe cases. It may, however, assume such marked proportions that we cannot believe it to be entirely due to pressure and soiling of the affected parts, but it must be assumed that trophic disturbances in addition are operative. It would appear that the form that I have described in connection with many cases of typhoid fever, and designated as subcutaneous phlegmonous decubitus, is also comparatively more frequent than any other in typhus fever. Without producing any marked pain or even any abnor-

mal sensation, a macular, yellowish-red or bluish-red discoloration of the skin, with more or less extensive induration and infiltration of the subcutaneous cellular tissue, develops over the nates, in the lower sacral region, or even in the depths of the fold between the buttocks. After a few days one or two small openings appear in the middle of the discolored area and discharge a thin, dirty-colored pus. If the openings are enlarged by incision or the diseased portion of the skin undergoes gangrenous suppuration, as not infrequently happens, a surprisingly large quantity of pus containing shreds of necrotic tissue is evacuated, and a large cavity, extending in all directions under the sound skin, is revealed, which, although it rarely extends deeper than the cellular tissue, may take a long time to heal.

The ordinary form of decubitus is more often followed by a deeper destructive process going on to necrosis and sequestration of bones, particularly in the sacrum and coccyx, and also in the scapula and the trochanters.

Closely related to actual decubitus there occurs furunculosis of the gluteal region and adjoining portions of the back. This complication, which is not very uncommon, often occasions great suffering and considerably protracts the period of convalescence. Occasionally, I have also met with furuncles in other regions or distributed over the entire body.

Once or twice I had the same experience that has been mentioned by other authors—of erysipelas following decubitus, furuncle, or abscess, but, fortunately, I never lost a patient from this cause.

In the case of a very few convalescent patients we had a good deal of trouble with diffuse phlegmons beginning during the febrile period. I have seen them on the arms and on the skin of the abdomen, and believe that they were due to traumatism, probably self-inflicted injuries during delirium. One of these patients died of septicopyemia in the fourth week of defervescence.

VERY SEVERE AND FATAL CASES. PROGNOSIS AND MORTALITY.

The cases with moderately severe and severe symptoms in the ordinary sense having been fully discussed in the general description of the clinical picture, for which they supplied the basis, will be touched upon but lightly in connection with prognosis and mortality.

In this section only those cases will be particularly mentioned that present unusually severe symptoms, and in which the prognosis is exceedingly unfavorable or absolutely fatal.

In this class we have certain cases of very short duration, others of usual length, and even some of abnormally long duration, all, however, characterized by unusually high fever. They are the so-called **hyperpyretic cases.** In most of them, after a single violent chill, the temperature rises in a short time, or at one bound, or with very slight remissions, to an unusual height, 41° or even 42° C. being often attained under such conditions as early as the evening of the second or the third day, and this level is, as a rule, maintained for days or until the second week, either with marked morning remissions or with less than the physiologic daily variations. Such cases early exhibit marked enlargement of the spleen; occasionally, the organ may become palpable with the first appearance of the febrile symptoms. Severe bronchitis is usually present from the beginning. Along with the unusually high temperature there are often an excessive increase in the pulse-rate and an alarming diminution in the tension.

In almost all the cases the central nervous system becomes involved very early: violent delirium on the first evening, rapidly developing hebetude, with subsultus tendinum and carphology, going on to the deepest coma, in which the majority of the patients die between the ninth and eleventh days, sometimes after an excessive preagonic rise in the temperature (Fig. 59). In a smaller number of the hyperpyretic cases the fatal termination is preceded by an unusual drop in the temperature, as shown in Fig. 60. Recovery in these cases is exceedingly rare.

Cases beginning with hyperpyrexia and running an unusually protracted course to a fatal termination are much less frequent than those just described. The temperature-curve frequently presents marked variations during the course of such cases. At first it is excessively high, then it falls to, or even below, the normal. I have seen cases belonging to this group (Fig. 69) in which death was delayed until the second, or even the middle of the third, week, and the temperature continued excessively low for days or weeks before the fatal termination.

Closely related to this group is a variety characterized by unusual severity and almost constantly fatal termination, in which the temperature continues comparatively low throughout the duration of the disease.

Subfebrile and Afebrile Cases.—True afebrile cases, such as occur in typhoid, appear to be extremely rare in typhus fever. I have not seen a single definite case of the kind, nor do I find mention of them by the most experienced authors. On the other hand, it quite commonly happens in the cases that I am now considering that the temperature during the entire period of the disease does not exceed 40°

or even 39° C. This is observed particularly in older individuals or in young persons whose strength has been reduced by poverty, vice, or chronic disease before their infection with typhus.

Instead of a general description of this variety, which has never been

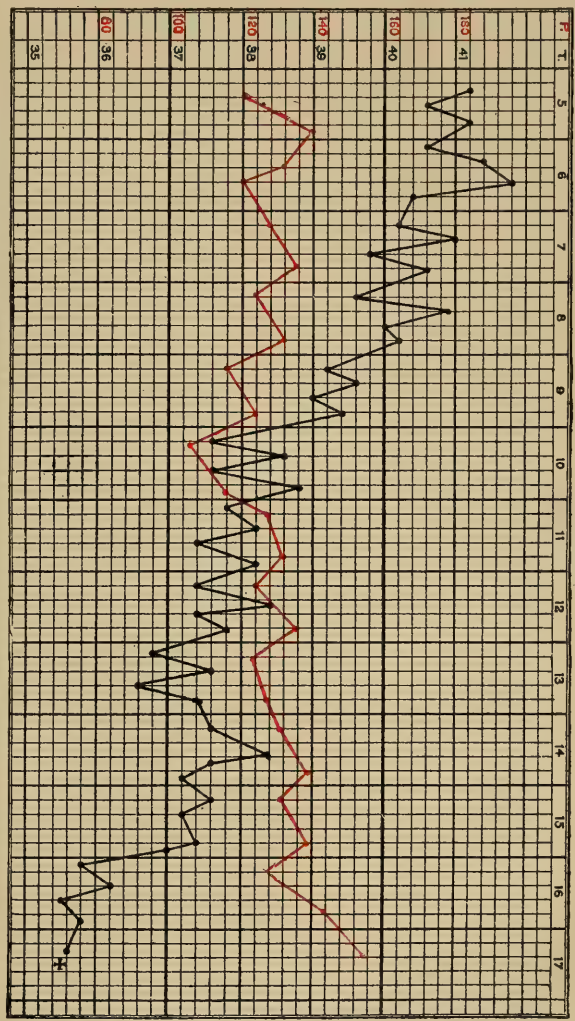

FIG. 69.—Male, aged thirty-eight. Excessively high temperature, lasting until the end of the first week. After the tenth day, low temperature with very high pulse-rate. Death on the seventeenth day.

fully described, I will give three temperature-charts with short notes of the corresponding case histories.

The first case (Fig. 70) was that of a feeble old man, sixty-three years of age, who for months before he was taken ill had lived amid the most destitute circumstances. His illness began with a series of slight chills, after which the temperature gradually rose, although it did not exceed 39° C., except on two days—the fourth and fifth days of the disease. With the beginning of the second week the temperature gradually and steadily began

to fall to the normal, with a slight rise shortly before death. Splenic enlargement was absent during the entire course of the disease. Rose-spots were

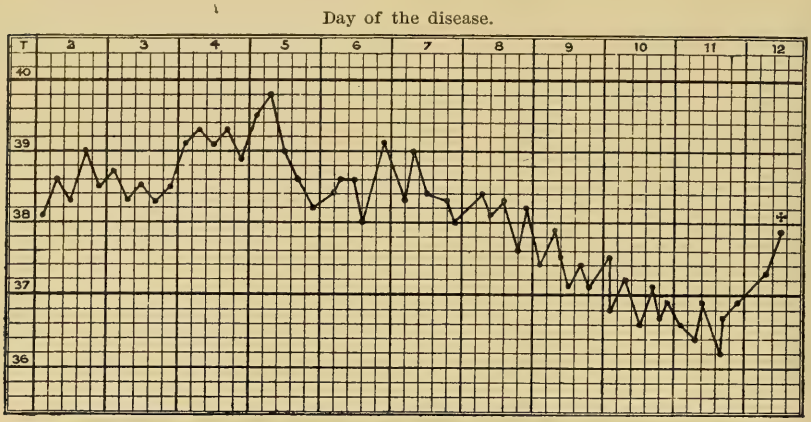

FIG. 70:—Male, aged sixty-three. Fatal termination with relatively low fever.

present in small numbers and were very indistinct; but, on the other hand, numerous petechiæ made their appearance early among the roseola lesions.

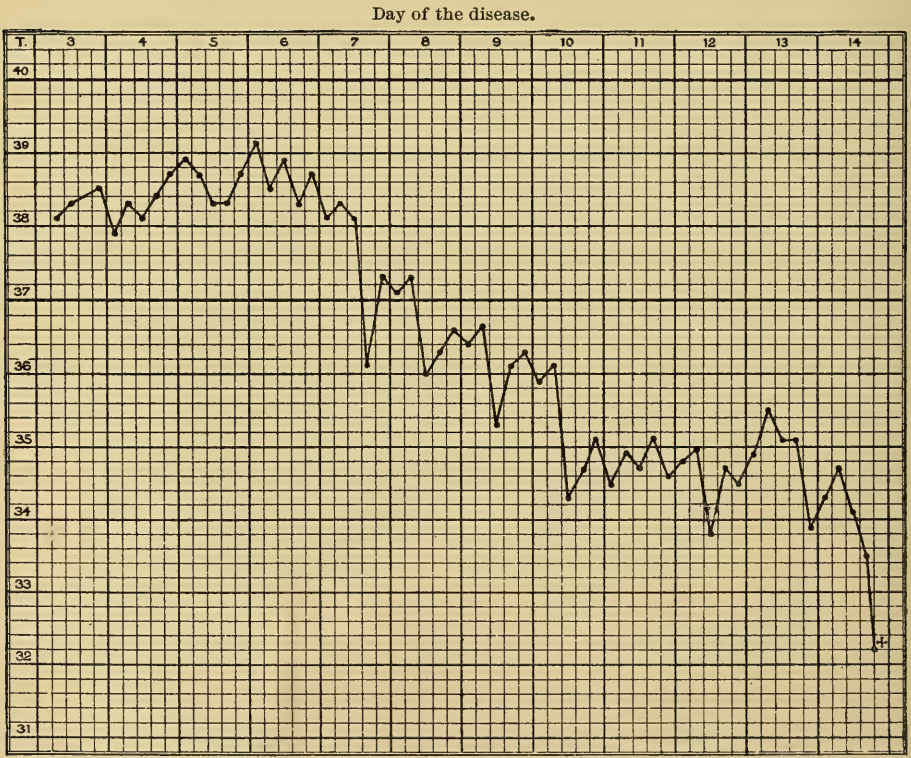

FIG. 71.—Male, aged thirty. Temperature was relatively low from the very beginning, and during the last week fell below the normal.

A considerable quantity of albumin was found in the urine from the third day until death. Coma developed on the second day, accompanied by subsultus tendinum, carphology, and muttering delirium, and continued until death.

The history of the second case, that of a laborer, thirty years of age, is even more remarkable (Fig. 71). The highest temperature, attained only once during the entire course of the disease, was 39.1° C., and from the seventh to the fourteenth day, when death occurred, the temperature continued to fall to so marked a degree that during the last four days it ranged between 34° and 35°, and eventually dropped to 33.3° and 32.2° C. immediately before death. In spite of this unusually low temperature the patient continued in violent delirium, and was entirely unconscious until two days before death. He was too weak to rise, and lay in bed in a state of constant restlessness, crying and yelling, at last quieting down and falling into distinct coma-vigil during the last forty-eight hours preceding death. For three months

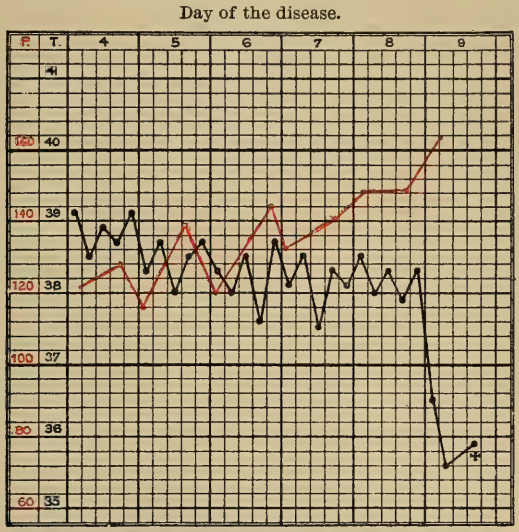

FIG. 72.—Male, aged thirty-five. Fatal case with very low temperature. Febris exanthematicus renalis.

before his admittance the patient had been without a home, had scarcely eaten anything, and had drunk large quantities of whisky.

Combemale reports 2 very similar cases with a marked fall of temperature in the last days, in one case to 33.7°, in the other to 33.2° C. This contribution is the only one on this subject found in recent literature, and even the oldest authors, such as Hildenbrand, refer to the condition in very indefinite terms.

A third case that I should like to add was that of a man, thirty-five years of age, who died on the ninth day of the disease (Fig. 72). The temperature in this case ran a remarkably regular and constant course at a comparatively low level—between 38° and 39° C.—and nothing but the excessive weakness and frequency of the pulse, which were present from the beginning, suggested a fatal termination. At the time of his admission the patient had a well-marked, closely aggregated roseolous eruption, which on the fifth day of the disease rapidly underwent almost complete hemorrhagic

transformation. In addition to this he presented on the day of his admission—the fourth day of the disease—symptoms of severe hemorrhagic nephritis that continued to dominate the clinical picture during the remainder of his illness. This and similar cases, which, it must be admitted, are very rare, might well be designated "*renal typhus*," in analogy to the corresponding forms occurring in typhoid fever.

Fatal cases of short or moderately short duration, which are described by the older authors under the term **typhus siderans,** vary in frequency in the different epidemics.

They appear to occur especially at the beginning and during the height of otherwise malignant epidemics, particularly such as occur on shipboard, in prisons, during a siege, or in badly managed armies. Hildenbrand, Murchison, Graves, and others among the older authors enjoyed an abundant experience from which to describe these varieties. It was quite prevalent during Napoleon's campaigns and in the Crimean war, especially among the French and Russians, who were not nearly so well looked after in the matter of health and general conditions as were the English.

This group includes cases ending fatally within a few days after the appearance of the first symptoms—usually between the third and fifth days, or even earlier. Most of them begin with a violent chill and a well-developed splenic enlargement. The temperature generally undergoes a rapid and uninterrupted rise, during which the patients complain of the most violent symptoms: unusually severe headache and pain in the back and limbs, accompanied not rarely by uncontrollable vomiting and retching. The temperature usually reaches a great, and sometimes an excessive, height. As early as the first day the pulse is unusually small, frequent, and may become irregular in volume and rhythm on the second day. The patients, whose mental condition becomes clouded on the evening of the first day, either develop violent delirium lasting until death or sink into coma-vigil.

Death is preceded by symptoms of extreme cardiac weakness, and usually by an excessive temperature—in one case I saw a hyperpyrexia of 42.6° C. The specific eruption is not rarely absent or but sparingly developed; to use an expression of the older physicians, it "sticks underneath the skin." Accordingly, the diagnosis, especially when the duration is very short, is particularly difficult, and during large epidemics can be made only by exclusion and by the determination of long-continued, close contact with well-marked typhus fever cases.

In this way one can understand certain cases described by reliable authors as lasting only one or two days or a few hours. Personally, I have never met with cases of such short duration. The quickest fatal

case I have had occasion to observe terminated in the night between the third and fourth days of the disease.

I must not omit to mention that a majority of these cases are characterized by marked albuminuria from the very beginning, and that diphtheric anginas are distinctly more frequent than in the other forms of typhus fever.

Among the forms that almost always end fatally must be included the so-called **hemorrhagic cases.**

Although this variety always receives careful consideration in descriptions of the acute exanthemata, but little attention is devoted to it even in careful descriptions of epidemics and in monographs on typhus fever. Exactly as in the acute exanthemata, these cases present a great variety of manifestations, and, for external reasons, they may be best divided into the fulminating form and the form having a somewhat longer duration.

Although cases of the fulminating hemorrhagic form of typhus fever are exceedingly rare in comparison with those of small-pox of the form designated as *purpura variolosa*, the two conditions nevertheless possess many points in common.

The temperature rises rapidly to a great height, and other severe initial phenomena are observed. With the first appearance of the rash—in the severest cases at the end of the second or beginning of the third day of the disease, before there is any sign of a rash—numerous petechiæ make their appearance and are immediately followed by extensive hemorrhages into the skin and subcutaneous cellular tissue of the trunk and extremities. The conjunctivæ are injected, and hemorrhages from the lips, tongue, gums, and nose make their appearance. This is followed by ecchymosis and softening of the pharyngeal structures and diphtheric exudation or gangrene of the mucous membrane. Soon hematuria of renal origin, with signs of severe nephritis, and also hematuria due to hemorrhage from the pelvis of the kidney and the bladder, are superadded. Many of the patients early expectorate a serosanguineous sputum; there are consolidations of the pulmonary tissues, sometimes ending in gangrene of the lung. Intestinal hemorrhages and, in the case of women, abundant metrorrhagia complete the horrible clinical picture, to which the older authors were in the habit of applying the term "Faulfieber."

In most cases the appearance and development of the hemorrhages are accompanied by a rapid fall of the temperature, which often sinks to an unusually low level just before the end. For days before death it is often impossible to feel the pulse. To this extreme prostration of

the circulatory organs is to be attributed, at least in part, the gangrene of the fingers, toes, tip of the nose, and ears, these organs often appearing suspiciously pale, livid, and cold even during the first twenty-four or thirty-six hours.

Although the number of these cases that I have seen personally is very limited, they are firmly impressed on my memory. Hematemesis never occurred among my cases, and appears to be rare. A case of Christie's [1] appears to me well worth quoting. A child, nine years of age, at first presenting a typical rash, which later became markedly hemorrhagic, died on the ninth day of the disease in consequence of an extensive hemorrhage from the stomach, the source of which was found at the autopsy to be, not a large vessel, as was expected, but an extensive capillary oozing.

The most malignant cases in this group—those that end fatally during the first days of the disease before the appearance of the true typhus rash—are comparable, as has been stated, to the variety of small-pox known as *purpura variolosa*. As I have shown in the discussion of that disease,[2] we have to deal with an affection that has become hemorrhagic in the very beginning of the initial stage.

It goes without saying that the hemorrhagic process, which, strictly speaking, belongs to the typical course of the disease, especially as regards the cutaneous changes, may become prominent during any other stage of the disease. Even then the prognosis is bad, although not quite so hopeless as in the form just considered. In general the prognosis is more favorable the later the hemorrhagic process makes its appearance.

These cases also present, in addition to the early and marked hemorrhagic transformation of the specific roseolous eruption, numerous independent petechiæ, as well as the previously mentioned extensive cutaneous hemorrhages.

The temperature-curve in these cases is variable: some cases are characterized by hyperpyrexia; others exhibit an irregular febrile course, with marked remissions or even intermissions suggesting collapse; again, there are cases in which the appearance of the hemorrhages is accompanied by a marked fall in the temperature, which remains subnormal and often exceedingly low until death.

These cases also are characterized from the very outset by pronounced weakness of the circulatory system, small, rapid, irregular pulse, pulmonary infarcts, and hypostatic congestion. In 2 instances I observed also intracranial hemorrhages: once into the brain-substance in the

[1] *Glasgow Jour.*, Dec., 1888.

[2] See Curschmann, "Die Pocken," *Ziemssen's Handb.*, second edition, vol. i.

region of the large ganglia, and another time into the meninges. Early and well-marked albuminuria is a constant feature of this variety, and abundant hemorrhages from the urinary passages are common occurrences.

Rapidly progressing loss of strength is a well-marked symptom from the beginning; the patients soon become unconscious and many are violently delirious, although the majority present the so-called "ataxo-adynamic" form of the disease.

PROGNOSIS; MORTALITY.

General Consideration of the Mortality-rate.—The question as to the mortality of typhus fever in its broadest sense is not easy to answer. The older statistics, although extensive, are of no value, because typhoid and relapsing fever were not distinguished from typhus fever with sufficient exactness, and the figures given are therefore too low.

Even in later times, however, when this distinction was more accurately made, discrepancies are found that cannot be attributed altogether to variations in the disease, but depend rather on errors of observation and diagnosis.

These errors usually result in an excessively high estimate of the mortality, especially when, as was the case in certain regions and at certain periods, medical men were not sufficiently trained to recognize all the various forms of the disease, especially the milder and imperfectly developed forms, and therefore based their statistics exclusively on the well-developed and severe cases that came under their observation.

Again, although the attempt might be made to correct errors incidental to statistics based on a small number of cases by comparison with a large number of reports derived from various epidemics occurring at various times, it is to be remembered that the malignancy of the disease is subject to the greatest variations, not only in different localities and at various periods, but even during different periods of the same epidemic.

Taking all the difficulties into account as well as possible, the mortality of typhus fever in general may be placed at from 15 to 20 per cent. It follows, therefore, that typhus fever is one of the most dangerous of infectious diseases—far more dangerous than typhoid fever.

Some vague idea of the nature of typhoid fever in Griessinger's time may be obtained from the statement of that author that typhus fever, the general mortality of which he estimated at from 15 per cent. to 20 per cent., is "considerably less dangerous than typhoid."

Murchison, whose statistics on the general mortality are most elaborate and based on the largest number of cases, on the basis of 4787 cases treated in the London Fever Hospital between 1848 and 1862, calculated the mortality at 20.89 per cent. Among 9485 cases admitted to the Infirmary at Glasgow during a period of eleven years, he reports a mortality of 18 per cent., and among 1370 patients treated in another Glasgow hospital the mortality was 236, or 17.23 per cent. After collecting the enormous number of 18,592 cases observed by himself and other authors, Murchison finally determined the mortality to be 18.78 per cent.

From my analysis of the 676 cases that I observed in Moabit in the years from 1876 to 1879, almost all of which came from the most destitute classes of the population, I obtained the alarming figure of 23.4 per cent. The distribution of the cases for the three years was as follows:

Admitted in 1876, 148; deaths, 40—27 per cent.; in 1878, 87; deaths, 22—25.3 per cent.; in 1879, 441; deaths, 97—21.8 per cent.

A mortality of from 15 to 12 per cent. or even 10 per cent. and less has been reported in a few epidemics of minor extent, characterized by unusually favorable conditions. It far more frequently happens that the mortality rises above 20 and as high as 30 per cent. Such high figures are reached in epidemics when the social, and consequently the individual, conditions are particularly unfavorable—as, for instance, when the disease breaks out in times of war or famine, on shipboard, in prisons, and under other especially unhygienic circumstances. Under such conditions the mortality has risen as high as 50 per cent. Again, I may cite the Crimean war and Napoleon's campaigns. In very recent times reports of an unusually severe form of the disease have been received from various regions. Thus, Dardignac[1] calculated the mortality at 36.3 per cent.

In hospitals a mortality of from 22 to 25 per cent. is quite common. It is often greater than it is among the outside population during the same epidemic, obviously owing to the fact that a relatively large number of severe cases are admitted. The high mortality of 21.14 per cent. that we had in 1879 in Moabit could be brought down to 18.8 per cent. if the cases admitted in a moribund condition and those that died before the end of forty-eight hours were deducted from the total. Murchison also states that the mortality-rate in his 4787 cases would be reduced from 20.89 to 17.9 per cent. if he were to make the same reservation.

The conditions that determine the character, and especially the malignancy, of the disease are as numerous as they are variable.

The peculiarities of the life-history of the specific organism and the reaction of the body to this organism are unquestionably most important factors, and we cannot hope fully to understand these until a more thorough knowledge of the micro-organism is obtained.

[1] *Depart. Oise*, 1893.

General **external** and **personal conditions** having an influence are, relatively speaking, much better known.

Among the general external conditions **geographic distribution, weather,** and **time of year** were, no doubt, formerly of much greater importance than they are to-day. Certain of the older authors state that they observed a distinct increase in the virulence of typhus fever in certain countries and during certain seasons and weather conditions, but at present we know that such factors are only indirectly important in so far as they affect the social and personal conditions of the populations.

Reference has frequently been made to the fact that great national destitution, famine, war, and sieges favor the development and materially increase the malignancy of the disease.

Among individual conditions **age** undoubtedly exerts the greatest influence on the mortality.

In children and young individuals under the age of twenty, just as in typhoid fever, the mortality is low—not more than from 2 to 5 per cent. It is materially higher between the ages of twenty and thirty, and in severe epidemics may be doubled or more than doubled. Between the ages of thirty and forty the mortality is four times as high as among individuals of under twenty, and after forty it rises to a stupendous height. Thus, in Moabit in 1879 almost two-thirds of all the deaths occurred in individuals over forty years of age, although of the entire number of patients admitted only one-quarter were of this age. Approximately the same proportion has been observed in other epidemics.

There is an interesting difference in the mortality in the three periods of childhood. This difference is sharply defined and has been observed with great regularity, but no satisfactory explanation has so far been offered. Children under five years of age are in greatest danger from the disease, whereas the period between ten and fifteen years exhibits the most favorable mortality. In the latter period the mortality ranges between 0.5 and 4 per cent., whereas among children under five it varies from 6 to 12 per cent. The intermediate class, comprising children between the ages of five and ten, occupies a corresponding intermediate position as regards the mortality (4 to 7 per cent.). In illustration of this point statistical tables of Murchison and Grätzer are added. The former collected his statistics from the records of 563 children in the London Fever Hospital:

	Admitted.	Died.	Per cent.
Under 5 years	17	3	17.65
Between 5 and 10 years	183	14	7.65
" 10 " 15 "	363	18	4.95

Grätzer based his calculations on 158 cases of children in the Breslau epidemic of 1869:

	Admitted.	Died.	Per cent.
Under 5 years	15	1	6.66
Between 5 and 10 years	42	2	4.76
" 10 " 15 "	101	1	0.99

To illustrate the mortality among all ages I give two tables based on very large figures, one by Murchison, based on 3506 cases admitted to the London Fever Hospital during ten years, and a later one by Guttstadt, based on 5545 cases admitted to Prussian hospitals during the years from 1878 to 1880.

The following are the statistics of Murchison:

Age.	Number admitted.	Died.	Per cent
Under 5 years	17	3	17.65
Between 5 and 10 years	183	14	7.65
" 10 " 15 "	363	18	4.95
" 15 " 20 "	546	26	4.76
" 20 " 25 "	495	47	9.05
" 25 " 30 "	343	52	15.15
" 30 " 35 "	323	55	17.02
" 35 " 40 "	270	89	32.96
" 40 " 45 "	292	87	29.79
" 45 " 50 "	212	83	39.15
" 50 " 55 "	150	78	52.00
" 55 " 60 "	100	51	51.00
" 60 " 65 "	88	49	55.68
" 65 " 70 "	42	28	66.66
" 70 " 75 "	24	17	70.83
" 75 " 80 "	6	5	83.33
Over 80 "	2	2	100.00
Age unknown	50	11	22.00
	3506	715	

Guttstadt's statistics are:

	Males. Per cent.	Females. Per cent.
Under 10 years	2.2	3.3
Between 10 and 15 years	3.0	1.5
" 15 " 20 "	5.2	4.5
" 20 " 30 "	8.2	10.1
" 30 " 40 "	16.0	11.2
" 40 " 50 "	31.9	20.2
" 50 " 60 "	43.7	35.5
Over 60 "	57.1	45.2

My own material, consisting of 410 cases treated in 1879 in the lazaretto at Moabit, yielded, according to the figures of my assistant Salomon, the following mortality for the different ages:

	Per cent.
From 10 to 20 years	2.50
" 20 " 30 "	5.49
" 30 " 40 "	20.00
" 40 " 50 "	48.53
" 50 " 60 "	63.63
" 60 " 70 "	62.50
" 70 " 80 "	100.00

The oft-repeated statement that the effect of age on the prognosis is to be attributed to the diminished powers of resistance against the micro-organism and its toxins, just as in the other acute infectious diseases, is a mere platitude. A much more tangible reason for the rapid rise of mortality after the age of forty is to be found in the cardiac weakness that is much more prominent during this period of life and in the pulmonary complications, especially hypostatic inflammations, directly dependent upon it.

The high mortality during the period between thirty and forty, in proportion to that observed in other acute infectious diseases, is probably due to the fact that typhus fever, which preferably attacks the poorer classes, generally selects those individuals who have suffered most in the struggle for existence and whose strength has been sapped by worry, vice, and general destitution.

As regards the remarkable differences in the mortality observed during the three periods of childhood, we still lack the necessary data to offer an explanation. It might be said of the period between the tenth and the fifteenth year that the clinical material is selected, inasmuch as only children of good constitution and good powers of resistance attain that age; and as regards the first period, the death-rate is perceptibly increased by the fact that the children are still contending with the difficulties of early feeding and with inherited weakness and the like, and have not yet developed a strong constitution.

Next in importance to the age are **occupation** and **mode of life.** The theory that certain conditions of life and occupations, owing to some inherent favorable or unfavorable conditions, exert a peculiar influence on the prognosis has been abandoned in the light of more recent experience. The effect of these two factors can only be indirect, and they are of influence only in so far as they determine bodily and mental overexertion, insufficient or improper feeding and modes of life, and general hardships, or as they favor the development of chronic disease, and the acquirement of passions and vices, especially alcoholism.

The marked influence to be attributed to poverty, disease, and vice in general is illustrated by one of Murchison's tables, in which the 3506 patients admitted to the London Fever Hospital are divided into three classes: *First*, those in good circumstances; *second*, those in moderately good circumstances; *third*, the poor. The results are as follows:

	Admitted.	Died.	Per cent.
First class	94	15	14.89
Second "	2674	497	18.6
Third "	738	204	27.64

The mortality, considered with reference to social status and occupation, is found to be greatest wherever these either permanently or temporarily necessitate a combination of bodily and mental overexertion with worry, care, and destitution. Tradesmen and day laborers attacked by the disease while out of work and without a home, travelling about the country in search of work or living in asylums, huts, or overcrowded tenements, die in very great numbers. Persons on shipboard, in camps, and in cities after a long siege are also under similar conditions of unfavorable prognostic omen. For many years "*febris castrensis pete-*

chialis," "*typhus carcerum,*" and "*febris nautica*" have been known as the most dreaded forms of the disease.

In regard to the **constitution,** those who are naturally deficient in this respect or have injured their health by bad habits and an irregular and dissipated mode of life are, even without regard to age, most likely to succumb to the disease. Again, alcoholism exerts a most baneful influence: 50 per cent. is not too high an estimate for the mortality of drunkards, even in those between the ages of twenty-five and forty.

That chronic diseases, as tuberculosis, syphilis, malarial cachexia, chronic gastric and intestinal affections, and recent recovery from severe acute infectious diseases, appreciably augment the danger of typhus fever need hardly be mentioned.

That bodily and mental overexertion exercises a marked influence on the prognosis, even when the individuals possess a strong constitution, are well fed and of a favorable age, is shown by the fact that in all the more extensive epidemics an unusually large number of victims were drawn from among physicians, hospital attendants, ministers, and officials in public institutions.

Whether mental depression, worry, and excitement without accompanying bodily disturbances tend to increase the danger from the disease, as has been insisted upon particularly by the older authors, cannot with certainty be determined, because it is rarely possible to estimate their influence apart from the above-mentioned factors.

Not only the surroundings of the patient before he was attacked, but also the conditions under which he lives during his illness, have an important bearing on the mortality. Proper treatment unquestionably lowers the mortality-rate. Among experienced hospital physicians it is generally accepted that any delay in removing the patient from his miserable social conditions into the more favorable surroundings of the hospital seriously affects the prognosis.

The effect of **sex** on the mortality of typhus fever is purposely treated at the end of our remarks on the prognosis, because it apparently does not exert any direct influence upon it. The lower mortality observed among women is explained by the circumstance that the female sex is much less exposed to the deleterious influences that are naturally incident to the life of man. In times of hardship, famine, and siege, when the two sexes share equally in want and misery and the epidemic spreads to the permanent population, the differences in the mortality practically disappear.

Guttstadt's table, given on page 586, shows clearly the difference in the mortality of the two sexes, especially during advanced age. In the Infirm-

ary at Edinburgh, Peacock[1] lost 114 out of 748 patients, 377 of whom were men and 371 women. Among the fatal cases 69—18.3 per cent.—were men and 45—12.5 per cent.—women. In 1847, during a severe epidemic in Glasgow, 32.4 per cent. of the men and only 20.7 per cent. of the women succumbed to the disease. The mortality among Murchison's 3506 patients, already discussed from other points of view, among whom there were almost as many men as women, was 21.18 per cent. for the men and 19.61 per cent. for the women.

Whether certain races possess a diminished power of resistance to the disease is a difficult question to determine, and we have no means of judging whether any particular race is more susceptible to infection than another. The fact that where the colored and white races are attacked side by side a greater number of the former succumb to the disease is probably due to the circumstance that they are, generally speaking, placed amid much more unfavorable external and social surroundings.

Of no less importance than the above-mentioned factors which determine the general mortality are those features of a case which need to be considered in judging of the probable course and outcome.

The question whether the **mode of onset,** and the **severity of the symptoms** during the stage of invasion afford any clue to the future course of the disease has received different answers from different authorities. High fever and grave general manifestations during this time certainly possess no prognostic significance. They are just as likely to usher in a short or even an abortive case of the disease as a severe one. On the other hand, it may be said that a mild stage of invasion almost always indicates that the subsequent course of the disease will also be mild. Very rarely, chiefly in the senile forms, it may happen that a comparatively quiet and apparently mild initial stage leads to a protracted illness with a fatal result.

During the subsequent course of the disease certain **general symptoms** and the action of **individual organs** and systems exert a decisive influence on the prognosis.

Among these features, the most conspicuous manifestation of the fever, the elevation in temperature, is undoubtedly of great prognostic importance, although its significance has in many respects been exaggerated.

Very high temperature during the initial stage or during the first week does not absolutely justify the expectation of a severe illness or even a fatal termination. On the other hand, the prospect is not bright if a continued or continued remittent fever, with a very high average

[1] Quoted by Murchison.

temperature, persists after the first week. Conversely, a favorable prognosis based on the mere fall in the temperature after the first week is not justifiable. It has been shown by several examples (Figs. 69 and 71) that fatal protracted cases may show a persistently low temperature during the last few days, or even a week, before death, during which time other ominous symptoms continue without abatement.

It is not possible to state with certainty whether a fall of temperature on the seventh day, which, according to Wunderlich, is typical of a favorable case, may be considered a favorable prognostic sign. Personally, I have rarely met with this phenomenon. On the other hand, marked remissions and intermissions occurring early are undoubtedly of favorable omen.

The action of the circulatory organs is of far greater importance in the prognosis, and affords a reliable means of judging the course of the disease. As has been stated elsewhere, the pulse in typhus fever, not only in women, children, and old persons, but also in vigorous men, is often proportionately very rapid, both early in the course of the disease and during the entire febrile period, the phenomenon being in accord with the violence of the mode of onset and presenting a certain contrast to what is observed in typhoid fever. The pulse-rate itself, although it indicates the early and distinct involvement of the heart, is of even less importance than other qualities of the pulse, especially volume, tension, and regularity. The earlier the pulse becomes soft and easily compressible, or unequal and irregular, the more unfavorable the prognosis. Early irregularity of the pulse I believe to be an especially useful sign. It must, however, always be remembered that recovery has been known to occur even in cases in which the pulse was barely perceptible for days, and so rapid that it could hardly be counted.

Next in importance to the behavior of the circulatory system from a prognostic point of view is that of the nervous system. It is evident that severe disturbances of the central nervous system indicate that the effect of the toxin has been particularly marked or that the individual's power of resistance is much reduced; and thus the earlier the appearance of nervous symptoms, the more unfavorable the prognosis.

One should be particularly guarded in one's prognosis when stupor and coma manifest themselves early. Such cases are usually graver than cases in which the mind is less markedly affected, even than those in which there is violent delirium in the evening and during the night.

Complete insomnia manifesting itself during the first days of the disease was justly considered a very suspicious symptom by the older

authors. It is not infrequently a precursor to the hopeless manifestation of the disease that has been aptly designated coma-vigil.

Many physicians regard the occurrence of subsultus tendinum, carphology, and choreic twitchings and tremors as among the most dangerous signs, and it is certainly true that they occur only in very severe cases. These symptoms do not, however, affect the prognosis to the same extent as they do in typhoid fever. Owing to the self-limited and relatively short duration of typhus fever, the patient is able to withstand, until the occurrence of the crisis, morbid conditions that, if they were to continue longer, would certainly kill him.

General convulsions are of unfavorable omen. The great majority of adults attacked by convulsions die; whereas children, who, as is well known, are attacked by convulsions in a large number of much less grave conditions, are more likely to recover.

Although we are still in the dark in regard to the causes of many changes in the pupil in typhus fever, we know from clinical experience that a few of them are of undoubted value in prognosis. In severe cases during the height of the disease and, what is even worse, during the first week, a very sluggish reaction to light is often observed. If this is accompanied by a high degree of myosis producing a "pin-point" pupil, the combination is of the worst significance. This phenomenon, designated by Graves and the older English authors as "pin-hole pupil," I have observed most often in cases that ended in coma-vigil.

The condition of the respiratory organs deserves some attention in determining the prognosis. Reference has already been made to the severe consequences that may be expected to follow any marked involvement of the larynx for either the future health or the life of the patient.

The significance of catarrhal and pulmonary affections varies widely and depends chiefly on the age of the patient. Whereas children and young healthy adults under twenty-five years of age usually bear an extensive attack of bronchitis or pneumonia fairly well, these complications seriously threaten the life of older persons.

It is not too much to say that after the age of forty most of the deaths are directly or indirectly attributable to extensive bronchitis with lobular pneumonia, to hypostases, or to the frequent complication of lobar pneumonia.

The condition of the digestive organs is of subordinate importance, both from a clinical and prognostic point of view. Diarrhea is rare, but I have met with it both in mild and in severe cases. Complications with dysenteric phenomena, which have rarely been observed

during the most recent epidemics, were justly regarded as grave accidents by the older authors (Barallier, Peacock, and others).

My experience leads me to regard severe meteorism, which is fortunately a rare occurrence and is undoubtedly the result of a severe intoxication of the nerves supplying the muscular walls of the intestines, as of the worst prognostic significance.

The condition of the urine, both physical and chemical, affords the physician many valuable hints. A marked diminution in the amount of urine, or complete anuria lasting many days, indicates a degree of cardiac weakness that eventually proves fatal to many patients—to the older ones almost without exception. A careful determination of the amount of albumin in the urine is not without its importance for the prognosis. The early appearance of considerable amounts of albumin is observed only in severe cases. If, in addition, there is hematuria, with the microscopic findings characteristic of nephritis, one has to deal with a very grave complication. Among all cases in persons between thirty and forty years of age with nephritis the majority die; among patients of more advanced age recovery is distinctly exceptional. It seems to me rather significant in this connection that in all my fatal cases, excepting a few in which death was due to special accidents, the urine persistently showed a large amount of albumin.

Much prognostic importance has been attributed by many authors to the condition of the skin, by the older writers partly because they were still under the influence of the humoral theories of disease. Personally, I believe that the importance of the cutaneous manifestations has been greatly exaggerated. I cannot bring myself to agree with those who believe that the abundance of the roseolous rash is proportional to the severity of the case. It cannot be denied that a pale, scanty, rapidly disappearing rash is found more frequently in mild cases; but in any epidemic examples are found of very severe and fatal cases in which the typical roseolous rash was slow to appear and developed imperfectly or even remained altogether absent. When it is remembered, moreover, that many of the abortive cases with severe onset often present from the beginning a well-marked and extensive rash, I think it will be admitted that the eruption in itself is of little value in determining the prognosis.

The hemorrhagic phenomena, on the other hand, are of much more serious import. Early and extensive hemorrhagic transformation of the rose-spots, and particularly the occurrence of petechiæ and extensive hemorrhages under the skin and in the subcutaneous cellular tissue, as has already been stated, is always a grave sign. Cases that present in

addition gangrene of the skin, tip of the nose, ears, fingers, and toes are almost certain to end fatally.

In connection with the typhus fever rash and its secondary alterations, mention must be made of the diffuse cyanosis of the face and hands that, inasmuch as it indicates cardiac weakness, is a particularly bad sign. I have rarely seen a patient with this symptom recover. A few who at first promised to get well eventually died of some grave complication.

Among the many systemic and organic diseases so far referred to that may shorten the life of the patient, there are some that may be regarded as localizations of the disease, while others are complications in the strict sense of the word. It is, of course, impossible to draw a sharp line of demarcation between the two groups. It is not too much to say, however, that the true complications exert a special influence on the prognosis, inasmuch as they claim many victims after the primary disease has been successfully overcome. In this connection let me remind the reader of the grave sequels in the region of the pharynx and larynx, abscess of the lung, purulent and necrotic pleurisy, nephritis, phlegmon of the skin, and malignant forms of decubitus. Guttstadt's repeatedly quoted statistics from the Prussian hospitals show that in one-sixth of 796 fatal cases death occurred after the fifteenth day of the disease, and in half of these death occurred even after the thirtieth day.

In the foregoing pages the prospect of recovery from typhus fever has been shown to be in general quite gloomy, and the many dangers threatening the life of the patient in all the stages of the disease have been enumerated; in conclusion, we may add a somewhat more cheering observation.

Typhus fever, like pneumonia and a few other acute infections, belongs to the diseases characterized by a relatively short duration, the morbid process ending by crisis, the extreme date of which can almost always be determined beforehand. In the very worst and apparently desperate cases one may still continue to hope for the crisis and ultimate recovery, and the latter can often be directly attributed to careful nursing and skilful handling of the patient during collapse. The regular self-limited course of the disease partly offsets its severity and its danger.

DIAGNOSIS.

General Considerations.—Whenever it is possible to observe a well-marked, typical case of typhus fever throughout or during the greater part of the course, the diagnosis presents very few difficulties. Even at the beginning of the disease, or after a few days' observation during the later stages, without any knowledge of the previous history, it is often quite easy to recognize the disease if an epidemic exists, and if it is found that the patient has been in close relations with patients undoubtedly suffering from typhus fever, or if he has been in their houses or used the same utensils.

If, however, we have to deal with an isolated case, which is perhaps the first that has occurred in the district, or if the disease presents unusual phenomena and the course is irregular, the diagnosis may be more difficult.

In the former case one or two examinations will rarely enable the physician to arrive at a definite opinion, and if the case has been under observation some time, he will realize the fact that typhus fever does not present any pathognomonic train of symptoms, but that the mode of onset and subsidence of the various symptoms, as well as their coexistence and duration, have important parts in the production of the characteristic clinical picture.

Even during an epidemic unusual manifestations of the disease may cause great diagnostic difficulty, or even make it quite impossible to recognize the disease.

Enough has been said about the marked infectiousness of the disease and the universal predisposition found at all ages and under the greatest variety of external circumstances to show the importance of making a clinical diagnosis as soon as possible, not only for the patient himself, but to a much greater degree for those surrounding him and for the entire population of the town or district.

Even the morbid anatomy, which in many infectious diseases affords the means of deciding a doubtful case, is not in itself sufficient to clear up the diagnosis in a doubtful case. It has been shown that no distinct alterations peculiar to the disease are found in the cadaver, and the autopsy in itself rarely reveals more information than that death has occurred as the result of some acute infectious disease.

The attempt to demonstrate a pathogenic micro-organism which should enable one to diagnose the disease has so far failed on account of insurmountable difficulties. From what has been said about the present state of the question it will be seen that we are still without any knowledge of the most essential data. It is probable that for some time we shall have to depend on clinical observation alone, and the question naturally presents itself whether there are any reliable data on which to base a diagnosis during the initial stage of typhus fever. The objective symptoms alone, without any knowledge of the existence of an epidemic or other possibilities of infection, enable one at best to make only a provisional diagnosis. In most cases it is impossible to say more than that some acute infectious disease is impending.

The most important diseases in the differential diagnosis are the acute exanthemata, especially small-pox and scarlet fever, relapsing fever, cerebrospinal meningitis, and cryptogenic septicopyemia—much more rarely typhoid fever.

Differential Diagnosis in Initial Stage.—The initial stage of typhus fever presents many points of resemblance to that of **small-pox:** the same sudden onset with chills, a rapidly rising pyrexia without or with relatively slight remissions, early, profound prostration, severe pain in the head and limbs, and splenic enlargement, which usually can be demonstrated at the beginning of the first week of the disease.

The fact that pain in the back is a much more frequent and violent symptom in the initial stage of variola than in that of typhus fever is of slight diagnostic significance, for the symptom in itself is rather vague and is not rarely absent in the milder forms of small-pox. On the other hand, the early appearance of an initial scarlatinal rash[1] on the thigh and upper arm is of some importance and strongly points to small-pox, as it is particularly likely to occur in the severe forms of that disease and does not occur either in typhus fever or in any other of the acute infectious diseases. On the other hand, an initial measly rash is of secondary importance. Very similar and rapidly disappearing rashes occur, as we have seen, shortly before or with the first appearance of the specific typhus fever rose-spots; but the diagnosis is soon cleared up by the appearance of the latter or by the eruption of typical small-pox lesions, the nature and distribution of which are characteristic even during the initial stage.

Finally, it may be well to point out how slightly the face is involved

[1] Compare Curschmann, "Die Pocken," *von Ziemssen's Handb.*, Bd. i., second edition.

in comparison with other parts of the body in typhus fever, in contradistinction to small-pox, in which the characteristic rash appears early and is very abundant on the face.

The temperature in both diseases at the end of the initial stage and at the beginning of the eruption is of some importance. While in typhus the fever is high during this time and not rarely continues to rise, there is always a marked fall in temperature in variola down to and even below the normal in ordinary cases.

The diagnosis may be well-nigh impossible when there is a question between the fulminating hemorrhagic form of typhus fever and the analogous form of small-pox—so-called *purpura variolosa*. Both represent a hemorrhagic initial stage of the disease and end fatally before the typical symptoms, especially the rash, become fully developed. Even after an autopsy has been held it may not be possible to arrive at a definite conclusion, and the diagnosis may have to be decided by the prevalence of one or the other of the two diseases in the district and the possibility of the patient having become infected. Similar difficulties are encountered in the differential diagnosis from severe hemorrhagic forms of other acute infectious diseases. I need refer only to the corresponding forms of scarlet fever and even of typhoid fever.

The differential diagnosis from **relapsing fever** during the first, or even the second, attack, if the first has not been sufficiently well observed, is extremely difficult, especially if one remembers that the disease often coexists with typhus fever, as was the case in Berlin in 1879. In many cases there is nothing characteristic about the mode of onset, rise, and ultimate height of the fever. The appearance and general condition of the patient are of much more importance in the diagnosis of relapsing fever. As a rule, the general condition is remarkably good in comparison to the height of the fever, there is little involvement of the sensorium, and the only symptom complained of is a painful tugging sensation in the calf of the leg. Although these points are more or less in favor of relapsing fever, nevertheless it cannot be said that more severe initial symptoms, such as violent headache and pain in the limbs, with profound prostration and even petechiæ (I need only remind the reader of the well-known "flea-bite rash"), absolutely exclude the existence of relapsing fever.

Many relapsing fever patients present, at the very beginning of the disease, a peculiar color of the skin, a point that we frequently utilized with remarkable success during the epidemic in Berlin, and that decided the admittance and assignment of the patients to the various wards. It is a peculiar, dull, yellowish-gray discoloration, which may best be com-

pared to the color of anemic individuals who have been for some time exposed to the sun.

As regards the spleen, I cannot agree with authors who affirm that it presents any characteristic enlargement during the initial stage of either disease.

The diagnosis of relapsing fever, however, can always be established by the finding of spirilla in the blood, and these organisms are usually demonstrable shortly before or after the first and every succeeding attack.

During their subsequent course the two diseases present such marked differences that the diagnosis cannot, except under very special circumstances, remain in doubt for any length of time.

Of course, the diagnosis may present peculiar difficulties when a convalescent from relapsing fever is immediately attacked by typhus fever. Reference has been made to this comparatively frequent possibility (see Fig. 57). It need hardly be emphasized that the absence of spirilla during the beginning of the fever, and the appearance of rose-spots a few days later, suffice to remove any doubts that may exist.

Relapsing fever leads us naturally to the discussion of **malarial fever.** It will readily be seen that first attacks of this disease in countries where it, as well as typhus, is endemic may easily lead to error. Difficulties may especially be encountered in severe forms of malaria with early involvement of the sensorium and great prostration, such as occur in the tropics and also in Holland, Hungary, and Italy. As in relapsing fever, the examination of the blood and the finding of the plasmodium will at once clear up the diagnosis without the necessity of waiting for the characteristic fall in temperature.

It may be exceedingly difficult, especially when an epidemic of typhus fever exists, to distinguish isolated cases of **cryptogenic septicopyemia** in its early stages from the initial or eruptive stage of typhus fever. An initial chill and a rapid rise of the temperature to a considerable height, early marked involvement of the whole system, especially affecting the nerves, are common to both diseases, and the difficulty may be further increased, particularly at the beginning, by the mode of appearance and distribution of the cutaneous rash.

I recently saw an interesting case of this kind. A young man who had recently come from Silesia was seized with violent chills, headache, retching and vomiting, and was admitted to my clinic with a high fever and marked splenic enlargement. There was great disturbance of consciousness. The fever-curve at first presented the character of a high continuous remittent fever. Between the third and fourth days, after a slight transitory morbilliform rash on the arms and thighs had appeared, an ill-defined, livid, small

macular rash made its appearance, which soon became petechial in character and presented a suspicious distribution, being more abundant on the hands and feet, especially the backs of the feet, and much less marked on the trunk. As a precautionary measure the patient was isolated for a few days.

The rash continued to appear in successive crops, the patient had several chills, and a few hemorrhagic spots appeared on the soles of the feet, the palmar surfaces of the fingers, the plantar surfaces of the toes, and under the nails. On the sixth day of the disease the sudden appearance of a loud, blowing endocarditic murmur confirmed the diagnosis of septicopyemia with mitral verrucose endocarditis, which diagnosis had already been made on the strength of the changes in the eruption and the appearance of chills. The diagnosis was confirmed at the autopsy, which, however, failed to reveal the original cause of the condition.

The clinical picture in a typical case of **cerebrospinal meningitis** would seem to differ sufficiently from that of typhus fever to preclude all danger of error, but it is true, nevertheless, that irregular cases, in the initial stages of the two diseases, often present considerable difficulties. It cannot be denied that there are cases of cerebrospinal meningitis that begin with a chill and, after a rapid rise of temperature, soon lead to disturbances of consciousness or even to coma. If we remember also the violent headache from which the patients suffer, the pain in the back, which does not by any means always manifest itself in the form of a characteristic rigidity of the neck, and the occasional appearance of a roseolous rash during the very first days—even before the rigidity of the neck—we have sufficient explanation for occasional errors in diagnosis.

Diagnosis in the Stage of Eruption.—Even after the end of the initial stage and after the typhus fever rash has made its appearance and begun to spread, the differential diagnosis may present some difficulties. There is a lamentable want of unanimity in the opinions of many physicians and even in the better text-books in regard to the form, distribution, and development of the eruption. It should be distinctly remembered that the specific rose-spots are always, at least in the beginning, purely hyperemic, often very pale and indistinct, and that only a portion of them later become more or less markedly hemorrhagic. There is a wide-spread erroneous belief, and one that has been perpetuated in the vicious name of "*petechial typhus*," that the eruption of typhus fever from the very outset takes the form of small hemorrhages. On the contrary, it may be stated definitely that any febrile case in which the cutaneous changes at once appear in the form of larger or smaller hemorrhages, without any prodromal stage, is not typhus fever.

Diagnostic Significance of the Eruption.—Another point

of general importance may be mentioned. It is the great variability of the eruption as regards its abundance and distribution. From the rare cases with abundant eruption covering the trunk and extremities, we have every possible gradation, down to those cases in which, from the very beginning of the disease and throughout its entire duration, it is practically impossible to demonstrate any characteristic changes in the skin. Even cases of so-called "*febris exanthematica sine exanthemate*" although rare, cannot be entirely excluded. It is owing to this want of uniformity in the eruption, both as regards its general appearance during different epidemics and also in individual patients during the same epidemic, that the diagnosis from other infectious diseases characterized by high fever without, or at best with very slight, changes in the skin, may be exceedingly difficult.

Difficulties of this kind present themselves especially when it is necessary to decide between typhus and typhoid fever, the disease which, in all its stages and in all features, stands in closest diagnostic relationship to it and which undoubtedly presents the greatest difficulties in differential diagnosis.

Typhus and Typhoid Roseolæ.—In regard to the roseolous eruption, which is so often considered diagnostic, it may be equally abundant or equally scanty in both diseases. It has already been pointed out that cases of typhus fever, however severe from the very beginning, may present only a few roseolæ scattered exactly as in typhoid fever, and, conversely, typhoid fever may be combined with a rash that even in typhus fever would have to be regarded as abundant. Since, then, the number of the rose-spots cannot be depended upon, it is all the more important to make a careful study of their mode of development, distribution, and individual characteristics. In regard to the development, it is to be noted that the rash of typhus fever appears very much earlier than that of typhoid fever—between the second and fifth days of the disease—that the lesions continue to appear in unbroken succession instead of in successive crops, and reach their ultimate number and development within a few days.

The distribution of the rose-spots over the surface of the body is next in importance. Whereas in typhoid fever the trunk is most thickly covered and the extremities escape altogether, or the spots become less and less numerous the greater the distance of the parts from the trunk, the eruption in typhus fever is fairly uniform and covers both the trunk and the extremities.

Rose-spots on the forearms and legs and on the hands and feet are extremely rare in typhoid fever, whereas involvement of the backs of

the hands and feet is extremely common, not to say typical, in typhus fever, so that I always subject these places to a careful examination in any suspicious case.

Although the appearance of the face in the two diseases is to a certain extent similar in so far as it never becomes the seat of rose-spots in typhoid, and very rarely in typhus fever, yet there is a marked contrast between the intensely swollen, reddened facies, with deeply injected or even hemorrhagic conjunctivæ and wild look of a typhus fever patient, and the pallid, stuporous, and prostrated appearance in typhoid fever.

The individual lesions present very considerable and distinct differences in the two diseases. Whereas the rose-spots of typhoid fever are from the beginning elevated, papular, with sharp, circular outlines, and retain their purely hyperemic character throughout, the eruption of typhus fever at first appears in the form of pale, indistinct, hyperemic patches, with irregular, ill-defined borders, which gradually become darker and eventually somewhat hemorrhagic (compare Plates 1 and 2). Hence the non-papular character of the eruption during and after the height of its development is an important diagnostic feature. The spots are pale, and only during the first few hours are they slightly elevated—never so distinctly papular as in typhoid fever.

OTHER DIFFERENTIAL SIGNS BETWEEN TYPHUS AND TYPHOID.

Second only in importance to the condition of the skin is the fever in the differential diagnosis between the two diseases. In contradistinction to the slow, step-like ascent of the curve in typhoid fever, we have seen that in typhus fever, after an initial chill, the temperature rapidly—within from twenty-four to forty-eight hours—and with much smaller morning remissions, rises to a height rarely reached in the former disease. Temperatures of 40.5° C. or even 41° are, as we have seen, quite common at this stage, and may persist and even continue to increase with relatively slight morning remissions until the end of the first week. The character of the temperature-curve during the first week positively distinguishes typhus from typhoid fever. As even the most severe cases of typhus fever rarely last more than from fourteen to seventeen, or at most twenty, days before defervescence begins, and the fever falls by crisis or at least by a succession of rapid declines, we are not without important differential signs, even during the latter period of the disease.

In accordance with the rapid rise and great intensity of the fever during the first days of the disease the disturbances of the patient's general condition are much more severe and manifest themselves much earlier than in typhoid fever.

Whereas a typhoid fever patient not infrequently remains at work or at least does not go to bed during the first week of the disease, the prostration in typhus is so great from the very beginning that the patients are forced to take to their beds on the first or the second day. Delirium, stupor, and coma declare themselves during the first week in typhus fever, but their appearance is delayed much longer in typhoid, or, if they do exceptionally occur early, they are due to some cerebral complication.

In many respects the pulse in typhus differs considerably from that usually observed in typhoid fever. The relatively low rate characteristic of the latter disease in youthful individuals, especially of the male sex, is not observed in typhus fever. In both sexes and in all ages the pulse is comparatively rapid from the very beginning—110 and more in the evening is not unusual even during the first week in vigorous men. The characteristic dicrotism seen in typhoid is only exceptionally observed in typhus fever.

Enlargement of the spleen is a more regular and lasting phenomenon in typhoid than in typhus fever. The time of its appearance also differs in the two diseases. In typhus fever, if it is present at all, it appears early and disappears at a time when it would still be present in typhoid fever.

The abdominal symptoms are of very little importance as diagnostic signs between the two diseases. Thus a moderate degree of meteorism quite commonly develops in severe cases of typhus, while, on the other hand, it may be absent during the entire duration of a typhoid fever attack and usually is so during the early stages. Diarrhea[1] is not by any means so constant in typhoid fever as is usually supposed, while in typhus thin stools of a pale yellow color are not at all uncommon.

Some of the newer methods of examination will, no doubt, prove of the greatest value in future epidemics and will help to decide the diagnosis in many a doubtful case.

The demonstration of typhoid bacilli in the blood, urine, rose-spots, and feces, and the behavior of cultures of this bacillus when added to the blood-serum of the individual are the most important of these methods.

The Gruber-Widal agglutination test will enable us in many cases to differentiate the two diseases, although, it is true, only at a somewhat later stage.

Whether the absence of leukocytosis or hypoleukocytosis observed in typhoid fever will distinguish this from typhus, as it does from some

[1] Compare the chapter on this subject in the author's work on typhoid fever.

of the other acute infectious diseases, such as pneumonia and septic conditions, which, as we all know, regularly show a marked leukocytosis, has not yet been definitely decided. Combemale speaks of a moderate increase in the number of white blood-cells in the blood of typhus fever patients. Four cases recently treated in the Johns Hopkins Hospital showed a moderate degree of leukocytosis.

The diazo-reaction is probably not of any diagnostic value. Several authors (Eichhorst, Vierordt) have frequently found it to be positive in typhus fever.

While the differential diagnosis from small-pox, as we have seen, presents great difficulties, especially during the initial stage, other acute exanthemata, particularly measles, may, during the period of eruption, prove equally confusing. The eruption of **measles,** especially during the first few hours after its appearance, may closely resemble that of typhus fever, and, conversely, the rash of typhus fever before the beginning of hemorrhagic transformation, when it is abundant and confluent in places, and accompanied by the macular rash that has been described, may easily be confounded with the eruption of measles.

As a rule, the diagnosis can be made by a careful examination of the remainder of the skin. It is to be remembered that the face is first attacked in measles, while in typhus fever it escapes entirely, or, in rare cases, is the seat of a few isolated rose-spots which then are characteristic. In any case of typhus fever, even when the rash is abundant, areas will be found on the body where it is more sparsely distributed and where the spots are distinct enough to make them easily recognizable.

The conversion of at least a part of the rose-spots into petechiæ is of some diagnostic value for typhus fever. Hemorrhagic measles is rare and need hardly be taken into consideration in the differential diagnosis.

The condition of the mucous membranes (conjunctivæ, nasopharynx, bronchi) presents nothing distinctive. Catarrh of these structures occurs in both diseases, and the intensity and distribution are so variable that it is impossible to draw any definite conclusion.

If the patients are seen during the beginning of the fever before the eruption appears, or if reliable data in regard to this period can be obtained, the decision becomes much easier. The rapid rise and unusual height of the temperature, and its persistence or even subsequent rise after the appearance of the eruption and during the entire first week of the disease, are never observed in measles.

Other diseases that are occasionally mentioned in this connection are

of secondary importance in the differential diagnosis. In very rare cases a central **pneumonia** may become a source of error. Even more rarely, and only under special conditions, an error might occur in **scarlatina, certain infectious exanthemata,** and in severe cases of **purpura.**

Anthrax and possibly **glanders** might for a time give rise to doubt, the former only in the extremely rare cases of cerebral or intestinal anthrax without edema or furunculosis; the latter, when the characteristic manifestations in the mucous membrane of the nose, trachea, and bronchi are less marked and the changes in the skin are imperfectly developed. In the case of anthrax the question would be decided at once by the bacteriologic examination, which in glanders is often more difficult.

PROPHYLAXIS.

ALTHOUGH we have no exact knowledge of the nature and mode of development of the micro-organism that is the cause of typhus fever, its effects, so far as they relate to the origin and spread of the disease, are sufficiently well known to enable us to adopt certain definite precautions which are very efficient, if properly carried out, against the transmission of the disease from patient to patient and its general spread.

The most important points in the prevention of the disease have been embodied in a few conclusions at the end of the chapter on Etiology.

REGULATION OF GENERAL AND LOCAL HYGIENIC CONDITIONS.

The precautionary measures based on these considerations may be divided into those that, by improving the general and local hygienic conditions, deprive the disease of a proper medium for its development, and those that are calculated to prevent the spread of the disease from one patient or articles used by him to other persons, or the spread from one town to a neighboring town or to remote regions and countries.

Many of the most important prophylactic principles were first laid down by the older authors, among whom no one has expressed them more clearly and more unequivocally than Hildenbrand. But even he, like Murchison and Griessinger, was never quite able to rid himself of the idea that the disease might arise spontaneously, a theory that to-day has been permanently refuted.

However, to say, as some authors have done, that anything that does not directly affect the development and spread of the specific contagium is of no consequence, would be to overlook the most important general principles in the prevention of the disease. We know that hunger and misery, insufficient food, overcrowding in badly ventilated rooms, filth, and the accumulation of decomposing substances cannot, it is true, produce the contagium of typhus fever, but we are more fully than ever convinced that they afford a most favorable soil for its development. Hence the name, hunger typhus; hence the distinctly social nature of this disease, which attacks the individual whenever his health has been

undermined by hunger and vice and his body has been prepared for the reception and development of the germ.

The shortest way for the state and society in general to deprive the disease of its soil is to improve the well-being and sanitary conditions of the less favored classes, especially in regions and during times when there is danger of the disease-poison being imported.

In large cities, especially during times of epidemic, the tenements of the poorer population, the poorer inns and cheap lodging-houses (known in Berlin as "Pennen"), all institutions for those who have no homes, workhouses, poorhouses, and prisons should be carefully inspected by the authorities. All ships, especially emigrant ships, should also be subjected to a careful inspection.

When war is being waged in a country in which the disease is presumably epidemic, the greatest attention should be given to a proper housing of the troops, the arrangement of the camp, and the feeding and general care of the soldiers' bodies.

How much can be accomplished in this direction was shown during the Crimean war, in 1856, especially during the siege of Sebastopol, by the different conditions of the French and English armies, which fought shoulder to shoulder. Whereas the disease carried off but few victims among the English, whose hygiene was well looked after and who were rationally fed, the neglect of the simplest hygienic measures avenged itself among the French by a decimation of their army by the disease, which claimed more victims than musket and saber.

During the approach of an epidemic the **passenger** as well as **freight traffic** from neighboring countries, including all objects to which the poison could adhere, requires the most careful attention. Clothing, washing, and anything that is suspicious in this respect should either be excluded altogether or be subjected to a systematic disinfection before it is allowed to pass the frontier.

Passenger traffic cannot nowadays be interrupted, as it could formerly in the days of land quarantine; it can, however, be kept under supervision by the sanitary police. Attention should be directed especially to tramps and vagabonds and their lodgings, to taverns, asylums, prisons, railroad stations, etc. Every suspicious case of disease should, if possible, be at once isolated either on the spot or in the nearest suitable hospital. Even the dwellings of healthy immigrants from infected regions, the streets and districts in large cities where they are in the habit of lodging and carrying on their business, ought to be under constant sanitary supervision, so that any one attacked by the disease may at once be sent to the nearest hospital, and, if possible, the other

members of the household, even if healthy, be kept under careful observation.

It is a good plan, when an epidemic is approaching, to make a regular evening examination of the inmates of houses of refuge and lodging-houses. In 1877, while I was visiting the asylums and suspicious lodging-houses ("Pennen") in Berlin, I found, in one night, 5 typhus fever patients scattered among the healthy inmates. I immediately referred them to the lazaretto in Moabit.

I need only mention in passing the desirability of a well-organized Bureau of Statistics in times of impending epidemic, for the purpose of keeping the authorities informed of the state of the disease and the general hygienic conditions in neighboring districts.

Isolation.—If, in spite of all precautionary measures, the disease obtains a foothold in a given region, everything may depend on early recognition of the first cases and energetic measures directed to the isolation of the patients. An epidemic may be confined within narrow limits, or may even be nipped in the bud if the authorities can succeed in protecting the immediate vicinity of the infected district and the remaining population from the disease, and so preventing new cases from developing, or at least in isolating, so soon as possible, those that have developed.

In the prophylactic treatment of typhus fever patients one should carefully bear in mind what we have learned by experience, namely, that the exciting cause of typhus fever emanates exclusively from the patient himself, from his immediate surroundings, and from objects that he has used, and, given the same predisposition, the virulence of the poison is inversely proportional to the amount of space and ventilation.

These facts must be remembered in the **transportation of patients.** Whenever the disease is prevalent, public conveyances should never be used for the transportation of well-pronounced or suspicious cases, or even of individuals suffering from an indefinite fever.

In large cities there is, as a rule, no lack of proper facilities for transportation in our day. In smaller places an efficient service can easily be improvised.

If the regular patrols designed for this purpose are inadequate in large cities, none but persons well acquainted with the special dangers of the disease should be intrusted with the transportation of patients, and this should not be left to police officials, prison wardens, or more ignorant persons. The drivers of such vehicles should not be allowed to drive any other conveyance, and they, as well as the remainder of the force, and even the wagons, should be furnished by the hospitals,

and these men should also lodge in the hospital and be placed under sanitary supervision.

The method of housing and isolating the patients, the choice and arrangement of wards in the hospitals or of sick-rooms in private houses, as well as the situation and internal arrangements of hospitals, will be discussed in the section on Treatment, together with other general principles to be observed in the care of patients. In the same place will be given a few necessary precautions which should be observed by those in immediate attendance on the patients—physicians, hospital attendants, and officials connected with the institution.

Immediately after admittance to the hospital the patients should receive a bath and be carefully cleansed; their clothing and underwear should be properly disinfected and kept in large, well-ventilated rooms at some distance from the wards until the patient is discharged. The patients should be dressed in clothing provided by the hospital, and should be strictly prohibited from using any other garments. Any part of the clothes or other effects belonging to the patients that cannot be easily disinfected or that is worn out, torn, or of no value, should be destroyed by fire. It is less costly to pay the patients a small indemnity for such destruction of clothing than to run the risk of infecting an entire district by the disregard of this precaution.

Even in smaller towns, where no time has been given for preparation when the first cases are discovered, infected material can easily be burned in the open air in some vacant field. If this should not be feasible, the offending objects can be rendered harmless by burying them in the ground at a depth of from one and a half to two meters.

The most careful directions should be given in regard to the **washing of hospital clothing,** particularly when patients with other diseases are treated in the same institution.

Soiled outer garments, underwear, and bed-linen must be immediately removed from the wards, sprinkled with a 3 per cent. solution of carbolic acid, or, better, with a solution of lysol, and kept in earthenware or tin receptacles with perforated lids until such time as they can be taken away, which should be done with the greatest possible despatch. The method of keeping the soiled clothing in water-tight and air-tight bags, which answers very well in the case of typhoid fever, cholera, and dysentery, I do not care to recommend for typhus fever patients, for I have great faith in the disinfecting power of the atmospheric air, and believe that objects that have been kept from contact with the air are doubly dangerous.

In the interest of laundry employees it is advisable, and indeed it is absolutely necessary, if the clothing of other patients is washed in the same laundry, to disinfect the clothing of typhus fever patients by means of boiling or exposure to superheated steam before beginning the process of washing.

In order to prevent the clothing from becoming spotted by the boiling it

is well to use a weak solution of soapsuds with a little soda and petroleum (Gärtner). This precaution, however, will not prevent materials soiled with mud, blood, or pus from becoming spotted, but even hospital authorities will resign themselves to this inconvenience when the great prophylactic value of the precaution has been made clear to them. When typhus fever patients are treated in private houses the question of washing is exceedingly complicated and will depend largely on the facilities at hand.

If the inhabitants and the authorities can be persuaded to do their part, it will usually be possible to utilize public institutions for the disinfection of clothing, and perhaps even the laundries of hospitals, considering the small number of cases usually treated in private houses, can be used for this purpose.

A safe method of **disinfecting washing, bed-linen,** and **outer clothing** consists in the use of live steam in the well-known apparatus now in use everywhere. Furs and leather garments cannot be subjected to this process, as they are completely destroyed by it. They must be carefully treated with a 5 per cent. carbolic acid solution and exposed to the air for a number of days.

It may be interesting to note that during my experience in Moabit, which antedates the introduction of steam sterilization by Koch, we succeeded in completely disinfecting clothing and underwear by exposing them for from one to two hours to a temperature of 110° to 112° C. in a specially constructed apparatus. The clothing was not tied together in bundles, but hung free, or at least was arranged in loose piles and thus exposed to the heat much in the same way as the material is arranged in the present method of treatment with live steam.

The disinfection of beds, like that of the body linen, should be done by live steam. Blankets, pillows, and mattresses of any kind may be exposed without suffering any damage. Even iron bedsteads, which should always be of the folding variety in epidemic hospitals, may be exposed to hot steam. Wooden bedsteads should be taken apart and thoroughly cleansed with carbolic acid or lysol solutions and then exposed to the air for a number of days.

In fitting up a temporary hospital, and whenever sufficiently large disinfecting apparatus cannot be obtained, the beds should be provided with straw mattresses, the hardness of which may be overcome by spreading several blankets upon them. As the material with which these mattresses are filled is of little value, they may be destroyed by fire; blankets, coverings, and other materials may be disinfected by boiling; blankets can be disinfected by merely exposing them to the sun for a few days.

The care of **other articles used by patients** is less important in typhus fever than in many other acute infectious diseases. Plates,

glasses, spoons, and forks require only washing in hot water, as the contagium does not adhere to objects with a smooth, non-porous surface. Bed-pans, specimen glasses, and water-closets should, of course, be carefully cleansed and disinfected with lysol solution or chlorid of lime. They are doubtless, however, much less dangerous than in typhoid fever, since the bacillus of typhoid fever is found chiefly in the feces and urine.

The exact relation of the feces and urine, as well as that of the other excretions of the body, to the poison of typhus fever is imperfectly known. The stools I believe to be least dangerous, while the urine, sputum, and perspiration deserve more careful attention in the matter of disinfection. Accordingly I always add some disinfectant to the water used in washing patients after profuse perspiration, or even have them sponged with brandy.

Typhus cadavers do not appear to be specially contagious: not more so at least than other inanimate objects to which the poison adheres mechanically. It was my practice to wash the cadavers with a 5 per cent. carbolic acid solution and wrap them in cloths saturated with the same solution; this I believe to be all that is necessary. Although we held a great number of autopsies, and had but a small room in which to perform them, I never had a case of infection among the physicians or attendants.

The **disinfection of wards** or **private sick-rooms** after the patient has recovered or died must be carried out with scrupulous care. The peculiar character of the poison of typhus fever calls for certain deviations from the ordinary procedure adopted in such cases.

In the first place the rooms should not be kept closed for a time, as is the practice in other diseases; but, on the contrary, they should be kept open for a number of days and well ventilated by throwing open windows, doors, dampers, and other vent-holes. In the section on Etiology I took occasion to remark that ventilation is the most powerful agent we have with which to combat the poison of the disease.

Disinfection of Furnishings.—After ventilation has been completed the furniture, pictures, and other ornaments on the walls are removed, and the walls, as well as the ceiling, subjected to a careful disinfection. The disinfection of the ceiling is much more necessary in typhus fever than in many of the other acute infectious diseases. If the walls and ceiling are papered, they should be rubbed down with bread-crumbs that are afterward carefully collected and burned. If the walls are painted in oil colors, they should be brushed down with a solution of carbolic acid or lysol. If they are whitewashed, they should be

scraped off, disinfected with chlorid of lime, and treated to a fresh coat of whitewash.

The floor is scrubbed carefully with soft soap and carbolic acid, special attention being paid to the joints; it is afterward rubbed off and waxed or painted.

Unpainted furniture and furniture painted with oil should be washed with a 3 to 5 per cent. solution of carbolic acid. Varnished and polished pieces are best cleaned with bread. The same method is employed with varnished pictures, mirrors, oil paintings, and their frames.

If the furniture is upholstered, the covering should be removed, horsehair should be disinfected by boiling, and other inexpensive material burned. Simple sponging or sprinkling of the upholstered surface with carbolic acid, which may suffice after many other infectious diseases when there has been no direct pollution, is utterly inadequate to destroy the poison of typhus fever.

As it is exceedingly difficult to disinfect woolen materials and upholstered objects generally, it is advisable to remove all but the most necessary objects from the sick-room and adjoining rooms from the beginning.

In the disinfection of ships, railroad cars, and vehicles that have been used by typhus fever patients, the methods prescribed for dwellings and furniture will suffice with proper modifications.

Disinfection of hospital wards by formaldehyd, which has recently been recommended, has never been tried in typhus fever. From what we know of the nature of the poison it seems probable that this method would be efficient. It is much to be hoped that careful experiments will be made during the next epidemic, since, if they prove successful, the present rather complicated measures will be immensely simplified.

The disinfection of private houses cannot be carried out successfully by any one who is not an expert. Even intelligent and well-informed persons who have not been specially trained are practically always found to be unequal to the task. In all the larger cities we now have regular disinfecting officials, whose services can be obtained by application to the Board of Health or to the hospital authorities. In smaller places the hospital attendants and nurses should be instructed properly and drilled in the necessary methods.

Regulations Regarding the Discharge of Convalescents.—Before allowing convalescents to return to their families and to private life it should be remembered that they are capable of carrying the poison if the necessary precautions have been neglected, just as other healthy persons may do if they have come in contact with patients or have been in an infected ward.

For several days before they are discharged convalescents should

take warm baths with carbolized soap and water, careful attention being given to the proper cleansing and disinfection of the hair, beard, and other hairy portions of the body. The last bath should be taken, if possible, at a distance from the hospital in a place that has not been contaminated by patients or their belongings. After they have taken this final bath, the convalescents are to dress in new clothing, or in their old clothing if this has been carefully disinfected and preserved from contact with the poison of the disease.

TREATMENT.

SPECIFIC TREATMENT.

Up to the present time there have been no noteworthy attempts at specific treatment of typhus fever in the modern sense.

Even the epidemic appearance of the disease in France in 1893 does not appear to have led to any careful attempts in this direction, although a number of French physicians were at the time well trained and competent to make the necessary experiments.

The fact that it is so dangerous a disease that the mortality is three times as great as it is from typhoid fever should induce us to devise new and more efficient methods of treatment than those at present in use.

Even the manifest difficulties encountered in the study of the nature and life-history of the cause of typhus fever and the absence of any definite knowledge in regard to it should not deter us in future epidemics from making experiments in immunization and serotherapy. We ought to feel encouraged by the results of vaccination in preventing small-pox and by the famous achievements of Pasteur in the treatment and prevention of rabies. Whether experiments in connection with typhus fever will also be crowned by success and of what nature the results of these experiments will be cannot, of course, be predicted to-day. I have already, in the chapter on the treatment of typhoid fever, had occasion to point out the fallacy of reasoning by analogy, and I feel impelled to repeat the warning in this place.

As opinions in regard to the nature of typhus fever changed, numerous attempts were made to shorten or abort the disease by blood-letting, by emetics, and by a long series of specific drugs, such as quinin and others. All these methods have now been abandoned.

An interesting paragraph on this subject is found in Hildenbrand's famous monograph, which dates from the beginning of the present century, and I am tempted to quote a few especially pregnant sentences from this work.[1]

"After a dispassionate survey of all these hypothetic methods of treatment, it is noted at once how short-lived they were, how little, therefore, was their true value, and how inadequate they were in practice. We may in the future expect as many more such doctrines and systems of therapeutics as there will be hot-heads and visionaries in our art. But if, on the contrary, we follow the path of observation and successful experience in these cases—in other words, the path of empiricism guided by reason—our free and untrammeled judgment will lead us on to new and better views than can be hoped for from a brain that is ruled by hypotheses."

[1] *Loc. cit.*, p. 178.

The most successful empirical method of treatment at the present day directs attention, above all, to the proper care of the patient in the broadest sense, including appropriate diet in all stages of the disease, with a due regard to individual peculiarities, and to the treatment of the fever and its concomitant symptoms, and also special localizations and complications of the disease, with physical and medicinal agents.

GENERAL TREATMENT, NURSING, AND DIET.

Owing to the intensity of the initial phenomena, even in cases that later turn out to be mild, it is rarely necessary to order the patients to bed; they are, without exception, so prostrated from the very beginning that they cannot keep on their feet, and therefore go to bed of their own accord.

It goes without saying that **absolute rest in bed** during the entire course of the disease and for at least a week after the complete disappearance of fever should be an absolute rule, as it is in any other severe infectious disease.

Patients should not be allowed to sit up, even while the bed-clothing is being changed. They should never be allowed to get out of bed to void feces or urine, but should be compelled to use the bed-pan and urine bottle from the very beginning.

In the arrangement of the bed the former habits of the patients may be consulted to a certain extent. It should be moderately cool and easy to clean and air. If at all feasible, a second bed should be prepared, so as to allow the patient to change. If a prolonged and severe case is expected, it is well to provide a water-bed from the outset.

The **sick-room** should be as large and airy as possible. It should afford the greatest possible amount of rest to the patient and allow the strictest isolation.

The practice of darkening the room, formerly recommended, is as harmful as is excessive illumination. It is only necessary to place the patient with his face turned away from the window, which need not be covered with a shade.

The hospital attendants should, if possible, be individuals who have been rendered immune by an attack of the disease; although such persons are usually protected against a second attack, they should, nevertheless, be carefully isolated from healthy persons, for they are very likely to spread the disease by means of the poison that adheres to their clothing and other personal effects.

During a large epidemic and in places where the disease is not endemic it is difficult, if not impossible, to procure immunes for hospital attendants. The contagiousness of the disease and, in case of infection, the severity of

its course, may be somewhat combated by protecting the attendants from excessive exertion, by careful attention to their diet and personal cleanliness, and, above all, by insisting on the prophylactic value of careful ventilation of the wards. After the work of hospital attendants is finished, they should be subjected to a strict quarantine, lasting a little longer than the average period of incubation, before they are allowed to mingle with the general population.

Whenever strict isolation of the patient is impossible, his immediate admission to a hospital should be insisted upon. This point will be discussed in detail further on.

If the patient can be nursed at home, the first question to be decided is what arrangements are necessary for his own welfare and to guard against the spread of the disease. The sick-room, in the first place, should contain only what is indispensable for the care of the patient. Mirrors, wall-paper of glaring design, conspicuous pictures, and any other brightly colored or otherwise unpleasantly prominent objects should be covered or removed. This precaution is more necessary even than in typhoid fever. Any physician of experience knows how such objects feed the imagination of the delirious patient, and to what an extent they enter into his hallucinations, aggravate his delirium to the point of mania, and thus give rise to incalculable harm.

I remember a patient who smashed into fragments a mirror that hung opposite his bed, because he mistook his own image for an enemy, and another who jumped through the window because he was terrified by a painted head, in the side of a porcelain stove, which he thought was alive and seemed to him to bear a frightful expression.

All woolen objects, blankets, window curtains, rugs, upholstered furniture, and other objects to which the poison, as we know, clings with the greatest obstinacy, should be removed at once from the room. If circumstances permit, the carpets should be replaced by linoleum, which is easily cleansed and disinfected.

These precautions, often carried out with difficulty in private practice, are properly observed in all well-regulated hospitals, but there are many directions to be observed in regard to the placing of the patients.

Removal to Hospitals.—Whenever it is at all possible, typhus fever patients should not be admitted to general hospitals, but if this cannot be avoided, it must at least be remembered that mere isolation in special wards near those occupied by other patients does not suffice. The proper degree of isolation can be obtained only by placing the patients in a special ward at some distance from all the others—if possible, it should be at the top of the building and provided with a separate entrance.

It is always much better to have special epidemic hospitals or isolated

buildings connected with the general hospital, such as are in use in all large cities.

In the construction of buildings of this kind, designed for the reception of small-pox and typhus fever patients, the barracks-system is to be preferred. If no permanent pest-house is available, wards can be constructed on this system easily and rapidly; many of the best epidemic hospitals to-day—I need refer only to the lazaretto in Moabit—began their existence as makeshifts of this kind.

Ventilation.—The barracks-system affords the readiest means of carrying out perfect ventilation, so necessary for both the patients and their attendants.

The windows should be open by day and night; in winter there should be correspondingly increased heating facilities. During the milder seasons of the year I make a practice of keeping my patients in the open air, properly protected against sun and rain.

Open-air Treatment.—I cannot say too much in favor of the open-air treatment. Although the hope I entertained in the beginning of reducing the fever by this means was never realized, the procedure proved to have a very favorable effect on the nervous system, which is always so severely implicated in typhus fever. The patients became quiet, and the symptoms of the initial stage—the violent headache and insomnia—were more favorably influenced by the open-air treatment than by any other means. The intensity of the delirium was held in check, and the mental condition of stuporous and comatose patients often seemed to be very favorably influenced.

The open-air method is of value not only as a symptomatic, but also as a directly curative, treatment, since we known that the chief danger to the central nervous system lies in excessive excitation or excessive depression.

Aside from the benefit to the patient, thorough ventilation and the open-air treatment afford the most effectual means of guarding against the spread of the disease.

It is to the strict use of these measures that I attribute the fact that not a single physician was infected, and that the percentage of hospital attendants who contracted the disease was conspicuously low during the three years from 1876 to 1878, when all the cases of typhus fever occurring in Berlin were admitted to Moabit and treated by the open-air method. The great majority of the hospital infections that did occur might have been avoided if the individuals had not neglected my instructions. I had issued strict orders that the necessary baths were to be given exclusively in the large wards, instead of in the narrow and poorly ventilated bath-rooms. Most of the attendants who contracted the disease had, merely out of laziness, repeatedly neglected to obey this order.

I may remark that I am not alone in maintaining these views. Even the older authors, Hildenbrand in particular, advocated the method of treatment with cool, fresh air. I am pleased to note that several physicians after me have recommended the open-air treatment as the most efficacious antipyretic remedy. The excellent works of Kaczerowski, published in 1878 and 1879, and the statistics collected by Barrault during the Lille-Paris epidemic of 1893, are particularly worthy of mention. The latter goes so far as to affirm that he actually reduced the mortality by energetic open-air treatment.

Diet.—The diet in typhus fever should be based on the same principles as those that guide us in the treatment of the acute exanthemata and not on those that obtain in the treatment of typhoid fever and the other infectious diseases especially characterized by intestinal lesions.

The choice of food in typhus fever is limited only by the deleterious effects of the toxin on the various secretions and mechanisms of digestion.

During the initial stage, when appetite is absent in nearly all patients, when every form of nourishment is repulsive to them and they are tormented by a constant desire to vomit, and also during the entire febrile stage, the diet should consist exclusively of liquids.

Of all foods, milk is the one that most nearly fulfills the requirements in the matter of supplying albumin, carbohydrates, and fat, and it is to be regretted that a large number of patients, especially during the febrile period, are unable to take it, at least in unmodified form. The physician should not, however, allow himself to be too easily deterred from prescribing it. In some cases the milk may be rendered palatable by diluting it with Seltzer or lime-water; in other cases the addition of cognac or of common salt may be found to answer. A very good plan consists of mixing the milk with semifluid substances, such as sago, rice, farina, arrow-root, Kindermehl, and the like, because it affords the best means of preventing the formation, in the stomach, of coarse coagula that interfere so much with digestion. An equally efficient breaking-up of the casein takes place in buttermilk, which many patients find palatable. Again, the patient's objections are sometimes successfully overcome by giving the milk in the form of kephyr. The carbonic acid contained in this is, for obvious reasons, much less objectionable in typhus than it occasionally proves to be in typhoid fever.

In some cases I have prescribed cold or tepid whey, and have often obtained very favorable results from this when there was intense catarrh of the respiratory passages.

If the milk is well borne, it may with advantage be enriched by an admixture of cream.

Apart from milk, the most useful foods are the carbohydrates, given in a fluid form, especially as thick soups. As has been said in connection with the treatment of typhoid fever,[1] in order to render such a diet palatable for any length of time the substances used must frequently be varied. Oatmeal, rice, farina, sago, green wheat, tapioca, and aleuronat flour may be used to break the monotony of the liquid diet. Even during the height of the fever soups containing evaporated fruits or, better, soups prepared with Hartenstein's leguminose, may be permitted.

It is well to alternate the thick soups with clear broth containing eggs, or we may add Leube-Rosenthal's meat-solution, sweet-breads, calves-brains, chicken, or pigeon ; this may be done during any stage of typhus fever.

It should be distinctly understood that eggs are better borne, as a rule, by typhus patients than by patients suffering from typhoid fever. As many as three or four eggs may be taken in the twenty-four hours, either stirred in with the soup—the best method—or soft boiled, or beaten up with a small quantity of bouillon, sweet wine, or cognac (egg-nog).

It is customary at the present day to enrich the soups by the addition of all kinds of artificial albuminous foods and condiments, such as somatose, nutrose, eucasin, meat peptones, and various meat extracts, among which may be mentioned Liebig's extract and Valentine's meat juice, the latter containing very little albumin.

On the whole, I prefer beef-tea prepared in the house to the artificial meat-extracts, and believe that for patients whose sensibilities are so dulled by the disease that they are not disgusted by the appearance and unpleasant odor of *succus carnis recens expressus* (beef-juice), the latter preparation, which also contains extractives of meat albumin in a very digestible form, should be used freely.

The *succus carnis* can readily be prepared with Klein's meat press, either in the hospital or in a private house. Patients who are fully conscious sometimes take to it quite kindly if it is mixed with wine or bouillon and served in a green glass to disguise the bloody color.

Patients in good mental condition who are able to chew and swallow may be allowed solid food in addition to the liquid preparations during any stage of the disease, even during the height of the fever. They may be given rolls, Zwieback, cakes, or perhaps raw chopped meat, spring chicken, squab, and the like.

The general rule is to feed patients regularly every two to three hours, a little at a time, and to endeavor by all possible means to induce them to eat when they are stuporous. Patients should receive some food two or three times during the night—for example, milk, bouillon

[1] *Loc. cit.*, p. 426.

with egg, and the like. It is well to offer them some little refreshment between meals—wine or meat-jelly in teaspoonful doses, or, what is equally as good, Brandt's essence of beef.

In the same way the patients should receive drinks at regular intervals, even if they must be persuaded to take them. Ordinary water is best, but Seltzer, Giesshübler, or Biliner may be given. Artificial mineral waters should be given only after effervescence has subsided.

A little fruit-juice, either lemon or raspberry, may be added to the water, but if possible the juice should be sweetened with saccharine instead of sugar. If alcohol is indicated, the water may be mixed with cognac or wine. Cold tea, coffee, or bouillon may with advantage be given either in the place of, or alternating with, the beverages mentioned. All drinks should be iced, or at least cold, unless this is contraindicated by some especial gastric or intestinal condition. With proper care, the mouth and the gums of the patient should never become dry, and, of course, they should be kept scrupulously clean.

In regard to the administration of alcoholic liquors opinions have undergone a marked change in the last few years. The practice of administering alcohol regularly and in large quantity in febrile diseases has been almost universally abandoned.

With a nutritious and well-regulated diet alcohol may usually be dispensed with in typhus fever, at least as a part of the regular treatment.

It is best to withhold alcohol until its use is indicated, when it will be doubly efficacious, especially when used to stimulate a failing heart. In any condition of collapse the indication for alcohol is urgent, and its free use may be the means even of saving life.

It is scarcely necessary to mention that a heavy drinker or one who has been accustomed to the regular use of a moderate amount of spirituous liquors must not be deprived entirely of alcohol during the disease. Its administration often has a very good effect when the patient is restless and cannot sleep, while its complete withdrawal not infrequently induces violent delirium and other severe symptoms. These patients may be allowed light Rhine wines or Moselle, or even well-matured beer of a good quality, especially Pilsner.

Usually with the beginning of defervescence, and almost regularly after the period of defervescence is over, the patient's appetite rapidly begins to improve. Since there are no counterindications on the part of the intestine, as in typhoid fever, there is no objection to gratifying the patient's appetite by allowing him semiliquid and solid food in addition to milk and soups. Such articles as roast veal, roast beef, roast mutton, venison, and poultry, with rice, farina, mashed potatoes, or green vegetables, may be permitted. The ordinary diet, with the

exception of articles which are especially difficult to digest, may be resumed before long. This is a good plan, especially for persons in moderate circumstances who must return to their work and their former mode of life within a short time.

Among the special methods of treatment, those that are directed toward combating the febrile condition and its consequences—the **so-called antipyretic methods**—occupy the first place.

The fact that these methods have not been discussed in detail in their bearing on typhus fever is owing, probably, to the great press of work and the many demands on the physician in times of extensive epidemics, so that he has neither the opportunity nor the time for careful observation. As a rule, however, most physicians place much reliance on these methods, especially on hydrotherapy and the use of antipyretic drugs.

I have already spoken of the undoubted value of fresh, frequently renewed air in combating the fever. It is to be hoped that in future epidemics the open-air treatment will be more extensively employed in suitable cases. I am inclined to go so far as to keep the patients in the open air even during the night, providing them, of course, with the proper protection.

Among the various uses of **hydrotherapy,** the simplest and the most indispensable methods are bathing, local application of cold, and the use of the water mattress.

In severe cases, as has been stated elsewhere, it is best to put the patient on a water-bed from the beginning. The mechanical reduction in temperature may be still further increased by changing the water several times a day, a procedure that can easily be carried out without altering the patient's position. The water should not be colder than 18° to 20° C. No advantage is secured from the use of water of a lower temperature, or even iced water, as has been recommended, and it is certain to distress the patient.

In all severe cases an ice-cap should be placed on the head from the beginning and during the entire febrile period. If the patient is very irritable, the use of Leiter's tubes is preferable, for they avoid the disturbance of changing and refilling the ice-cap.

When there is severe headache, especially in the beginning of the disease, a small pillow filled with iced water is valuable. Both the ice-cap and the water mattress are reliable means for combating the insomnia, which is often very troublesome.

An ice-bag may often with advantage be applied to the precordial region, especially when the pulse is very rapid and irregular and the heart begins to fail.

Every patient should be thoroughly sponged two or three times a day. The practice of French physicians of adding a little vinegar to the water will often be found grateful. Under certain circumstances partial or total wet-packs may be employed after the sponging. In many cases it may be advisable to use them in place of the sponging, but they must be carefully regulated to suit individual conditions in the matter of temperature, duration, and extent of body-surface to which they are applied.

In many patients a cool or lukewarm wet-pack applied to the trunk and lower extremities during the first half of the night is successful in allaying restlessness and inducing sleep.

As a rule, one should guard against the too frequent use of very cold packs, as they have an undesirable exciting effect on many patients.

Treatment by Baths.—Although opinions may differ as to the number of cool or lukewarm baths that it is desirable to employ, and as to the way in which they act, no one will deny the value of employing them freely in typhus fever.

I have long held the opinion, which I find agrees with that of the majority of physicians at the present time, that the principal object aimed at and the value of the bath treatment lie not so much in the reduction of the temperature as in the favorable effect produced on the entire symptom-complex of the fever, particularly on certain vital centers that are especially implicated—namely, the respiratory and circulatory centers. The truth of this appears more forcibly in typhus fever than in any other febrile disease. Whereas I frequently observed an exceedingly slight and very temporary influence on the temperature, the effect of the baths on the cerebral functions and on the respiratory and circulatory organs was always so marked and persistent that I do not believe typhus fever can possibly be treated without frequent regular baths.

The method to be pursued in the bath treatment must be strictly regulated according to the individual case. I have already dealt with this method at some length in the section on Typhoid Fever,[1] to which I refer the reader for further details. I will only say that in typhus, as in typhoid fever, I never use cold baths except under special circumstances, and usually prefer Ziemssen's method of gradually reducing the temperature of the bath. I place the patient in a bath of 24° to 26°, and gradually cool the water to 20° or 18°, rarely lower. A cold, damp cloth or an ice-cap is applied to the patient's head during the bath.

Except in cases of extreme debility or with some local contraindicating affection it is a good practice, in stuporous and comatose patients,

[1] See *Typhoid Fever*, p. 456.

to give a cold douche over the head and trunk, either at intervals during the bath or at the end of the bath. Again, however, I use cold water or even iced water only in special cases, contenting myself with water at a temperature of 18°, gradually reduced to 10°, although others, on Currie's recommendation, have advised the use of ice-water as a routine practice.

The frequency of the baths should depend not alone or even chiefly on the body-temperature, as I must again emphasize, but on the general condition, and particularly on the condition of the central nervous system, the pulse, and the respiration. As these symptoms are likely to be so much more obstinate and severe in typhus, a greater number of baths will, as a rule, be necessary than in typhoid fever.

When the facilities are limited, as in private practice, where it is not always possible to give a full bath, it may be advisable to use, instead, lukewarm and cool sponging combined with douches. Personally I have very little experience in regard to their efficacy, but on general principles I do not believe their value can be as great as that of a regular course of bathing.

Cold douches in an empty bath-tub, as first recommended by Currie and after him employed by many physicians, some of whom carried it to an unreasonable extent, I believe to be a much inferior method. I employ it only in conditions of deep coma and stupor, or occasionally in marked cataleptic conditions, providing they are not complicated by a subnormal temperature. My experience is strongly against the advisability of employing it in conditions of marked excitement.

In place of cold baths Hermann, on the strength of his experiences during the Petersburg epidemic of 1874 and 1875, advocates the use of protracted lukewarm baths. His ultimate results—he had a mortality of 16.6 per cent.—are not very encouraging.

In a few instances I have seen favorable results, especially as regards the sedative effect, from baths of this kind combined with cold compresses or an ice-bag to the head. I should advise that the method be tested carefully in future epidemics, especially as certain modern authors in Germany (Riess, Unverricht, and Eichhorst) have warmly recommended it in the treatment of typhoid fever.

In accordance with the then accepted principles of therapeutics I made a very extensive use of **antipyretic remedies** during the years from 1876 to 1878, without, however, any marked result.

Now that opinions on the treatment of fever have undergone so marked a change, and, as has been repeatedly stated, the advantage of reducing the temperature alone is accounted of much less importance

than formerly, I am inclined to make but a very limited use of such remedies, and would recommend great care in their selection. This precaution is all the more necessary as typhus fever patients are much more liable to be attacked by sudden heart-failure than are patients suffering from typhoid fever.

The use of salicylic acid, sodium salicylate, kairin, thallin, and antifebrin should be abandoned altogether, on account of their marked effect on the heart. Quinin, antipyrin, phenacetin, and lactophenin may be used in certain cases, according to the principles laid down for the treatment of typhoid fever.[1]

Of all these remedies, lactophenin is the one I am most inclined to recommend, and I have recently had considerable experience with it. It is practically without any injurious effect on the heart and respiration, and, in addition to its marked antipyretic action, it is especially useful for allaying excitement, delirium, and insomnia.

Other remedies hardly come into consideration in an ordinary case of typhus fever. In private practice and for hospital patients who are fond of taking medicine, the usual hydrochloric acid mixture or a decoction of quinin with hydrochloric acid may be prescribed.

TREATMENT OF SPECIAL CONDITIONS AND ORGANIC CHANGES.

In speaking of the events and conditions that may call for especial therapeutic intervention in the course of typhus fever I may mention particularly **weakness of the circulation, cardiac and vasomotor palsy,** and **collapse in general.**

In a disease which is relatively so short in duration and so severe in its symptoms, where the crisis may be expected at a definite period, the patient's life may depend on beginning a rational treatment to combat impending collapse at the proper moment, and gradually increasing its force. Everything may depend on keeping the patient alive until the fifteenth or seventeenth day, when the crisis and a spontaneous change for the better may be expected.

Although stimulating remedies should be strictly withheld in any uncomplicated case, they should be employed unhesitatingly to their fullest extent at the first sign of impending failure of the circulation.

Among stimulating remedies the first place is accorded to alcoholic beverages, although their manner of action may not be quite fully understood. At the first sign of weakness, old Rhine wine, Bordeaux, or Burgundy, according to the individual's circumstances, should be given;

[1] *Typhoid Fever*, p. 461.

if more active stimulants are required, port, heavy Hungarian wines, sherry, or champagne. Patients of the poorer classes may be given brandy, either with or without water. If cyanosis is present, and the extremities are cold and the temperature is subnormal or the patient is in collapse, grog, mulled wine, or cognac in strong black coffee or tea may be used with advantage.

I particularly recommend the use of alcohol in the form of the well-known Stokes' mixture, on account of the ease with which the dose may be regulated, and because, being in the form of a medicine, it may be given without the patient's knowledge. The formula in use in my clinic is as follows:

℞. Spirit. vin. cognac, 50.0;
Vitell. ov., No. 1;
Syr. cinnamom., 25.0;
Aquæ dest., 150.0.
M. Sig.—One or two tablespoonfuls every two hours.

Occasionally I add tinct. valer. æther., 3.0 to 5.0, as a nerve tonic. If the patient cannot swallow or absolutely refuses to take alcohol, it may be administered in a nutritive enema of the following formula:

℞. Spirit. vin. cognac, 40.0;
Tinct. valer. æther., 5.0;
Vitell. ov., No. 1;
Muc. gum arab., 20.0;
Aqua, q. s. ad 180.0.
M. Sig.—To be given as enema and repeated three times.

To combat the collapse I prefer camphor to caffein. Both are administered exclusively in the form of hypodermic injections, caffein in the form of caffein. natr. salicyl., on account of the greater solubility in this form.

I never use hypodermic injections of ether, as they are neither so quick nor so lasting in their effects as camphor, and are, besides, very painful and frequently produce abscesses and necrosis of the fatty tissues.

For the hypodermic injection of camphor a freshly prepared solution is to be preferred to the official camphor oil found in the stores. I use a strong and a weak solution, according to the formulas:

℞. Camphor. trit., 1.0;
Æth. sulph., 2.0;
Ol. oliv. puriss., 8.0.

Or as solutio camphori fortius:

℞. Camph. trit., 1.0;
Ol. oliv. puriss., 5.0.

If the use of camphor has been decided upon, it should be given in generous doses. One or two syringefuls of the weaker solution may be given every one to three hours, and, under certain circumstances, the same amount of the stronger may be similarly administered. No disagreeable results will be experienced, and the effect is often exceedingly good.

Caffein is no less efficacious than camphor. As vasomotor paralysis probably plays an important part in the production of collapse in typhus fever, as it does in other infectious diseases, caffein, owing to its special action on the vasomotor system, is often found extremely useful.

When the pulse is very rapid, irregular, and low in tension, digitalis is indicated and may prove useful. If, however, the collapse continues, it is better to substitute caffein.

These procedures should, of course, be combined with other, especially physical, methods of treatment, either cooling applications—as, for example, the ice-bag to the head or the precordia, and the use of the water mattress, with or without changing the water, and cool sponging—or the application of warmth. In impending heart-failure cold or even lukewarm baths must be used with caution. None but a bigoted fanatic on the subject of hydrotherapy will deny that they tend to bring on collapse.

When the pulse is thready, the temperature is subnormal, and the face and extremities are cyanotic, much good may be accomplished by filling the water mattress with warm water, by applying hot-water bottles, by wrapping the extremities in flannels, and by the application of Leiter's apparatus—using warm water—to the precordia.

Nervous Symptoms.—Among other symptoms and complications requiring special treatment those affecting the nervous system occupy the first place.

The intolerable **headache,** which frequently declares itself at the beginning of the disease, requires energetic treatment. A water pillow and an ice-cap should first be ordered, followed in many cases by cold douches to the head. These may be given almost without changing the patient's position, merely by holding his head over the edge of the bed and placing a vessel under it.

Many patients find compresses of cold water, to which is added a little vinegar, alcohol, or eau de cologne, grateful. Warm compresses are sometimes soothing, especially in old, anemic, or very feeble persons.

In youthful, plethoric individuals no hesitation should be felt in applying artificial leeches behind each ear or to the temporal region.

If these measures fail to relieve the headache, antipyrin, phenacetin, and lactophenin may be resorted to. Even opiates, especially hypodermic injections of morphin (0.01 to 0.015 gm. per dose in adults),

may be given without the slightest hesitation and are often of great use.

Another equally important symptom requiring special treatment is **insomnia.** If this continues uninterruptedly for several days, it may threaten the patient's life, and in any stage of the disease a reasonable amount of normal sleep exerts a marked influence on the cerebral centers, which are often so profoundly involved, and, through them, on the entire course of the disease.

The open-air and bath treatment is extremely valuable and often suffices to overcome the insomnia.

If the patient is accustomed to the use of alcohol, a small quantity of beer, either one of the darker varieties or porter, may with advantage be given in the evening. Some few patients are relieved by bromid or valerian, or the two drugs in combination. The insomnia as well as the headache may require opium or morphin, and these drugs should be given unhesitatingly. I strongly object to chloral on account of the unfavorable effect it exerts on the circulation. Some of the newer hypnotics, which have been found so useful in various conditions, will require testing in future epidemics of typhus fever.

In the treatment of the **delirium** hydrotherapeutic procedures are, of course, the most efficacious, and their skilful use, with due regard to individual peculiarities, may often prevent the occurrence of violent excitement.

If, however, in spite of their use, violent excitement and delirium develop, lukewarm packs or lukewarm baths should be used in addition to the application of the ice-bag or cold compresses to the head. The lukewarm packs or baths are to be preferred to cold douches or cold tub-baths.

The drugs to be preferred in combating this symptom include bromid, valerian, and the opiates, even morphin. I am in the habit of giving bromid and opium together in the following formula:

℞.	Sod. brom.,	10.0;
	Tinct. opii simpl.,	2.0;
	Spir. vin. cog.,	10.0;
	Aquæ menth.,	q. s. 200.0.

The psychic treatment is of the greatest importance in violent delirium. A great deal may depend on the manner of physician and attendants. The room and its immediate surroundings should be absolutely quiet, and no one but those whose presence is absolutely required should be allowed to come near the patient. He should not be spoken

to unnecessarily, and force should never be used except in extreme cases. Firmness and a confident demeanor on the part of his attendants give the greatest amount of encouragement to the patient.

If deep **coma** and **stupor** develop, stimulants may be required. Under such conditions cold douches in a lukewarm bath or in an empty bath-tub may be useful. The importance of careful attention to the urinary secretion, and the free use of the catheter, if necessary to combat ischuria and overfilling of the bladder, cannot be too strongly insisted upon, particularly in the case of a stuporous patient.

The **vomiting** that often accompanies the headache and is evidently of cerebral origin will require the treatment appropriate to that condition. Small pieces of ice and the application of the ice-bag to the epigastric region will be found of value. I have often obtained good results from the use of aqua amygdalæ amaræ.

To relieve the troublesome **hyperesthesia** of the skin and muscles and the obstinate pains in the fingers, toes, and soles of the feet, which are particularly common during the initial stage and again during the period of defervescence, cool or lukewarm Preissnitz bandages should be tried. If drugs are resorted to, chloroform liniment or menthol should be preferred, the latter either in a solution of olive oil or, what I believe to be even better, in the form of a paste:

℞. Menthol,
Amyl, āā 2.0;
Vaselin. puriss., 50.0.
M. Sig.—Spread thickly on a piece of lint and apply.

The **respiratory organs** may require treatment in various ways.

The greatest attention should be paid to the condition of the nose, the nasopharynx, and the larynx.

Attendants should be instructed to pay special attention to the care of the nose and mouth. Irrigation of the nose with weak salt solution or some disinfecting solution may occasionally be necessary.

For the milder affections of the throat and larynx the usual gargles are quite appropriate. If the voice begins to change and hoarseness develops, the greatest vigilance is necessary. The great liability to severe and rapidly progressing changes in the larynx in typhus fever and the sudden development of edema of the glottis, often leading to asphyxia, must always be borne in mind. Under such circumstances the patient, especially if he is unconscious, should be watched day and night by a responsible person to ascertain the proper moment for tracheotomy.

Tracheobronchitis is one of the commonest symptoms of the disease and requires no special treatment. It is likely to be followed by hypostatic congestion of the lungs, which event may occasionally be prevented by strengthening the heart and frequently changing the position of the patient.

The **digestive organs** do not, as a rule, require treatment. During the height of the disease and during convalescence obstinate constipation sometimes occurs and may be treated by means of enemata, mild abdominal massage, and, in contradistinction to typhoid fever, by the administration of cathartics.

Diarrhea and meteorism rarely require therapeutic intervention. Meteorism is usually a most ominous symptom, and, when it is present, all remedies are valueless.

The **changes in the skin** that frequently occur during the period of convalescence are to be treated exactly as in typhoid fever.

As regards the development of bed-sores, the greatest watchfulness is necessary, for the patients are usually profoundly prostrated and unconscious from the beginning. Great care is necessary not only to keep the bedding clean and smooth, but also to subject the body to careful daily examination. It has been shown how quickly the most extensive subcutaneous bed-sores, which at first are not noticeable, may develop.

The **treatment during convalescence,** if no complications develop, is simpler than in any other acute infectious disease.

After the end of the febrile period the patients, as a rule, recover very rapidly, and the physician is more often called upon to restrain and admonish than to encourage.

The appetite, when it returns, may be gratified without any special restrictions, as has already been shown. I refer the reader to the directions previously given as to diet.

The nervous system and the heart call for more careful attention at this time than do the digestive organs. In many convalescents there is a persistent nervous irritability or a condition of depression, with marked deterioration of the intellect and memory. Such conditions require complete rest and freedom from exertion. Too early mental effort or excitement, whether pleasurable or the reverse, are likely to retard recovery.

A prolonged period of rest is necessary, especially if, after defervescence, the pulse continues slow and weak. Under such conditions the patient should be kept in bed until the symptoms have improved, after

which he may be allowed to get up for an hour at a time. Any neglect may lead to syncope and directly endanger the patient's life.

After a severe attack of typhus fever, a **period of recuperation,** protracted according to the individual's needs, should be insisted upon before allowing him to resume his usual activity. If the patient's circumstances permit, a sojourn in a southern climate, in the mountains, or at the seashore may be prescribed. For poorer patients a prolonged stay in the hospital or in a convalescent's home in the country is advisable.

LITERATURE.

Jacobus de Partibus, Commentar. ad Avicenn., 1498.

Frascatori, Opera omnia. De contagionibus et morbis contagiosis. Venet., 1555.

Massa, De febr. pestil. cum petechiis. Venet., 1556. Haller's Bibl. med. pract. I.

Andr. Gratioli, Commentar. de Peste. Venet., 1556.

Lebenwald, Chronik aller denkwürdigen Pesten. Nürnberg, 1615.

Huxham, Observ. de aere et morbis epidemicis. London, 1752.

— Essay on Fevers, IInd Ed. London, 1757.

Hasenöhrl, Histor. medic. morbi epidemici etc. Vindob., 1763.

Strack, Observ. med. de morbo cum petechiis. Carlsruhe, 1786.

Rennebaum, Histor. morb. contag. anni 1793 et 1794 a Francogallis captivis Culmbacium delati. Erlangen, 1796.

Schäfer, Ueber das in und um Regensburg 1793 herrschende Nervenfieber. Erlangen, 1796.

Currie, Medical Reports on the Effects of Water as a Remedy in Fever. London, 1797.

J. Hartmann, Der ansteckende Typhus. Med. chirurg. Zeitung, Nr. 45, 1807.

A. Fr. Hecker, Ueber die Nervenfieber, welche in Berlin 1807 herrschten. Erfurt, 1809.

v. Hildenbrand, Ueber den ansteckenden Typhus, nebst einigen Winken zur Beschränkung oder gänzlichen Tilgung der Kriegspest und mehrerer anderer Menschenseuchen. Wien, 1810. (A book for its time remarkably objective, and even to-day still well worth reading.)

Wedemeyer, De febr. petechial. Göttingen, 1812.

Hartmann, Theorie des ansteckenden Typhus. Wien, 1812.

Rasori, Storia della febr. petech. de Genova 1799—1800. Milano, 1813.

Hufeland, Ueber die Kriegspest. Berlin, 1814.

Ackermann, Von der Natur des ansteckenden Typhus. Heidelberg, 1814.

Horn, Erfahrungen über die ansteckenden Nerven- und Lazarethfieber. 2. Aufl. Berlin, 1814.

Wolff, Bemerkungen über die Krankheiten, welche im Jahre 1813 in Warschau herrschten, besonders über den ansteckenden Typhus. Hufel. Journ., 1814.

Renard, Beiträge zur Geschichte der Hirnentzündung und des ansteckenden Typhus. Hufel. Journ., 1815.

Reuss, Identität des Fleckfiebers mit der oriental. Pest. Nürnberg, 1815.

Armstrong, A Pract. Illustr. of Typhus Fever. London, 1819.

R. Jackson, A Sketch of the History of Contagious Fever. London, 1819.

Barker and Cheyne, An Account of the Fever Lately Epidemical in Ireland. London. 1821.

Marsh, Observ. on the Origin and Latent Periods of Fevers. Dublin Hosp. Rep., 1827, Vol. 4.

Corrigan, On the Epidemic Fever of Ireland. Lancet, 1829 and 1830.

Gaultier de Glaubry, De l'identité du typhus et de la fièvre typhoide. Mém. de l'Acad. de méd., T. VII, 1835.

Pfeuffer, Beiträge zur Geschichte des Petechialtyphus. Bamberg, 1831.

Perry, Letter on Typhus Fever. Dublin Journ. of Med. Sc., 1836.
Gerhard and Pennok, On the Typhus Fever which occurred at Philadelphia in 1836. Amer. Journ. of Med. Science, Vol. 19 and 20, 1837.
Thomson, A Statistical Inquiry into Fever. Edinb. Journ., Vol. 50, 1838.
Graves, On the State of the Pupil in Typhus and the Use of Belladonna in Certain Cases of Fever. Dubl. Journ., 1838.
Valleix, Du "Typhus fever" et de la fièvre typhoide d'Angleterre. Arch. gén. de méd., 1839.
Roupell, Treatise on Typhus Fever. London, 1839.
Anderson, Observ. on Typhus. Glasgow, 1840.
Christison, Art. Continued Fever in Twedie, Syst. of Pract. Med., Vol. I., London, 1840.
Landouzy, Sur l'epidémie de typhus carcéral qui a regné a Reims en 1839—1840. Arch. gén. de méd., 1842.
Kennedy, On the Connex. Between Famine and Fever in Ireland etc. Dublin, 1847.
Stokes and Cusak, On the Mortality of Med. Practitioners in Ireland. Dublin, Journ. of Med. Sc., 1847, 1848.
Omerod, Clin. Observ. on Continued Fever at St. Bartholomew's Hosp. London, 1848.
Graves, Clin. Lect. on the Practice of Medicine. II. Ed. Dublin, 1848.
Virchow, Mittheilungen über die in Oberschlesien herrschende Typhusepidemie. Virch. u. Reinh. Archiv, Bd. II, 1849.
Stich, Zur patholog. Anatomie des oberschles. Typhus. Ebenda, S. 323.
v. Bärensprung, Ueber den Typhus in Oberschlesien. Haeser's Arch. X, 4, 1849.
Virchow, Kritisches über den oberschles. Typhus. Virch. Arch., Bd. III, 1849.
Suchanek, Mittheil. über die Typhusepidemie im Teschener Kreise. Prager Vierteljahrschr., Bd. 21, 1849.
Schütz, Ueber Typhus exanthematicus, beobachtet in den Wintermonaten des Jahres 1847, 1848.
— Ebenda, Bd. 22, 1849.
Finger, Die während der Jahre 1846—1848 im Prager allg. Krankenhause beobachteten Epidemien, 1846—1848.
— Ebenda, Bd. 23, 1849.
Jenner, Typhus and Typhoid. Edinb. Monthly Journ. of Med. Science, Vols. IX and X, 1849—1850.
Christioson, On the Distribution of Fever Patients in a Hospital. Monthly Med. Journ., 1850.
Flint, Clinical Reports on Continued Fevers Based on an Analysis of 164 Cases. Buffalo, 1852.
Lindwurm, Der Typhus in Irland, beobachtet im Sommer 1852. Erlangen, 1853.
Forget, Preuves cliniques de la non-identité du typhus et de la fièvre typhoïde. Gaz. méd. de Paris, 1854.
Virchow, Die Noth im Spessart. Würzburger Verhandl., Bd. III, S. 105.
— Die Hungerepidemie in Unterfranken etc. Ebenda, S. 161. (Both articles also in Ges. Abhandl. aus d. Geb. d. öffentl. Med. u. Seuchenlehre.)
Bartlett, The Fevers of the United States, 4th Ed. Philadelphia, 1856.
Jaquot, Du typhus de l'armée d'Orient. Paris, 1856.
Peacock, On the Varieties of Continued Fever and their Discrimination. Med. Times, 1856.
Godelier, Résumé d'une mémoire sur le typhus, observé en Val-de-Grâce etc. Gaz des hôp., Juli, 1856.
Mayer Das Typhusexanthem etc. Wochenblatt der Wiener Aerzte, 1856.
Merentie, Rech. clin. et anatom. sur quelques points de l'hist. du typhus. Thèse, Paris, 1857.

Murchison, History of the Distinction of Typhus and Typhoid Fever. Med. Times, 1857.
Bryce, England and France before Sebastopol, etc. London, 1857.
Theuerkauf, Typh. exanthemat. in Göttingen 1856/57. Virch. Arch., Bd. 43.
Wunderlich, Ueber den Normalverlauf einiger typischer Krankheitsformen. Arch. f. physiolog. Heilkunde, 1858.
Rühle, Anatom. Mittheil. über Typh. exanthemat. Günsb. med. Zeitsch. 1858 u. Greifswald. med. Beitr., Bd. II.
Murchison, On the Classification and Nomenclature of Continued Fevers. Edinb. Med. Journ., Oct., 1858.
Barallier, Du typhus épidémique à Toulon. Paris, 1861.
Schnepp, Des fièvres typhiques et de l'apparition du typh. exanthemat. en Égypte. Un. méd., Oct., 1861.
Cazalas, Examen théorique et pratique de la question relative à la doctrine de l'identité ou de la non-identite du typhus de la fièvre typhoide. Un méd., 1861.
Rühle, Differentielle Diagnose des exanthem. vom Abdominaltyphus. Ber. d. 36. Naturforsch.-Vers., 1861.
Griesinger, Ueber Fleckfieber etc. Arch. d. Heilkunde, Bd. II, 1861.
— Acute Infectionskrankheiten: Abschn. Fleckfieber. Virch. Handb. d. spec. Pathol. u. Therap., 2. Aufl., 1864.
Wunderlich, Beiträge zur Beurtheil. der typhös. Kranken mit Hilfe der Wärmemessung. Arch. für phys. Heilk., 1861.
Duncan, On the Introduction of Fever into Liverpool, etc. Med. Times, 1862.
Gourrier, Relat. d'une épidém. du typhus observé à Toulon 1864. Thèse Montpellier, 1866.
Murchison, Die typhoiden Krankheiten. Uebers. von Zülzer. Berlin, 1867. (Very complete collection of the literature, especially of the older English and French works.)
Rosenstein, Mittheilungen über das Fleckfieber. Virch. Arch., Bd. 43, 1868.
v. Treskow, Vorl. Mittheil. über Vork. d. Typh. exanthem. etc. Berl. klin. Wochenschr., Nr. 7 u. 8, 1868.
Naunyn, Bericht über den exanthem. Typhus in Ostpreussen. Berl. klin. Wochenschr., Nr. 22, 1868.
Schieferdecker, Verhandl. der Berl. med. Ges. Berl. klin. Wochenschr., Nr. 28, 1868.
Becher, Mittheilungen aus der Typhusepidemie in Ostpreussen. Berl. klin. Wochenschr., Nr. 49, 50 u. 51, 1868.
Mosler, Erfahrungen über die Behandlung des Typh. exanthemat. etc. Greifswald, 1868.
Varrentrapp, Die Fleckfieberepidemie in Frankfurt a. M. Correspondenzblatt für die mittelrhein. Aerzte, Nr. 10 u. 11, 1868.
Virchow, Ueber den Hungertyphus und einige verwandte Krankheitsformen. Berlin, 1868. (Virch. ges. Abhandl. aus d. Geb. d. öffentl. Med. u. Seuchenlehre, S. 433.)
Wegener, Zur Pathol. u. Therap. des Typh. exanthemat. Jahrb. f. Kinderheilk., 1868.
Vital, Le typhus dans la prov. de Constantine en 1866. Rec. des mém. de méd. milit., 1869.
Kanzow, Der exanthemat. Typhus im ostpreuss. Reg.-Bez. Gumbinnen während des Nothstandes im Jahre 1868. Potsdam, 1869.
Grätzer, Statistik der Epidemie von Typh. exanthemat. in Breslau i. d. Jahren 1868 u. 1869. Deutsch. Arch. f. klin. Med., Bd. VII.
Lebert, Aetiologie und Statistik des Rückfallfiebers und des Flecktyphus in Breslau i. d. Jahren 1868 und 1869. Deutsch. Arch. f. klin. Med., H. 3, 4 u. 5, Bd. VII.
v. Pastau, Statist. Bericht über das Allerheiligenhospital Breslau, 1870. (S. 105 ff.)
Passauer, Ueber den exanthemat. Typhus in klin. und sanitätspoliz. Beziehung. Nach

Beobachtungen während der ostpreuss. Typhusepidemie i. d. Jahren 1868 u. 1869. Erlangen, 1870.

Perrier, Effets de la misère et typhus dans la province d'Alger. Rec. des mém. de méd. milit., 1870.

Wunderlich, Ueber die Diagnose des Flecktyphus. Volkm. Samml. klin. Vorträge, Nr. 21, 1871.

Murchison, On the Period of Incubat. of Typhus, Relapsing Fever, etc. St. Thomas Hosp. Rep., Vol. III, 1871.

Obermeier, Die ersten Fälle der Berliner Flecktyphusepidemie von 1873. Berl. klin. Wochenschr., Nr. 30 u. 31, 1873.

— Zur Contagion des wiederkehrenden und des Flecktyphus. Centralbl. f. d. med. Wissensch., Nr. 36, 1873.

Zülzer, Zur Aetiologie des Flecktyphus. Nach Beobachtungen aus der Berliner Epidemie von 1873. Vierteljahrschr. f. gerichtl. Med., Jan., S. 183, und Zeitschr. f. prakt. Med., Nr. 4, 1874.

Behse, Beobachtungen über Typh. exanthemat. und Febricula. Dorpat. med. Zeitschr., Bd. V, 1874.

Heitler, Bericht über die im Jahre 1875 auf der Klinik und Abth. des Prof. Löbel beobachteten Fälle von Flecktyphus. Wiener med. Jahrb., 1875.

Lebert, Flecktyphus. v. Ziemssen's Handb. d. spec. Path. u. Therap., 2. Aufl., Bd. II, 1876.

Wyss, Fleckfieber. Gerhart's Handb. der Kinderkrankh., Bd. II, 1876.

F. Herrmann, Die Flecktyphusepidemie von 1874 und 1875. Petersb. med. Wochenschr., Nr. 16, 1876.

Martin, Etude sur l'endémicité du typhus dans le départ. du Finistère. Thèse, Paris, 1876.

Kaczorowski, Ueber die Epidemie des Typhus exanthemat. im Spital der barmherz. Schwestern in Posen. Deutsche med. Wochenschr., 1877.

— Die kalte Luft als Antipyreticum. Ebenda, 1879.

Oser, Ueber den Typhus exanthemat. in Wien. Med. Jahrb., H. 4, 1877.

Dangy des Deserts, Relations de l'épidém. de typh. pétéchial de l'île Molène. Arch. de méd. navale, 1877.

v. Scheven, Ueber die gegen den exanthemat. Typhus in der Armee zu ergreifenden sanitätspoliz. Massregeln. Vierteljahrschr. f. gerichtl. Med., 1877.

Gestin, Rapport sur les épidémies de 1877. Mém. de l'acad. de méd., T. 32, 1878.

Benary, Kurzer Bericht über die während des Jahres 1878 im Berl. städt. Barackenlazareth vorgekomm. Fälle von Typhus exanthemat. Deutsche med. Wochenschr., Nr. 46, 1878.

Hartmann, Die bei Typhus exanthemat. auftretenden Erkrankungen der Hörorgane. Arch. der Ohrenheilk., 1879.

Salomon, Bericht über die Berliner Flecktyphusepidemie im Jahre 1879. Inaug.-Diss., Berlin, 1880 und Deutsch. Arch. f. klin. Med., 1880. (The articles of Benary, Hartmann, and Salomon refer to the material observed by me at the Berl. städt. Barackenlazareths at Moabit.)

Pistor, Die Flecktyphusepidemie in Oberschlesien 1876—1877. Vierteljahrschr. f. gerichtl. Med., Bd. 29, 1, 1880.

Goltdammer, Ueber die Kost- und Logirhäuser für die ärmeren Volksclassen. Vierteljahrschr. f. gerichtl. Med., Bd. 29, 2, 1880.

Krukenberg, Zur Pathologie und Therapie des Typh. exanthemat. Deutsche med. Wochenschr., Nr. 49—51, 1880.

Hampeln, Ueber Flecktyphus. Deutsch. Arch. f. klin. Med., 1880.

Moritz, Kurzer Bericht über den Flecktyphus im weibl. Obuchowspital 1879—1880. Petersb. med. Wochenschr., Nr. 17, 1881.

Herrmann, Beitrag zur Anwendung warmer, prolongirter Bäder im Flecktyphus. Petersb. med. Wochenschr., Nr. 26, 1881.

Janeway, Typh. Fever in New York. Bost. Med. and Surg. Journ., 1881.

Guttstadt, Fleck- and Rückfallfieber in Preussen. 11. Ergänz.-Heft zur Zeitschr. d. königl. preuss. statist. Bureaux. Berlin, 1882.

Michaelis, Der exanthemat. Typhus in der russischen Armee auf der Balkanhalbinsel 1877/78. Oesterr. militärärztl. Zeitsch., 1882.

Mott and Blore, Micro-organisms in Typhus Fever. Brit. Med. Journ., Dec., 1883.

Weichselbaum, Ueber einige seltene Complicationen des Typh. exanthemat. in anatom. u. aetiolog. Beziehung. Allgem. Wiener med. Zeit., Nr. 22—23, 1883.

Curschmann, Fleckfieber. Ziemssen's Handb., Bd. 2, 3. Aufl., 1886.

Mantzel, Ueber die Verbreitung des Flecktyphus in Preussen (bis 1885). Diss. Berlin 1887. (Unter Guttstadt's Leitung bearbeitet.)

Janowsky, Ueber das Exanthem des Flecktyphus. Internat. klin. Rundschau, 1888.

Seeliger, Die Flecktyphusepidemie in der städt. Krankenanstalt zu Königsberg 1880 bis 1882. Berl. klin. Wochenschr., Nr. 51 u. 52, 1888.

Reichsgesundheitsamt, Veröffentlichungen des, Ueber eine Flecktyphusepidemie in Magdeburg, 1888.

Christie, A Case of Typhus Fever Complic. with Hematemesis. Glasgow Med. Journ., Dec., 1888.

Moreau et Cochez, Contribut. à l'étude du typh. exanthemat. Gaz. hebd., Nr. 28, 1888.

Hlawa, Etude sur le typh. exanthemat. Arch. Bohême de méd. III, 1, 1889.

Thoinot, Le typh. exanthemat. de l'île Tudy. Ann. de hyg. publ. et de méd. légale, 1891.

Mey, Zur Kenntniss des Hämoglobingehaltes des Blutes beim Typh. exanthemat. Diss. Dorpat, 1891.

Thoinot et Calmette, Note sur quelques examens de sang dans le typh. exanthemat. Ann. de l'Institut Pasteur, 1892.

Thoinot, Art. Fleckfieber. Traité de méd., 1892.

Lewaschew, Ueber die Mikroorganismen des Flecktyphus. Deutsche med. Wochenschr., Nr. 13, 1892.

— Ueber die Mikroparasiten des Flecktyphus. Ebenda, Nr. 34, 1892.

Erismann, Flecktyphus und Cholera. Morbidität des ärztl. Standes. Petersb. med. Wochenschr., 1892.

Brannan and Cheesman, A Study of Typhus Fever, etc. Med. Record, 1892.

Netter, Etiologie et prophylaxe du typh. exanthémat. Union méd., 1893.

— Origine brettonne de l'épidémie typhique de 1892/93 en France. Semaine méd., Juni, 1893.

— Un cas de typhus méconnu. Soc. méd. des hôpit., Juni, 1893.

— Etiologie et prophylaxie du typh. exanthémat. Ebenda, Juli, 1893.

De Brun, Note sur le typhe exanthémat. observé à Beyrouth dans les premiers mois d'année 1893. Bull. de l'Acad., 1893.

Combemale, Deux cas de typh. exanthémat. avec hypothermie. Gaz. hebd., Nr. 30, 1893.

— Soc. méd. des hôpit., 1893.

Lanceraux, Sur l'épidémie de typh. exanthémat. Bull. de l'acad. de méd., 1893.

Proust, Note sur le typh. exanthémat. en France 1893 etc. Bull. de l'acad. de méd., 1894.

— Typh. exanthémat. au Hâvre en 1893, etc. Paris, 1893.

Barrault, Gaz. hebd., Nr. 35 u. 36, 1893. — Chantemesse, Société méd. des hôpit., 1893. — Dubief et Brühl, Semaine méd., 1893. (These works treat of an epidemic which broke out in Lille in 1893, and spread from there to the prisons of Paris and environs.)

Kelsch, Traité des maladies épidémiques. Paris, 1894.
Dubief et Brühl, Contrib. à l'étude anatom.-pathol. et bactériolog. du typh. exanthémat. Arch. de méd. expér., Nr. 2, 1894.
Combemale, Le typh. exanthémat. chez les vieillards. Bull. gén. de thérap., 1894.
— Des complications pulmon. graves dans le typh. exanthémat. Ebenda, 1894.
Dardignac, Le typhus dans l'Oise en 1893. Gaz. hebd., Nr. 39—42, 1895.
Richter, Ueber Flecktyphus. Deutsche med. Wochenschr., Nr. 34, 1895.
Mosler, Flecktyphus. Eulenberg's Encyklopädie, 3. Aufl., 1895.
Spillmann, Contribut. à l'histoire du typh. exanthémat. Rév. de méd., Nr. 8, 1895.
Pietrusky, Ueber das Auftreten des Fleckfiebers in Schlesien und die zu dessen Verhütung geeigneten Massregeln. Vierteljahrschr. f. öffentl. Gesundheitspfl., 1895.
Leonhardt, Ueber das Vorkommen von Fleckfieber und Recurrens in Breslau. Zeitschr. für Hygiene und Infect.-Krankh., Bd. 24, 1897.
Filatow, Vorlesungen über acute Infectionskrankheiten im Kindesalter Aus dem Russischen. Wien, 1897.
Netter, Flecktyphus. Traité de méd. par Brouadel, 1898.
Mac Weeney, Note on the Etiology of Typhus Fever. Brit. Med. Journ., Apr., 1898.
Balfour and Porter, A Research into the Bacteriology of Typhus Fever. Prelimin. Notice, Edinb. Med. Journ., Nr. 2, 1899.
Pelc, Verbreitung des Flecktyphus in Böhmen. Prag. med. Wochenschr., Nr. 18, 1899.
Littlejohn and Ker, An Outbreak of Typhus Fever. Edinb. Med. Journ., 1899.

The above bibliography is not intended to be comprehensive. It includes the more important publications dealing with the epidemiology, and a number of others which contain some specially valuable data.

For the older literature, especially the English and French up to 1865, the reader is referred to the classical work of Murchison. The same work and Hirsch's Handbuch der histor.-geograph. Pathologie contain a detailed account of the history and geographic distribution of typhus fever.

INDEX.

Catalogue of the Medical Publications

OF

W. B. SAUNDERS & COMPANY

PHILADELPHIA — 925 Walnut Street
LONDON, W. C. — 161 Strand

Arranged Alphabetically and Classified under Subjects

See page 20 for a List of Contents classified according to subjects

THE books advertised in this Catalogue as being *sold by subscription* are usually to be obtained from travelling solicitors, but they will be sent direct from the office of publication (charges of shipment prepaid) upon receipt of the prices given. All the other books advertised are commonly for sale by booksellers in all parts of the United States; but books will be sent to any address, carriage prepaid, on receipt of the published price.

Money may be sent at the risk of the publisher in either of the following ways: A postal money order, an express money order, a bank check, and in a registered letter. Money sent in any other way is at the risk of the sender.

SPECIAL OFFER To physicians of approved credit books will be sent, post-paid, on the following terms: $5.00 cash upon delivery of books, and monthly payments of $5.00 thereafter until full amount is paid. Any one or two volumes will be sent on thirty days' time to those who do not care to make a large purchase.

An American Text-Book *of* Applied Therapeutics.

Edited by JAMES C. WILSON, M. D., Professor of Practice of Medicine and of Clinical Medicine, Jefferson Medical College, Philadelphia. Handsome imperial octavo volume of 1326 pages. Illustrated. Cloth, $7.00 net; Sheep or Half Morocco, $8.00 net. *Sold by Subscription.*

An American Text-Book *of the* Diseases *of* Children.

Second Edition, Revised.

Edited by LOUIS STARR, M. D., Consulting Pediatrist to the Maternity Hospital, etc.; assisted by THOMPSON S. WESTCOTT, M. D., Attending Physician to the Dispensary for Diseases of Children, Hospital of the University of Pennsylvania. Handsome imperial octavo volume of 1244 pages, profusely illustrated. Cloth, $7.00 net; Sheep or Half Morocco, $8.00 net. *Sold by Subscription.*

An American Text-Book *of* Diseases *of the* Eye, Ear, Nose, *and* Throat.

Edited by G. E. DE SCHWEINITZ, M. D., Professor of Ophthalmology, Jefferson Medical College, Philadelphia; and B. ALEXANDER RANDALL, M. D., Clinical Professor of Diseases of the Ear, University of Pennsylvania. Imperial octavo of 1251 pages; 766 illustrations, 59 of them in colors. Cloth, $7.00 net; Sheep or Half Morocco, $8.00 net. *Sold by Subscription.*

An American Text-Book of Genito-Urinary and Skin Diseases.

Edited by L. Bolton Bangs, M. D., Professor of Genito-Urinary Surgery, University and Bellevue Hospital Medical College, New York; and W. A. Hardaway, M. D., Professor of Diseases of the Skin, Missouri Medical College. Imperial octavo volume of 1229 pages, with 300 engravings and 20 full-page colored plates. Cloth, $7.00 net; Sheep or Half Morocco, $8.00 net. *Sold by Subscription.*

An American Text-Book of Gynecology, Medical and Surgical. Second Edition, Revised.

Edited by J. M. Baldy, M. D., Professor of Gynecology, Philadelphia Polyclinic, etc. Handsome imperial octavo volume of 718 pages; 341 illustrations in the text, and 38 colored and half-tone plates. Cloth, $6.00 net; Sheep or Half Morocco, $7.00 net. *Sold by Subscription.*

An American Text-Book of Legal Medicine and Toxicology.

Edited by Frederick Peterson, M. D., Chief of Clinic, Nervous Department, College of Physicians and Surgeons, New York; and Walter S. Haines, M. D., Professor of Chemistry, Pharmacy, and Toxicology, Rush Medical College, Chicago. *In Preparation.*

An American Text-Book of Obstetrics.

Edited by Richard C. Norris, M. D.; Art Editor, Robert L. Dickinson, M. D. Handsome imperial octavo volume of 1014 pages; nearly 900 beautiful colored and half-tone illustrations. Cloth, $7.00 net; Sheep or Half Morocco, $8.00 net. *Sold by Subscription.*

An American Text-Book of Pathology.

Edited by Ludwig Hektoen, M. D., Professor of Pathology in Rush Medical College, Chicago; and David Riesman, M. D., Demonstrator of Pathologic Histology in the University of Pennsylvania. Handsome imperial octavo, over 1200 pages, profusely illustrated. *By Subscription.*

An American Text-Book of Physiology. Second Edition, Revised, in Two Volumes.

Edited by William H. Howell, Ph. D., M. D., Professor of Physiology, Johns Hopkins University, Baltimore, Md. Two royal octavo volumes of about 600 pages each. Fully illustrated. Per volume: Cloth, $3.00 net; Sheep or Half Morocco, $3.75 net.

An American Text-Book of Surgery. Third Edition.

Edited by William W. Keen, M. D., LL. D., F. R. C. S. (Hon.); and J. William White, M. D., Ph. D. Handsome octavo volume of 1230 pages; 496 wood-cuts and 37 colored and half-tone plates. Thoroughly revised and enlarged, with a section devoted to "The Use of the Röntgen Rays in Surgery." Cloth, $7.00 net; Sheep or Half Morocco, $8.00 net.

THE NEW STANDARD **THE NEW STANDARD**

The American Illustrated Medical Dictionary.

Second Edition, Revised.

For Practitioners and Students. A Complete Dictionary of the Terms used in Medicine, Surgery, Dentistry, Pharmacy, Chemistry, and the kindred branches, including much collateral information of an encyclopedic character, together with new and elaborate tables of Arteries, Muscles, Nerves, Veins, etc.; of Bacilli, Bacteria, Micrococci, Streptococci; Eponymic Tables of Diseases, Operations, Signs and Symptoms, Stains, Tests, Methods of Treatment, etc., etc. By W. A. NEWMAN DORLAND, A. M., M. D., Editor of the "American Pocket Medical Dictionary." Handsome large octavo, nearly 800 pages, bound in full flexible leather. Price, $4.50 net; with thumb index, $5.00 net.

Gives a Maximum Amount of Matter in a Minimum Space and at the Lowest Possible Cost.

This Edition contains all the Latest Words.

"I must acknowledge my astonishment at seeing how much he has condensed within relatively small space. I find nothing to criticise, very much to commend, and was interested in finding some of the new words which are not in other recent dictionaries."—ROSWELL PARK, *Professor of Principles and Practice of Surgery and Clinical Surgery, University of Buffalo.*

"I congratulate you upon giving to the profession a dictionary so compact in its structure, and so replete with information required by the busy practitioner and student. It is a necessity as well as an informed companion to every doctor. It should be upon the desk of every practitioner and student of medicine."—JOHN B. MURPHY, *Professor of Surgery and Clinical Surgery, Northwestern University Medical School,* Chicago.

The American Pocket Medical Dictionary. **Third Edition, Revised.**

Edited by W. A. NEWMAN DORLAND, M. D., Assistant Obstetrician to the Hospital of the University of Pennsylvania; Fellow of the American Academy of Medicine. Containing the pronunciation and definition of the principal words used in medicine and kindred sciences, with 64 extensive tables. Handsomely bound in flexible leather, with gold edges. Price $1.00 net; with thumb index, $1.25 net.

The American Year-Book *of* Medicine *and* Surgery.

A Yearly Digest of Scientific Progress and Authoritative Opinion in all branches of Medicine and Surgery, drawn from journals, monographs, and text-books of the leading American and Foreign authors and investigators. Arranged with critical editorial comments, by eminent American specialists, under the editorial charge of GEORGE M. GOULD, M. D. Year-Book of 1901 in two volumes—Vol. I. including *General Medicine;* Vol. II., *General Surgery.* Per volume: Cloth, $3.00 net; Half Morocco, $3.75 net. *Sold by Subscription.*

Abbott on Transmissible Diseases. **Second Edition, Revised.**

The Hygiene of Transmissible Diseases: their Causation, Modes of Dissemination, and Methods of Prevention. By A. C. ABBOTT, M. D., Professor of Hygiene and Bacteriology, University of Pennsylvania. Octavo, 351 pages, with numerous illustrations. Cloth, $2.50 net.

Anders' Practice *of* Medicine. Fifth Revised Edition.

A Text-Book of the Practice of Medicine. By JAMES M. ANDERS, M. D., PH. D., LL. D., Professor of the Practice of Medicine and of Clinical Medicine, Medico-Chirurgical College, Philadelphia. Handsome octavo volume of 1292 pages, fully illustrated. Cloth, $5.50 net; Sheep or Half Morocco, $6.50 net.

Bastin's Botany.

Laboratory Exercises in Botany. By EDSON S. BASTIN, M. A., late Professor of Materia Medica and Botany, Philadelphia College of Pharmacy. Octavo, 536 pages, with 87 plates. Cloth, $2.00 net.

Beck on Fractures.

Fractures. By CARL BECK, M. D., Surgeon to St. Mark's Hospital and the New York German Poliklinik, etc. With an appendix on the Practical Use of the Röntgen Rays. 335 pages, 170 illustrations. Cloth, $3.50 net.

Beck's Surgical Asepsis.

A Manual of Surgical Asepsis. By CARL BECK, M. D., Surgeon to St. Mark's Hospital and the New York German Poliklinik, etc. 306 pages; 65 text-illustrations and 12 full-page plates. Cloth, $1.25 net.

Boisliniere's Obstetric Accidents, Emergencies, *and* Operations.

Obstetric Accidents, Emergencies, and Operations. By L. CH. BOISLINIÈRE, M. D., late Emeritus Professor of Obstetrics, St. Louis Medical College. 381 pages, handsomely illustrated. Cloth, $2.00 net.

Böhm, Davidoff, *and* Huber's Histology.

A Text-Book of Human Histology. Including Microscopic Technic. By DR. A. A. BÖHM and DR. M. VON DAVIDOFF, of Munich, and G. CARL HUBER, M. D., Junior Professor of Anatomy and Director of Histological Laboratory, University of Michigan. Handsome octavo of 503 pages, with 351 beautiful original illustrations. Cloth, $3.50 net.

Butler's Materia Medica, Therapeutics, *and* Pharmacology. Third Edition, Revised.

A Text-Book of Materia Medica, Therapeutics, and Pharmacology. By GEORGE F. BUTLER, PH. G., M. D., Professor of Materia Medica and of Clinical Medicine, College of Physicians and Surgeons, Chicago. Octavo, 874 pages, illustrated. Cloth, $4.00 net; Sheep or Half Morocco, $5.00 net.

Cerna on *the* Newer Remedies. Second Edition, Revised.

Notes on the Newer Remedies, their Therapeutic Applications and Modes of Administration. By DAVID CERNA, M. D., PH. D., Demonstrator of Physiology, Medical Department, University of Texas. Rewritten and greatly enlarged. Post-octavo, 253 pages. Cloth, $1.00 net.

Chapin on Insanity.

A Compendium of Insanity. By JOHN B. CHAPIN, M. D., LL. D., Physician-in-Chief, Pennsylvania Hospital for the Insane; Honorary Member of the Medico-Psychological Society of Great Britain, of the Society of Mental Medicine of Belgium, etc. 12mo, 234 pages, illustrated. Cloth, $1.25 net.

Chapman's Medical Jurisprudence and Toxicology.

Second Edition, Revised.

Medical Jurisprudence and Toxicology. By HENRY C. CHAPMAN, M. D., Professor of Institutes of Medicine and Medical Jurisprudence, Jefferson Medical College of Philadelphia. 254 pages, with 55 illustrations and 3 full-page plates in colors. Cloth, $1.50 net.

Church and Peterson's Nervous and Mental Diseases.

Third Edition, Revised and Enlarged.

Nervous and Mental Diseases. By ARCHIBALD CHURCH, M. D., Professor of Nervous and Mental Diseases, and Head of the Neurological Department, Northwestern University Medical School, Chicago; and FREDERICK PETERSON, M. D., Chief of Clinic, Nervous Department, College of Physicians and Surgeons, New York. Handsome octavo volume of 875 pages, profusely illustrated. Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.

Clarkson's Histology.

A Text-Book of Histology, Descriptive and Practical. By ARTHUR CLARKSON, M. B., C. M. Edin., formerly Demonstrator of Physiology in the Owen's College, Manchester; late Demonstrator of Physiology in Yorkshire College, Leeds. Large octavo, 554 pages; 22 engravings and 174 beautifully colored original illustrations. Cloth, $4.00 net.

Corwin's Physical Diagnosis. Third Edition, Revised.

Essentials of Physical Diagnosis of the Thorax. By ARTHUR M. CORWIN, A. M., M. D., Instructor in Physical Diagnosis in Rush Medical College, Chicago. 219 pages, illustrated. Cloth, $1.25 net.

Crookshank's Bacteriology. Fourth Edition, Revised.

A Text-Book of Bacteriology. By EDGAR M. CROOKSHANK, M. B., Professor of Comparative Pathology and Bacteriology, King's College, London. Octavo, 700 pages, 273 engravings and 22 original colored plates. Cloth, $6.50 net; Half Morocco, $7.50 net.

DaCosta's Surgery. Third Edition, Revised.

Modern Surgery, General and Operative. By JOHN CHALMERS DA COSTA, M. D., Professor of Principles of Surgery and Clinical Surgery, Jefferson Medical College, Philadelphia; Surgeon to the Philadelphia Hospital, etc. Handsome octavo volume of 1117 pages, profusely illustrated. Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.

Enlarged by over 200 Pages, with more than 100 New Illustrations.

Davis's Obstetric Nursing.

Obstetric and Gynecologic Nursing. By EDWARD P. DAVIS, A. M., M. D., Professor of Obstetrics in Jefferson Medical College and the Philadelphia Polyclinic; Obstetrician and Gynecologist to the Philadelphia Hospital. 12mo volume of 400 pages, fully illustrated. Crushed Buckram, $1.75 net.

DeSchweinitz on Diseases *of the* Eye. Third Edition, Revised.

Diseases of the Eye. A Handbook of Ophthalmic Practice. By G. E. DE SCHWEINITZ, M. D., Professor of Ophthalmology, Jefferson Medical College, Philadelphia, etc. Handsome royal octavo volume of 696 pages; 256 fine illustrations and 2 chromo-lithographic plates. Cloth, $4.00 net; Sheep or Half Morocco, $5.00 net.

Dorland's Dictionaries.

[See *American Illustrated Medical Dictionary* and *American Pocket Medical Dictionary* on page 3.]

Dorland's Obstetrics. Second Edition, Revised and Greatly Enlarged.

Modern Obstetrics. By W. A. NEWMAN DORLAND, M. D., Assistant Demonstrator of Obstetrics, University of Pennsylvania; Associate in Gynecology, Philadelphia Polyclinic. Octavo volume of 797 pages, with 201 illustrations. Cloth, $4.00 net.

Eichhorst's Practice *of* Medicine.

A Text-Book of the Practice of Medicine. By DR. HERMAN EICHHORST, Professor of Special Pathology and Therapeutics and Director of the Medical Clinic, University of Zurich. Translated and edited by AUGUSTUS A. ESHNER, M. D., Professor of Clinical Medicine, Philadelphia Polyclinic. Two octavo volumes of 600 pages each, over 150 illustrations. Prices per set: Cloth, $6.00 net; Sheep or Half Morocco, $7.50 net.

Friedrich *and* Curtis on *the* Nose, Throat, *and* Ear.

Rhinology, Laryngology, and Otology, and Their Significance in General Medicine. By DR. E. P. FRIEDRICH, of Leïpzig. Edited by H. HOLBROOK CURTIS, M. D., Consulting Surgeon to the New York Nose and Throat Hospital. Octavo, 348 pages. Cloth, $2.50 net.

Frothingham's Guide for *the* Bacteriologist.

Laboratory Guide for the Bacteriologist. By LANGDON FROTHINGHAM, M. D. V., Assistant in Bacteriology and Veterinary Science, Sheffield Scientific School, Yale University. Illustrated. Cloth, 75 cts. net.

Garrigues' Diseases *of* Women. Third Edition, Revised.

Diseases of Women. By HENRY J. GARRIGUES, A. M., M. D., Gynecologist to St. Mark's Hospital and to the German Dispensary, New York City. Octavo, 756 pages, with 367 engravings and colored plates. Cloth, $4.50 net; Sheep or Half Morocco, $5.50 net.

Gould and Pyle's Curiosities of Medicine.

Anomalies and Curiosities of Medicine. By GEORGE M. GOULD, M. D., and WALTER L. PYLE, M. D. An encyclopedic collection of rare and extraordinary cases and of the most striking instances of abnormality in all branches of Medicine and Surgery, derived from an exhaustive research of medical literature from its origin to the present day, abstracted, classified, annotated, and indexed. Handsome octavo volume of 968 pages; 295 engravings and 12 full-page plates. Popular Edition. Cloth, $3.00 net; Sheep or Half Morocco, $4.00 net.

Grafstrom's Mechano-Therapy.

A Text-Book of Mechano-Therapy (Massage and Medical Gymnastics). By AXEL V. GRAFSTROM, B. Sc., M. D., late House Physician, City Hospital, Blackwell's Island, New York. 12mo, 139 pages, illustrated. Cloth, $1.00 net.

Griffith on the Baby. Second Edition, Revised.

The Care of the Baby. By J. P. CROZER GRIFFITH, M. D., Clinical Professor of Diseases of Children, University of Pennsylvania; Physician to the Children's Hospital, Philadelphia, etc. 12mo, 404 pages; 67 illustrations and 5 plates. Cloth, $1.50 net.

Griffith's Weight Chart.

Infant's Weight Chart. Designed by J. P. CROZER GRIFFITH, M. D., Clinical Professor of Diseases of Children, University of Pennsylvania. 25 charts in each pad. Per pad, 50 cts. net.

Hart's Diet in Sickness and in Health.

Diet in Sickness and Health. By MRS. ERNEST HART, formerly Student of the Faculty of Medicine of Paris and of the London School of Medicine for Women; with an Introduction by SIR HENRY THOMPSON, F. R. C. S., M. D., London. 220 pages. Cloth, $1.50 net.

Haynes' Anatomy.

A Manual of Anatomy. By IRVING S. HAYNES, M. D., Professor of Practical Anatomy in Cornell University Medical College. 680 pages; 42 diagrams and 134 full-page half-tone illustrations from original photographs of the author's dissections. Cloth, $2.50 net.

Heisler's Embryology. Second Edition, Revised.

A Text-Book of Embryology. By JOHN C. HEISLER, M. D., Professor of Anatomy, Medico-Chirurgical College, Philadelphia. Octavo volume of 405 pages, handsomely illustrated. Cloth, $2.50 net.

Hirst's Obstetrics. Third Edition, Revised and Enlarged.

A Text-Book of Obstetrics. By BARTON COOKE HIRST, M. D., Professor of Obstetrics, University of Pennsylvania. Handsome octavo volume of 873 pages; 704 illustrations, 36 of them in colors. Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.

Hyde *and* Montgomery on Syphilis *and the* Venereal Diseases. **Second Edition, Revised and Greatly Enlarged.**

Syphilis and the Venereal Diseases. By JAMES NEVINS HYDE, M. D., Professor of Skin and Venereal Diseases, and FRANK H. MONTGOMERY, M. D., Associate Professor of Skin, Genito-Urinary, and Venereal Diseases in Rush Medical College, Chicago, Ill. Octavo, 594 pages, profusely illustrated. Cloth, $4.00 net.

The International Text-Book of Surgery. **In Two Volumes.**

By American and British Authors. Edited by J. COLLINS WARREN, M. D., LL. D., F. R. C. S. (Hon.), Professor of Surgery, Harvard Medical School, Boston; and A. PEARCE GOULD, M. S., F. R. C. S., Lecturer on Practical Surgery and Teacher of Operative Surgery, Middlesex Hospital Medical School, London, Eng. Vol. I. *General Surgery.*—Handsome octavo, 947 pages, with 458 beautiful illustrations and 9 lithographic plates. Vol. II. *Special or Regional Surgery.*—Handsome octavo, 1072 pages, with 471 beautiful illustrations and 8 lithographic plates. *Sold by Subscription.* Prices per volume: Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.

"It is the most valuable work on the subject that has appeared in some years. The clinician and the pathologist have joined hands in its production, and the result must be a satisfaction to the editors as it is a gratification to the conscientious reader."—*Annals of Surgery.*

"This is a work which comes to us on its own intrinsic merits. Of the latter it has very many. The arrangement of subjects is excellent, and their treatment by the different authors is equally so. What is especially to be recommended is the painstaking endeavor of each writer to make his subject clear and to the point. To this end particularly is the technique of operations lucidly described in all necessary detail. And withal the work is up to date in a very remarkable degree, many of the latest operations in the different regional parts of the body being given in full details. There is not a chapter in the work from which the reader may not learn something new."—*Medical Record*, New York.

Jackson's Diseases *of the* Eye.

A Manual of Diseases of the Eye. By EDWARD JACKSON, A. M., M. D., Emeritus Professor of Diseases of the Eye, Philadelphia Polyclinic and College for Graduates in Medicine. 12mo volume of 535 pages, with 178 illustrations, mostly from drawings by the author. Cloth, $2.50 net.

Keating's Life Insurance.

How to Examine for Life Insurance. By JOHN M. KEATING, M. D., Fellow of the College of Physicians of Philadelphia; Ex-President of the Association of Life Insurance Medical Directors. Royal octavo, 211 pages. With numerous illustrations. Cloth, $2.00 net.

Keen on *the* Surgery *of* Typhoid Fever.

The Surgical Complications and Sequels of Typhoid Fever. By WM. W. KEEN, M. D., LL. D., F. R. C. S. (Hon.), Professor of the Principles of Surgery and of Clinical Surgery, Jefferson Medical College, Philadelphia, etc. Octavo volume of 386 pages, illustrated. Cloth, $3.00 net.

Keen's Operation Blank. **Second Edition, Revised Form.**

An Operation Blank, with Lists of Instruments, etc., Required in Various Operations. Prepared by W. W. KEEN, M. D., LL. D., F. R. C. S. (Hon.), Professor of the Principles of Surgery and of Clinical Surgery, Jefferson Medical College, Philadelphia. Price per pad, blanks for fifty operations, 50 cts. net.

Kyle on *the* Nose and Throat. Second Edition.

Diseases of the Nose and Throat. By D. Braden Kyle, M. D., Clinical Professor of Laryngology and Rhinology, Jefferson Medical College, Philadelphia. Octavo, 646 pages; over 150 illustrations and 6 lithographic plates. Cloth, $4.00 net; Sheep or Half Morocco, $5.00 net.

Lainé's Temperature Chart.

Temperature Chart. Prepared by D. T. Lainé, M. D. Size 8 x 13½ inches. A conveniently arranged Chart for recording Temperature, with columns for daily amounts of Urinary and Fecal Excretions, Food, Remarks, etc. On the back of each chart is given the Brand treatment of Typhoid Fever. Price, per pad of 25 charts, 50 cts. net.

Levy, Klemperer, *and* Eshner's Clinical Bacteriology.

The Elements of Clinical Bacteriology. By Dr. Ernst Levy, Professor in the University of Strasburg, and Felix Klemperer, Privatdocent in the University of Strasburg. Translated and edited by Augustus A. Eshner, M. D., Professor of Clinical Medicine, Philadelphia Polyclinic. Octavo, 440 pages, fully illustrated. Cloth, $2.50 net.

Lockwood's Practice *of* Medicine. Second Edition, Revised and Enlarged.

A Manual of the Practice of Medicine. By George Roe Lockwood, M. D., Professor of Practice in the Woman's Medical College of the New York Infirmary, etc.

Long's Syllabus *of* Gynecology.

A Syllabus of Gynecology, arranged in Conformity with "An American Text-Book of Gynecology." By J. W. Long, M. D., Professor of Diseases of Women and Children, Medical College of Virginia, etc. Cloth, interleaved, $1.00 net.

Macdonald's Surgical Diagnosis *and* Treatment.

Surgical Diagnosis and Treatment. By J. W. Macdonald, M. D. Edin., F. R. C. S. Edin., Professor of Practice of Surgery and Clinical Surgery, Hamline University. Handsome octavo, 800 pages, fully illustrated. **Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.**

Mallory *and* Wright's Pathological Technique.

Second Edition, Revised.

Pathological Technique. A Practical Manual for Laboratory Work in Pathology, Bacteriology, and Morbid Anatomy, with chapters on Post-Mortem Technique and the Performance of Autopsies. By Frank B. Mallory, A. M., M. D., Assistant Professor of Pathology, Harvard University Medical School, Boston; and James H. Wright, A. M., M. D., Instructor in Pathology, Harvard University Medical School, Boston.

McFarland's Pathogenic Bacteria. Third Edition, increased in size by over 100 Pages.

Text-Book upon the Pathogenic Bacteria. By Joseph McFarland, M. D., Professor of Pathology and Bacteriology, Medico-Chirurgical College of Philadelphia, etc. Octavo volume of 621 pages, finely illustrated. Cloth, $3.25 net.

Meigs on Feeding in Infancy.

Feeding in Early Infancy. By ARTHUR V. MEIGS, M. D. Bound in limp cloth, flush edges, 25 cts. net.

Moore's Orthopedic Surgery.

A Manual of Orthopedic Surgery. By JAMES E. MOORE, M. D., Professor of Orthopedics and Adjunct Professor of Clinical Surgery, University of Minnesota, College of Medicine and Surgery. Octavo volume of 356 pages, handsomely illustrated. Cloth, $2.50 net.

Morten's Nurses' Dictionary.

Nurses' Dictionary of Medical Terms and Nursing Treatment. Containing Definitions of the Principal Medical and Nursing Terms and Abbreviations; of the Instruments, Drugs, Diseases, Accidents, Treatments, Operations, Foods, Appliances, etc. encountered in the ward or in the sick-room. By HONNOR MORTEN, author of "How to Become a Nurse," etc. 16mo, 140 pages. Cloth, $1.00 net.

Nancrede's Anatomy *and* Dissection. Fourth Edition.

Essentials of Anatomy and Manual of Practical Dissection. By CHARLES B. NANCREDE, M. D., LL. D., Professor of Surgery and of Clinical Surgery, University of Michigan, Ann Arbor. Post-octavo, 500 pages, with full-page lithographic plates in colors and nearly 200 illustrations. Extra Cloth (or Oilcloth for dissection-room), $2.00 net.

Nancrede's Principles *of* Surgery.

Lectures on the Principles of Surgery. By CHAS. B. NANCREDE, M. D., LL. D., Professor of Surgery and of Clinical Surgery, University of Michigan, Ann Arbor. Octavo, 398 pages, illustrated. Cloth, $2.50 net.

Norris's Syllabus *of* Obstetrics. Third Edition, Revised.

Syllabus of Obstetrical Lectures in the Medical Department of the University of Pennsylvania. By RICHARD C. NORRIS, A. M., M. D., Instructor in Obstetrics and Lecturer on Clinical and Operative Obstetrics, University of Pennsylvania. Crown octavo, 222 pages. Cloth, interleaved for notes, $2.00 net.

Ogden on *the* Urine.

Clinical Examination of the Urine and Urinary Diagnosis. A Clinical Guide for the Use of Practitioners and Students of Medicine and Surgery. By J. BERGEN OGDEN, M. D., Instructor in Chemistry, Harvard Medical School. Handsome octavo, 416 pages, with 54 illustrations and a number of colored plates. Cloth, $3.00 net.

Penrose's Diseases *of* Women. Fourth Edition, Revised.

A Text-Book of Diseases of Women. By CHARLES B. PENROSE, M. D., PH. D., formerly Professor of Gynecology in the University of Pennsylvania. Octavo volume of 538 pages, handsomely illustrated. Cloth, $3.75 net.

Pryor—Pelvic Inflammations.

The Treatment of Pelvic Inflammations through the Vagina. By W. R. PRYOR, M. D., Professor of Gynecology, New York Polyclinic. 12mo, 248 pages, handsomely illustrated. Cloth, $2.00 net.

Pye's Bandaging.

Elementary Bandaging and Surgical Dressing. With Directions concerning the Immediate Treatment of Cases of Emergency. By WALTER PYE, F. R. C. S., late Surgeon to St. Mary's Hospital, London. Small 12mo, over 80 illustrations. Cloth, flexible covers, 75 cts. net.

Pyle's Personal Hygiene.

A Manual of Personal Hygiene. Proper Living upon a Physiologic Basis. Edited by WALTER L. PYLE, M. D., Assistant Surgeon to the Wills Eye Hospital, Philadelphia. Octavo volume of 344 pages, fully illustrated. Cloth, $1.50 net.

Raymond's Physiology. Second Edition, Revised and Greatly Enlarged.

A Text-Book of Physiology. By JOSEPH H. RAYMOND, A. M., M. D., Professor of Physiology and Hygiene and Lecturer on Gynecology in the Long Island College Hospital.

Salinger *and* Kalteyer's Modern Medicine.

Modern Medicine. By JULIUS L. SALINGER, M. D., Demonstrator of Clinical Medicine, Jefferson Medical College; and F. J. KALTEYER, M. D., Assistant Demonstrator of Clinical Medicine, Jefferson Medical College. Handsome octavo, 801 pages, illustrated. Cloth, $4.00 net.

Saundby's Renal *and* Urinary Diseases.

Lectures on Renal and Urinary Diseases. By ROBERT SAUNDBY, M. D. Edin., Fellow of the Royal College of Physicians, London, and of the Royal Medico-Chirurgical Society; Professor of Medicine in Mason College, Birmingham, etc. Octavo, 434 pages, with numerous illustrations and 4 colored plates. Cloth, $2.50 net.

Saunders' Medical Hand-Atlases.

See pages 16 and 17.

Saunders' Pocket Medical Formulary. Sixth Edition, Revised.

By WILLIAM M. POWELL, M. D., author of "Essentials of Diseases of Children"; Member of Philadelphia Pathological Society. Containing 1844 formulæ from the best-known authorities. With an Appendix containing Posological Table, Formulæ and Doses for Hypodermic Medication, Poisons and their Antidotes, Diameters of the Female Pelvis and Fetal Head, Obstetrical Table, Diet List for Various Diseases, Materials and Drugs used in Antiseptic Surgery, Treatment of Asphyxia from Drowning, Surgical Remembrancer, Tables of Incompatibles, Eruptive Fevers, etc., etc. Handsomely bound in flexible morocco, with side index, wallet, and flap. $2.00 net.

Saunders' Question-Compends.

See page 15.

Scudder's Fractures. Second Edition, Revised.

The Treatment of Fractures. By CHAS. L. SCUDDER, M. D., Assistant in Clinical and Operative Surgery, Harvard University Medical School. Octavo, 460 pages, with nearly 600 original illustrations. Polished Buckram, $4.50 net; Half Morocco, $5.50 net.

Senn's Genito-Urinary Tuberculosis.

Tuberculosis of the Genito-Urinary Organs, Male and Female. By NICHOLAS SENN, M. D., PH. D., LL. D., Professor of the Practice of Surgery and of Clinical Surgery, Rush Medical College, Chicago. Handsome octavo volume of 320 pages, illustrated. Cloth, $3.00 net.

Senn's Practical Surgery.

Practical Surgery. By NICHOLAS SENN, M. D., PH. D., LL. D., Professor of the Practice of Surgery and of Clinical Surgery, Rush Medical College, Chicago. Handsome octavo volume of 1200 pages, profusely illustrated. Cloth, $6.00 net; Sheep or Half Morocco, $7.00 net. *By Subscription.*

Senn's Syllabus *of* Surgery.

A Syllabus of Lectures on the Practice of Surgery, arranged in conformity with "An American Text-Book of Surgery." By NICHOLAS SENN, M. D., PH. D., LL. D., Professor of the Practice of Surgery and of Clinical Surgery, Rush Medical College, Chicago. Cloth, $1.50 net.

Senn's Tumors. Second Edition, Revised.

Pathology and Surgical Treatment of Tumors. By NICHOLAS SENN, M. D., PH. D., LL. D., Professor of the Practice of Surgery and of Clinical Surgery, Rush Medical College, Chicago. Octavo volume of 718 pages, with 478 illustrations, including 12 full-page plates in colors. Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.

Starr's Diets for Infants *and* Children.

Diets for Infants and Children in Health and in Disease. By LOUIS STARR, M. D., Editor of "An American Text-Book of the Diseases of Children." 230 blanks (pocket-book size), perforated and neatly bound in flexible morocco. $1.25 net.

Stengel's Pathology. Third Edition, Thoroughly Revised.

A Text-Book of Pathology. By ALFRED STENGEL, M. D., Professor of Clinical Medicine, University of Pennsylvania; Visiting Physician to the Pennsylvania Hospital. Handsome octavo, 873 pages, nearly 400 illustrations, many of them in colors. Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.

Stengel *and* White on *the* Blood.

The Blood in its Clinical and Pathological Relations. By ALFRED STENGEL, M. D., Professor of Clinical Medicine, University of Pennsylvania; and C. Y. WHITE, JR., M. D., Instructor in Clinical Medicine, University of Pennsylvania. *In Press.*

Stevens' Therapeutics. **Third Edition, Revised and Greatly Enlarged.**

A Text-Book of Modern Therapeutics. By A. A. STEVENS, A. M., M. D., Lecturer on Physical Diagnosis in the University of Pennsylvania.

Stevens' Practice *of* Medicine. **Fifth Edition, Revised.**

A Manual of the Practice of Medicine. By A. A. STEVENS, A. M., M. D., Lecturer on Physical Diagnosis in the University of Pennsylvania. Specially intended for students preparing for graduation and hospital examinations. Post-octavo, 519 pages; illustrated. Flexible Leather, $2.00 net.

Stewart's Physiology. **Fourth Edition, Revised.**

A Manual of Physiology, with Practical Exercises. For Students and Practitioners. By G. N. STEWART, M. A., M. D., D. Sc., Professor of Physiology in the Western Reserve University, Cleveland, Ohio. Octavo volume of 894 pages; 336 illustrations and 5 colored plates. Cloth, $3.75 net.

Stoney's Materia Medica for Nurses.

Materia Medica for Nurses. By EMILY A. M. STONEY, late Superintendent of the Training-School for Nurses, Carney Hospital, South Boston, Mass. Handsome octavo volume of 306 pages. Cloth, $1.50 net.

Stoney's Nursing. **Second Edition, Revised.**

Practical Points in Nursing. For Nurses in Private Practice. By EMILY A. M. STONEY, late Superintendent of the Training-School for Nurses, Carney Hospital, South Boston, Mass. 456 pages, with 73 engravings and 8 colored and half-tone plates. Cloth, $1.75 net.

Stoney's Surgical Technic for Nurses.

Bacteriology and Surgical Technic for Nurses. By EMILY A. M. STONEY, late Superintendent of the Training-School for Nurses, Carney Hospital, South Boston, Mass. 12mo volume, fully illustrated. Cloth, $1.25 net.

Thomas's Diet Lists. **Second Edition, Revised.**

Diet Lists and Sick-Room Dietary. By JEROME B. THOMAS, M. D., Visiting Physician to the Home for Friendless Women and Children and to the Newsboys' Home; Assistant Visiting Physician to the Kings County Hospital. Cloth, $1.25 net. Send for sample sheet.

Thornton's Dose-Book *and* Prescription-Writing.

Second Edition, Revised and Enlarged.

Dose-Book and Manual of Prescription-Writing. By E. Q. THORNTON, M. D., Demonstrator of Therapeutics, Jefferson Medical College, Philadelphia.

Van Valzah *and* Nisbet's Diseases *of the* Stomach.

Diseases of the Stomach. By WILLIAM W. VAN VALZAH, M. D., Professor of General Medicine and Diseases of the Digestive System and the Blood, New York Polyclinic; and J. DOUGLAS NISBET, M. D., Adjunct Professor of General Medicine and Diseases of the Digestive System and the Blood, New York Polyclinic. Octavo volume of 674 pages, illustrated. Cloth, $3.50 net.

Vecki's Sexual Impotence. Second Edition, Revised.

The Pathology and Treatment of Sexual Impotence. By VICTOR G. VECKI, M. D. From the second German edition, revised and enlarged. Demi-octavo, 291 pages. Cloth, $2.00 net.

Vierordt's Medical Diagnosis. Fourth Edition, Revised.

Medical Diagnosis. By DR. OSWALD VIERORDT, Professor of Medicine, University of Heidelberg. Translated, with additions, from the fifth enlarged German edition, with the author's permission, by FRANCIS H. STUART, A. M., M. D. Handsome octavo volume, 603 pages; 194 wood-cuts, many of them in colors. Cloth, $4.00 net; Sheep or Half Morocco, $5.00 net.

Watson's Handbook for Nurses.

A Handbook for Nurses. By J. K. WATSON, M. D. Edin. American Edition, under supervision of A. A. STEVENS, A. M., M. D., Lecturer on Physical Diagnosis, University of Pennsylvania. 12mo, 413 pages, 73 illustrations. Cloth, $1.50 net.

Warren's Surgical Pathology. Second Edition.

Surgical Pathology and Therapeutics. By JOHN COLLINS WARREN, M. D., LL. D., F. R. C. S. (Hon.), Professor of Surgery, Harvard Medical School. Handsome octavo, 873 pages; 136 relief and lithographic illustrations, 33 in colors. With an Appendix on Scientific Aids to Surgical Diagnosis, and a series of articles on Regional Bacteriology. Cloth, $5.00 net; Sheep or Half Morocco, $6.00 net.

SAUNDERS'

QUESTION-COMPENDS.

ARRANGED IN QUESTION AND ANSWER FORM.

The Most Complete and Best Illustrated Series of Compends Ever Issued.

NOW THE STANDARD AUTHORITIES IN MEDICAL LITERATURE

WITH

Students and Practitioners in every City of the United States and Canada.

Since the issue of the first volume of the Saunders Question-Compends,

OVER 200,000 COPIES

of these unrivalled publications have been sold. This enormous sale is indisputable evidence of the value of these self-helps to students and physicians.

SEE NEXT PAGE FOR LIST.

SAUNDERS' QUESTION-COMPEND SERIES.

Price, Cloth, $1.00 net per copy, except when otherwise noted.

"Where the work of preparing students' manuals is to end we cannot say, but the Saunders Series, in our opinion, bears off the palm at present."—*New York Medical Record.*

1. **Essentials of Physiology.** By SIDNEY BUDGETT, M. D. *A New Work.*
2. **Essentials of Surgery.** By EDWARD MARTIN, M. D. Seventh edition, revised, with an Appendix and a chapter on Appendicitis.
3. **Essentials of Anatomy.** By CHARLES B. NANCREDE, M. D. Sixth edition, thoroughly revised and enlarged.
4. **Essentials of Medical Chemistry, Organic and Inorganic.** By LAWRENCE WOLFF, M. D. Fifth edition, revised.
5. **Essentials of Obstetrics.** By W. EASTERLY ASHTON, M. D. Fourth edition, revised and enlarged.
6. **Essentials of Pathology and Morbid Anatomy.** By F. J. KALTEYER, M. D. *In preparation.*
7. **Essentials of Materia Medica, Therapeutics, and Prescription-Writing.** By HENRY MORRIS, M. D. Fifth edition, revised.
8. 9. **Essentials of Practice of Medicine.** By HENRY MORRIS, M. D. An Appendix on URINE EXAMINATION. By LAWRENCE WOLFF, M. D. Third edition, enlarged by some 300 Essential Formulæ, selected from eminent authorities, by WM. M. POWELL, M. D. (Double number, $1.50 net.)
10. **Essentials of Gynecology.** By EDWIN B. CRAGIN, M. D. Fifth edition, revised.
11. **Essentials of Diseases of the Skin.** By HENRY W. STELWAGON, M. D. Fourth edition, revised and enlarged.
12. **Essentials of Minor Surgery, Bandaging, and Venereal Diseases.** By EDWARD MARTIN, M. D. Second edition, revised and enlarged.
13. **Essentials of Legal Medicine, Toxicology, and Hygiene.** This volume is at present out of print.
14. **Essentials of Diseases of the Eye.** By EDWARD JACKSON, M. D. Third edition, revised and enlarged.
15. **Essentials of Diseases of Children.** By WILLIAM M. POWELL, M. D. Third edition.
16. **Essentials of Examination of Urine.** By LAWRENCE WOLFF, M. D. Colored "VOGEL SCALE." (75 cents net.)
17. **Essentials of Diagnosis.** By S. SOLIS-COHEN, M. D., and A. A. ESHNER, M. D. Second edition, thoroughly revised.
18. **Essentials of Practice of Pharmacy.** By LUCIUS E. SAYRE. Second edition, revised and enlarged.
19. **Essentials of Diseases of the Nose and Throat.** By E. B. GLEASON, M. D. Third edition, revised and enlarged.
20. **Essentials of Bacteriology.** By M. V. BALL, M. D. Fourth edition, revised.
21. **Essentials of Nervous Diseases and Insanity.** By JOHN C. SHAW, M. D. Third edition, revised.
22. **Essentials of Medical Physics.** By FRED J. BROCKWAY, M. D. Second edition, revised.
23. **Essentials of Medical Electricity.** By DAVID D. STEWART, M. D., and EDWARD S. LAWRANCE, M. D.
24. **Essentials of Diseases of the Ear.** By E. B. GLEASON, M. D. Second edition, revised and greatly enlarged.
25. **Essentials of Histology.** By LOUIS LEROY, M. D. With 73 original illustrations.

Pamphlet containing specimen pages, etc., sent free upon application.

Saunders' Medical Hand-Atlases.

VOLUMES NOW READY.

Atlas and Epitome of Internal Medicine and Clinical Diagnosis.

By Dr. Chr. Jakob, of Erlangen. Edited by Augustus A. Eshner, M. D., Professor of Clinical Medicine, Philadelphia Polyclinic. With 179 colored figures on 68 plates, 64 text-illustrations, 259 pages of text. Cloth, $3.00 net.

Atlas of Legal Medicine.

By Dr. E. R. von Hofmann, of Vienna. Edited by Frederick Peterson, M. D., Chief of Clinic, Nervous Department, College of Physicians and Surgeons, New York. With 120 colored figures on 56 plates and 193 beautiful half-tone illustrations. Cloth, $3.50 net.

Atlas and Epitome of Diseases of the Larynx.

By Dr. L. Grunwald, of Munich. Edited by Charles P. Grayson, M. D., Physician-in-Charge, Throat and Nose Department, Hospital of the University of Pennsylvania. With 107 colored figures on 44 plates, 25 text-illustrations, and 103 pages of text. Cloth, $2.50 net.

Atlas and Epitome of Operative Surgery.

By Dr. O. Zuckerkandl, of Vienna. Edited by J. Chalmers DaCosta, M. D., Professor of Principles of Surgery and Clinical Surgery, Jefferson Medical College, Philadelphia. With 24 colored plates, 217 text-illustrations, and 395 pages of text. Cloth, $3.00 net.

Atlas and Epitome of Syphilis and the Venereal Diseases.

By Prof. Dr. Franz Mracek, of Vienna. Edited by L. Bolton Bangs, M. D., Professor of Genito-Urinary Surgery, University and Bellevue Hospital Medical College, New York. With 71 colored plates, 16 illustrations, and 122 pages of text. Cloth, $3.50 net.

Atlas and Epitome of External Diseases of the Eye.

By Dr. O. Haab, of Zurich. Edited by G. E. de Schweinitz, M. D., Professor of Ophthalmology, Jefferson Medical College, Philadelphia. With 76 colored illustrations on 40 plates and 228 pages of text. Cloth, $3.00 net.

Atlas and Epitome of Skin Diseases.

By Prof. Dr. Franz Mracek, of Vienna. Edited by Henry W. Stelwagon, M. D., Clinical Professor of Dermatology, Jefferson Medical College, Philadelphia. With 63 colored plates, 39 half-tone illustrations, and 200 pages of text. Cloth, $3.50 net.

Atlas and Epitome of Special Pathological Histology.

By Dr. H. Durck, of Munich. Edited by Ludwig Hektoen M. D., Professor of Pathology, Rush Medical College, Chicago. In Two Parts. Part I. *Ready*, including Circulatory, Respiratory, and Gastro-intestinal Tract, 120 colored figures on 62 plates, 158 pages of text. Part II. *Ready Shortly*. Price of Part I., $3.00 net.

Saunders' Medical Hand-Atlases.

VOLUMES JUST ISSUED.

Atlas and Epitome of Diseases Caused by Accidents.

By Dr. Ed. Golebiewski, of Berlin. Translated and edited with additions by Pearce Bailey, M. D., Attending Physician to the Department of Corrections and to the Almshouse and Incurable Hospitals, New York. With 40 colored plates, 143 text-illustrations, and 600 pages of text. Cloth, $4.00 net.

Atlas and Epitome of Gynecology.

By Dr. O. Shaeffer, of Heidelberg. *From the Second Revised German Edition.* Edited by Richard C. Norris, A. M., M. D., Gynecologist to the Methodist Episcopal and the Philadelphia Hospitals; Surgeon-in-Charge of Preston Retreat, Philadelphia. With 90 colored plates, 65 text-illustrations, and 308 pages of text. Cloth, $3.50 net.

Atlas and Epitome of the Nervous System and its Diseases.

By Professor Dr. Chr. Jakob, of Erlangen. *From the Second Revised and Enlarged German Edition.* Edited by Edward D. Fisher, M. D., Professor of Diseases of the Nervous System, University and Bellevue Hospital Medical College, New York. With 83 plates and a copious text. Cloth, $3.50 net.

Atlas and Epitome of Labor and Operative Obstetrics.

By Dr. O. Schaeffer, of Heidelberg. *From the Fifth Revised and Enlarged German Edition.* Edited by J. Clifton Edgar, M. D., Professor of Obstetrics and Clinical Midwifery, Cornell University Medical School. With 126 colored illustrations. Cloth, $2.00 net.

Atlas and Epitome of Obstetric Diagnosis and Treatment.

By Dr. O. Schaeffer, of Heidelberg. *From the Second Revised and Enlarged German Edition.* Edited by J. Clifton Edgar, M. D., Professor of Obstetrics and Clinical Midwifery, Cornell University Medical School. 72 colored plates, text-illustrations, and copious text. Cloth, $3.00 net.

Atlas and Epitome of Ophthalmoscopy and Ophthalmoscopic Diagnosis.

By Dr. O. Haab, of Zürich. *From the Third Revised and Enlarged German Edition.* Edited by G. E. de Schweinitz, M. D., Professor of Ophthalmology, Jefferson Medical College, Philadelphia. With 152 colored figures and 82 pages of text. Cloth, $3.00 net.

Atlas and Epitome of Bacteriology.

Including a Text-Book of Special Bacteriologic Diagnosis. By Prof. Dr. K. B. Lehmann and Dr. R. O. Neumann, of Wurzburg. *From the Second Revised German Edition.* Edited by George H. Weaver, M. D., Assistant Professor of Pathology and Bacteriology, Rush Medical College, Chicago. Two volumes with over 600 colored lithographic figures, numerous text-illustrations, and 500 pages of text.

ADDITIONAL VOLUMES IN PREPARATION.

NOTHNAGEL'S ENCYCLOPEDIA

OF

PRACTICAL MEDICINE

Edited by ALFRED STENGEL, M. D.

Professor of Clinical Medicine in the University of Pennsylvania; Visiting Physician to the Pennsylvania Hospital

IT is universally acknowledged that the Germans lead the world in Internal Medicine; and of all the German works on this subject, Nothnagel's "Encyclopedia of Special Pathology and Therapeutics" is conceded by scholars to be without question the **best System of Medicine in existence.** So necessary is this book in the study of Internal Medicine that it comes largely to this country in the original German. In view of these facts, Messrs. W. B. Saunders & Company have arranged with the publishers to issue at once **an authorized edition** of this great encyclopedia of medicine in English.

For the present a set of some ten or twelve volumes, representing the most practical part of this encyclopedia, and selected with especial thought of the **needs of the practical physician,** will be published. The volumes will contain the real essence of the entire work, and the purchaser will therefore obtain at less than half the cost the cream of the original. Later the special and more strictly scientific volumes will be offered from time to time.

The work will be translated by men possessing thorough knowledge of both English and German, and **each volume** will be **edited by a prominent specialist** on the subject to which it is devoted. It will thus be brought thoroughly up to date, and the American edition will be more than a mere translation of the German; for, in addition to the matter contained in the original, it will represent the **very latest views of the leading American specialists** in the various departments of Internal Medicine. The whole System will be under the editorial supervision of **Dr. Alfred Stengel,** who will select the subjects for the American edition, and will choose the editors of the different volumes.

Unlike most encyclopedias, the publication of this work **will not be extended over a number of years,** but five or six volumes will be issued during the coming year, and the remainder of the series at the same rate. Moreover, each volume will be revised to the date of its publicatfon by the American editor. This will obviate the objection that has heretofore existed to systems published in a number of volumes, since the subscriber will receive the completed work while the earlier volumes are still fresh.

The usual method of publishers, when issuing a work of this kind, has been to compel physicians to take the entire System. This seems to us in many cases to be undesirable. Therefore, in purchasing this encyclopedia, physicians will be given the opportunity of subscribing for the entire System at one time; but any single volume or any number of volumes may be obtained by those who do not desire the complete series. This latter method, while not so profitable to the publisher, **offers to the purchaser many advantages** which will be appreciated by those who do not care to subscribe for the entire work at one time.

This American edition of Nothnagel's Encyclopedia will, without question, form **the greatest System of Medicine ever produced,** and the publishers feel confident that it will meet with general favor in the medical profession.

NOTHNAGEL'S ENCYCLOPEDIA

VOLUMES JUST ISSUED AND IN PRESS

VOLUME I

Editor, William Osler, M. D., F. R. C. P.

Professor of Medicine in Johns Hopkins University

CONTENTS

Typhoid Fever. By DR. H. CURSCHMANN, of Leipsic. **Typhus Fever.** By DR. H. CURSCHMANN, of Leipsic.

Handsome octavo volume of about 600 pages.

Just Issued

VOLUME II

Editor, Sir J. W. Moore, B. A., M. D., F. R. C. P. I., of Dublin

Professor of Practice of Medicine, Royal College of Surgeons in Ireland

CONTENTS

Erysipelas and Erysipeloid. By DR. H. LENHARTZ, of Hamburg. **Cholera Asiatica and Cholera Nostras.** By DR. K. VON LIEBERMEISTER, of Tübingen. **Whooping Cough and Hay Fever.** By DR. G. STICKER, of Giessen. **Varicella.** By DR. TH. VON JÜRGENSEN, of Tübingen. **Variola (including Vaccination).** By DR. H. IMMERMANN, of Basle.

Handsome octavo volume of over 700 pages.

Just Issued

VOLUME III

Editor, William P. Northrup, M. D.

Professor of Pediatrics, University and Bellevue Medical College

CONTENTS

Measles. By DR. TH. VON JÜRGENSEN, of Tübingen. **Scarlet Fever.** By the same author. **Rotheln.** By the same author.

VOLUME VI

Editor, Alfred Stengel, M. D.

Professor of Clinical Medicine, University of Pennsylvania

CONTENTS

Anemia. By DR. P. EHRLICH, of Frankfort-on-the-Main, and DR. A. LAZARUS, of Charlottenburg. **Chlorosis.** By DR. K. VON NOORDEN, of Frankfort-on-the-Main. **Diseases of the Spleen and Hemorrhagic Diathesis.** By DR. M. LITTEN, of Berlin.

VOLUME VII

Editor, John H. Musser, M. D.

Professor of Clinical Medicine, University of Pennsylvania

CONTENTS

Diseases of the Bronchi. By DR. F. A. HOFFMANN, of Leipsic. **Diseases of the Pleura.** By DR. ROSENBACH, of Berlin. **Pneumonia.** By DR. E. AUFRECHT, of Magdeburg.

VOLUME VIII

Editor, Charles G. Stockton, M. D.

Professor of Medicine, University of Buffalo

CONTENTS

Diseases of the Stomach. By DR. F. RIEGEL, of Giessen.

VOLUME IX

Editor, Frederick A. Packard, M. D.

Physician to the Pennsylvania Hospital and to the Children's Hospital, Philadelphia

CONTENTS

Diseases of the Liver. By DRS. H. QUINCKE and G. HOPPE-SEYLER, of Kiel.

VOLUME X

Editor, Reginald H. Fitz, A. M., M. D.

Hersey Professor of the Theory and Practice of Physic, Harvard University

CONTENTS

Diseases of the Pancreas. By DR. L. OSER, of Vienna. **Diseases of the Suprarenals.** By DR. E. NEUSSER, of Vienna.

VOLUMES IV, V, and XI

Editors announced later

Vol. IV.—**Influenza and Dengue.** By DR. O. LEICHTENSTERN, of Cologne. **Malarial Diseases.** By DR. J. MANNABERG, of Vienna.

Vol. V.—**Tuberculosis and Acute General Miliary Tuberculosis.** By DR. G. CORNET, of Berlin.

Vol. XI.—**Diseases of the Intestines and Peritoneum.** By DR. H. NOTHNAGEL, of Vienna.

CLASSIFIED LIST

OF THE

MEDICAL PUBLICATIONS

OF

W. B. SAUNDERS & COMPANY

ANATOMY, EMBRYOLOGY, HISTOLOGY.

BACTERIOLOGY.

CHARTS, DIET-LISTS, ETC.

CHEMISTRY AND PHYSICS.

CHILDREN.

DIAGNOSIS.

DICTIONARIES.

EYE, EAR, NOSE, AND THROAT.

GENITO-URINARY.

GYNECOLOGY.

HYGIENE.

MATERIA MEDICA, PHARMACOLOGY, AND THERAPEUTICS.

MEDICAL JURISPRUDENCE AND TOXICOLOGY.

NERVOUS AND MENTAL DISEASES, ETC.

NURSING.

OBSTETRICS.

PATHOLOGY.

PHYSIOLOGY.

PRACTICE OF MEDICINE.

SKIN AND VENEREAL.

SURGERY.

URINE AND URINARY DISEASES.

MISCELLANEOUS.

THE LATEST BOOKS.

Bergey's Principles of Hygiene.

The Principles of Hygiene: A Practical Manual for Students, Physicians, and Health Officers. By D. H. BERGEY, A. M., M. D., First Assistant, Laboratory of Hygiene, University of Pennsylvania. Handsome octavo volume of about 500 pages, illustrated.

Brower's Manual of Insanity.

A Practical Manual of Insanity. By DANIEL R. BROWER, M. D., Professor of Nervous and Mental Diseases, Rush Medical College, Chicago. 12mo volume of 425 pages, illustrated.

Gorham's Bacteriology.

A Laboratory Course in Bacteriology. By F. P. GORHAM, M. A., Assistant Professor in Biology, Brown University. 12mo volume of about 160 pages, handsomely illustrated.

Gradle on the Nose, Throat, and Ear.

Diseases of the Nose, Throat, and Ear. By HENRY GRADLE, M. D., Professor of Ophthalmology and Otology, Northwestern University Medical School, Chicago. Handsome octavo volume of 800 pages, profusely illustrated.

Sollmann's Pharmacology.

A Text-Book of Pharmacology. By TORALD SOLLMANN, M. D., Lecturer on Pharmacology, Western Reserve University, Cleveland, Ohio. Royal octavo volume of about 700 pages.

Wolf's Examination of Urine.

A Handbook of Physiologic Chemistry and Urine Examination. By CHAS. G. L. WOLF, M. D., Instructor in Physiologic Chemistry, Cornell University Medical College. 12mo volume of about 160 pages.