# THE DUCTS OF THE HUMAN SUBMAXILLARY GLAND.

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WITH 9 TEXT FIGURES.

The ducts of the salivary glands have a peculiar interest because they represent the paths of development followed by the more highly organized secretory portions of the organ. Excepting possibly certain parts of the intralobular system comparatively little work has been done on the ducts of the human submaxillary gland. Owing to the important embryological relations of the ducts and the interest associated with their functions of providing a channel for the secretion, accurate information concerning their course and structure should be obtained. With this end in view, therefore, the following work was undertaken.

## METHODS.

Studies of the gross anatomy of the ducts and the gland were carried on in the dissecting rooms during the regular work of a class in systematic anatomy. The material was embalmed with a bichloride, glycerine and alcohol fluid and injected with red lead and starch. On the whole the cadavers were in very good condition so that the relations and structure of the tissues under investigation and those about them were very well preserved. Entirely outside of the value of the study itself, the pedagogical effect of demonstrating to a working class of students some of the simpler research methods is not to be underestimated. We are indebted to Schwalbe, Cunningham and Mall for the extensive use of dissecting-room material for the purposes of research.[1] The material for the corrosions on which this study of the ducts is largely based was likewise obtained from the cadavers. The submaxillary gland was carefully dissected from its bed with a portion of the D. submaxillaris and injected. Corrosions of the ducts can be easily obtained with the ordinary celloidin carriers, colored with chrome

[1] Bardeen: Bulletin of the Johns Hopkins Hospital, Vol. xii, 1901.

yellow, cinnabar, or Prussian blue. Prussian blue is the best pigment for this purpose as its dark color renders the smallest ramifications visible and its fine granulation often allows the mass to pass easily through the intralobular ducts into the alveoli themselves. When it is desired to inject only the sublobular or lobular ducts chrome yellow or cinnabar should be used, for such masses do not, as a rule, pass beyond these structures into the finer ducts. Celluloid colored by victoria blue is a good mass, its advantage lying in the fact that it can be kept in the air as a dry preparation without shrinkage and does not have to be preserved in glycerine like the celloidin injections. For these corrosions commercial celluloid dissolved in acetone can be used or the celluloid may be made by adding camphor and acetone to celloidin. Apparently the granular pigments do not give such good results with the celluloid mass for the corrosion is liable to crumble after the surrounding tissue has been destroyed. Both the celluloid and celloidin can be freed from the glandular tissue surrounding them by the pepsin hydrochloric digestion fluid or a more rapid destruction of the gland is easily effected by immersing the injected organ in commercial hydrochloric acid. Inasmuch as the ducts are small, the acid does not make the preparations too brittle to be handled. All of our injections have been prepared in this way rather than by the use of the more tedious pepsin method. The stereoscopic microscope proved to be of the greatest service in the study of the corrosions. By its use we can follow, owing to its deep field, the course of the finer branches accurately in three dimensions and get much sharper pictures of the relations of these structures than by the old flat field microscope.

By far the best way of showing ducts in relation to the frame-work of the glands is by a method devised by the writer[2] while working in the laboratory of Prof. Spalteholz in the Anatomical Institute of Leipzig. Small blocks of tissues are hardened in the graded alcohols, bichloride or Van Gehuchten's fluid, dehydrated and then repeatedly extracted with the (Soxhlet) apparatus and digested until all of the glandular elements are dissolved and nothing but the frame-work remains. Up to this point this is the method of piece digestion devised by Spalteholz[3] for the demonstration of connective tissue in sections. After the digestion is complete, the digested frame-work of the organ is then cleared in glycerine, creosote or xylol and is then ready for preliminary study. This block of tissue, owing to the fixation and hardening, retains

[2] Flint: Johns Hopkins Hospital Bulletin, Feb., 1902.
[3] Spalteholz: Arch. f. Anat. u. Phys., Suppl. Bd., 1897.

perfectly the form and relations of the original tissue. It is the delicate opaque skeleton of the original tissue formed by the connective tissue frame-work, and when viewed through the stereoscopic microscope, shows in three dimensions all of the normal relations of the frame-work to the original structures of the organ. Owing to the high diffraction of the fibrils many of the finest details of structure are brought out, as for example, the basement membranes of the alveoli, ducts, vessels, perilobular membranes, etc. When pieces of the submaxillary gland are digested and cleared in this way, the ducts and their accompanying vessels are shown beautifully, both in the interlobular spaces and as they enter the lobule and ramify in its substance.

After careful drawings have been made of these thick preparations in glycerine, they can be utilized for further study with the finer methods according to the original procedure of Spalteholz. When embedded in paraffin and cut in thin sections, they can be stained on the slide with iron hæmatoxylin. Numerous variations in the stains are, of course, possible although iron hæmatoxylin and aniline blue give by far the sharpest pictures. Beautiful specimens can be obtained by using celloidin as an embedding medium and cutting thick sections which are stained in an eight per cent solution of acid fuchsin. They are then washed rapidly in distilled water and the graded alcohols until the celloidin is decolorized, and finally cleared in creosote and mounted. These preparations show the fibrils distinctly for naturally the staining adds greatly to the clearness of the picture, but, at the same time, it is necessary to sacrifice some of the depth as the stained sections cannot be cut over a certain thickness, depending partially on the nature of the tissue and partly on the density of the meshwork.

For the study of the ducts in sections most of the ordinary procedures were employed. Several proved especially useful for this purpose, among which was the method of slide digestion perfected by Spalteholz and his pupils.[4] This consists, briefly, in mounting an alternate series of paraffin sections and digesting one with pancreatin, while the other is stained as a control. To complete this comparison the writer treated a third section by Weigert's elastic tissue method counterstained with picric acid, so as to have, side by side, successive sections prepared by three different methods instead of two. Hensen's modification of the Van Gieson stain[5] proved of value in the study of the connective tissue

[4] Spalteholz: loc. cit. Hoehl: Arch. f. Anat. u. Phys., Anat. Abtlg., 1897. Clark: Ibid., 1898.

[5] Hensen: Anat. Anzeiger., Bd. xv.

in sections, especially in the comparison with digested sections. Many other methods were used and modified as the exigencies of the research required.

## Gross Relations.

The Ductus submaxillaris joins the submaxillary gland with the Caruncula sublingualis. Its length varies between four and five cm., its diameter is between two and three mm. The duct first becomes visible as it emerges from the hilus of the gland which is situated usually near the central portion of the medial surface. From the hilus it runs downwards, inwards, and forwards, upon the external surface of the M. hypoglossus running between it and the M. mylohyoideus. After passing the M. hyoglossus it passes in its course between the Glandula sublingualis, the M. genioglossus and M. lingualis inferior. As it runs by the medial surface of the sublingual gland it is usually in intimate connection with the N. lingualis and A. sublingualis. It then terminates in the Caruncula sublingualis which opens into the mouth just at one side of the Frenulum linguae. The walls of the duct are rather thin when the diameter of its lumen is taken into consideration, but it is well provided with elastic and fibrous tunics as well as a few smooth muscle fibres. The contrast in the thickness of the walls of the D. submaxillaris and D. parotideus is at first sight rather surprising, especially as the former carries the thick viscid secretion of the submaxillary gland while the latter forms the channel through which the thin serous product of the parotid is poured into the mouth. When one considers, however, the fact that the duct of the parotid is relatively exposed as it lies covered simply by skin and fascia, this is not so surprising, for the submaxillary duct is well protected and sheltered by the numerous firmer structures forming its environment.

The Gl. submaxillaris lies in the Regio submaxillaris, adapting its form apparently to the shape of the space in which it lies. It is irregularly prismatic or triangular in shape with its large axis directed dorsoventrally, slightly downward and inward so that it lies parallel to the axis of the ramus of the mandible. Below it is covered by the cervical fascia and M. platysma. The V. facialis communis and sometimes the A. maxillaris externa passes over the inferior surface of the gland. Medialwards the Gl. submaxillaris rests upon the M. mylohyoideus, M. stylohyoideus, and M. hyoglossus, while lateralwards the ramus of the mandible forms its chief boundary. On the internal surface is the hilus where the D. submaxillaris leaves the gland. Often there is a posterior prolongation of the organ but this is usually poorly marked. A small lobe or prolongation, however, is usually observed passing beneath the M. mylohyoideus with the D. submaxillaris in rather intimate association with it. This portion may be completely free from the major part of the gland forming an aberrant lobe, the duct of which joins the D. submaxillaris at a point somewhat below the hilus.

In taking up the description of the course of the secretory channels within the organ it is perhaps best for the sake of clearness to begin with the main duct and then proceed through its complex ramifications to the alveoli, although this course is opposite that taken by the secretion. On the other hand from an embryological point of view, it is, of course, obvious that in adopting this method of description we follow the path taken by the gland in its development. In discussing the course of the ducts it will be necessary to refer, from time to time, to certain facts concerning their development, accordingly, at the outset, it may be well to recapitulate briefly certain details of the organogenesis of the submaxillary which are to form the substance of a later communciation. The first *anlage* consists of a spur from the epithelium of the mouth which marks the beginning of the duct. This *anlage* is a solid cylindrical column of cells which grows and finally begins to branch. The branching portion becomes encapsulated and indicates the primitive form of the organ as we know it in adult life. At this stage it is composed of a blastema of branching nucleated cells in which the growing ducts are embedded. The growth at this stage is chiefly apical and the branches of the simple little tree which later is transformed into the major ducts of the gland terminate in little buds or swellings that form the growing points at the apices. As the gland develops these simple cell columns divide and ramify and become more complex until, after giving rise to the ducts of the first order, interlobular, lobular and intercalary ducts, they produce finally the alveoli and secreting elements of the gland. In their growth, the ducts and their accompanying vessels are surrounded by strands of connective tissue which form later the interlobular spaces. At the time when the ramification has proceeded to a certain point, the growing ends become surrounded by a fine capsule or membrane which marks the initial formation of the lobule and its membrana limitans. This membrane is attached to the growing duct at the future site of the lobular hilus and forms the one firm point of attachment of the lobule. Within this membrane, the intralobular ducts and alveoli are developed. At first the lobules are comparatively free but later become, as they increase in size, closely packed together, forming the irregular polygonal shapes observed in adult life. It is in this way that the limiting membranes of adjacent lobules are pressed in close apposition, and yet, as a general rule, the attachment between them consists simply of a few fine fibrils of reticulum (Fig. 8). In its early stages, the organ in pigs, as a whole, is regularly symmetrical and the future ducts, marked by the growing columns of cells, branch with great regularity, the larger divisions alternately passing first to one side and then to the other of the gland. They can be followed with some distinctness in ordinary sections but in injected specimens better results are obtained when the gland is divided and viewed with the stereoscopic microscope which shows these relations in three dimensions. In the simplest forms the blood-vessels form a fine plexus about these growing columns of cells and, as they develop and ramify, the arteries and vessels supplying them follow the same line of growth so that we have an artery and veins developing with each branch of the duct.

It has been shown[6] that the intrinsic vessels of an organ indicate in general the paths along which the different parts of that organ have developed, a principle which is expressed in the following paraphrase of a well-known scientific aphorism, viz.: the angiology of an organ in a measure recapitulates its ontogeny. In the case of the submaxillary this principle obtains and the blood-vessels of the organ represent the lines of its development. Therefore, in injected preparations of the developing gland we can follow accurately the course of the ducts from the vessels that always accompany them. Were it essential, this relation of the blood-vessels to the ducts would afford another proof that the ducts themselves also form a record of the development of the gland. It follows, therefore, that the youngest parts of the organ are the terminals of the ducts or alveoli while the oldest portion is the main duct itself. It is also apparent that this relationship of the ducts and vessels gives rise to the invariable conditions observed in the interlobular spaces where an artery and its venæ comites accompany every duct. So constant and regular is this condition that these vessels may be justly termed the vasa comites of the ducts. In embryo pigs the Gl. submaxillaris in gross appearance is a small opalescent organ lying near the angle of the mandible covered by the developing platysma and fascia. At this stage it is not situated in a fossa, nor is it jammed up beneath the mandible. From the earliest period that it can be distinctly seen with the naked eye it is reniform in shape and perfectly symmetrical;

[6] Flint: Monograph on the Adrenal. Contributions to the Science of Medicine, dedicated to Dr. William H. Welch by his Pupils. Johns Hopkins Hospital Reports, Vol. ix, Baltimore, 1900.

the vessels and ducts enter the gland at the hilus. At this stage in its development the organ is encapsulated.

Before the duct of the human gland penetrates the hilus of the organ, it is often joined by a small duct, either from the aberrant lobes which so frequently occur or from the anterior prolongation of the

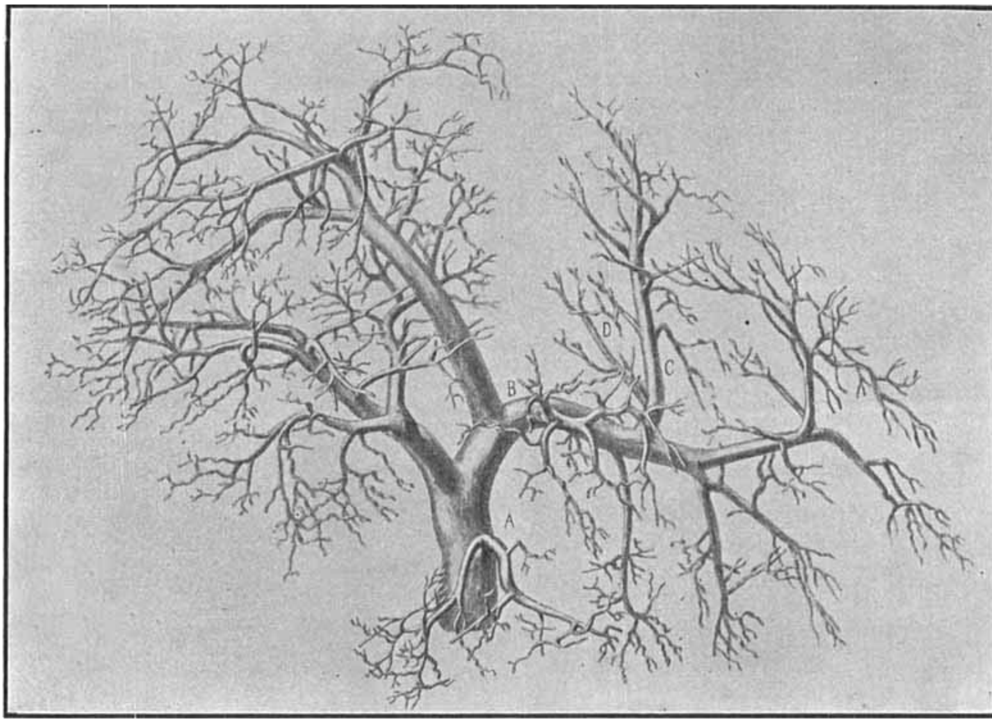


FIG. 1.—*Celloidin corrosion of the ducts of the human submaxillary gland.* Magnified 4 diameters. The Ductus submaxillaris is shown as the main trunk in this tree, giving off the primary branches just within the boundaries of the gland which are here roughly marked out by the terminal twigs. The secondary divisions are the interlobular ducts. These radiate from the central to the peripheral portion of the gland. The secondary branches of the interlobular ducts form the sublobular system. These divide once or twice and at this point the injection mass has usually stopped, although in a few places it has penetrated into the lobular ducts. The interlobular ducts may divide into one or two larger branches before exhausting themselves in the sublobular system. *A*, Ductus submaxillaris; *B*, primary ducts; *C*, interlobular ducts; *D*, sublobular ducts.

gland which extends with the duct between the M. hyoglossus and mylohyoid. The corrosions by means of which the ducts are studied look remarkably like miniature representations of certain species of trees, especially the California live oak. That this parallel is not fanciful can be shown by a glance at a corroded preparation of the human submaxillary, where Wharton's duct represents the trunk, the interlobular ducts the branches, the intralobular ducts the twigs, and the alveolar ampullæ the foliage. When the injections are incomplete (Fig. 1) they look like the naked limbs of the oak, but if the mass has passed into the alveoli the corrosion resembles that tree in full foliage. In the corrosion preparations the form of the gland is preserved by the tree as a whole, and these naturally vary in the same wide limits noted in the gross relations of the organ. When aberrant lobes or prolongations are present their ducts usually look like branches arising from the trunk of a tree some distance below the usual branching zone. The size of these portions varies a good deal, but in general they may be said to correspond to that part of the gland which is drained by a duct of the first order.

The submaxillary duct and its ramifications may be classified in the following general scheme, each subdivision representing one of its main divisions, which has, in general, fairly definite relations to the glandular units:

1. Ductus submaxillaris.
2. Primary ducts.
3. Interlobular ducts.
4. Sublobular ducts.
5. Lobular ducts.
6. Intralobular ducts. (Salivary tubes of Pflüger.)
7. Intercalåry ducts.
8. Alveolar ampullæ.

At the hilus there is a considerable amount of connective tissue through which the duct penetrates as it enters the gland. In most human submaxillaries the duct divides shortly after entering the hilus; in pigs, apparently, it always does. It is not uncommon, however, to observe in human glands instances where the main duct preserves its identity, penetrating directly through the substance of the gland and exhausting itself by manifold lateral branching instead of dividing into several chief primary divisions just after entering the hilus.

It is somewhat difficult to obtain the diameter of the duct between the hilus and papilla in corroded specimens owing to the nature of the material used since we employed for this purpose the glands removed from bodies in the dissecting room. The walls of the ducts had lost their tonicity and this, together with shrinkage of the celloidin during the digestion, rendered the corrosions unreliable as a means of determining accurately the caliber of the ducts. These data are naturally best obtained by direct measurements of the distended duct in fresh subjects. In a general way, however, the relations in size are well preserved, although one would hesitate to apply methods of accurate mensuration to them. Of course the ducts in all parts of the gland are under the same general conditions so that the effect of shrinkage in one part would be about commensurate with that in another. And even while we can assume that this method gives a general idea of the relative size of these structures, under no circumstances, however, would we be justified in drawing conclusions from material of this nature as to their exact caliber in life.

In general the method of branching appears to be dichotomous, although often unequally so. The diameter of the two branches after a division is usually unequal, a fact which is especially true of the larger divisions. The rule of dichotomy holds nevertheless throughout the entire secretory system, both intra- and extralobular, with the single exception of the intercalary ducts where three or even four ducts are often given off at a single node. The ultimate alveolar ampullæ, likewise, violate this law since three, four, or five of them always terminate the secretory system (Fig. 3).

The commonest distribution of the ducts is represented in Fig. 1, where the primary branches or ducts of the first order spread out irregularly from a short and twisted trunk radiating in various directions from the hilus. Since the Glandula submaxillaris is about three times as long as it is thick, the branching must be less in the plane of lesser than in the one of greater dimension. Except at the hilus the ducts run, in general, as far away from the capsule as the anatomical conditions which require the drainage of the entire organ will permit. In the human gland the primary ducts do not pass alternately to one and then the other side of the organ, as they do in embryo pigs, but arise rather irregularly from the main trunk. They correspond, however, to the primary divisions of the ducts in embryo pigs and if they had preserved the same regularity of distribution observed in the embryo they might perhaps be justly called lobar ducts. Owing, however, to the mechanics of development which crowd the gland into the small angle between the mandible and adjacent muscles the organ becomes distorted and its different portions have unequal opportunities for growth. Apparently these primary ducts have the same general caliber, although it is not uncommon to observe considerable variations in their diameter indicating that they drain unequal volumes of glandular substance. Their number is not constant but varies in different glands between three and six. In the cases observed by the author there have been, as a rule, three ducts of the first order.

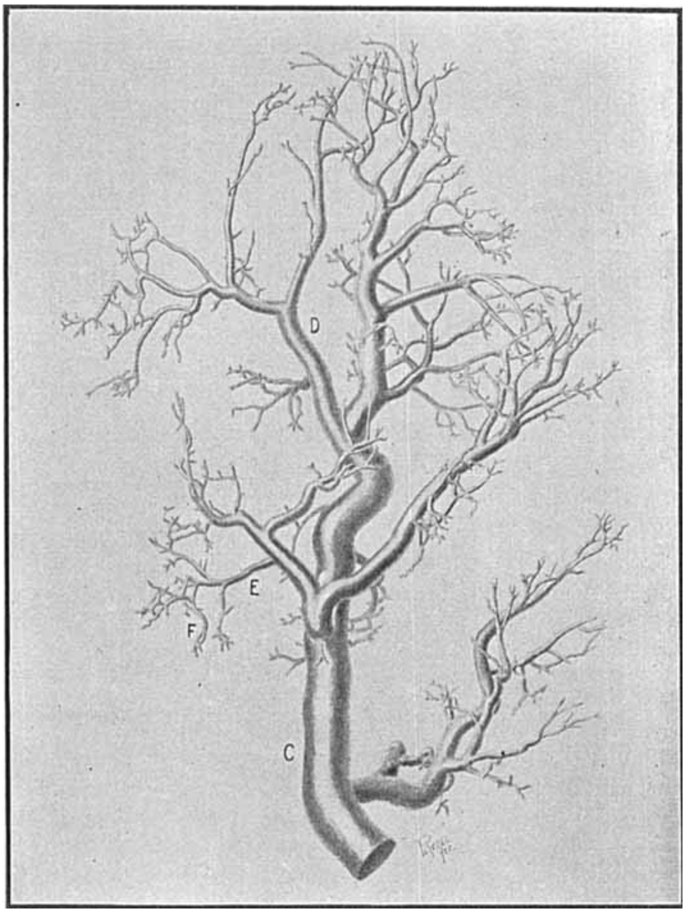


FIG. 2.—*Celloidin corrosion of an interlobular duct.* Magnified 12 diameters. The interlobular duct is shown taking a rather tortuous course and giving off sublobular ducts of the first and second order. From these the lobular ducts are derived and can be easily seen together with the larger portion of the intralobular system. The lobular ducts in proportion to their diameters appear rather long. *C*, interlobular duct; *D*, sublobular duct; *E*, lobular duct; *F*, intralobular duct.

From these main divisions arise the ducts of the second order which are usually termed the interlobular ducts. They are of large caliber, ramify extensively, and run for a considerable distance before giving off the individual branches. There is often considerable tortuosity observed in their course (Fig. 2). They run between the lobules embedded in the thick fasciculated connective tissue of the interlobular spaces and are accompanied by the vasa comites. From these occasional lobular ducts are derived. As a rule, however, they break up into the sublobular ducts which leave the interlobular ducts at sharp angles and ramify among the lobules. They are called sublobular because it is from them or their chief divisions that the great majority of lobular ducts are derived. The latter are proportionately longer than ducts in other parts of the system and pass without dividing through the hilus of the lobule to ramify in the substance of the lobule itself. The position of the lobular ducts in corrosions can be identified by comparing them with the ducts of the same nature in digested preparations and sections of injected glands, the size of the ducts as well as their course corresponding perfectly in preparations made by both methods. When viewed under the stereoscopic microscope the lobular ducts ramify through three or four divisions which often follow in such close succession that the general rule of dichotomy seems to be violated. the case, for two complete trunks can always Careful study, however, shows that this is not be found after a division has taken place although they may occur very close together. The division is rapid so that the terminal ducts are thoroughly distributed throughout the lobule. These intralobular ducts which are synonymous with the salivary tubes of Pflüger, pass towards the center of the lobules and then radiate towards the periphery without ever quite reaching it, owing to the layers of acini which are interposed between them and the limiting membrane.

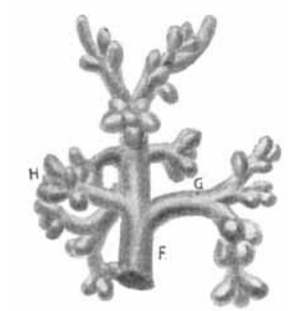


FIG. 3. *Celloidin corrosion of terminal ducts and alveolar ampullæ.* Magnified about 115 diameters. The main trunk in this preparation represents the end of one of the intralobular ducts which exhausts itself in giving off the intercalary branches. These may be divided once or twice and then terminate in the alveolar ampullæ which look like little ovoid or pear-shaped ends of the corrosions.

*F*—intralobular duct.
*G*—intercalary duct.
*H*—alveolar ampullæ.

When the terminal branches of the intralobular ducts are reached the law of dichotomy is often violated; branches occur more frequently and more abruptly, three or four sometimes arising at the same level. These divisions are the intracalary ducts which are usually about one-third the diameter of the terminal intralobular ducts in injected preparations. They run at obtuse angles from the ducts from which they spring. These intercalary ducts are of variable length and often branch, although they not infrequently end in ampullæ without giving rise to a single vessel of a similar nature, especially in the mucous parts of the gland.

At the ends of the intercalary ducts are the ampullæ of the alveoli in which they terminate. These are surrounded by the secreting epithelium of the alveolus and represent moulds of the spaces into which the secretion is poured from the cells before it passes into the intercalary ducts. They have constricted necks marking the termination of the ducts and the end of this portion of the secreting system. Beyond the constriction their greatest diameter may be twice as large as the duct from which they spring. In corrosions they (Fig. 3) appear like ovoid knob-like endings to the intercalary ducts occurring in groups or clusters. As a rule they are slightly longer than they are wide, occasional ampullæ, however, are much longer than others, showing that they must have been derived from longer alveoli. In Fig. 3 the two apical ampullæ represent alveoli of this nature. Apparently the number of these structures arising from an intercalary duct varies between three and six, four perhaps representing the average number. This means, of course, that four alveoli, on an average, empty into each of the termini of the intercalary ducts. Whether they represent primary reservoirs for the storage of the products of glandular metabolism before they are emptied into the ducts it is as yet impossible to say.

In the course of development of the submaxillary gland the growing ducts, as we have already seen, are accompanied by blood-vessels which maintain throughout life this close and intimate association. Since blood-vessels follow in general certain laws of ramification, each trunk of the same size in an organ tending to give off an equal number of branches, it is not unreasonable to assume that the ducts may perhaps obey some similar law. Blood-vessels, of course, are not in stable equilibrium but are continually subjected to progressive and regressive changes which depend upon certain well-known laws.[7] The caliber of the vessel, for example, depends on the velocity of the current within it and this, in turn, depends partly on the nature and number of its branches. So far as we know the cross-section of the ducts is not the resultant of the action of any mechanical factors like those influencing the progressive and regressive changes in vessels, although it is by no means certain that some such mechanical control is not exerted. But even while it is true that there is a general tendency for ducts of the

[7] Thoma's Untersuchungen über die Histogenese und Histomechanik des Gefäss-systems. Stuttgart, 1893.

same size to give rise to the same number of branches, this is by no means so definite and well marked as it is in the case of blood-vessels. In the submaxillary gland the following general quantitative relations are found in the successive ramifications of the ducts.

The Ductus Submaxillaris divides into
3 Primary Ducts which divide into
18 Interlobular Ducts which divide into
96 Sublobular Ducts which divide into
1500 Lobular Ducts.

Obviously a table of this nature must be interpreted liberally inasmuch as it indicates only the average scheme of division in a system which varies within wide limits. As an absolute standard it is worthless, its chief service being to indicate the general plan of ramification of the ducts, estimated from corrosion preparations of several glands. Since the lobules are always drained by a single duct we find from the above table that there must be approximately 1500 lobules in the entire submaxillary gland.

In the corrosions one is often struck by an apparent similarity between the ducts of the lobule and the ducts of the gland as a whole, the former appearing much like a miniature reproduction of the latter. When attention is called to this analogy it becomes immediately patent and may, indeed, be extended to many other features of the gland as we shall have occasion to show later. The duct enters the gland at the hilus; the lobular duct passes into the lobule through a similar portal. There is but one submaxillary duct to each gland; there is likewise but one lobular duct to each lobule. In the gland the ducts ramify through the central portion without ever reaching the capsule, keeping, indeed, as far away from it as the anatomical conditions which require the drainage of the whole gland will permit. In the lobule the intralobular ducts take the same course with reference to the Membrana limitans and and the drainage of the lobular alveoli. This analogy may be of more interest than importance. Its explanation affords no difficulty since the lobular and intralobular ducts are formed by the same laws of growth and mechanics of development which give rise to the larger ducts of the gland as a whole.

## The Ducts in Sections and Digested Preparations.

In preparations made by the method of piece digestion which have been cleared by glycerine, xyol or creosote, the form of the lobule, the frame-work, and particularly the distribution of the interlobular and intralobular ducts, can be easily seen. The relations of the ducts to these structures are likewise sharply defined so that one obtains by the use of the stereoscopic microscope the relations of the vascular and secretory units to the frame-work and the structures of the gland. In these specimens the interlobular septa and their relation to the capsule can be easily determined. The larger ducts and vessels in the interlobular septa are readily followed, owing to the difference in diffrac-


FIG. 4—*Piece digestion of dog's submaxillary.* Magnified 10 diameters. This specimen shows the sublobular interspaces and the passage of lobular ducts and connective tissue from the interspace into the lobule through its hilus. The relation of the membrana limitans to other lobules is shown as clearly in this specimen as in figure 8. The course of the intralobular ducts is plain as they pass through the fine supporting meshwork formed by the basement membranes of the alveoli. *A*, Sublobular interspace with artery, duct, and veins; *M*, Membrana limitans; *C*, Capsule.

tion between them and the frame-work of other portions of the organ. The ducts, vessels, and septa appear in these specimens, when viewed by transmitted light, considerably darker than the fine lobular framework in which they run and they can be easily distinguished from each other by their size. The ducts are considerably larger than either of the vasa comites which run in the same interspace. Embracing the group of vessels are fine fasciculated bands of connective tissue which form the interlobular spaces. These can be made out in digested specimens both by the position of the vessels and the darker areas which they produce as they pass between the lobules. Fig. 4 is a representation of the submaxillary of a dog prepared by this method. The ducts and vessels lie in a sublobular interspace embraced by the connective tissue which is seen in cross-section at the edge of the block of tissue. The larger duct in this space runs for only a short distance before entering the lobules and is, therefore, of the order of sublobular ducts. The lobular ducts which are given off from this branch pass through the hilus of the lobules carrying with them considerable connective tissue derived from the interspace from which they come (Figs. 4 and 5). After penetrating the lobule they run to the center of that structure and then begin to radiate towards its periphery. The intralobular ducts can be distinguished from the blood-vessels by their caliber and the delicacy of the walls. Isolated terminal branches are seen towards the periphery of the lobule, but in no instance does a duct ever seem to reach the limiting membrane, a layer of one or two alveoli always intervening. The frame-work within the lobule and its relation to the ducts is exquisitely shown in these preparations; the strands of connective tissue entering at the hilus, the fine delicate limiting membrane embracing it, and the basement membranes of the alveoli are all patent, the latter appearing like a delicate web throughout the whole lobule. This is firmly attached to the limiting membrane on the one hand where it forms a sort of mosaic, and to the walls of the ducts and vessels on the other, so that the support of these structures is given by the alveolar frame-work, and they are, as it were, swung in the meshwork of delicate reticulated basement membranes.

In ordinary sections, the Ductus submaxillaris is lined by a double layer of epithelial cells, the inner of which is irregularly columnar and has oval nuclei which stain deeply and show distinct gatherings of chromatin substance upon the linin filaments. These cells interdigitate with those of the outer layer which are more conical and polyhedral in shape, and are, as a rule, considerably smaller. The nuclei of the latter are smaller, somewhat more deeply stained and often more vesicular in shape. The two layers of epithelial cells rest upon the basement membrane of the duct which is immediately embraced by the fasciculated intertwining strands of white fibrous tissue and reticulum. Immediately external to the epithelial layer of basement membrane is a dense meshwork of elastic fibres which interlace with the fibres of reticulum and white fibrous tissue. The few smooth muscle fibres described by von

Kölliker can be seen in specimens stained by Van Gieson's method, and the lumina of the rich plexus of arterioles, venules and capillaries that surround the duct are often seen in cross-section. Ducts of the first order present no characteristic differences from those observed in the Ductus submaxillaris, except that the connective tissue which em-

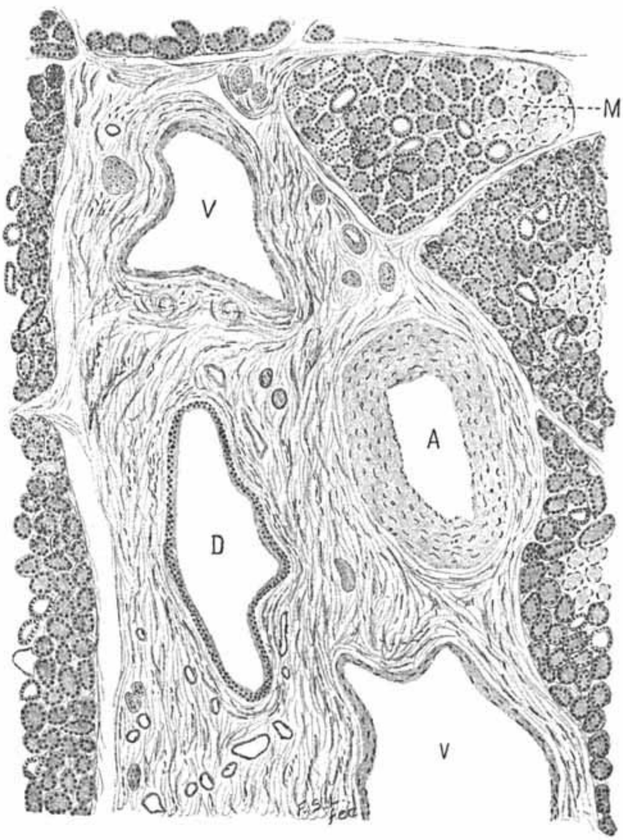


Fig. 5.—*Sections of a human submaxillary gland stained by Henson's modification of Van Gieson's stain.* Magnified about 85 diameters. This section shows one of the interlobular spaces with the duct and its vasa comites. Adjacent lobules show the mucous and serous portions of the gland. *D*, Interlobular duct; *V*, Interlobular vein; *M*, Mucous alveoli; *A*, Interlobular artery.

braces them is far richer owing to the fact that it now carries not only the excretory channels and the blood-vessels of the organ, but, in addition, forms the main interlobular support of the gland as a whole. This connective tissue is continuous with that which enters the gland at the hilus and forms the main support of the glandular lobules. The interlobular spaces in the submaxillary gland may be compared to those in the liver, except that in the case of the former we have usually two veins accompanying the duct instead of the single branch of the portal vein which we are accustomed to see in the liver. The interlobular

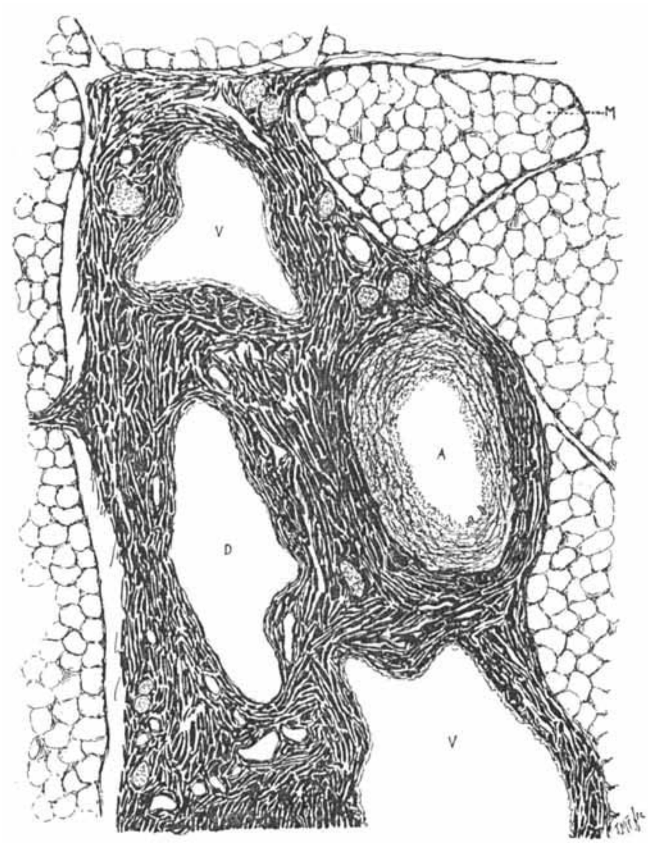


FIG. 6.—*Slide digestion after Spalteholz.* Magnified about 85 diameters. The section is the one just following that shown in figure 5. All of the cells have been removed from the specimen which shows fasciculi in the interlobular spaces and the basement membranes about the alveoli. It is at once apparent that without the control specimen it would be impossible to distinguish the sections of the intralobular ducts from the alveoli. The basement membranes of both structures have practically the same arrangement. *D*, Interlobular duct; *A*, Interlobular artery; *V*, Interlobular vein; *M*, Mucous alveoli.

ducts (Fig. 5) like the other main channels are lined by two layers of epithelial cells which possess all the chief characteristics of those we have just described in ducts of a lower order. They also rest on the basement membranes. In preparations that have been digested on a slide (Fig. 6) this basement membrane can be distinguished at the inner edge of the lumen of the duct where it appears as a delicate irregular line. The slight clear area just outside of the basement membrane is caused by the spaces left by the elastic tissue, the fibres of which have been entirely dissolved from the specimens by the action of the enzyme. The connective tissue embracing the duct is now distinctly fasciculated and arranged so that its bundles seem, at the same time, to give the greatest strength and elasticity to that part of the duct. Numerous connective tissue corpuscles, endothelial cells lining the lymph spaces and capillaries, can be seen in the frame-work just about the interlobular ducts, the vasa comites cut in cross-section are also evident. Specimens stained with Weigert's elastic tissue method (Fig. 7) show external to the basement membrane, a dense, deeply-staining, elastic membrane, composed of interlacing elastic fibres which entirely embraces the duct and appears, in these specimens, like an irregular black line just external to the epithelium. Numerous elastic fibres having a concentric lamellar arrangement are found outside of the main elastic membrane. Some fibres connect the different concentric elastic lamellæ, while others, variously arranged, appear to be extensively distributed throughout the entire interspace. Ducts of the next higher order, namely the sublobular ducts (Figs. 4 and 8), are likewise embraced by the connective tissue of the sublobular spaces, but this is now greatly diminished in amount. The sublobular ducts like those of the lower orders are lined by a double layer of epithelial cells. The cells of the inner columnar layer are much lower than those of the corresponding layer of interlobular ducts or ducts of the first order. The nuclei are more nearly spherical, the cytoplasm is somewhat diminished in quantity and appears slightly more granular. These cells are likewise slightly smaller and more compact than those of the corresponding layer of the larger ducts, the basement membranes are clearly marked and the connective tissue has the same characteristic fasciculated appearance noted in the larger interspaces, except that the fasciculi are much smaller and more compactly arranged. Connective tissue cells, endothelial cells and blood-vessels are also found in these spaces bearing ostensibly the same relation to the ducts and connective tissue which we have observed about the larger branches.

The elastica of the sublobular ducts is very well marked, forming a thick mesh-work of anastomosing and interlacing fibrils lying just beneath the membrana propria. As in the larger ducts there is the same concentric arrangement of the elastic lamellæ, the latter alternating with layers made of white fibrous tissue and reticulum with numerous coarse elastic fibres running in between the elastic tissue bundles. In the meshes of the elastica are found numerous bundles of ordinary fibrous tissue so that in digested specimens the position of the elastica,

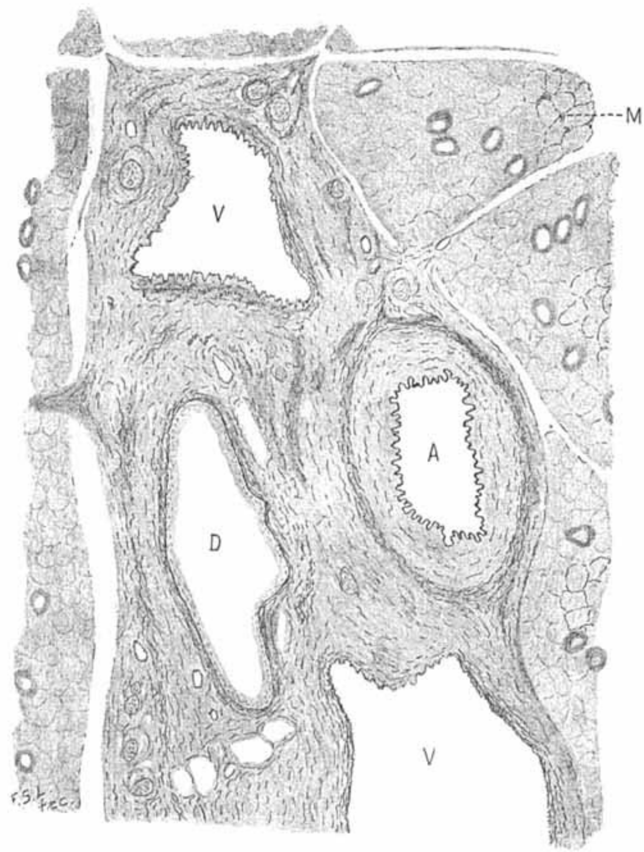


FIG. 7.—*Section preceding the one shown in figure* 5.—*Stained by a modified Weigert's elastic stain.* Magnified about 85 diameters. The elastic membrane, the concentric lamellæ about the interlobular duct are clearly shown together with the elastic fibres scattered throughout the interlobular space. The characteristic arrangement of the fibres about the blood-vessels can also be noted. In comparing this figure with the preceding one the mucous alveoli are seen to be surrounded by a delicate elastic membrane while only occasional fibrils are found about either the serous alveoli or the intralobular ducts. *D*, Intralobular duct; *V*, Intralobular vein; *A*, Intralobular artery; *M*, Mucous alveoli.

even though it has been dissolved by the enzymes, is indicated by the fact that the frame-work is more open at the points previously occupied by the elastic fibres.

As the duct enters the hilus of the lobule (Fig. 8) a considerable portion of the sublobular connective tissue is carried in with it, a relation between the lobular duct and lobule similar to that observed between the Ductus submaxillaris and the gland as a whole. The connective tissue which enters the lobule at this point, is continuous with that of the sublobular space from which it springs and possesses ostensibly the same characteristics and relations. It may be observed that the spaces containing the sublobular ducts are the points of origin of several lobules which may be seen in sections and piece digestions as arising from these centers (Figs. 4 and 8). That is to say, the hilus of the lobule is attached at these points and this intimate association with the sublobular interspaces is the only firm point of union between the lobules and the glandular frame-work, inasmuch as the fibrils connecting adjacent limiting membranes are, as a rule, too scant and delicate to have an extensive supporting function (Figs. 5 and 8). This is a point of considerable importance when the origin of the lobule in the development of the gland is considered. As soon as the duct is within the lobule the same relations observed in corrosions and digestions are seen in ordinary sections, namely that the ducts which are cut in various directions, transversely, longitudinally and obliquely, are observed to lie in the central portions of the lobule away from the membrana limitans. Indeed, it is only very rarely that sections of the ducts are seen nearer the perilobular membranes (Fig. 8) than the

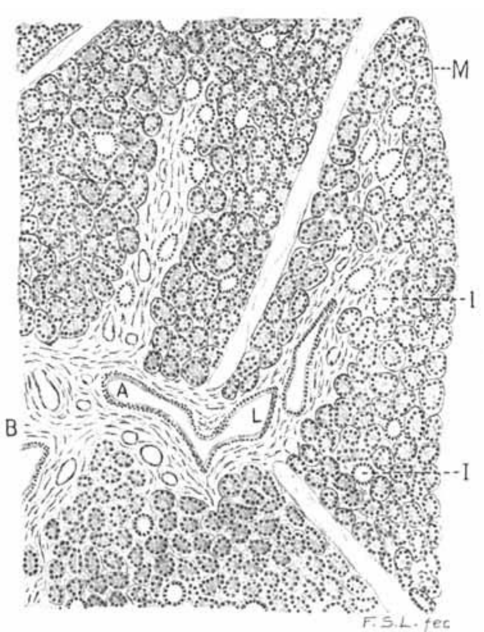


FIG. 8.—*Lobule of the human submaxillary gland, showing the hilus and the lobular ducts.* Magnified about 85 diameters. Same stain as Fig. 5. The attachment of the lobule to the sublobular interspace is clearly shown and the arrangement of the connective tissue as it enters the lobule with the lobular duct, is evident. The membrana limitans has very few connections with those of the adjacent lobules, the main attachment of the lobule being the portion at the hilus. The distribution of the intralobular ducts in the central portion of the lobules away from the membrana limitans is well represented. *A*, Sublobular duct; *B*, Sublobular interspace; *M*, Membrana limitans; *L*, Lobular duct at hilus of lobule; *I*, Intralobular duct.

width of two alveoli. Sometimes they may approach as near as one alveolus but an instance of a duct lying adjacent to the limiting membrane is almost impossible to find, except at the hilus, where the lobular duct enters the lobule. Once in the lobule the duct loses its double layer of epithelium and is lined from this point with a single layer of short columnar or cubical cells which are characteristic of the ducts in this region. These intralobular ducts are known throughout the literature as the "salivary tubes of Pflüger" who believed that they were concerned in the metabolic activities of the gland and took an active part in the phenomena of secretion. These cells have oval or vesicular nuclei which are situated about the center of the cells. As a rule they take the stain somewhat more deeply than the nuclei of the epithelium in the extralobular ducts. The portion of the cell towards the lumen of the duct is composed of granular cytoplasm which stains deeply with the ordinary acid contrast dyes, such as congo red, eosin, or the picric acid element of the Van Gieson stain. The pole of the cell external to the nucleus shows a characteristic appearance of longitudinal striations which run from the central portion just below the nucleus to the end of the cell near the basement membrane. In cells that have been isolated from the ducts the portion of the cytoplasm occupied by these striations splits into little staves which often spread out much like the sticks of a fan. Protoplasmic bridges have been described running between the individual filaments composing these striations.

As we have seen from the corrosions, the intercalary ducts form the termination of the intralobular ducts and connect them with the alveoli. They are seen readily in sections where they appear when undistended only about one-third of the diameter of the intralobular ducts. The epithelium of these structures changes suddenly from the striated cubical cells and is composed of rather long, flattened epithelium cells with their major axis running parallel to the axis of the duct. The nuclei are elongated, less deeply staining than the nuclei of the cells in ducts of the next lower order. The cytoplasm is neither so rich in quantity nor does it have the same affinity for the acid dyes that we have observed in the cells of the intralobular ducts. The boundaries of the cells, moreover, are somewhat obscured. When cut in cross-section the lining cells of these ducts appear as flattened cuboidal epithelial elements. There is little elastic tissue about either the lobular or intralobular or intercalary ducts, only an occasional fibril can be made out surrounding them. The regular elastic membranes described in the extralobular system cease shortly after the ducts become intralobular. Sometimes, however, they may be observed following the lobular ducts for some little distance into the lobule, but these cases are exceptional. Both the interlobular and intercalary ducts are provided with basement membranes which differ so little from the membranæ propriæ of the acini that it is usually necessary to orient them in digested specimens in order to distinguish ducts from alveoli (Fig. 6). These basement membranes consist of a delicate network of interlacing fibrils of reticulum which appear in sections cut tangentially to the membrane as a cross-hatch or mesh-work of interlacing fibrils which are only visible with the immersion lens. When viewed with the lower powers the membrana propria usually appears practically homogeneous.

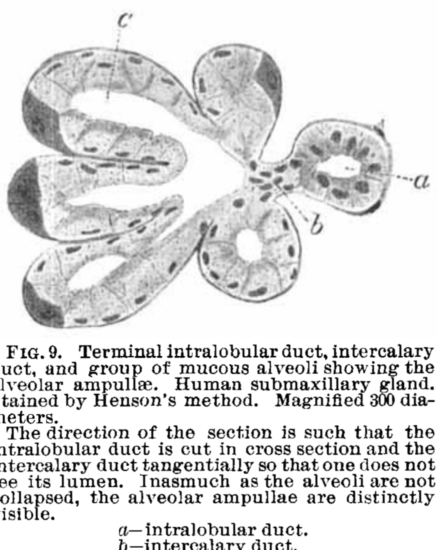


FIG. 9. Terminal intralobular duct, intercalary duct, and group of mucous alveoli showing the alveolar ampullæ. Human submaxillary gland. Stained by Henson's method. Magnified 300 diameters.
The direction of the section is such that the intralobular duct is cut in cross section and the intercalary duct tangentially so that one does not see its lumen. Inasmuch as the alveoli are not collapsed, the alveolar ampullae are distinctly visible.

*a*—intralobular duct.
*b*—intercalary duct.
*c*—alveolar ampulla.

At the point of termination of the intercalary ducts a slight constriction is noted, in corrosions, just as they widen into the ampullæ. In sections the flattened epithelium at this point changes abruptly into the regular epithelium of the alveolus. In sections cut in the right plane it is possible not only to see the intercalary duct terminating in the alveoli but to make out the little ovoid spaces forming the ampullæ as well (Fig. 9). As a rule, however, the inner borders of the cells of the alveolar epithelium are in close approximation so that in the collapsed state of the alveolus only a small chink is left between them. About the serous alveoli there are only a few occasional elastic fibres; about the mucous alveoli, however, these fibres are numerous, as has been shown by Livini.[8] Their nature and relations, however, Livini did not describe. It appears that these fibres, which under the lower power of the lens look homogeneous, are in reality very delicate elastic membranes made up of an intertwining and interlacing mesh-work of fibres which have a reticulated appearance similar to that of the regular membrana propria. This elastic membrane appears to lie outside of the regular membrana propria of the mucous alveoli. As Livini pointed

[8] Livini: Monitore Zoologico Italiano, vol. x, 1899.

out, the thick, ropy, tenacious secretion of the mucous alveoli is partly expelled from the alveolus into the ducts by the assistance of the mechanical action of this elastic membrane. He did not suggest, however, the interesting corollary that, in the secretion of this substance, the elastic tension of this same mebrane must be overcome, which means that secretion in the mucous alveoli must at least be accomplished under a sufficient pressure to overcome this elastic tension. It is, of course, well known that secretion takes place under a pressure higher than that of the blood, and this, together with the recent work which seems to indicate that the osmotic pressure within the cell is twenty times greater than the blood pressure, would explain how the stretching of this elastic membrane could be easily accomplished during the activity of the glandular cells.

There are several characteristic staining reactions of the duct epithelium which can be observed with more or less distinctness from the Ductus submaxillaris to the alveoli. The duct cells take the ordinary contrast stains deeply. They exhibit especially a peculiar affinity for congo red. Accordingly as in the case of demilunes of Gianuzzi, congo red may almost be considered as the special selective stain for the duct epithelium. When elastic tissue preparations are made and contrasted with picric acid the epithelial cells of both intra- and extralobular ducts take a rather yellowish-green tint, while the rest of the epithelium is only a pale yellow (Fig. 7). In Van Gieson preparations or modifications of this method the duct epithelium stains a pale yellow while the serous alveoli are a deep purple and the mucous alveoli stain a dark blue.

## Discussion of the Literature.

Comparatively little work has been done upon the ducts of the salivary glands alone, most of the research appearing as collateral study in course of work upon other portions of the organs. Von Kölliker[9] states that the ducts of the salivary glands are made up of a single layer of cylindrical epithelium which is surrounded by connective tissue and some elastic fibres. Those about the D. submaxillaris according to Kölliker are arranged in the form of a double membrane. As we have seen, however, there is just one well-marked elastic membrane located external to the membrana propria and several concentric, less regularly arranged lamellæ situated external to the regular elastic tunic. It was one of these, no doubt, which von Kölliker believed was the second elastic sheath. He states, moreover, that this double arrangement of

[9] Kölliker: Gewebelehre. Bd. ii, Leipzig, 1852.

the elastic fibres was limited solely to the main duct, whereas by means of improved elastic tissue stains we can show that these concentrically arranged elastic fibrils embrace ducts of all orders as high as those which drain the lobules.

According to the Tobiens[10] the ducts of the glands in general consist of connective tissue. Those of the salivary glands in addition possess muscle fibres, which are arranged in an outer longitudinal and an inner circular layer. All the ducts of man, horse, dog, and cat have, according to this investigator, elastic fibres which vary inversely with the amount of muscle present. The arrangement of the fibres is inconstant, but there is usually an inner circular layer, while in man spirally arranged fibrils situated outside of this layer can occasionally be found. The results of Tobiens' work, however, has never been confirmed.

Krause[11] describes the ducts as consisting of fine-meshed connective tissue with numerous longitudinal or transversely-running elastic fibres. With the exception of Wharton's duct, muscle fibres do not occur in the walls of the submaxillary ducts. Previous to the work of Henle[12] the epithelium of the Ductus submaxillaris has always been described with a single layer of epithelium. He states definitely, however, that the epithelial lining of Wharton's duct is made up of a double row of cells. This observation has now been shown to be true of all the ducts of the extralobular system as well.

Von Ebner[13] supports the work of Pflüger on the structure and nature of the salivary tubes and describes, for the first time, the intercalary ducts. These, he states, are clothed by cubical epithelium and form that portion of the excretory system between the alveoli and the salivary tubes of Pflüger.

This fact was emphasized by Klein[14] and Heidenhain.[15] Klein described the epithelium of the ducts of the human submaxillary as consisting of an inner layer of cylindrical cells with long nuclei and a deeper layer of small cells with oval nuclei. In his later paper Klein goes extensively into the origin and relation of the ducts. Among other things he states that the amount of connective tissue supporting

[10] Tobiens: De glandularum ductibus efferentibus ratione imprimis habita te; ae muscularis. Inaug. Diss. Dorpat, 1853. Cited by Oppel.

[11] Krause: Zeit. f. rat. Med. Bd. 21, 1864.

[12] Henle: Eingeweidelehre, 1871.

[13] Von Ebner: Arch. f. mik. Anat., Bd. VIII, 1872.

[14] Klein: Quar. Jour. of Mic. Science, N. S., vol. XIX, 1879.
Klein: Quar. Jour. of Mic. Science,, vol. XXII, 1882.

[15] Heidenhain: Hermann's Handbuch d. Physiologie, Bd. V, 1880.

the interlobular ducts and vessels is subject to considerable variation in different glands, but in all instances this connective tissue is proportionate to that penetrating into the interior of the lobules with the chief ducts and vessels. In sections of the submaxillary of man the connective tissue around the larger ducts and vessels appears to be of the same nature as in the organs where the fibrous tissue is arranged in continuous and compact masses, that is to say groups, bundles, or trabeculæ of fibrous tissue running in various directions are seen cut at various angles. Between these fasciculi are the interfascicular spaces more or less dilated according to the method of hardening. Among the connective tissue fibrils Klein found branched cells, plasma cells of Waldeyer, and some *Mastzellen* of Ehrlich. The important point is that the groups or bundles are arranged into definite plates which vary greatly in breadth and thickness. These Klein calls the fasicle plates, each of which is composed of a number of fasciculi or bundles of connective tissue fibrils which are continued into the lobule in company with the lobular ducts. The interlobular ducts in most glands, according to Klein, are lined by a double layer of cells, the inner of which are cylindrical and the outer, next to the membrana propria, conical. The cytoplasm of these cells shows occasionally a tendency to fibrillation similar to the striations observed by Henle and Pflüger in the intralobular ducts. This observation, however, has not been repeated by other investigators nor is supported by the preparations used in this study. The intralobular ducts are lined by a single layer of columnar cells, showing the characteristic fibrillations which are joined by short lateral branchlets, and, therefore, converted into reticulum. Distinct from these are the spindle-shaped or staff-shaped cells which are in communication with the membrana propria and extend from this structure up between the epithelial cells, and in some cases, form a sort of inner membrane within the lumen. Klein states that these cells are particularly well marked in the parotid gland of guinea-pigs. No other investigator, however, has described their existence nor have they been found in the ducts of the human submaxillary. As the intralobular ducts pass over into the intercalary portion there is a distinct shorter portion which Klein calls the neck. This is characterized by the lumen and the whole breadth of the salivary tube becoming here suddenly smaller. In the submaxillary of the pig Klein says there is no intercalary portion, in the submaxillary of man he finds in the serous portions a short neck passing over into a long, fine, intermediary duct, while in the mucous parts the neck terminates directly in the alveoli.

Kultschultzky[16] describes in the epithelium of the intralobular ducts of the submaxillary of the hedge-hog three distinct cytoplasmic zones, an inner mucous zone, a protoplasmic zone, and a rodded zone next to the membrana propria. In the human gland three zones can be distinctly seen, but whether the deeply-staining portion adjacent to the lumen is due to a mucous zone has not yet been definitely settled.

Toldt[17] divided the excretory system into three portions, branches extending from the hilus of the gland to the points where they enter the lobule, branches given off within the lobule, and finally the so-called intercalary ducts connecting the alveoli with Pflüger's salivary tubes. These ducts, according to Toldt, do not have the same arrangement in all glands and may even vary in the mucous and serous alveoli of the same gland. Toldt first called the attention to the fact that the nature of the division of the ducts is dichotomous and that this plan occurs both within and without the lobule.

According to Krause,[18] the height of the epithelium depends on the diameter of the duct, the one varying directly with the other. He shows also in one of the figures, viz., Fig. 7, an ampulla within the alveolus but does not seem to recognize its importance as a definite part in the secretory system. In the schema given in Fig. 10, Krause also represents long serous alveoli given off from the intercalary ducts; the regularity of the ovoid ampullæ found in corrosion preparations shows that the alveoli of both mucous and serous portions possesses also this same general shape, with perhaps a more marked constriction at the end where they rise from the intercalary ducts. This fact is also emphasized by the work of Maziarski,[19] who has used in two splendid researches on the classification and structure of different glands, Born's wax-plate method for the reconstruction of their terminal ducts and alveoli. Among other glands, both mucous and serous portions of the submaxillary were studied by this investigator. The results show that the salivary tubes or intralobular ducts in the serous parts of the gland break up after a short course into the intercalary ducts. These subdivide again until they terminate finally in the alveoli. The alveoli are slightly oval or pear-shaped and look like a bunch of grapes hanging on a stem. In the mucous portions of the gland the intralobular ducts seem larger than the serous parts. The intercalary portion which is also

[16] Kultschultzky: Zeit. f. Wiss. Zool., XLI, 1885.

[17] Toldt: Gewebelehre, Stuttgart, 1888.

[18] Krause: Arch. f. Mik. Anat., Bd. XLV, 1895. Bd. XLIX, 1897.

[19] Maziarski: Bull. Internat. de l'Acad. d. Scien. de Cracovie, 1900. Anat. Hefte, Bd. XVIII, Heft I, 1901.

smaller forms, according to Maziarski, the duct for the whole group of alveoli.

If one were to take a piece of the corrosion, as for example, Fig. 3, and clothe different portions with the epithelium which they normally possess, a picture would be obtained in this way almost identical with that given by Maziarski, except that owing to the regular distension of the system with the injection mass the form in this case would be somewhat more regular than that observed in Maziarski's reconstruction. The latter did not recognize the ampullæ within the alveoli as they were collapsed by the fixation of the tissue, and therefore, are not rendered patent except, perhaps, in exceptional cases.

In conclusion, I wish to express my great indebtedness to Dr. Revell, of the Department of Anatomy of the University of Chicago, for the drawings of the corrosions.