

longer foveolae and shorter necks. They are as follows, taken from glands of the middle of the greater curvature of the stomach:

Thickness of tunica mucosa	1.200 to 1.320 mm
Combined length of foveolae and collecting duct.....	.358 to .539 "
Neck of gland.....	.147 to .220 "
Body of gland414 to .526 "

The differences between these two sets of measurements possibly indicate that there is considerable individual variation in the relative lengths of the foveolae and the necks of the glands.

The fact that the fundus glands of the stomach are composed of several kinds of cells was discovered in 1850 by von Kölliker, who described them as composed of very large mononucleated cells, located immediately beneath the membrana propria, and of smaller rounded cells which formed a complete tube around the very narrow lumen. This discovery, however, attracted little attention from histologists, and even von Kölliker himself failed to mention it in the subsequent editions of his text-book. The two kinds of cells were subsequently rediscovered in 1870, independently of one another, by Heidenhain and Rollett. The former called the chief cells and parietal cells respectively *Hauptzellen* and *Belegzellen*. By Rollett the chief cells were called "*adelomorphe Zellen*," the parietal cells, "*delomorphe Zellen*."

The descriptions of Heidenhain and Rollett differed in some important respects. The former described the neck of the gland as being composed of both chief and parietal cells, and mentioned the occasional occurrence of parietal cells under the cylindrical epithelium. Rollett denied both the existence of chief cells in the neck of the gland, which he supposed to be wholly composed of parietal

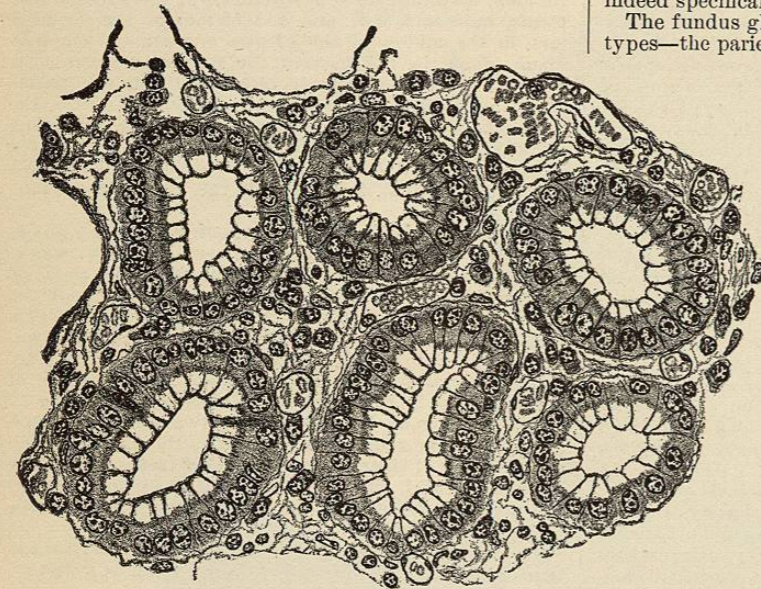


FIG. 4501.—Section Cut Parallel to the Surface of the Mucous Membrane of the Greater Curvature of the Human Stomach, Across Six Foveolae Gastricae, showing the Type of the Epithelium and the Tissue of the Lamina Propria Mucosae. Note the large number of plasma cells in the latter. × 394.

cells, and the occurrence of the latter in the foveolae. The researches of subsequent investigators, in particular those of Stöhr, have amply sustained Heidenhain in both these respects. In 1892 Bizzozero called attention to the

fact that the chief cells in the neck of the gland differed somewhat from those in the body of the gland. The question as to the nature of these cells has since been investigated by Oppel, Bensley, Zimmermann, Cade, and

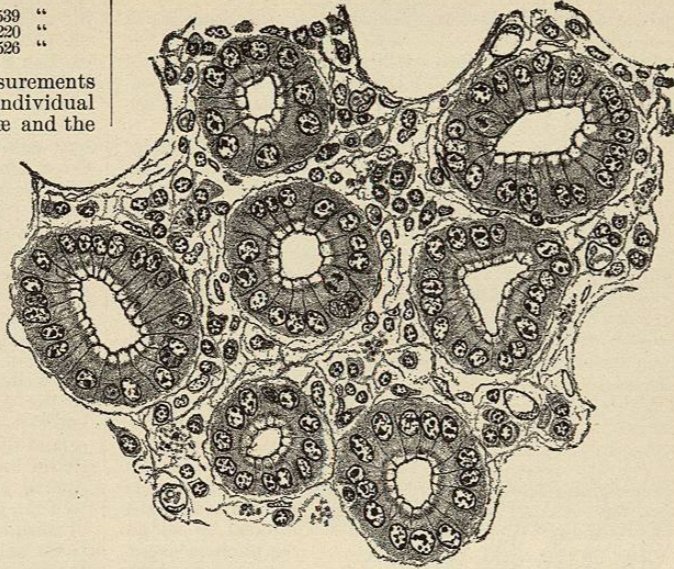


FIG. 4502.—Section Across the Foveolae Near their Outer Ends. Note the smaller size of the foveolae as compared with Fig. 4501; the smaller mucigenous border (theca) of the epithelial cells; the mitoses; and the larger amount of interglandular tissue. × 394.

others, and it has been shown that the transition which Bizzozero supposed to exist between the chief cells of the neck of the gland and those of the body of the gland does not occur, and that the two kinds of chief cells are indeed specifically different.

The fundus gland is composed of cells of three distinct types—the parietal cells, large, ovoid elements projecting on the outside; the mucous cells of the neck of the gland (*Halshauptzellen* of Oppel); and the pepsin-forming chief cells of the body of the gland (*Grundhauptzellen* of Oppel).

In the body of the gland, the large, wedge-shaped or cuboidal chief cells form an almost continuous lining for the narrow lumen, the large ovoid parietal cells being displaced to the periphery of the gland away from the lumen, with which they are only connected by narrow ductlets which pass between the adjacent surfaces of the chief cells.

In sections of fresh mucous membrane, mounted in an indifferent fluid (aqueous humor or blood serum), the portions of the chief cells of the body of the gland which border the lumen are seen to be occupied by closely packed minute refractive granules. These granules have been shown by Langley in a number of mammals and lower vertebrates to diminish in number during secretory activity and to accumulate during rest. Langley has also shown that the amount of pepsin which may be extracted from the mucous membrane is proportional to the extent of this superficial granule-filled zone of the chief cells. The granules are therefore composed of the antecedent substance of the enzyme, and are called zymogen granules. The zymogen granules in the gastric mucosa of man are exceedingly diffi-

cult to preserve, and for this reason are usually not visible in stained sections. In material fixed in alcohol or in aqueous solutions of mercuric chloride they have, as a rule, completely disappeared. They may be retained by fixation of the tissue in alcoholic solutions of mercuric chloride or in solutions containing four per cent. of formaldehyde.

In sections of tissue fixed by mercuric chloride in alcohol and stained in hæmatoxylin, or, better, in toluidine blue, the chief cell of the body of the gland exhibits two well-defined zones—a deeply stained proximal zone containing the nucleus, and a pale distal zone bordering the lumen. The relative sizes of these two zones depend on the physiological condition of the cell, the clear zone being larger in a resting cell, smaller in a cell which has been actively secreting for several hours. The cytoplasm of the basal zone stains intensely in nuclear dyes such as hæmatoxylin, toluidine-blue, thionin, methylene-blue, etc., and exhibits an indistinct radial striation, which has been interpreted by some observers as due to the presence in the cytoplasm of groups of parallel filaments (the basal filaments of Solger). The intense staining of the basal zone has been shown by the writer to be due to the presence in it of substances chemically similar to the chromatin of the nucleus. This may be shown by the employment of Macallum's microchemical tests for iron and phosphorus, both of which give distinct positive reactions, quite as intense as those given by the nuclear chromatin. There is a reciprocal relation between the amount of these substances and the number of zymogen granules bordering the lumen of the gland, the latter being formed apparently in part at the expense

of the former. These substances, on the presence of which depends the deep staining character of the basal zone, may therefore be termed prozymogens. The amount of prozymogen and of zymogen present in any cell depends on the phase of physiological activity in which it happens to be, and on the specific secretory equilibrium of the cell. Macallum has shown in the pancreatic cell, and Carlier in the cells of the gastric glands of Triton, that the increase of prozymogen in the basal cytoplasm is accompanied by an exhaustion of the nuclear chromatin, indicating an actual participation of the latter in the secretory metabolism of the cell.

The transparent distal zone of the chief cells of the body of the gland, that is, the zone that is next the lumen of the gland, exhibits a finely reticular structure, the meshes of the network being of wonderful regularity and corresponding in size to the zymogen granules observable in the living cell. This reticular appearance has been interpreted by Théohari and others as due to the presence of a true cytoplasmic reticulum or spongioplasm. The more probable explanation is that the cytoplasm of the portion of the cell nearest the lumen contains innumerable small granules of zymogen, each granule enclosed in a space separated from the neighboring spaces by the continuous cytoplasm. In sections stained in alum hæmatoxylin and eosin or in toluidine-blue,

the granules remain unstained and the spaces they occupy appear as tiny vacuoles, so closely aggregated that the portion of the cell in which they occur appears reticulated. The correspondence between the granules and the meshes of the cytoplasmic network may be demonstrated by staining sections of material fixed fresh in formalin or in alcoholic solution of mercuric chloride, in iron alum hæmatoxylin, or in neutral gentian. By these methods the zymogen granules are intensely stained, and it may be readily seen that each granule is enclosed in a mesh of the network.

The nucleus of the chief cell of the body of the gland is located at the junction of the two zones, is spherical in outline, and possesses one or two oxyphile nucleoli and a well-defined chromatin network.

It has been shown by the writer and confirmed by Cade that the chief cells of the neck of the gland differ in several important points from those of the body of the gland. These cells lack both prozymogens (there is no indication of basal filaments in them) and zymogen granules. In the living gland the contrast between the two portions of the gland is very striking, owing to the fact that the zymogen granules are entirely confined to the body of the gland.

The neck chief cells resemble very closely the mucous cells from salivary glands. For the most part they appear triangular when seen in longitudinal sections of the gland, the broad base of the triangle directed toward the lumen, the narrow apex toward the outside, where the cells are crowded by the presence of the parietal cells. The nucleus is located in the proximal attached end of the cell and is spherical, oval, or crescentic in outline, ac-

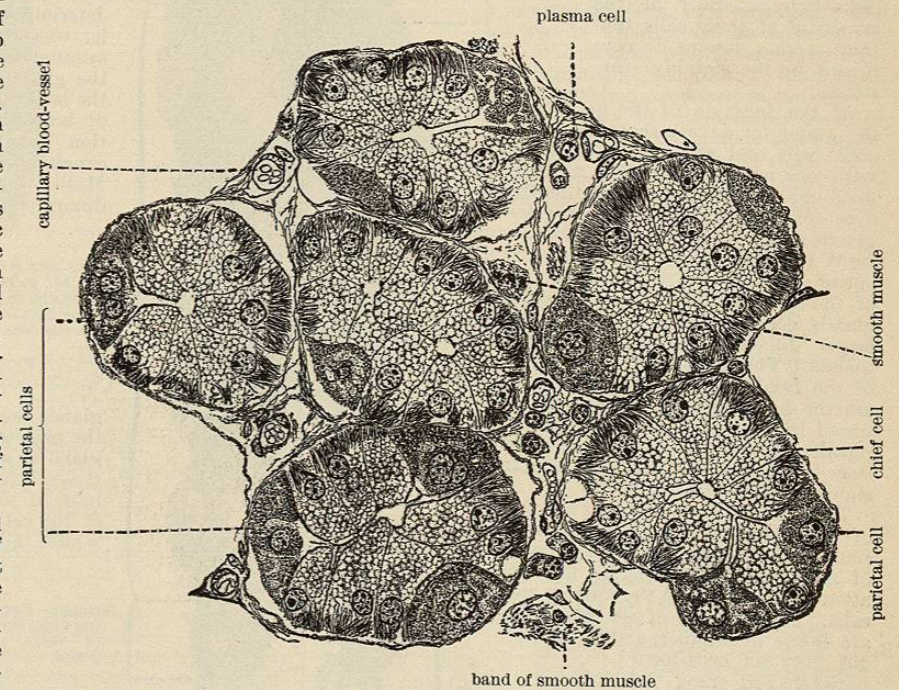


FIG. 4503.—Section Across Six Fundus Glands from the Greater Curvature of the Human Stomach, Near the Outer Ends. In the chief cells may be seen the two characteristic zones: the outer zone containing basal filaments of prozymogen; the inner zone a fine network enclosing the spaces in which the zymogen granules are lodged. × 500.

ording to the degree of loading of the cell with secretion. The contents of the cell appear in hæmatoxylin-eosin sections clear and transparent, and exhibit a reticular structure, the large meshes of which are separated by delicate protoplasmic trabeculae. The meshes or clear spaces in such preparations are the cavities of the cell in which the secretion is stored. Usually there is in these cells a condensation of the cytoplasm in the

middle of the cell in the form of a transverse band, incompletely subdividing the secretion into a proximal and a distal mass. The nature of the secretion contained in these cells may be determined by staining in a modified form of P. Mayer's mucicarmine solution of the following composition: Hematein, 1 gm.; aluminum chloride, 0.5 gm.; seventy-per-cent. alcohol, 100 c.c. The sections fastened to the slide are stained in this solution under the microscope until the mucin of the surface epithelial cells is a deep blue; the stain is then washed off with ninety-five-per-cent. alcohol, and the sections are dehydrated, cleared, and mounted in xylol balsam. In such preparations the contents of the secretion spaces of the neck chief cells, as well as the mucin of the surface cells, are stained intensely blue. A similar result is obtained by staining sections with Mayer's mucicarmine, freshly prepared and undiluted, the contents of the neck chief cells and of the theca of the epithelial cells of the foveolæ gastricae staining in this solution intensely red. Thus the impression gained by a study of the structure of these cells that they secrete mucus is confirmed by the staining reactions.

At the junction of the neck and body of the gland for a very short distance the mucous cells and zymogenic cells are mixed with one another, affording at this place a good opportunity to compare their respective cytological characters. In a very few of the glands of the fundus the mucous cells extend right to the bottom of the gland, replacing entirely in this case the ordinary chief cells of the body of the glands. Such mucous glands contain fewer parietal cells and a larger lumen than the ordinary fundus glands. The mucous chief cells of the neck of the fundus gland of man and mammals are the homologues of the large clear cells found in the necks of the gastric glands of reptiles and anurous Batrachians, with which they correspond in position, structure, and staining characters.

The parietal cells occur in all parts of the gland, although they may be found in greatest numbers in the necks of the gland, alternating in this situation with groups of the mucous neck cells. In the body of the gland they are fewer in number, and in the foveolæ only an occasional parietal cell may be seen.

The parietal cells are of ovoidal shape with centrally placed nuclei. In the neck of the gland they have a broad surface of contact with the lumen, but in the body of the gland they are crowded to the outside of the gland, and are connected with the lumen only by narrow ductlets which pass between the adjacent surfaces of the chief cells. In each parietal cell,

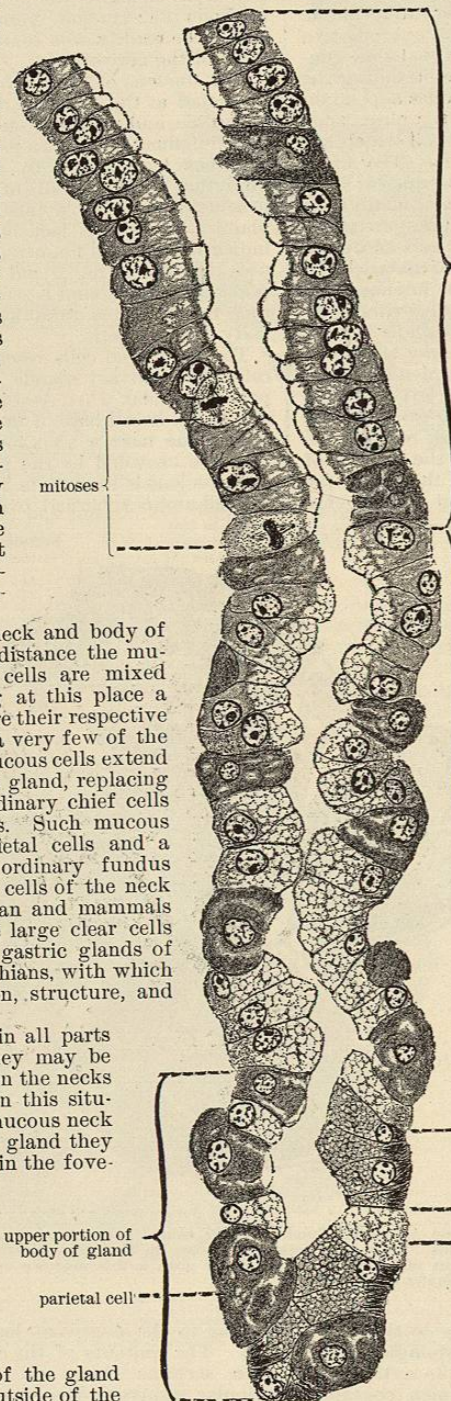


FIG. 4504.—Longitudinal Section of Part of a Foveola Gastrica, of the Neck, and of Part of the Body of a Fundus Gland of the Stomach of Man. $\times 580$.

according to Zimmermann, three zones of structure can be made out, a central mass of coarsely granular structure, containing the spherical nucleus or nuclei, for the latter are often multiple, a peripheral zone of similar structure, and an intermediate zone of finely granular structure. The differences between these various zones are best brought to view by staining sections according to Heidenhain's iron hematoxylin method, in which the coarse granules of the middle and outer zones stain deeply. The intermediate zone forms the free surface of the cell on the lumen or on the minute ductlets above described.

For a long time it was thought that the parietal cells in the body of the gland were completely shut off from the lumen by a layer of chief cells. Stöhr was the first to point out that the parietal cells also came into contact with the lumen. According to him this connection

was effected by the parietal cell possessing a pointed projection which penetrated between the adjacent surfaces of the chief cells and thus reached the lumen of the gland. It was not, however, until the introduction of the rapid Golgi method for the impregnation of tissue spaces that the real nature of the ductules of these cells was determined. By this means Erik Müller was able to show not only that a minute canal ran from the lumen of the gland to the parietal cell, but that the latter possessed an intricate system of branching and anastomosing secretion canaliculi. These intracellular canaliculi have since been observed by Müller, Zimmermann, and others in ordinary stained preparations, especially

in sections stained by the ferric alum hematoxylin method of M. Heidenhain, in which the intracellular and intercellular secretion canaliculi may be readily seen. In Golgi preparations of the gastric glands the fine ductule which connects the parietal cell with the lumen of the gland is seen to divide, on arriving at the cell, into a group of fine branches, most of which penetrate the substance of the cell, in the intermediate zone of which they ramify (intracellular canaliculi); others penetrate

a short distance between the parietal cell and the adjacent chief cells (intercellular canaliculi). The true intercellular character of the latter may be determined, as Zimmermann has shown, by the presence of the intercellular cement lines. The ductules of the intracellular canaliculi frequently contain transparent globules of coagulated secretion, which may also be observed in the lumen of the gland as far as its opening into the foveola gastrica.

The theory of Heidenhain that the parietal cells are the sole source of the

hydrochloric acid of the gastric juice rests at present on a very insecure foundation. The argument commonly employed, that the parietal cells are absent from the pyloric glands which produce an alkaline secretion, would be equally true of the chief cells of the body of the fundus glands. Moreover, the difference in acidity of the mucous membrane of the fundus and greater curvature of the stomach of the rabbit, which, according to Langley, corresponds to differences in the number of parietal cells present, could be equally well explained by

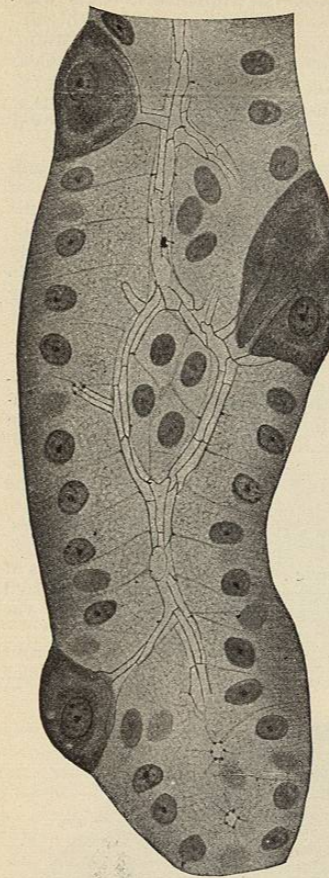


FIG. 4505.—Lower End of Fundus Gland, Chief and Parietal Cells. In the latter the intracellular ducts may be seen. (After K. W. Zimmermann, *Arch. f. mikr. Anat.*, Bonn, Bd. III.)

the obvious differences in secretory equilibrium of the chief cells from these two sources.

The mucous membrane of the greater part of the pars pylorica is thinner than that of the greater curvature, although thicker than that of the fundus and cardia. The thickness in material examined by the writer was 0.832-0.955 mm. Near the sphincter pylori, however, it again increases in thickness to 1.3 mm., or in places as much as 1.8 mm.

The glands of the pyloric region are much less closely set than in the fundus region, and are separated from one another by a larger amount of tissue belonging to the lamina propria mucosæ.

The foveolæ into which the pyloric glands open are much narrower in man than in most mammals. They rapidly diminish in diameter, to become narrow tubes, which branch as they descend in the mucous membrane, and at about the junction of the middle and outer thirds of the mucous membrane receive the pyloric glands. The long tubular branches of the foveolæ in the pyloric region may be compared to the short collecting ducts of the fundus glands. In view, however, of the fact that they are lined throughout by epithelium similar in character to that of the foveolæ, it seems to me better to consider them as part of the latter.

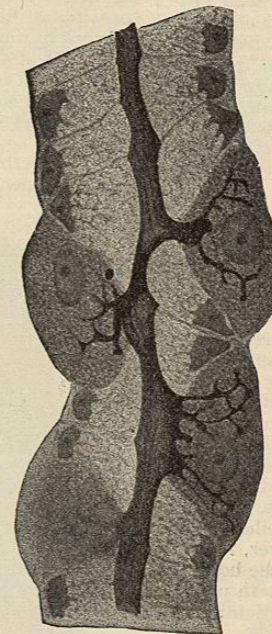


FIG. 4506.—Fundus Gland of Cat. Golgi preparation, fixed in ammonium sulphide and stained with hematoxylin and eosin; showing intracellular ducts of the parietal cells. (After K. W. Zimmermann, *Arch. f. mikr. Anat.*, Bonn, Bd. III.)

Into the bottoms of these foveolar branches open the pyloric glands. These are composed of a varying number of branching wavy tubules, into which open short, pear-shaped acini. Both tubules and acini are lined by the characteristic pyloric gland cells. The thickness of the portions of the mucous membrane occupying the foveolæ and glands respectively, I have determined as follows:

Length of foveolæ and branches	0.441-0.476 mm.
Width of portion of tunica mucosa occupied by the glands proper	.283-.301 "

In the thicker distal portion of the pyloric mucous membrane they are as follows:

Length of foveolæ and branches	0.735 mm.
Width of mucosa containing glands proper	.301 "

The narrow tubular branches of the foveolæ are lined by cells of the type of those found at the bottoms of the gastric foveolæ and in the short tubules which are intercalated between these and the neck of the glands in the fundus region. They are cylindrical cells, containing an oval nucleus and a considerable amount of cytoplasm. At the end of the cell which borders on the lumen a small theca is seen containing mucus, stainable in mucicarmine according to the method already described.

The terminal branches of the pyloric gland are made up of large, cubical cells surrounding an obvious lumen. These cells are usually found filled with secretion which occupies the meshes of a coarse network of cytoplasm. The nucleus is situated at the base of the cell and is spherical, flattened, or crescentic in outline, according to the amount of the secretion contained in the cell.

The theory of Heidenhain that the cells of the pyloric glands are pepsin-forming elements similar in character to the chief cells of the body of the fundus gland, has been shown to be incorrect.

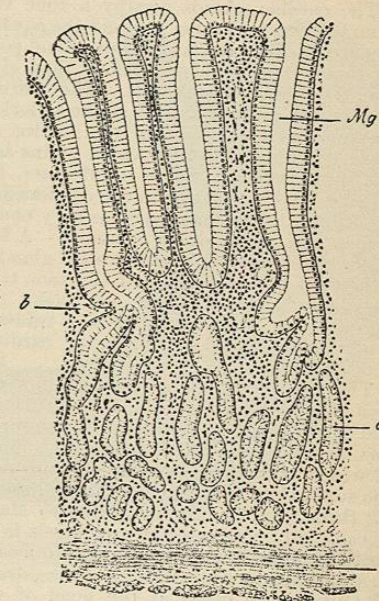


FIG. 4507.—Vertical Section of the Pyloric Mucous Membrane of the Stomach. $\times 85$. Mg, Foveolæ gastricae; b, blood-vessels of mucous membrane; d, glandular tubules; m, lamina muscularis mucosæ. (After V. von Ebner in von Kölliker's "Handbuch der Gewebelehre.")

gen, found in the form of coarse granules along its free surface. Neither of these substances occurs in the pyloric gland cells. The absence of the granules explains the greater transparency of the pyloric mucous membrane.

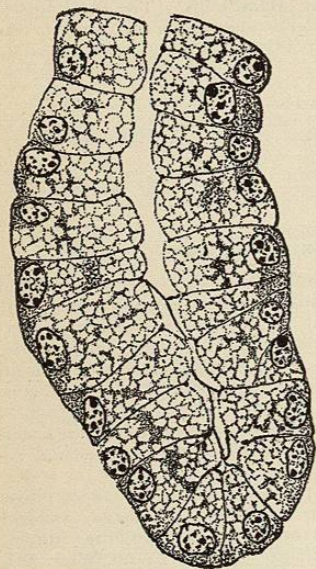


FIG. 4508.—Tubule of Pyloric Gland of Man. (Highly magnified.) Note the thin basal layer of cytoplasm; the reticular cell body containing secretion; the subdivision of the latter in some cells into proximal and distal masses.

On the contrary, the meshes of the coarse network seen in the pyloric gland cells are filled with a substance which stains strongly in mucicarmine, when employed according to the methods indicated above. These facts, together with the strong resemblance of the pyloric gland cells to mucous cells from other sources, and the gradual transition in character from the gland cells to the cells of the superficial epithelium, indicate that the bulk of the secretion of the pyloric glands is simply mucus. What other subsidiary substances are secreted along with the mucin is at present unknown.

Morphologically and physiologically the cells of the pyloric glands are regarded by the writer as the equivalents of the mucous chief cells found in the necks of the fundus glands.

The same relation thus obtains between the pyloric glands and the fundus glands of mammals as between the corresponding structures in Reptilia and Anura.

The cardiac glands occupy a zone varying in width from 0.5 cm. to 4.3 cm. around the cardiac orifice of the stomach. The glands of the proximal portion of this area are much more richly branched than either the fundus glands or the pyloric glands. They are composed largely of cells similar in character to the pyloric gland cells and the mucous chief cells of the fundus glands, and like them contain a secretion which stains in mucicarmine and mucicarmine. Some tubules are, however, formed of cells similar in type to the chief cells of the body of the fundus gland, inasmuch as they contain both prozymogen and granules of zymogen. A few parietal cells may also be present in the cardiac glands.

Toward the distal part of the zone the glands become less branched, and chief cells make their appearance regularly at their outer ends, a transition being thus gradually accomplished from the cardiac glands to the fundus glands.

The framework of the tunica mucosa is composed of reticulum, which forms a delicate network supporting and separating the glands and containing the blood-vessels, nerves, etc., of the membrane. The delicate fibrils of which this tissue is composed are condensed around the surfaces of the glands to form basement membranes for them. In the dog, according to Mall, the reticulum is especially condensed at two levels in the mucosa, one just above the lamina muscularis mucosæ, corresponding to a rudimentary stratum fibrosum (stratum compactum of Oettel); the other at the level of the necks of the glands. In man the glands reach almost to the muscularis mucosæ, so that here also the stratum fibrosum of Mall is rudimentary.

Here and there in the tunica mucosa branching bands of smooth muscle extend between the glands from the muscularis mucosæ in the direction of the free surface.

These also receive a delicate investment of reticular fibrils, containing a network of fine elastic fibres.

In the meshes of the reticular framework many wandering cells occur. In the superficial portions of the mucous membrane Unna's plasma cells are especially abundant (Figs. 4501 and 4502). A few polymorphonuclear neutrophile and eosinophile leucocytes, and lymphocytes, are present, and in sections stained in polychrome methylene-blue numerous mast cells may be seen among the glands.

Solitary lymph nodules (noduli lymphatici solitarii) occur in varying numbers in the mucous membrane of the stomach. They are particularly abundant in the cardiac and pyloric regions, where they occupy the deeper layers of the mucous membrane. Occasionally they may be found in the superficial tela submucosa, in which case they are often continuous through an opening in the lamina muscularis mucosæ with the reticular tissue of the tunica mucosa.

The deepest layer of the tunica mucosa is formed by the lamina muscularis mucosæ, a double layer of unstriated muscle fibres, 50-100 μ in thickness. It consists, according to Klein, of an inner circular and an outer longitudinal layer of fibres, which intercross and pass into one another. According to Böhm and von Davidoff it is composed of three layers. Between the constituent fibres of this layer may be seen a delicate network of reticulum and a rich network of elastic fibres. The fibres of the latter, for the most part, run in a direction parallel to the muscle fibres. From both layers of the lamina come off the groups of muscle fibres referred to above, ascending in the tunica mucosa among the glands.

The tela submucosa is a loose layer of collagenic fibrous tissue, connecting the tunica mucosa with the tunica

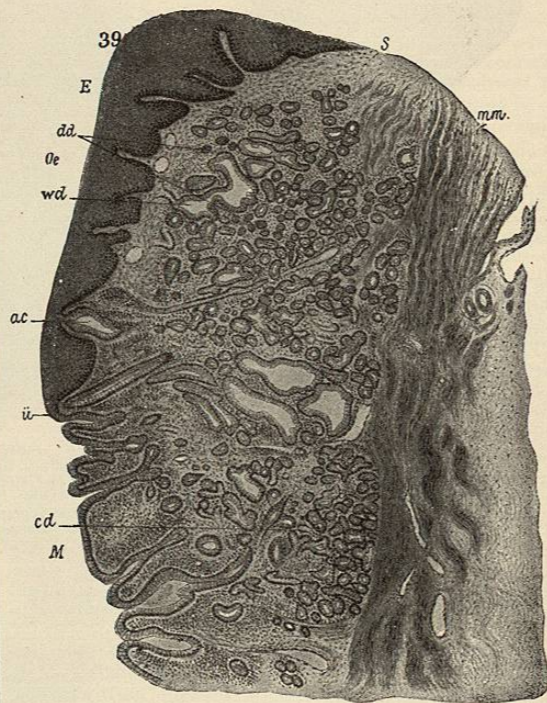


FIG. 4509.—Section through the Junction of Esophagus and Stomach of Man, showing Cardiac Glands. $\times 121$. *Oe.*, Esophagus; *m.*, stomach; *cd.*, cardiac glands; *wd.*, dilated ducts of cardiac glands. (After J. Schaffer, *Sitzungsber. d. k. Akad. d. Wissensch.*, Wien, Bd. cvl., Abth. iii.)

muscularis, and containing the large blood-vessels and lymphatics and the nerves and ganglia forming the plexus of Meissner. This layer is poor in elastic fibres

except in the neighborhood of the tunica muscularis, where the rich network of elastic fibres may be seen. Here and there, in the tela submucosa, are to be seen larger and smaller accumulations of adipose tissue.

In the description of the muscular coat, the recent account given by Birmingham will be followed. The tunica muscularis is composed of three layers, the outermost layer (stratum longitudinale) being a continuation of the corresponding layer of the esophagus. The fibres of which it is composed form on each curva-

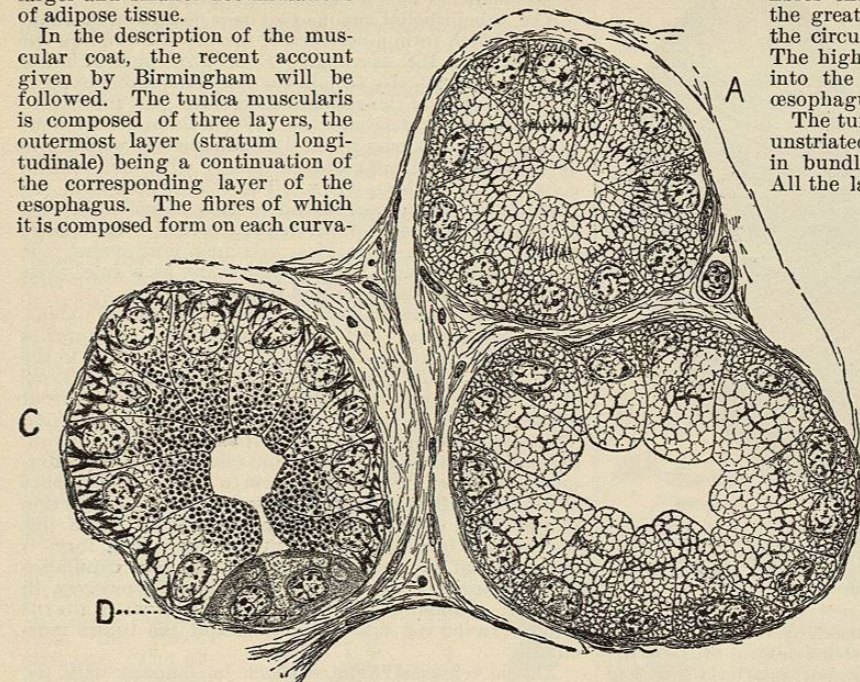


FIG. 4510.—Cross-section of Three Tubules of the Cardiac Glands of Man. $\times 1,000$. *A.*, Mucous tubule, showing cells in early stage of mucin formation; *B.*, mucous tubule, showing cells in various stages of mucin formation up to complete loading; *C.*, tubule composed of cells similar to the chief cells of the body of the fundus glands. These cells contain basal filaments (prozymogen) and zymogen granules; *D.*, binucleate parietal cell with intracellular secretion channels. (After R. R. Bensley, '02.)

ture, but particularly on the curvatura minor, a well-marked layer of numerous distinct bundles. On the anterior and posterior surfaces the layer exists as a very thin sheet, the fibres being less distinctly longitudinal in places, particularly near the middle of the surfaces beneath the cardia, than in the neighborhood of the curvature (Fig. 4511). The middle layer (stratum circulare) is best developed at the pylorus, where it forms a thickened muscular ring, musculus sphincter pylori, surrounding this aperture. In the adjacent narrow portion of the stomach the fibres are also well developed, and the resulting rings are numerous and closely placed. As we pass on toward the left the layer becomes thinner and the rings correspondingly fewer, but they still form a distinct and well-defined continuous sheet, the fibres of which can be easily seen even through the peritoneum, forming very symmetrical rings, disposed at right angles to the long axis of the organ. This regular arrangement is continued as far as the region of the esophagus, where it is interrupted. To the left of the cardia the layer is continued for some distance in the form of oblique fibres, which radiate from the right side of the esophageal opening above, downward, and to the left on the two surfaces of the stomach. These fibres, becoming more and more oblique, are continued above into the superficial circular fibres of the lower end of the esophagus. The internal layer is composed, like the middle layer, of circular and oblique fibres; but while the oblique fibres are but slightly developed in the middle layer, they form an important part of the internal layer. Beginning as a series of circles at the summit of the fundus, it extends in the form of a layer of rings, disposed at right angles to the axis of the stomach, as far as the cardia. Beyond this it is continued by a number of fibres—the well-known oblique muscular fibres of the stomach—which radiate from the left

side of the esophageal opening, downward, and to the right on both surfaces of the stomach, some of them reaching almost as far as the antrum pylori. These fibres end by turning abruptly toward the greater curvature and passing into the circular fibres of the middle layer. The highest of these oblique fibres pass into the deeper circular fibres of the esophagus.

The tunica muscularis is composed of unstriated muscle fibres bound together in bundles by delicate reticular tissue. All the layers of this coat contain many elastic fibres forming networks, the meshes of which are elongated in the direction of the long axis of the fibres.

Between the strata is a thin layer of collagenic connective tissue, containing numerous blood-vessels and the nerves and ganglia of the plexus of Auerbach.

The peritoneal coat of the stomach (tunica serosa) consists of collagenic tissue, composed of crossing and intercrossing fasciculi and containing elastic fibres. The free surface is covered by a layer of flat, irregularly shaped nucleated endothelial cells, which give to the external surface its smooth, glistening appearance. Under the endothelium is a thin layer of connective tissue, containing in its deeper half a network of fine elastic fibres. The deeper layers of the tunica serosa, formed of connective tissue composed

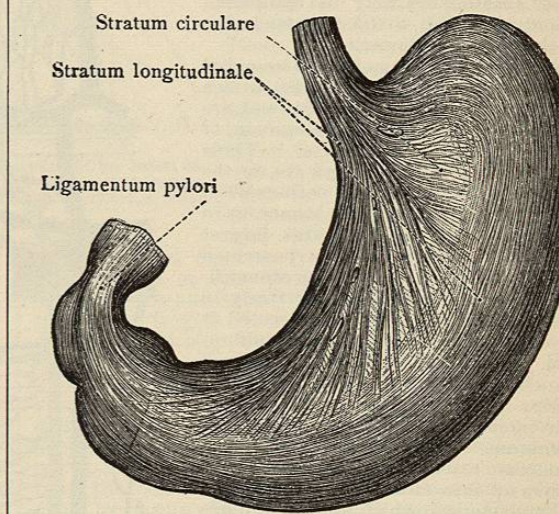


FIG. 4511.—The Superficial Layers of the Tunica Muscularis of the Stomach. Stratum longitudinale. (After C. Toldt, "Anatomischer Atlas," Zweite Auflage.)

of loosely interlaced fasciculi of collagenic fibrils and a few elastic fibres, contain the blood-vessels and nerve bundles.

The blood-vessels of the stomach are derived from all three branches of the arteria coeliaca, which form arterial