Pool, of Dutch Guiana, says it is better than thymol for the anchylostomum duodenale.

Thymol urethane has a similar use and dosage.

W. A. Bastedo.

THYMUS.—Introduction.—The thymus gland (also known in English as the thymus, or popularly as the neck or throat "sweetbread"; in German as the Thymus, Thymusdrüse, Brustdrüse, Bries or Briesel; in French as thymus) enjoys the unique distinction not only of being a transitory organ of extra-uterine life in man, but also of existing in three or possibly four distinct and different morphological conditions during its life history.

Comparative Anatomy.—This organ is not, however, peculiar to man, being present in all vertebrata, including the lampreys (cyclostomata) in which its existence was considered doubtful until recently. Its development does not proceed so far in some of the lower vertebrate animals as in mammals, being often arrested at the epithelial stage as seen in certain fishes where, during life, the thymus is an epithelioid organ, or rather an epithelial, mucus-secreting gland. In other fishes, in reptiles, and in birds it usually attains the condition of a lymphadenoid structure and persists through life, though it may undergo retrograde metamorphoses. In mammals the thymus passes through certain changes leading to its complete transformation into indifferent tissue before adult life is attained, but to this rule there are many exceptions, as one may discover by careful dissection of such animals as the rabbit, guinea-pig, dog, cat, cow, and horse. It is by no means uncommon to find large, well-developed thymus glands apparently quite like the "sweetbread" of the calf or lamb among adult animals of the varieties mentioned. This is the case in man, as we shall see later.

Embryology.—Until comparatively recent years the embryology of the thymus was obscure; but the observations of Renaut, Kölliker, Stieda, Born, Rabl, and Mall have pretty thoroughly established the developmental history of the organ. The generally accepted idea now is that in the higher orders, and probably in all vertebrata, the thymus develops as a paired organ from the third pair of gill clefts, and according to most authorities from the endodermal lining of these clefts, though His first held that the ectoderm furnished the component cells of the thymus anlage, and Kastschenko maintained that both ecto- and endodermal cells participated in forming the primary organ. The anlage of the thymus is a pouch of endoderm forming in the third gill cleft, and in a human embryo of the fifth week His found this pouch open. Originally the thymic pouch communicates with the fore gut or pharynx, but this connection is soon lost and the elongated sac with thickening epithelial walls, first lying transversely across the future neck, becomes free from its moorings to the gill clefts and shifts toward the tail, the larger dorsal end becoming the future head of the organ. The lumen of this cylindrical sac remains open, how long is still unsettled, though the twelfth week in man is the period usually assigned, after which the anlage becomes a solid cord of cells with numerous buds. Thus in its first appearance this organ is similar to a secreting tubular or acinous gland. A shifting of the endodermic anlage continues in the direction of the future thoracic cavity along the vagi and carotid arteries, reaching almost to the heart, finally making the lobes into which the fully formed organ is divided.

But the anlage does not long enjoy a strictly endodermal structure, for blood-vessels push in from the mesoderm and soon after round cells, presumably also of mesodermic origin, insinuate themselves into the epithelial cords, while others gather about to form investing masses which soon predominate. As we shall see later, these mesodermic cells form the larger bulk of the fully developed thymus, which, even in the fœtus, attains great size.

The preceding account represents the most widely accepted views relative to the origin of the thymus in man, though such points as the possible participation of other (the fourth) gill clefts and of the ectoderm should be mentioned. In vertebrates below mammals variations are seen, the second gill cleft in the frog, the first four in fishes, and the second, third, and fourth being at times called upon. The questions as to the time of closure of the lumens of the tubules in the anlage and the relation of these tubules to the corpuscles of Hassall (*vide infra*) are still under discussion.

It is at least worthy of passing notice that some similarity exists in the development of the thymus and several organs in its immediate neighborhood, like the tonsils, thyroid, and parathyroids, though the full details regarding their embryology have not been established.

Anatomy.—The fully formed human thymus makes an organ of considerable size lying in the anterior mediastinum at or near the median line. It generally consists of two broad and flat lobes more or less closely united with vascular connective tissue, and enveloped by a continuous sheath of fascia partly from the deep fascia of the neck and in part a reflection of the cephalic portion of the pericardial sac. As this smooth capsule is stripped from the organ several layers of loose areolar tissue come into evidence, the deeper ones of which send offshoots into the substance of the gland. The cephalic extensions of the thymus bring it almost in touch with the lateral lobes of the thyroid, to which it is united by a cord-like mass of dense connective tissue containing branches of the inferior thyroid artery and some veins. Downward, the thymic lobes reach well upon the pericardium, a distance of two or three finger-breadths, and to the interval between the second and fourth ribs. Its ventral surface is separated from the manubrium sterni by loose areolar tissue. Dorsally, its thoracic portion lies in relation to the arch of the aorta, the aortic branches, and the left innominate vein. The body and edge of the right lobe adjoin the innominate artery, superior vena cava, and right phrenic nerve; while the left lobe comes close to the common carotid artery and left phrenic nerve. Both vagi and the recurrent laryngeal nerves lie well behind the lobes of the thymus, and this is the case with the carotids in the cervical region. Here, also, the continuation of the organ brings it to lie beneath the origin of the sterno-hyoid and sterno-thyroid muscles, and in front of the trachea, everywhere more or less separated by loose connective tissue and fat. Thus it is seen that the thymus lies partly in the neck and partly in the chest, its thoracic portion being the expanded leaflets or lobes, its cervical portion consisting of the narrow finger-like extensions of these lobes. The organ might aptly be compared to two small, rather thin hands in the index attitude, the two fingers lying closely together and pointing upward. As a whole the organ is loosely held in position; it can be easily moved sidewise and lifted somewhat, and, after severing its thyroid connections, it shortens and sinks into the chest.

The blood supply of the organ is derived principally from the mediastinal branches of the internal mammary artery, and from the inferior thyroid. Its dorsal surface, applied to the pericardium, is penetrated by minute branches of the pericardial arteries. All its arteries are comparatively small, thus differing from those feeding the thyroid. On the contrary, the thymic veins are large, making a stem 3 mm. in diameter lying between the lobes and terminating in the left vena innominata (Dwornitschenko).

The lymphatics are numerous and large. They enter the glands of the anterior mediastinum and, according to Astley Cooper, two large vessels proceed, one from each lateral lobe, to open by one or more orifices into the internal jugular vein (Quain's "Elements of Anatomy," tenth edition, vol. ii., pt. ii., p. 556).

When fully exposed by dissection the thymus, in the height of its development, is a soft, smooth, pinkish, or pinkish-gray, bilobed, flattened organ, slightly concave dorsally where it lies against the heart's sac, widest below and tapering above. Because of the penetration of connective-tissue bands into its substance it is mapped out into distinct lobules and sublobules, giving it the

"sweetbread"-like appearance, not unlike that shown by the pancreas or the salivary glands. Within the lobules it is often possible to make out distinct rounded or polygonal follicles. A milky juice has been described by the older anatomists as coming from the cut organ especially in young children, or in adults in whom the organ was persistent and enlarged, and this circumstance has recently been alluded to as possibly of pathological significance. Probably, however, this condition is the result of a post-mortem softening; one of the artifacts to which the organ is prone. Of the same nature is the central canal with its lateral branches, or the "central cavity" so persistently mentioned in descriptions of the human thymus even in some present-day treatises on anatomy.

At the height of its normal growth the thymus attains a length of 9.5 cm., a width of 5 cm., a thickness of 1 cm., and weighs 20 gm. It sinks in water with a displacement of 21 c.c. But the organ may depart widely from the average standard; it may be larger or smaller. Its relations will vary according to its size, and it may lie to the left or right of the median line. A bridge of true thymic tissue may come in direct contact with the thyroid gland, or 3 or 4 cm. may intervene between the thyroid lobes and the cephalic extensions of the thymus. Sometimes the distinct divisions into lobes may be lost, or one lobe may greatly exceed its fellow in size. Multiple lobes, from three to seven or eight, may at times be found. Small lobes or islets of thymus tissue are sometimes found at a considerable distance from the organ proper, making *accessory thymuses,* as also seen in the case of the spleen and thyroid.

Histology.—The connective-tissue envelope of the active thymus sends offshoots or septa into the gland, dividing the lobes into lobules, and these again into secondary lobules from 4 to 11 mm. in size, finally separating the lobules into smaller, roughly spherical foci of solid thymic tissue termed follicles or acini, from 0.4 to 0.7 mm. in size. Ordinary white fibrous tissue mixed with elastic fibres makes the principal part of the enveloping sheath or capsule surrounding the thymus; in this more or less fat is mixed, depending upon the proportion of adipose tissue in the body at large. In the finer septa isolating the follicles or acini only loose white fibres with delicate elastic fibrils are present (Mall).

The follicles consist throughout of adenoid tissue, giving the impression made by the follicles of the lymph glands, even to the extent of showing a lighter central portion and darker periphery. This resemblance is heightened by the fact that the vast proportion of the elements composing the thymic acini are lymphoid cells. But more careful examination with higher magnifying powers brings out an evident difference between the central portion or medulla, as it is called, and the germinal centre seen in the follicle of lymph nodes. The darker, more solid peripheral portion of the acinus (cortex) is quite similar to the bulk of tissue composing the follicle of a lymph gland.

The cortical and medullary portions of the thymic acini are not sharply circumscribed. In general the reticulum of the medullary substance forms a network or framework of branching cells whose processes communicate with each other and with the walls of the blood-vessels. The nuclei of these radiating cells are 6–8 μ in size and rather poor in chromatin. In the meshes of the network lie small mononuclear leucocytes with nuclei 3–5 μ in diameter (lymphocytes); larger leucocytes with polymorphous nuclei are more seldom present, along with the eosinophilous cells described by Schaffer, which are also found along the blood-vessels of the interlobular connective tissue. Multinuclear (giant) cells are also to be found in the medulla, which, according to Watney, are derived in part from the cells of the framework. But, as Schaffer finds, there are also multinuclear cells which are united with the capillaries at the ends of which they are located and with whose retrogression they are related. At certain points the constituent cells of the framework press closely together, making flattened polyhedral objects whose arrangement resembles that of stratified epithelium. Here the extraneous (multinuclear) cells are entirely absent or only sparingly found. These nests or cords of epithelium, deprived of blood-vessels, show, at certain places where they adjoin the connective tissue, a layer of higher cells which resemble those in the basement layer of a stratified epithelium. That the medullary substance of the thymic follicle arose from an epithelial anlage cannot well be doubted from the outspoken epithelial nature of the cells just described, which must be regarded as direct descendants from the anlage. It is more difficult to decide whether the radiating cells of the medullary framework are epithelial in origin. In preparations stained after Van Gieson's method a portion of the medullary framework shows connective-tissue fibres, indicating that a part at least of this network is mesodermic in origin.

Besides the epithelial islets just described one finds in the thymus of advanced embryos, in greater numbers in the fully developed organ, and in the early stages of its retrogression, numerous characteristic objects varying in size and condition. These bodies are known as the concentric or lamellated corpuscles of Ecker, Hassall's corpuscles, or thymic corpuscles. They abound in the medulla exclusively. In the simplest form they are spherical bodies 13–22 μ in diameter, with a central portion feebly refractive, homogeneous, or granular, surrounded by shell-like flattened epithelial cells. The nuclei of the epithelial cells are plainly discernible, or they may be swollen, with their chromatin dispersed or even entirely missing. Here and there between the constituent cells leucocytes appear which may even penetrate to the central mass of the corpuscle. These bodies closely resemble the epithelial cell-nests or pearls seen in epitheliomas. Their nature and origin was long obscure, but the embryological studies of His and Stieda have thrown light on the question, which is not, however, even now definitely settled. According to the authorities just quoted the formation of these bodies is due to the separation of the primary thymic epithelium into isolated portions by the ingress of mesodermic elements, the pressure apparently producing their spherical contour, after which a degeneration of the central cells ensues, though this degeneration does not follow a uniform course. Usually a homogeneous refractive mass appears; at other times refractive granules, droplets, or flakes form. Whether the homogeneous substance is colloid, or not, is undetermined, though the microchemical test of Amman shows the same color-reaction as that given by the colloid of the thyroid gland. The substance is compared to that of prostatic stones by Kölliker. It certainly is a proteid and not a fatty substance, though both fatty and calcareous changes occur in Hassall's corpuscles. Frequently concentric corpuscles are seen in which the nuclei have entirely disappeared and the cell substance has become reticulated; or it undergoes transformation into soft masses which give a mucin reaction.

Along with the simple concentric corpuscles, bodies appear with multiple centres from which the cell layers radiate. Irregular forms, spindle- or club-shaped, or variously bent and knotted, also abound. But in all these corpuscles the concentric disposition of the component parts is retained. These bodies may reach a size of 0.1 mm. It is important not to confuse with these true thymic corpuscles epithelial cell-masses devoid of the concentric arrangement, found especially in individuals of advanced age, in which the thymus is well along in its retrogression; they attain a diameter of 0.2–0.3 mm., and may be designated epithelial spherules.

In poorly fixed or macerated specimens the Hassall corpuscles and epithelial spherules readily fall out during preparation; and where several of them have been in contact, a space is left which may easily be mistaken for a central canal. The loss of large epithelial spherules from the medulla may give the impression of considerable cavities here, but these artifacts are not to be confounded with cavities clad with ciliated epithelium, first noticed by Remak, which are of embryonic origin due to imperfect closure of the primitive epithelial canals of the thymic anlage. It is also advisable to have in mind the occasional presence of aberrant parathyroids which may find their way into the medulla of the thoracic portion of the thymus.

The cortical portion of the thymic follicle is characterized by the possession of abundant blood capillaries, and has much similarity with the structure of lymphatic glands. It has a delicate reticulum whose meshes are packed with cells which are for the most part small, mononuclear lymphocytes. In sections stained with nuclear dyes this preponderance of lymphocytes gives the cortex a dark hue, plainly outlining it from the lighter medulla. As to the nature of the reticulum, whether entirely cellular or partly fibrillar, it is a question still undecided, as is the case in reference to the lymph glands. Watney holds that the reticulum is a dual structure, both cellular and fibrillar. It is highly probable, however, that it does not develop from the ectodermic thymic anlage.

In conjunction with the cortical reticulum and lymphoid elements one finds the eosinophilic cells, described by Schaffer and by Sultan, scattered through the whole cortex, especially along the surface and in the neighboring connective tissue. Further, there are peculiar round or branching cells reaching a diameter of 12–30 μ thickly disposed about the capillaries, and containing strongly refractive granules, differing from those of eosinophilic cells, but more closely resembling the colloid-like droplets in the centre of the Hassalian corpuscles because of their insolubility in acids and alkalies. These granules vary in size, the average being 4 μ in diameter; they stain but faintly in eosin and differ from fat by their insolubility in ether. These cells can most readily be demonstrated by treating sections of thymus hardened in alcohol with dilute caustic soda, which clears the tissue, bringing out the granules in the cells that lie along the capillary walls of the cortical portion only.

Of especial importance is the fact pointed out by Schaffer that in smear preparations of the thymus nucleated red blood corpuscles are to be found, as is the case in the spleen and bone marrow. They are hard to find in sections. They are especially abundant in the cortex, though present in the medulla.

As first pointed out by Kölliker, the blood-vessels of the thymus are peculiar. The arteries following the central cords in the interior of the lobules penetrate the follicles and pass into a network of capillaries along the inner side of the cortex. The central portion of the medulla is largely free from capillaries. The branching arterial capillaries at the border of the medulla pass into capillaries which mostly penetrate perpendicularly, making a radial network with numerous anastomoses. Immediately beneath the connective-tissue envelope this radial capillary network becomes a narrow-meshed plexus of rather wide capillaries which surround the cortex and communicate with numerous venous branches passing into interlobular veins. Together with venous trunks coursing along the surface of the cortical substance numerous veins and arteries are found in the medulla. In consequence there exists a double venous system, a superficial one between the adjoining cortices and a deeper one in the medulla; there is also a double capillary plexus, one superficial, the other radial.

The lymphatics of the thymus are still but little understood, our knowledge remaining practically where it was after His completed his studies upon the thymus of the calf, supplemented by the contributions of Watney and Renaut. According to His the larger blood-vessels, which run along the central cord (calf's thymus) are accompanied by two or more lymph vessels, which receive one or more rootlets from each acinus. When these lymph vessels are traced, it is seen that in their further branching in the interlobular septa they soon lose their valves and muscular coat and become delicate-walled lymph spaces. These spaces plentifully surround the follicles. The lymph spaces provide an easy avenue for the thymic cells which are numerous in the thymic lymph.

The nerves accompanying the thymic arteries are easily discovered. According to the investigations of Boveri, who employed the Golgi method, the nerves form a fine plexus upon the vessels and in the interlobular connective tissue, from which some fibrils penetrate into the medulla, terminating there with slightly swollen extremities (A. Kölliker).

Retrogression of the Thymus.—It has already been mentioned that the thymus is a temporary organ in man; that is to say, it does not remain in its condition of morphological (and presumably, therefore, physiological) perfection during life. That the thymus disappears more or less completely in adult life has long been known, but data relative to the exact time at which it passes away, and as to the stages leading to its backward metamorphosis, were not available until recent years. Indeed, even at the present time authorities are far from being in accord on all these points.

The views of Friedleben, whose work now over half a century old must be regarded as the classic on the thymus, are most generally accepted. He held that the organ reached its complete development at birth, remained in this condition (with some increase in size) until the second year of life, then gradually altered and atrophied, the retrograde process being well advanced by puberty. Variations in the course of these changes are by no means rare, and some of these are still misunderstood.

Accepting 20 gm. as the ordinary weight of the thymus, this remains fairly constant, under normal conditions, throughout life. But even with the unaided eye it may be seen that there is a marked difference between the thymus of a young child and that of an adult. In the first case the organ has a solid, flesh-like appearance, a uniform pinkish color, with well-defined and closely approximated follicles. No great excess of connective tissue is present, and but little fat occurs in the gland proper. In the case of the adult, however, all this is changed, and the organ appears as a fatty mass approximating the size and shape of the original organ. In this so-called "thymic fat body" of Waldeyer, reddish or dark yellowish foci, more or less discrete are to be seen up to the thirtieth year, and the microscope shows these foci to be remnants of the once voluminous gland. A marked change in the specific gravity of the thymus occurs with advancing years, as Dwornitschenko has shown, it being higher for the first thirty years and then becoming less. This is shown by its sinking in water during the first period and afterward floating, the fatty alteration being largely responsible for this variation. Such is the usual conduct under normal conditions, but the changes in the gland are profoundly affected by the general state of nutrition, and it also sometimes happens that the involution of the organ is retarded so that one finds in the adult an apparently perfect thymus, a solid mass of thymic tissue unchanged by fatty overgrowth, constituting the so-called "persistent" thymus. Persistent thymus is almost invariably an accompaniment of the dyscrasia known as status lymphaticus. (See *Status Lymphaticus.*)

So far as macroscopic evidences go we may summarize by stating that at the second year of extra-uterine life the thymus reaches its anatomical perfection, being a solid mass of adenoid tissue about 20 gm. in weight and sinking in water. From this period to puberty the organ gradually becomes smaller and distinctly tougher, owing to the increase of connective tissue in its substance; and at the same time its pinkish color fades. Between puberty and the twentieth year little change in bulk is noted, but it may be seen that adipose tissue is gradually appearing in the thymus, isolating the thymic substance into separate masses. This fatty alteration becomes more pronounced during the next two decades, the foci of thymic substance becoming smaller and more widely separated until finally a mass of yellowish fat, preserving the shape of the thymus, is all that the eye can detect—a mass that equals in bulk that attained at puberty, but that floats in water after the thirtieth year.

Histologically the evidences of a profound structural change during the retrogression of the thymus are well

marked, and differ strikingly from what has been portrayed as the microscopic anatomy of the thymus at the period of its perfect development. These changes, which begin at the second year, have been particularly studied and described by Friedleben, Watney, Waldeyer, Schaffer, Sultan, Dwornitschenko, Lochte, and others. By these studies it has been determined that several distinct metamorphoses manifest themselves, the most pronounced being the connective-tissue, endothelioid, and fatty; that is to say, the process is one that affects both the framework and the parenchyma of the organ.

One of the earliest changes is the increase of interlobular tissue by which the acini become more widely separated, and, even before pronounced alterations occur in the acini, fat begins to make its appearance in the framework. There being no increase in volume of the organ, it follows that the proliferation of connective tissue produces a shrinkage or atrophy of the proper thymic elements, and in this the fat also plays a part, as Waldeyer has claimed. But while it must be regarded as a factor, pressure-atrophy is not the only condition incidental to the retrogression of the thymus. There is an atrophic change seemingly inherent in the cells of the thymic parenchyma. Sultan has directed attention to the other important retrogressive process—the endothelioid, which seems to be present at some stage during the transformation of the adult thymus in all individuals. From the endothelial cells lining the small blood-vessels and capillaries, and from those of the adventitia, endothelioid cells proliferate and appear both at the border and at the centre of the thymic acini. Sultan believes that some of these cells undergo a metamorphosis into fat cells. Later, spindle cells largely replace the endothelioid elements. A distinctly glandular or epithelioma-like appearance may be given to the thymus at the height of its endothelioid transformation.

Physiology.—The function of this organ, whose life history is so peculiar, is still much in the dark. Apparently its functional activity continues only during the stage of lymphadenoid development, though even at this time the presence of the thymus does not seem essential to life and well-being, since, according to the testimony of Friedleben and other experimenters who have followed him, the organ may be extirpated in young animals without causing any serious disturbance. Apparently contradictory to this conclusion are the results obtained by Thiroloix and Bernard in thymectomized rabbits, which died in three or four weeks with hypopyrexia and convulsions.

A number of authors have looked upon the thymus as a blood-forming organ, and Schaffer is the most recent advocate of this view. He believes, from his studies upon cats and rabbits, that the hæmatopoietic function is, like that of the spleen, liver, and bone marrow, a temporary one corresponding to certain growing periods; and, furthermore, he believes that the spleen and thymus maintain a reciprocal relationship, in that a rich supply of nucleated red blood cells in one is attended with a sparseness in the other. Carbone believes that the hæmatopoietic function of the thymus is limited to intra-uterine life.

Since Friedleben's time the possibility of the thymus influencing the growth and nutrition has been considered. This point has been raised anew by Seydel, who, finding the thymus much atrophied or absent in infants dying from impoverished nutrition, concludes that the organ supplies blood or nutrient fluid. Tarulli, from his extirpation experiments, believes that increased appetite with augmented ingestion of food follows the operation, in spite of which the growth is retarded. There is also a diminution of hæmoglobin and of red blood cells with leucocytosis and eosinophilia. Von Braunschweig concurs with Tarulli in so far as denying a leucocyte-forming function to the thymus.

Experiments with extracts of the thymus have been made, particularly by Svehla, who used a ten-per-cent. aqueous extract of the organ from man, dogs, swine, and cattle, and experimented on dogs by injection into the portal vein. He noted a fall of blood pressure, presumably caused by paralysis of the vaso-motors, acceleration of the pulse due to direct action on the heart, and death in narcotized subjects. In non-narcotized animals small doses caused restlessness and dyspnœa, while larger doses caused death with pronounced dyspnœa. Svehla compares the symptoms of experimental thymus intoxication with those of thymic sudden death (see *Status Lymphaticus*), and concludes that the fatal ending in the latter affection is caused by hyperthymization of the blood. Before accepting fully the conclusions reached by Svehla we should recall the fact that Cunningham has found that the toxicity of thymus and thyroid extracts is largely determined by the post-mortem changes in the glands after their removal and before subjected to the extractive process.

Pathology.—Besides various anomalies in the size, shape, and anatomical location of the thymus or portions of it, the organ may be completely absent. A typical example of this congenital abnormality has been reported by Clark in a baby of eight months; and while this reporter concluded from his observation that no serious nutritive disturbance followed the anomaly, he endeavored to show a relationship between the absent thymus and a form of hæmophilia from which the infant was suffering.

Circulatory disturbances as part of general vascular disease occur in the thymus. Venous hyperæmia is particularly prone to occur in the well-developed thymus with its large venous trunks, and has been repeatedly observed in asphyxia of the new-born. Punctate hemorrhages are found in some cases of sudden death in victims of status lymphaticus, and in the persistent thymus of lymphatic epileptics dying of asphyxia. They have also been noted in some cases of ordinary suffocation and in fatal phosphorus poisoning.

Atrophy of the thymus is a coincidence of general wasting of the body like that accompanying exhausting acute diseases or various chronic diseases attended by cachexia and marasmus. A well-developed thymus in an infant or a persistent one in an adult may shrink until little more than a fibrous-tissue mass remains to mark the place it once filled. This fact is important in connection with the anatomical diagnosis of status lymphaticus, a condition in which persistent thymus is associated with general lymphadenoid hyperplasia; for, under the conditions just mentioned, the organ atrophies and practically disappears, and, as a rule, the other lymphadenoid accumulations suffer the same fate.

Hypertrophy with hyperplasia of the thymus, which has had an overwhelming amount of attention in the literature concerning diseases of this organ, is almost invariably associated with the general condition known as status lymphaticus (see *Status Lymphaticus*), and should not be regarded as an independent affection. Even in the several cases in which the thymus has been reported as enlarged in Basedow's disease, myxœdema, Addison's disease, and acromegaly, other evidences of status lymphaticus have usually been disclosed.

Acute non-suppurative inflammations of the thymus are not common, and while the organ may participate in an inflammatory affection involving contiguous anatomical structures, it usually escapes. Biedert has reported a case of primary acute inflammation of the thymus unknown in origin. In general hæmatogenous infections the specific micro-organism may find its way to the thymus; and in certain pyæmic affections metastatic abscesses may occur in the thymus. There are also several cases on record in which single or multiple abscesses of the organ were found, with no evidence of a primary suppurative process elsewhere. In the cases of this character reported by Schlossman, Demme, and Helm, the enlarged thymus with its abscesses was apparently responsible for the sudden death.

Primary tuberculosis of the thymus is unknown, unless the questionable case of Carpenter's is so considered; but a number of instances of secondary infection, either in the form of miliary tubercles or in that of caseous tuberculous foci, have been noted.

The thymus is the seat of various kinds of tumors, and is the starting-point of a considerable number of the neoplasms located in the anterior mediastinum. Various teratomas have been found in connection with it, the most common one being a dermoid cyst with hair, epithelium, and fatty contents similar to the dermoids of the ovary. A more frequent variety of thymic tumor is one taking a lymphoid structure and designated lymphoma or lymphosarcoma, depending on its extent and the production of metastases. However, since the lymphatic glands in the anterior mediastinum and about the bronchi may also become the seat of these tumors, it often becomes difficult to decide whether the thymus has been primarily or secondarily affected. The question may at times be determined histologically by the discovery of Hassall's corpuscles in the primary tumor. Besides the small-celled lymphosarcoma, other varieties of sarcoma may occur, and carcinoma, presumably originating from the remaining foci of epithelial tissue, is occasionally encountered.

Extensive lymphoid infiltration and enlargement of the thymus may attend leukæmia and pseudoleukæmia.

Peculiar cysts of the thymus, probably at one time misunderstood and consequently designated Dubois's abscesses, have been carefully studied by Chiari, who regards them as originating from a growth of thymic tissue into the corpuscles of Hassall. Besides these spurious abscesses there are cavities with softened contents, properly called Dubois's abscesses, due to the softening of syphilitic nodules (small gummas). Syphilitic infection of the thymus may also manifest itself by a hyperplasia of the organ, or by a diffuse connective-tissue overgrowth with consequent induration. *A. P. Ohlmacher.*

LITERATURE.

As has already been mentioned, much of the literature upon the thymus, especially as to its hypertrophy and hyperplasia, should properly be classed with that bearing upon status lymphaticus. A particularly valuable paper giving the historical references is Ducrot's thesis ("De la Mort subite chez les jeunes enfants par hypertrophie du thymus au point de vue médico-légal," Paris, 1901). A more extensive work dealing with the thymus as a whole is Friedleben's monograph ("Die Physiologie der Thymusdrüse in Gesundheit und Krankheit," 1858). A thorough summary of the more recent literature is to be found in Klein's review ("Neuere Arbeiten über die Glandula thymus," *Cent. f. allgemeine Pathologie*, Bd. ix., Nos. 16, 17, 1898). From these three sources the student can obtain a reference to most of the literature dealing with the thymus except as pertains to certain special aspects of the embryology, anatomy, and histology, for which the standard text-books may be consulted.

THYROID.—ANATOMY.—There are few organs in the body that show normally so many and so great variations in structure, both gross and minute, as the thyroid. This is to be explained by the fact that it has its origin in three independent embryonal structures, so that in their fusion there are many opportunities for variations. Again, the absence of any excretory duct probably permits of wider variations than might otherwise occur, for no matter how arranged or where located the gland can accomplish its entire function, provided only that it has proper circulation. Ordinarily it presents two lateral lobes connected by an isthmus, which latter lies across the trachea from the second to the fourth tracheal rings, inclusive. This isthmus is absent in from ten to fifteen per cent. of individuals. When present, it may merely consist of a mass of fibrous tissue containing a minimum of gland tissue, or it may form the largest of the three lobes, with all possible intervening variations. Quite rarely, *i.e.*, in about one per cent., the isthmus exists as an independent lobe. When the isthmus is absent the lateral lobes are often so closely applied that the absence of the isthmus may be completely overlooked. At the level of the isthmus, the recurrent laryngeal nerve lies in the angle between the œsophagus and the trachea, being covered externally by the lateral lobe on each side. In front, the gland is covered by the sterno-hyoid, the sterno-thyroid, and the omo-hyoid muscles. Laterally, the lobes extend outward in front of the common carotid arteries. The lower end of each lateral lobe is usually at the fifth or sixth ring of the trachea, and the upper end is at the middle of the thyroid cartilage. The lower edge is embedded in a mass of fatty connective tissue, which is of some surgical importance, since it passes without any demarcation into the anterior mediastinum. Behind, it is attached by tough fibrous tissue to the larynx and trachea, so that it moves with them in swallowing. When the head is thrown back, the distance of 2 mm. that lies between the lower border and the sternal notch is doubled (Sappey).

Frequently a conical process, called the "pyramid of Lalouette," extends upward to be attached to the hyoid bone, thyroid cartilage, or thyro-hyoid membrane. This may arise from the isthmus or from either or both lateral lobes, its shape and size also presenting wide variations. Its frequency varies greatly according to different observers. Marshall found it in 26 out of 60 thyroids, or 43 per cent.; Streckeisen in 104 out of 153; Zoja in 109 out of 147, or 74 per cent.; while the writer found it with 36 of 60 thyroids, or 60 per cent. In 10 of these last it arose from the right lobe, in 12 from the left, in 8 from the isthmus, in 5 from both lobes, and in 1 from the left lobe and from the isthmus. In 21 it was attached to the thyroid cartilage or thyro-hyoid membrane, and to the hyoid bone in 15. In one instance the pyramid was split up into a chain of isolated masses of gland tissue, which would have to be classified as accessory thyroids. In structure the pyramid generally consists of regular gland tissue near its base, but the colloid material disappears as it ascends, and the vesicles become mere groups of epithelial cells, which are gradually replaced by fibrous and muscular tissue, until near the upper part of the pyramid they disappear entirely. If the muscle fibres are numerous the upper part is considered a separate muscle, and called the *levator glandulæ thyroideæ*. The pyramids are considered by Bland Sutton to represent part of the original thyroglossal duct.

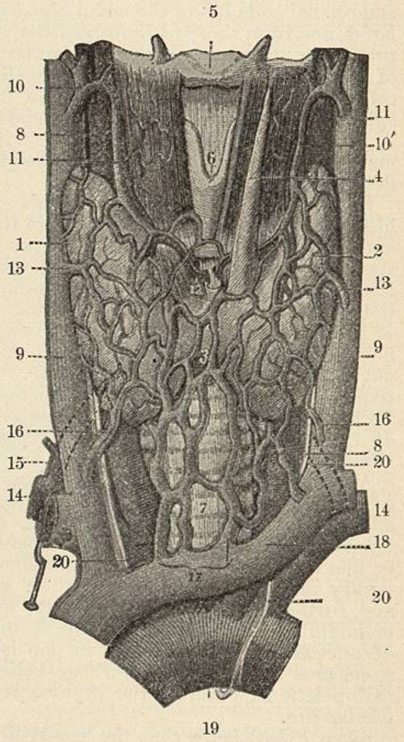

FIG. 4711.—The Thyroid Gland and its Relations. (Testut.) 1, Right lobe; 2, left lobe; 3, isthmus; 4, pyramid of Lalouette; 5, hyoid bone; 6, thyroid cartilage; 7, trachea; 8, carotid artery; 9, internal jugular vein; 10′, superior thyroid vein; 10, thyro-lingual-fascial vein; 11, superior thyroid artery; 12, inferior laryngeal vessels; 13, median thyroid vein; 14, subclavian artery; 15, inferior thyroid artery; 16, lateral inferior thyroid veins; 17, median inferior thyroid veins; 18, left brachiocephalic vein; 19, arch of the aorta; 20, pneumogastric nerve.

In proportion to its weight the thyroid has perhaps the largest blood supply of any organ of the body, the blood reaching it through the superior and inferior thyroid arteries on each side, and occasionally from the thyroidea ima. Following the trabeculæ these vessels break up into a rich meshwork of capillaries about the vesicles. In some places these capillaries even penetrate the basement membrane and come into direct contact with the

secreting cells. So great is the vascularity, that when an active dilatation of its vessels occurs the gland increases noticeably in size, and in this condition a distinct pulsation can be felt throughout the gland. The veins unite to form the superior, middle, and inferior thyroid veins, the two former of which empty into the internal jugular vein, the last into the innominate. They are devoid of valves, and a rich plexus surrounds the gland, often causing much bleeding in operations. Some authors have described collections of a colloid-like substance in the veins of the gland, and suggested that this was the method by which the gland disposed of its secretion, *i.e.*, directly into the circulation. However, these appearances are probably due to accidental extravasations occurring in the handling of the gland. It seems most probable that the excretion of the colloid substance occurs through the lymph channels, which are very numerous in the thyroid and lie in direct contact with the basement membrane of the vesicles, sometimes even with the gland cells themselves. In their lumen colloid is usually to be found, distinguished from other substances by its staining with Van Gieson's stain. After free anastomosis the lymph vessels leave the gland and pass through the superior and inferior deep cervical glands. (See description of lymphatics under "Tumors of the Thyroid.")

The nerves of the thyroid come from the middle and inferior cervical sympathetic ganglia, and pass into it with the blood-vessels. The recurrent and external laryngeal, the hypoglossal, and the vagus all send filaments to the gland, but these all seem to be vaso-motor or secretory, that is to say, they are all of sympathetic origin (Kölliker). The branches run to the bases of the epithelial cells, but the actual endings are not exactly determined.

The weight of the thyroid seems to vary greatly in different countries, since most German authors (Virchow, Rauber) place it at from 30 to 60 gm.; Schaefer in England gives it as 30–40 gm.; Poirier and Charpy in France give the average as 22–24 gm. In sixty thyroids removed in this country, I found the average weight but 22 gm. It would seem that in goitrous countries the normal gland is larger than in non-goitrous countries. The thyroid shows the effects of senility sooner and more than any other organ that is not essentially reproductive. In my series in persons over forty-five years of age the average weight was but 16 gm., while in people between twenty and forty-five years it averaged 25 gm. Differing from the other organs, it is larger, as a rule, in women than in men—a fact which, together with its early atrophy, indicates its close relation to the reproductive organs. It is relatively larger in infants than in adults; in the former the proportion to the body weight being 1 to 700 or 1,000, in the latter 1 to 1,500 or 2,200. According to Huschke there is even a decrease in size after birth, followed by a rapid growth at puberty. In the adult the transverse measurement is usually 50–60 mm., antero-posterior thickness of the lateral lobes 18–20 mm., of the isthmus 6–8 mm.; length of the lateral lobes 50 mm.; height of the isthmus, 5–15 mm. The right lobe is slightly larger when a considerable number of cases is averaged, although often in individual glands the opposite is true.

DEVELOPMENT.—Three separate "anlagen" unite to form the human thyroid. 1. A median diverticulum of the pharyngeal hypoblast pushes its way downward, and forms a tube that is connected with the base of the tongue. Subsequently it becomes solid, its upper end forming the foramen cæcum, from its lower end developing the isthmus, part of the lateral lobes, the pyramids (when they are present), and occasionally accessory thyroids. It sometimes happens that this structure remains in the adult as the "*ductus lingualis.*" 2. From the fourth visceral cleft on each side spring pouches which pass in front of the larynx and unite with the lower end of the median diverticulum, ultimately forming the outer part of the lateral lobes. These three masses fuse to form a horseshoe-shaped structure encircling the embryonic larynx, and are separated from their origin in the hypoblast. At first the gland consists merely of rod-like columns of epithelial cells, resulting from the division and branching of its original rudiments. The ingrowing connective tissue divides these cords of cells into short segments, which form the vesicles later, when colloid is secreted. Colloid formation begins in intra-uterine life, but the vesicles are not generally filled until some time after birth, section of the gland of a new-born child showing but few of the acini containing colloid. Because of the method of formation, in the fœtus a lobular structure is distinct, but in the adult this is generally absent or indistinct.

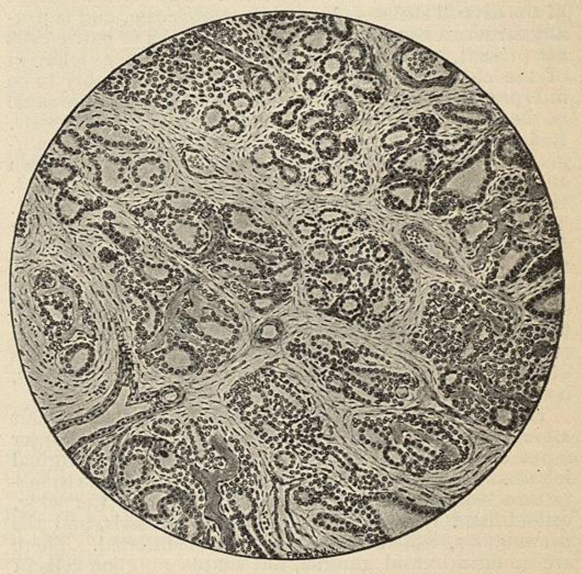
FIG. 4712.—Thyroid of Fœtus at Term. The lobular outlines are more prominent than in the adult; there is no colloid in the acini.

HISTOLOGY.—Fully as great variations are seen microscopically in the thyroids of persons who die of diseases that have no known effect on the thyroid, as have been noted in the gross anatomy. Study of the thyroids from consecutive autopsies shows such a variety of conditions as to suggest that perhaps this organ suffers much more in disease than we have reason to suspect from any clinical evidences. What may be considered the normal structure is described most briefly by saying that it differs from other tubular glands chiefly in having the tubules closed and filled with colloid to varying degrees of distention. The arrangement of capsule, septa, basement membrane, vessels, and nerves is that common to glandular organs in general. By reconstruction methods Streiff has shown that the vesicles are not always spherical sacs, but often are tubular, and frequently are sacculated. The size of the vesicles varies greatly, some being quite without lumen, while others are more than half a millimetre in diameter. As the epithelial cells are modified by the pressure of the colloid in the lumen of the acinus, they vary much in size and shape from those that are distinctly columnar in empty acini to those flattened, in distended sacs, to the nature of an endothelial cell. For the most part they are cuboidal, with a small spherical nucleus that stains more intensely than that of most epithelial cells. They are described as of two kinds—the chief cells and the colloid cells. The chief cells, which form by far the greater part, are clear or with very fine granules and have no distinct membrane, but seem to blend with one another, their outer ends resting on the basement membrane, the inner lying in the colloid substance. The colloid cells are characterized by a more granular and opaque appearance, obscuring the nucleus, and they are lower than the chief cells, from which they seem to be derived. The granules stain like colloid, and