

A STUDY OF THE PARATHYROID GLANDS IN MAN.

BY

E. T. RULISON, JR.

*From the Histological Laboratory, Cornell University Medical College,
New York City.*

The physiologic necessity of leaving the parathyroid glands uninjured in operations upon the thyroid region is now well known. It has also been demonstrated that the administration of beeves' parathyroids will to some extent relieve the postmortem tetany in man which follows the removal of the parathyroid glands (Halsted).

The number of parathyroid glands typically present has been quite generally stated as four, two posterior superior and two anterior inferior. Yet frequently at autopsy the typical four parathyroid glands are not to be found even after most careful dissection. The number which can actually be recovered varies from none to as many as six (Erdheim). This extreme variation has been ascribed to such causes as irregular number of glands in the individual, irregularities in their position, the presence of a varying number of accessory parathyroid glands, and even to the possibility of postmortem destruction of the small parathyroid glands by autolysis.

The reports of surgeons would lead one to believe that during operations upon the thyroid, the parathyroids are recognized with relative ease and can be preserved together with their blood supply. Parathyroid serums and extracts have been prepared, presumably without microscopical confirmation of the tissue used in their manufacture. If a relatively small percentage of the tissue so used is actually parathyroid, the serum or extract will certainly contain a considerable admixture of the products of such other tissues as thyroid gland, lymphatic nodes and thymus; and experimental results based upon the specificity of such extracts must be interpreted in the light of this possible source of error.

In view of these considerations further anatomical studies of the parathyroid glands for the purpose of providing a more firm and accurate foundation upon which to build and interpret physiologic experiment and surgical procedure appear most desirable.

RECOGNITION OF PARATHYROID GLANDS.

The following notes, based upon autopsies of bodies in the best state of preservation, one excepted, indicate that only 41 per cent of probable parathyroid glands, as identified by gross inspection, actually contain parathyroid tissue when examined microscopically. This percentage does not widely differ from the results obtained by Rogers and Ferguson, who found 61 parathyroids out of 189 pieces examined, or in 32.4 per cent (all suspicious looking pieces being included). In certain cases the gross appearance is undoubtedly misleading, tissue not resembling the classical type proving to be parathyroid after microscopic examination. Less frequently tissue presenting the typical macroscopic features of parathyroid is found to be lymphoid or other tissue.

The results of the gross dissection of the several autopsies are given somewhat in detail because of their relation to the question of the percentage of cases in which one may hope that the glands may be positively recognized by the unaided eye, without microscopical study.

Autopsy I.¹ W. M., aged 35; five hours post-mortem. Mental diagnosis, senile delirium. Cause of death, acute enteritis. In this case three pieces of tissue, none bearing the characteristic stamp of the parathyroid, were dissected, two from the posterior-superior aspect of the lateral lobes of the thyroid and one from the anterior surface of the esophagus on the right side. All proved to be adenoid tissue.

The failure to obtain the parathyroids in this case may have been due (1) to rapid autolysis, (2) neglect to secure all tissues bearing the slightest resemblance to a parathyroid, (3) the possibility of the

¹The material used was obtained in 1907 through the kindness of the Hudson River State Hospital, Poughkeepsie, N. Y. My thanks are due this institution for the opportunity offered.

glands being situated beyond the limited field of dissection, or (4) the remote possibility of an unobserved location within the thyroid gland.

Autopsy II. S. R., aged 55; twelve hours post-mortem. Mental diagnosis, epileptic insanity. Cause of death, appendicitis with perforation. In this case the tissue had undergone extensive post-mortem change. Only one very small piece of tissue resembling parathyroid was found, being located at the superior pole of the left thyroid lobe, posteriorly. Microscopical examination proved this to be thyroid tissue.

Autopsy III. D. W., aged 22; seven hours post-mortem. Mental diagnosis, epilepsy with insanity. Cause of death, septicæmia following carbuncle.

The two left parathyroids were readily recognized by (1) the yellowish brown color, (2) smooth, finely textured surface, (3) lack of the firmness which characterizes the thyroid and other tissue so often confused. Both left parathyroids were found on the posterior surface, the lower one, however, being anterior to the main branch of the thyroid artery. Six other suspicious looking pieces of glandular tissue were removed from the loose areolar tissue bordering on the right lobe and along the esophagus. One of these proved to be the right anterior parathyroid. The fourth parathyroid, if present, must have been outside the field of dissection.

Autopsy IV. L. W., aged 40; seven hours post-mortem. Mental diagnosis, general paresis. Cause of death, general paresis.

The two anterior parathyroids were recognized by the characteristics above mentioned. Both were located between the branches of the inferior thyroid artery and upon the lateral lobes of the thyroid gland. Two other pieces of tissue were examined, one from the superior pole of the left lobe of the thyroid and another from the anterior surface of the esophagus, on the right side. The former proved to be thyroid and the latter adenoid tissue.

Autopsy V. M. B., aged 36; two hours post-mortem. Mental diagnosis, imbecility with insanity. Cause of death, pulmonary tuberculosis.

The two anterior inferior parathyroids were immediately recog-

nized. The posterior glands were not found in the usual location, and having in mind the possibility of an internal position, large wedge-shaped areas of thyroid were excised from the upper posterior surface of the lobes. These were sectioned throughout, but no parathyroids were found. A search was made along the wall of the pharynx and esophagus, but no tissue resembling parathyroid was found.

Autopsy VI. A. P., aged 70; eight hours post-mortem. Mental diagnosis, melancholia simplex. Cause of death, carcinoma with multiple metastases.

The two posterior superior parathyroids were found, the right one being in direct relation to the esophagus. Just anterior to the main artery of the right thyroid lobe, a gland was removed, bearing all the characteristics of the parathyroid. On microscopical examination this proved to be adenoid tissue. This was the only instance in the ten autopsies in which a piece of tissue having the typical color, consistency and location proved not to be parathyroid. To secure the left inferior parathyroid a wedge-shaped area was excised from the thyroid and a small gland removed from the arcolar tissue just external to the left thyroid lobe. No parathyroid tissue was found in the thyroid and the small gland proved to be a bit of accessory thyroid tissue.

Autopsy VII. A. J. B., aged 55, eight hours post-mortem. Mental diagnosis, imbecility with insanity. Cause of death, lobar pneumonia.

The field of dissection was limited and but three blocks of tissue were obtained. At the extreme inferior pole of the left thyroid lobe, beneath the branches of the inferior thyroid artery, a parathyroid was found, the gland extending over upon the anterior surface of the thyroid. Two other pieces of tissue were removed, one from the esophagus at the level of the superior border of the cricoid cartilage and the other from the surface of the larynx on the left at the same level. Neither had all the essential attributes of parathyroid and both proved to be thyroid tissue.

Autopsy VIII. P. F., aged 40; twelve hours post-mortem. Mental diagnosis, epileptic insanity. Cause of death, asphyxia following convulsion.

The tissue was badly congested and no parathyroids were found in the customary locations. Four wedge-shaped pieces of tissue were excised from the thyroid at the most likely points, but no parathyroids were found.

Autopsy IX. E. K., aged 32; twelve hours post-mortem. Mental diagnosis, alcoholic psychosis. Cause of death, chronic interstitial nephritis.

All four parathyroids were readily recognized and secured. The inferior parathyroids were both at the extreme lower poles of the thyroid. The superior parathyroids were situated rather laterally than posteriorly. But four blocks of tissue were obtained in this case, the glands being characteristic. No search for accessory parathyroids was made.

Autopsy X. W. P. H., aged 48; twenty hours post-mortem. Mental diagnosis, maniacal depression. Cause of death, cardiac valvular disease with nephritis.

Three parathyroids were obtained in this case, all located upon the posterior surfaces of the thyroid lobes, two on the left, the other on the right. Of the two left parathyroids, one was found immediately beneath the superior pole, lying in the groove between the thyroid and esophagus, the other, three centimetres below in the same vertical line. The third was found in the same relative position on the posterior surface of the right lobe. No other tissue was searched for parathyroid, as it was badly congested.

With one or two exceptions all of the glands were fixed in Van Gehuchten's fluid. They were then hardened in graded alcohol, embedded in paraffin, sectioned and stained with hematein and eosin.

The following conclusions are based upon the dissection and microscopical study of the 17 parathyroids obtained:

1. *Size.* The size varied from 2 x 4 x 6 mm. to 4 x 6 x 10 mm. The average size was about 3 x 5 x 8 mm.
2. *Color.* Typical yellowish brown 13 glands
 Deep red brown (congestion) 3 glands
 Light yellow 1 gland

3. <i>Consistency.</i>	Typical, flaccid	12 glands
	Tense, hard	3 glands
	Medium	2 glands

4. *Number and location.*

Number of autopsies in which 4 glands were obtained.....	1
Number of autopsies in which 3 glands were obtained.....	2
Number of autopsies in which 2 glands were obtained.....	3
Number of autopsies in which 1 gland was obtained.....	1
Number of autopsies in which no glands were obtained....	3

Total number of glands obtained17

Number of <i>superior</i> glands obtained	6
Number of <i>inferior</i> glands obtained	11
Number of glands irregularly situated	7

Superior: found on esophagus	1
Inferior: found on esophagus	1
Inferior: found at extreme inferior pole	3
Inferior: found on posterior surface	2

D. A. Welsh (Jour. Anat. and Physiol., 1898, XXXII, page 383) says "the posterior-superior parathyroid of each side is much more constant in its position, and much more easily found than the anterior inferior glandule." Contrary to the experience of Welsh, the inferior parathyroids in the above series seem the more easily located, in all except two cases being found anterior to the inferior thyroid artery, and in all except four cases being located at the first branch of this artery on the thyroid lobe.

5. *Recognition of the glands.* In many cases the parathyroids can be definitely recognized by gross inspection if the tissue is fresh and not badly congested or pigmented or otherwise altered. In only one instance in ten did a gland with a smooth surface, of yellowish-brown color and flaccid consistency, fail microscopical confirmation, while seven atypical pieces of tissue proved to be parathyroids. In none of the ten autopsies were more than two parathyroids found in

their typical location, but in autopsy IX, in which four parathyroids were found, the superior were typically located while the two inferior were atypical only in that they were displaced toward the inferior pole of the thyroid and were inferior to the thyroid branch of the inferior thyroid artery. Although glands of typical parathyroid appearance rarely failed of confirmation, the converse was more frequently true, that in certain instances glands of variable color and consistency proved to be parathyroid.

Tissue resembling parathyroids on dissection would seem to be divisible into three groups: (1) in which the location, form, size and color appear wholly characteristic to the unaided eye—such tissue on sectioning rarely proves to be other than parathyroid; (2) in which location, form, size and color approximate the typical—a considerable portion of these prove not to be parathyroid on microscopical section; (3) in which the location, form, size or color are wholly atypical—such occasionally prove to be parathyroids.

The obvious surgical importance of the above seems to be two-fold, viz., the surgeon during thyroidectomy can be reasonably certain of his identification of certain of the parathyroid bodies when they can be found, but to insure the preservation of these glands they must leave intact much, if not all, of the glandular tissue found in the immediate vicinity of the thyroid gland, bearing in mind, also, that the number of parathyroids constantly present in each individual has not been demonstrated to be as many as the typical number, four.

To those studying the parathyroids it soon becomes evident that if four glands are to be obtained in each case very extensive search is necessary. Only very rarely can four glands be immediately and definitely recognized. In cases in which, for example, but three glands are identified one is obliged to preserve all possible tissue from the hyoid bone to the aortic arch before excluding the presence of a fourth gland. If this search fails to locate the missing gland a complete sectioning of the entire thyroid may produce it, owing to its occasional location within the capsule of the thyroid gland.

ANATOMY AND HISTOLOGY.

In man the parathyroids may be as many as four in number,

occasionally five or six (Erdheim). They vary in size from that of a grain of rice, or even smaller, to that of a small white bean. Their color is quite characteristic, a peculiar yellowish brown, in contrast to the deep red of the thyroid. Their surface is smooth and conveys the idea of a tissue of finer elements than that of the thyroid or other tissue, for example, lymphatic nodes, thymus rests, with which parathyroids may be confused. In many instances the parathyroid is situated in direct relation to the thyroid gland, less often in relation to the esophagus or trachea. The glandules have been found superiorly as far as the hyoid bone and inferiorly as far as the bifurcation of the trachea or upon the arch of the aorta in relation to the thymus (Welsh). The last named position is stated by Welsh as being the most common in the cow. The parathyroid glands most readily located are the ones known as the anterior inferior parathyroids, usually situated at the inferior poles of the lateral thyroid lobes, although there is much individual variation in their position (Rogers and Ferguson). Welsh however states that in his series of cases the superior were the more easily recognized, whereas in the present series of autopsies the inferior parathyroids were much the more easily recognized and more constantly present. The inferior thyroid artery forms a guide to the two inferior glands which often rest in the bifurcation of the artery upon the anterior inferior surface of the thyroid on either side. The two remaining parathyroid glands are most frequently found posteriorly at the superior pole of the thyroid. Very often one or both of the superior parathyroids is found upon the esophagus. In rare cases a human parathyroid may be embedded within the thyroid gland, and this location is quite the usual one for the inferior parathyroid of the dog, horse and goat (Rogers and Ferguson).

The parathyroid is described as an epithelial structure resembling the glandular portion of the hypophysis cerebri. The epithelial cells are of two varieties: (1) so-called *principal cells*, which have a distinct limiting membrane or wall and are outlined by the supporting stroma of reticulum, thus assuming a polygonal, often pentagonal shape; they have a clear cytoplasm, and a centrally situated and often vesicular nucleus; the principal cells predominate: (2) *oxyphile or*

acidophile cells, somewhat larger than the principal cells, and have distinct outlines, a finely granular and acidophile cytoplasm, and a centrally situated nucleus which is small in proportion to the size of the cell and often highly chromatic. The acidophile cells are irregularly placed among the masses of principal cells, either singly or in small groups. These groups are often situated immediately beneath the capsule in wedge-shaped areas, or in relation to blood-vessels.

The stroma includes a capsule, always present, consisting of delicate white fibrous connective tissue. From the inner surface of the capsule fine trabeculae are given off, which in some cases appear to divide the gland into lobules. In many glands there is a distinct hilum by means of which the arteries of supply—branches of the inferior thyroid—enter the glandular substance, supported by the trabeculae.

There is no duct through which a secretion may leave the gland. The tubular cysts found in the parathyroids of the goat, horse, and occasionally in other mammals (Kohn, Edmunds, Rogers and Ferguson) can not be considered as in any sense ducts, for they do not receive the secretion from the parathyroid parenchyma nor do they open upon any free surface. They are closed cysts and more nearly than anything else they simulate the branchial cysts which are frequently found in the connective tissue about the trachea, and which are of a congenital type, probably due to the embryonal dislocation of primordial epithelial cells from the branchial clefts. The embryology of the parathyroids would suggest a similar origin for the ciliated epithelium lining the occasional colloid-containing cysts within their substance.

No peculiar histology of the larger parathyroid blood-vessels presents itself, the coats being properly proportioned. The arterioles empty into an extensive sinusoidal system of capillary vessels which are then collected by the radicals of the venous system. The arrangement of the epithelial cells seems dependent upon the blood-vessels, the intimate contact of parenchymal cells and vascular epithelium suggesting the escape of secretion into the sinusoidal vessels. It is believed that the arrangement of cells varies somewhat with the age

of the individual. In young subjects the columnar arrangement of the epithelial cells seems to predominate (Ferguson). Later in life the cells show either a diffuse arrangement or assume something of an alveolar grouping. In rare instances within the parenchyma there are alveoli containing a colloid material, but in these cases the cells lining the alveoli are low columnar or cuboidal cells resembling the true glandular cells of the thyroid and bear no obvious resemblance to the parenchymal cells of the parathyroid. These alveoli would seem to form no essential part of the parathyroid structure.

Most parathyroid glands contain fat, either in discrete cells or in groups. The presence of fat, however, very probably does not account for the somewhat characteristic yellow tint of the yellowish brown parathyroid glands, which is apparently an intrinsic property of the parenchymal cells, for many of the glands of my series which possessed a most characteristic yellowish tint proved on sectioning to contain very few or no fat cells. The remaining brownish tint appears to be due to the extreme vascularity of the gland.

The following is a summary of the histological findings in the seventeen parathyroid glands removed from the above described autopsies.

Capsule.—The capsule was invariably present, varying greatly in thickness and structure. In most cases the capsule was found to consist of white fibrous tissue apparently containing some smooth muscle. From the inner surface, septa composed of a delicate reticulum of fibrous tissue were found to penetrate between the parenchymal cells. These septa support the blood-vessels.

Hilum.—A more or less distinct hilum was found in each gland, the arteries entering and veins leaving at this point.

Reticular Tissue.—After tryptic digestion for twenty-four hours of sections of the parathyroid gland—removing the white fibrous connective tissue, elastic tissue, muscle and epithelial cells—a delicate reticulum remains. Hence, it would seem that this is true reticular tissue; it appears to form the ultimate framework of the parathyroid. The distribution of the reticular tissue corresponds to the outlines of the capsule, septa and parenchymal cells, principal and oxyphile.

Blood-vessels.—The parathyroids were in all cases found to be

highly vascular. The histological study of the arteries and veins revealed nothing indicating any possible structural relation of the vascular system to the glandular secretion, such as is found in the excessive development of the longitudinal muscle of the media of the adrenal veins (Ferguson). The capillary network pervading the gland is very delicate and seems to determine the grouping of the cells, the resulting arrangement of the cells presenting either a columnar or alveolar form. The columnar grouping was not observed, this arrangement being more frequent on younger subjects. In five instances an acinar grouping was indicated. In one of these the acini seemed very distinct, and a few of them contained colloid. In many glands there were broad vascular spaces lined by a single layer of endothelium—so-called sinusoids.

Principal Cells.—The limiting membrane of the cell was usually distinct. Each cell most commonly had a pentagonal outline; its cytoplasm was clear, often taking a faint bluish tinge in sections stained with hematein and eosin. The nucleus was centrally situated and often vesicular in character.

Acidophile Cells.—In size these were somewhat larger than the principal cells. The limiting membrane was fairly distinct and the cells had a polygonal outline. The cytoplasm was finely granular and strongly acidophile. The nucleus was centrally situated and often deeply chromatic; occasionally multiple. In twelve cases the acidophile cells were found dispersed uniformly among the principal cells without evident relation to capsule, septa or blood-vessels. In the remaining five cases some of the acidophile cells were found in distinct, often wedge-shaped areas beneath the capsule or in relation to septa or blood-vessels.

Fat.—In five glands no fat cells were found either in the capsule or among the epithelial cells. In four glands the fat cells were found in discrete arrangement only. In two glands fat occurred in large masses only, and in the remaining six the fat cells were found in both discrete and grouped arrangement.

Color.—The distinctive yellowish brown color of the parathyroid has been attributed to the presence of fat (Welsh). A review of the five glands in which I found no fat shows that the color in each

instance was a characteristic yellowish brown, and it must, therefore, be an inherent property of the parenchymal cells; possibly the color may be due to reflected light from the masses of principal cells, the clear cytoplasm of which, together with the extreme vascularity of the gland, may combine to produce the characteristic yellowish brown.

PATHOLOGY.

Nothing of importance from a pathological viewpoint was noted in any of the glands. In one case, in which there was extreme congestion of all the organs, some pigmentary deposit was found in the small areas of hemorrhage. No evidences of degeneration were found unless the presence of colloid containing follicles in two glands may be considered. No new growths were found, not even a metastasis in the case of general carcinoma.

In closing, I desire to express my thanks to Dr. J. S. Ferguson, Assistant Professor of Histology, at whose suggestion and under whose direction the present study was undertaken.

Received for publication May 11, 1909.

BIBLIOGRAPHY.

- ERDHEIM. Beitr. z. path. Anat. u. z. allg. Path., 1904, xxxv, 366.
FERGUSON. Text-book of Histology, 1905, 456.
HALSTED. Am. J. Med. Sc., 1907, cxxxiv, 1.
HOWELL. Text-book of Physiology, 1906.
KOHN. Arch. f. mik. Anat., 1897, xlviii, 398.
ROGERS AND FERGUSON. Am. J. Med. Sc., 1906, cxxxI, 811.
WELSH, D. A. J. Anat. and Physiol., 1898, xxxii, 292, and 380.