It has been found that when the *Bacillus typhosus* is introduced into the bottles it is not destroyed by this treatment, but that multiplication occurs, and that this multiplication can be stimulated still further by the addition of 10 c.cm. of broth to the litre of water.

The residual water is put on Conradi-Drigalski plates (not adding more than 4 c.cm. to each plate), and smeared over them with a T-shaped glass rod. The more Conradi-Drigalski plates used and the more of the residual water examined, the better is the chance of finding the typhoid bacillus. However, such an amount of multiplication occurs that if the typhoid bacillus was present it will be found in 1 to 2 c.cm. of the residue.

The more or less anaërobic conditions prevailing and the high temperature favour the development of the typhoid bacillus, and are inhibitory to many water organisms.

After the water has been spread over the plates they are dried at 37° C. in the incubator, the covers put on, and the plates are inverted. It is best to stop the evaporation when 20 c.cm. of water remain in the bottle. If the evaporation is carried further the precipitated flocculent matter and the high concentration of salts may interfere with the growth of the colonies on the Conradi-Drigalski plates. I may add, however, that after evaporating to dryness, and then adding a few c.cm. of water to the bottle, and shaking and then transferring to Conradi-Drigalski plates, colonies of typhoid bacilli have developed.

Method of Ascertaining the Number of Bacilli added to the Water.

To judge of the efficiency of the method it is necessary to know the number of bacilli added to the bottles. For this purpose I have been in the habit of adding, by means of a fine capillary pipette, two drops of a 24-hours broth culture of the *Bacillus typhosus* to 100 c.cm. of sterile water in a flask; then, after shaking, taking 1 c.cm. of this and adding it to a second 100 c.cm.; then 1 c.cm. of this is added to a third 100 c.cm. After shaking, 1 c.cm. is taken from the last dilution and distributed over four Conradi-Drigalski plates, and at the same time 1 c.cm. is added to 1 litre of water. The number of colonies that develop on the plates gives approximately the number of bacilli added to the water.

Experiment.

To 1 litre of sterile tap water were added 10 c.cm. broth and seventeen typhoid bacilli. The evaporation was completed in twenty-two hours, 28 c.cm. being left in the bottle; 1 c.cm. of this residue was distributed over four Conradi-Drigalski plates. Forty-eight colonies developed on these plates. Therefore $28 \times 48 = 1344 =$ number of bacilli in bottle at end of process. And as there were seventeen bacilli present at the commencement there had been thus an 80-fold increase. The bacilli were proved to be typhoid bacilli by cultural and agglutination tests.

In this experiment sterile water was used, so that other organisms giving blue colonies on the Conradi-Drigalski plates might not be counted as typhoid. In other experiments ordinary tap water was used with equally satisfactory results. I have recovered the typhoid bacilli where as few as two have been added to a litre of water. The salts present in ordinary water do not, even in concentrated solution, destroy the typhoid bacillus.

Belfast tap water is a moderately hard water. A chemical examination gave the following result:

Free ammonia	...	...	0.001 part per 100,000
Albuminoid ammonia	...	...	0.020
Total solids	...	...	15 parts per 100,000
Total hardness	...	...	7
Chlorine	...	...	1 to 3

From some preliminary experiments it seems that the presence of *B. coli communis* does not interfere with the usefulness of the method; but it can especially be recommended where an attempt is made to isolate the typhoid bacillus from a suspected water which, according to ordinary standards, might be deemed free from pollution.

Finally, my best thanks are due to Professor Symmers for the interest he has taken in the method, and to Dr. Rankin for sketching the apparatus.

UNDER the will of the late Mr. William Guiver Wright, of Paddington, which has now been proved, St. Mary's Hospital, Paddington, receives a sum of £200.

THE SCIENCE COMMITTEE

OF THE

British Medical Association.

REPORT CI.

THE STRUCTURE AND SECRETION OF THE PARATHYROID GLANDS IN MAN.*

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THE histology of the parathyroid glands has already received attention from previous observers. In his original paper, Sandström¹ described it with detail and accuracy as far as he went. After pointing out how varied were the appearances presented by sections of the glands, he proceeded to recognise three main types. In the first the cells were arranged in a continuous mass; in the second the structure was more open, consisting of a reticulum of cells, the meshes of which were occupied by blood vessels; while the last type showed an arrangement of cells to form small vesicles, in some of which were drops of a substance possessing the staining properties of colloid.

While confirming the Swedish anatomist's work, Welsh² carried the subject further. He described four types: (1) The cells form a uniform mass, their protoplasm taking little if any stain, and there being but slight degree of vascularity. (2) The cell masses show a tendency to break up into anastomosing columns, between which are capillaries borne in a fine connective tissue stroma; the protoplasm stains somewhat more deeply than before. (3) The cells form branching columns between which lies a fine or dense stroma bearing blood vessels. These cells are larger and faintly staining. (4) The cells are arranged in a single layer around a central lumen to form definite acini. These cells are large, with protoplasm staining variously, and the lumen is usually occupied by a small globular mass of colloidal substance. Welsh specially notes that commonly several types coexist in one gland.

More important than this recognition of types is his description of what he terms "oxyphile cells." These he mentions as occurring in a very large proportion of cases, though not in all, and never attaining the same abundance as the above-mentioned cells ("principal cells"). They have a relatively large amount of protoplasm, which is usually full of fine oxyphile granules, and he thought he recognized differences between the nuclei of the two varieties of cells, those of the oxyphile being smaller, more nearly circular, and with their chromatin more densely plaited. According to their grouping he makes four types of these cells also. They occur as: (1) Uniform masses forming islets scattered irregularly through the gland; (2) anastomosing columns; (3) cells either singly or in groups of twos and threes; (4) cells forming definite acini, the lumina of which are occupied by colloid material—a very exceptional type. He does not offer any explanation of these cells, nor does he discuss their relation to the so-called principal cells.

In a preliminary communication to the Physiological Society in 1906, the cardinal points of the present paper were recorded. It will be found that while the following account corroborates the work of both Sandström and Welsh, certain hitherto undescribed points in the histology of the gland are brought forward, more especially as regards the interpretation of the two varieties of cells, and the nature of the secretion, and therefore of the function, of the parathyroids.

I.—STRUCTURE OF THE PARATHYROIDS.

The parathyroid is enclosed in a thin connective tissue capsule, from the deep surface of which delicate trabeculae

* From a paper read before the Pathological Society of London, February 19th, 1907.

pierce the interior of the gland, branching and uniting till the whole structure is cut up into small compartments polyhedral in section. This framework encloses in its mesh the cellular elements of the organ, and carries a rich vascular and lymphatic supply. In some specimens the connective tissue is increased in places, so that fairly strong septa are seen dividing the gland. In others the processes are so fine as scarcely to be discernible except under high magnifications.

Fig. 1.—Showing continuous mass of parathyroid cells; fat spaces absent.

The blood vessels which come from or drain into the adjacent branches of the carotid arteries and internal jugular vein respectively form a lavish network of capillaries throughout the organ, accepting as they run the support of the trabeculae. Not infrequently, however, the small vessels venture away from this shelter, and are seen lying among the cells; but for the most part there is no intercellular vascular plexus, and in many specimens large masses of cells are found unpenetrated by any blood vessel.

The lymphatic drainage of the gland is likewise free. In its finer ramifications it is traced with difficulty, but it

Fig. 2.—Showing collections of parathyroid cells separated by much fatty tissue.

begins as minute intercellular spaces, which drain into lymphatic capillaries. These, like the blood capillaries, may run in the connective tissue framework, and as they pass along the trabeculae gradually advance towards the surface, and at the same time unite to form larger channels, until finally they emerge from the gland as one—rarely as more than one—main lymphatic vessel. It is common for this latter to meander for some little distance over the capsule before quitting the gland.

The cellular structure of the parathyroid can be appreciated only after an examination of many sections

of many glands. Points which are obscure or absent in one specimen show clearly in another, and often a riddle set by some peculiarity of structure in this section finds its ready solution in that. It is supererogatory and confusing to indulge in a classification into types. The parathyroid has but one structure, and its variations are but expressions either of altered connective tissue contents or of changing activity. It has already been noted how the framework may vary, and this alone is responsible for

Fig. 3.—Showing active and inactive parathyroid cells. At the top right-hand corner is a large mass of resting oxyphil cells; another mass lies in the bottom left hand corner, and three or four smaller clusters appear elsewhere. The dark cells with no oxyphilic protoplasm represent the fatigued stage.

many differences. Most often wide divergences of appearance are introduced by the admixture of fat with the gland tissue. This fat may be entirely absent; it may occur as a few isolated fat spaces; these spaces may be in clusters, or finally whole fields may show fatty tissue, with scarcely any of the proper cellular element. The extent to which this cause alone accounts for differences between specimens is readily understood by comparing slides illustrating the two extremes. In the one containing no fat the cells from end to end

Fig. 4.—Showing many drops of colloid secretion lying irregularly among the parathyroid cells.

of the section are massed in a solid phalanx; in the other the large amount of fat confers a texture more open than the fattest of bone marrows (Figs. 1 and 2). Yet with all this alteration in non-essentials the parathyroid cells repeat their peculiarities of structure over and over again, and such variations as they undergo are always dependent on functional activity, usually on alternating rest and fatigue. The parathyroid cells in the elaboration of their secretion pass through the transformation to which, as Langley has shown, glandular cells are subject; and in the matter of the histological changes

associated with their secretion, the parathyroids fall into line with the other glands of the body.

The cells lie in the compartments made by the trabecular meshwork, and these spaces are filled by a varying number of cells arranged without order. According to the sectional outline of each mesh so will the clump of contained cells be circular, oval or columnar, single or branching. The impression obtained of a section under low power depends on the prominence of this com-

woven than in others. The protoplasm varies extensively with its functional activity. In a cell which has just ceased secreting it is comparatively small in amount and stains faintly or not at all with acid dyes. Later it grows more eosinophile, and appears of a pale pink, with perhaps a dubiously granular texture. Further rest leads to progressive changes, until the fully-rested cells ready to secrete again show a considerable increase in the amount of protoplasm and a marked affinity for eosin, with which

Fig. 5.—Showing two colloid-containing vesicles.

partition, the fields consisting of an apparently continuous mass of cells when the trabeculae are slight, of definitely isolated clumps when the septa are coarse. Naturally so delicate a structure as the parathyroid occasionally suffers in process of preparation and the soft protoplasmic cells may shrink. This results in the appearance of a clear space round each cluster of cells, between it and the limiting trabeculae. The mosaic character thus imparted to the section—each group of cells set in a clear back-

Fig. 7.—Showing stages in the arrangement of parathyroid cells to form regular vesicles.

ground—stain they colour so vividly as at once to arrest the eye in any field in which they occur. Even under a low power, but more clearly under a high, the protoplasm is seen to be crammed with oxyphile granules. In the last stage the granules are extruded into the surrounding lymph space and the cell assumes its fatigued characters, again to perform its functional cycle.

It is not all the cells in a gland, nor even all the cells in any field, that show the same stage of activity. It may

Fig. 6.—Showing much colloid secretion. Most of the drops lie in definite vesicles. The resemblance to normal thyroid tissue should be noted.

ground—is probably wholly factitious and is not seen in more successful preparations.

The cellular elements proper are found to approximate to the so-called "embryonic type." They are polyhedral in shape, each being modelled by its neighbours, and presenting at or near its centre a nucleus surrounded by an amount of protoplasm depending on the condition of the cell. The nucleus, which stains readily though with varying intensity with basic dyes, shows a marked chromatin skeir, which in some cells is more closely

Fig. 8.—Showing a small lymphatic capillary containing colloid.

be that no sign of activity can be found. Slightly more common is it for the whole field to consist of the distended oxyphile cells. Most frequently cells at every stage between rest and fatigue can be readily identified. Unlike other glands, such as the pancreas or the sub-maxillary, where the call for active functioning is intermittent and allows reciprocal periods of rest, there is, from the ductless glands, a constant demand for secretion. These organs must be unceasingly adding their quota to the blood stream, and we should therefore expect to find cells pregnant with secretion side by side with

others exhausted or in process of recovery. A study of but few specimens is needed to corroborate this presumption. The large eosinophile cell occurs in varied connexions. Grouped with many others, it may form clusters big or little. It may lie in small association with three or four of its fellows. It may stand isolated. For the same reason cells of intermediate type can be found, though these, from their less bright hue, require more careful seeking out. With similar irregularity of distribution occur the pale-staining fatigued cells. The appearance, therefore, of a parathyroid gland changes from field to field; and when it is remembered how the stroma and fat vary, it will be realized how apparently widely apart are the histological features of different glands. Yet the underlying explanation—that the gland cells require a rhythm of activity and rest no less than do the cells elsewhere in the body—harmonizes their varied features and arrangements, and enables a clear conception of their structure to be formed (Fig. 3).

II.—THE SECRETION OF THE PARATHYROIDS.

The presence in the parathyroid of minute drops of a colloid-like material has been noted by many, but none has fully interpreted their meaning, while on the secretion as a whole the literature is silent. This is a matter

Fig. 9.—Showing a medium-sized lymphatic channel lined by pavement endothelium and containing colloid.

for surprise, for the human parathyroid so often contains secretion that one would have expected its recognition to have been made earlier.

As regards the different macroscopic appearances of active and resting glands, it is not often possible to decide on the vigour of secretion by naked-eye examination alone. It will sometimes be found that the more darkly-coloured glands—those with the brown of a normal thyroid—represent an active state, while the pale pink bodies contain but little secretion. This distinction, however, is not infallible. Microscopically the examination of one section of any gland sometimes makes it possible to form an idea of the amount of secretion that will be found in subsequent sections. It may be noted as a general rule—subject, however, to exceptions—that the presence of many large clumps of active cells gives promise of plentiful secretion.

The present series provided examples of every stage in the secreting process, from the extrusion of the protoplasmic granules to the draining away of the secretion from the gland.

It has already been shown how the oxyphile cell, distended by its granules, extrudes them into the lymphatic space around. The secretion, as it leaves the cell and for some time afterwards, retains its granularity. The small amounts that lie between the cells are not readily identified under low powers, but with a $\frac{1}{2}$ in. objective they are not difficult to discover. This secretion may now find its way into the neighbouring lymphatic capillaries, but

frequently the products of adjoining cells aggregate to form minute drops of colloid lying in the midst of the cells (Fig. 4). The colloid is often found thus scattered, but there is another position the drop may assume relative to the cells. It is of common occurrence for the secretion to lie among cells grouped more or less regularly around. Naturally a drop is more likely to appear in the centre of a cell clump than near its boundary, since the former position is the nearest point to the greatest number of cells, and will therefore present most facilities for the aggregation of the colloid. Thus it comes that a drop of fair size is seen in the middle of a compartment, having pushed open the cells so that they appear to be grouped in a layer, one or more than one deep, around a central lumen. In this way a vesicle comparable to a thyroid vesicle comes into being (Fig. 5).

In some specimens the colloid will collect to one side of the centre, in which case the lumen lies eccentrically and will be bounded by more cells on one side than on the other; but by far the commonest result, at any rate in compartments containing small masses of cells, is for the colloid to occupy a central space bounded on all sides by a single layer of cells, beyond which comes the limiting trabecula (Fig. 6). With a sufficiently large series of specimens there is no difficulty in recognizing every variety of structure, from the continuous mass of cells to the fully formed vesicle lined by cells as regularly as any

Fig. 10.—Showing a very large lymphatic vessel, a smaller vessel about to open into it, and numerous lymphatic capillaries, all containing colloid. Serial sections proved that all these lymphatics finally poured their secretion into the main vessel.

thyroid vesicle (Fig. 7). Such cells subjected to mutual lateral pressure soon lose their polyhedral outline and become regular cubical epithelium. In the smallest of vesicles, where each cell occupies no inconsiderable segment of a circle, its shape is correspondingly modified, being broader at its base and tapering towards the lumen.

At this stage of the process of secretion the granules of the colloid have frequently merged their individuality, and a homogeneous mass results. A $\frac{1}{2}$ in. objective, however, will often reveal granularity where a $\frac{1}{4}$ in. is useless. Whether the secretion lies as scattered granules among the cells or as a drop in a vesicle, it passes into the lymphatics of the gland and trends to the surface, the smaller lymphatics uniting to form larger. Finally, it can be found, as already mentioned, lying on or in the capsule contained in a large lymphatic lined by the usual pavement endothelium. Along this channel it is led away from the gland (Figs. 8, 9, 10).

It is of interest to note that the cortex of the gland sometimes stains more deeply than the medullary tissue, and that drops of colloid and regular vesicles are met with more frequently near the surface than elsewhere. The latter occurrence is probably due to the flow of colloid being towards the cortex. The nearer the surface the more abundant will the secretion be, and consequently the superficial lymphatic spaces and vessels will be more liable to distension and fuller of secretion than those more deeply situated. Whether the deeply-staining cortex

bespeaks a more vigorous activity is not so certain, though this seems probable.*

It is desirable to emphasize the fact that neither by its appearance nor by its microchemical properties was it possible to distinguish parathyroid colloid from thyroid colloid. The two appear identical. Both may be granular, both may be homogeneous. In a thyroid vesicle the central part of the colloid is often homogeneous while the more recently elaborated secretion near the lining cells is granular. It has already been shown that the parathyroid colloid in its earlier stages is granular but later loses this property.

Both thyroid colloid and parathyroid colloid behave similarly to stains. Though both are usually oxyphile, thyroid colloid will occasionally stain with basic as well as with acid dyes—treated with haematoxylin and eosin a deep purple results. Parathyroid colloid is sometimes found to possess this peculiarity.

In the paraffin process thyroid colloid is apt to become hard and to tear before the razor into characteristic strips, the edges of which tend to crinkle. The larger collections of parathyroid colloid behave identically.

THE INFANTILE PARATHYROID.

There remains to notice a difference between the parathyroid as described above and the gland at or shortly after birth.

Fig. 11.—Infantile parathyroid gland, showing complete absence of all signs of functional activity.

Sections of the gland at this age present an immature appearance in contrast to that attained at a slightly later period. The parathyroid in an infant shows a connective tissue stroma similar in arrangement to that of an adult, but the trabeculae, although delicate, are less masked by the cells and therefore more distinct. These latter wholly fill the compartments and present a uniform aspect of inactivity, the protoplasm being comparatively large in amount but staining scarcely at all with acid dyes. As a result the cell walls are distinct. Cells in an active stage are wholly or almost wholly absent and no deposit of fat can be seen (Fig. 11).

The characteristics of the infantile parathyroid may persist till as late as the third or fourth year, and in one girl of 7 all the parathyroids were infantile. In these later examples, however, it is usual to see signs of awakening activity as marked by a greater affinity of certain cells for eosin. On the other hand, active parathyroids were found in a baby of 3 months. This specimen had none of the above peculiarities except an unwanted prominence of the connective tissue, and it showed the

* I have found in not a few animals (for example, the two-spotted paradoxure, the Beatrix antelope, the suricate, the fat-tailed desert mouse) the thyroid to be as much or more parathyroid than thyroid in structure, and in these instances thyroid characters predominated at the surface, gradually giving place to a parathyroid structure deeper down. Further, in a young four-horned antelope a parathyroid was found in which the whole of the cortex had already become definitely thyroidal, and the change was clearly spreading more deeply. A full description of these glands will be given in the *Journal of Anatomy and Physiology* in the course of a paper on the comparative anatomy and physiology of the thyroid and parathyroid glands in mammals and birds.

cells broken up into clumps and columns as in an adult. Once, in an infant of 6 days, the presence of many moderately active cells was noted, while in a baby of 3 months and in another of 11 months a drop of colloid was found, but this is exceptional.

CONCLUSIONS.

1. The parathyroid gland, like other glands, presents the histological variations of activity and rest. The so-called oxyphile cells are cells distended with granular secretion, and the so called principal cells represent the exhausted stage. Intermediate forms are common.

2. The granular secretion of the cells is extruded into the surrounding lymphatic spaces and often the product of many cells runs together to form a drop. This may either lie in an irregular space between the cells or occupy a central position around which the cells are grouped to form a vesicle. In either case the secretion passes into the smaller lymphatic vessels and gradually flows along larger vessels to reach the surface, whence it drains away from the gland.

3. The secretion of the parathyroid, both in its physical characters and in its microchemical reactions, appears indistinguishable from the colloid of the thyroid.

4. During the first few months of life the parathyroid glands show few if any signs of activity. By the end of the third month at latest colloid secretion may be found, though the infantile type may persist for some years.

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¹ Sandström. Läkareförenings Föreläsningar, Upsala, 1880 (Abstract in Schmidt's *Jahrbuch*, 1880.) ² Welsh, *Journ. Anat. and Physiol.*, 1898.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL.

ACUTE CYSTITIS IN INFANT TREATED WITH HELMITOL.

On December 21st, 1906, I was called to see E. S., a twin, aged 7 months. I found him with a temperature of 103.6°, and no definite symptoms except persistent vomiting and swollen gums, with a purple patch about the size of the head of a small nail on the upper one. On making inquiries, the mother told me that he was passing very little urine. The urine was loaded with albumen (only). I diagnosed infantile scurvy with renal symptoms, and the diagnosis was confirmed by the other twin developing infantile scurvy shortly afterwards. Under suitable treatment the patient made rapid progress, and on January 1st, 1907, the temperature was normal. I was under the impression he was over his troubles, but on the following day I was called in again, to find him with a temperature of 103.4°.

For the next fourteen days, in spite of frequent ice-cloths to the head, cold sponging, etc., and also the most devoted attention and care of the mother and nurses, there was no improvement, the temperature oscillating from 104° to 100°, coming down to normal on two occasions for a very short time. He had, however, developed, in addition to the already-mentioned condition, gastro-enteritis and bronchopneumonia. On January 12th he began to pass pus and blood with his urine, and seemed to feel great relief when he had done so. He showed symptoms of intense pain on pressure being made over the bladder. I now determined to try helmitol, giving 1 grain every three hours. In twenty-four hours the temperature came down to normal, and remained there. In forty-eight hours the pus had entirely disappeared. I persisted with the helmitol for three days more, during which time he passed astonishing quantities of urine. I was, of course, unable to estimate the amount, but the mother was certain he was passing three or four times the normal quantity. From this time onward he made steady progress, although his eventual recovery was somewhat retarded by an attack of whooping-cough.

The scorbutic condition I treated exactly on the lines suggested by Dr. G. F. Still in the *BRITISH MEDICAL JOURNAL* of July 28th, 1906, p. 186, the nurses being much taken aback at being told to give mashed potatoes to an infant of 7 months.

Sparkhill.

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