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REMARKS

ON TUMOURS AND ENLARGEMENTS OF THE THYROID GLAND TREATED SURGICALLY.*

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HAVING during the last few years operated upon twenty-three cases of various forms of enlargement of the thyroid gland, I hope it may prove of interest to give a short sketch of the cases so treated. They arrange themselves in three groups—tumours, parenchymatous goitre, and exophthalmic goitre; of the first 12 cases, of the second 5 cases, and of the last 6 cases.¹ Tumours and parenchymatous goitre are frequently confounded—a reasonable error, since structurally they are often identical, and not rarely are present together. Even Graves's disease in its early stages may be difficult to distinguish from some cases of tumour, as several similar symptoms may be presented by each before exophthalmos is fully developed. Here pathological anatomy is of service to us. The structural changes in Graves's disease are in a way unique, being neither inflammatory, degenerative, nor neoplastic, but more evolutionary as in the lactating mamma. This serves to distinguish it from all other affections of the thyroid. The pathological anatomy explains, too, on the theory that the symptom-complex of Graves's disease is due to the toxic secretions of the altered gland, how it is that similar symptoms may be met with in totally different affections of the gland, if the tissue changes are in any way allied.

GENERAL STRUCTURAL CHANGES.

The remarks contained in this paper are based upon the cases operated on, together with some half dozen cases of cancer. A careful examination has been made of each specimen, and whether speaking generally or in regard to a special point, I wish to be understood as referring to the results obtained from the examination of my own material, and not as quoting from the work of others, with which in most instances these results are in accord. In this sense the following are the structural changes met with in the epithelium, the connective tissue, and the vascular supply of the gland in the three groups of cases. The epithelium: New gland follicles originate in three ways. 1. By the enlargement of old follicles, and the budding into them of branching epithelial growths from their walls until a complete lobule takes the place of what was previously only a follicle. (Fig. 9.) This intrafollicular hypertrophy is characteristic of Graves's disease, except that it is closely mimicked by typical thyroid carcinoma. 2. By the development of new follicles from gland cells lying between the old follicles. (Fig. 4.) This intrafollicular mode of growth is usual in parenchymatous goitre and adenomata. 3. By the budding growth of foetal thyroid tissue (Fig. 6), sometimes met with in adenoma, and possibly originating in "rests," or parathyroid tissue. Normal gland follicles are lined with cubical epithelium. This may become flatter and less active when the follicles distend with colloid matter, and no clear fluid secretion is present, which is the case in parenchymatous goitre and the colloid forms of adenoma. (Figs. 3 and 7.) Or the epithelium may elongate and become more active when in the less advanced condition colloid is present in the follicles, but there are droplets of fluid secretion between it and the cells (Fig. 11); and in the

more advanced condition colloid is absent and the follicles contain fluid secretion only. (Fig. 3.) Elongation and increased activity of the epithelium occurs in Graves's disease and in the soft vascular forms of adenoma. The connective tissue of the gland may increase in the form of a tumour as fibro-adenoma—(Fig. 4)—(as well as pure fibroma and sarcoma, which are both probably very rare). It is also increased in ordinary goitre (Fig. 7), and is abundant, highly nucleated, and vascular in Graves's disease. (Fig. 10.) In the later stages of the latter, as in myxœdema, it may be present as a sclerosis. The thyroid is always well supplied with blood, but in the markedly colloid enlargements the vascular supply is relatively lessened. On the other hand, it is increased in Graves's disease, and in some forms of adenoma. (Fig. 8.) Hæmorrhages into the tissue occur frequently in parenchymatous goitre and adenoma, but appear rare in Graves's disease, in which I have only once seen it. The vessels may also increase in the form of cavernous tissue, which was present in one of the cases of adenoma. (Fig. 5.)

MINUTE STRUCTURE AND CLASSIFICATION OF THE ADENOMATA.

Without pretending that these twelve cases of thyroid adenoma cover the entire field, I believe I am fortunate enough to include amongst them what are probably the leading types of innocent glandular growth in this organ. They remind one of other and better known adenomata in their general characters, but they present special features of which the following are amongst the more important:—1. Their structure is generally purely glandular. 2. They are often multiple. 3. They are frequently cystic. 4. Hæmorrhages into them are very common. At first one is inclined to divide them into two chief groups, the cystic and the solid, but such a classification is unscientific, as the cysts are not derived from distended follicles, but except in rare instances are produced by the continuous breaking down of the walls of the follicles, until more or less of the tumour is converted into a cyst. (Fig. 1.) I have only met with one case in which the wall of the cyst was not composed of the remains of what had once been a solid adenoma, and in this case the cyst may have been derived from a blood clot. It is better, therefore, in classifying the adenomata to disregard the presence or absence of cysts, and to take into consideration only those features which constitute a fundamental distinction. My cases suggest the four following types:—1. The colloid type. 2. The mucous type. 3. The fibrous type. 4. The cavernous type. Colloid adenoma is an encapsuled tumour fairly firm to the touch and easily enucleated. It may be multiple and grow to a considerable size, but sets up no symptoms except such as depend upon mechanical causes. Patients generally seek surgical help on account of some impediment to free respiration, perhaps accompanied with giddiness and congestion of the head; or on account of appearance alone. To the naked eye the tumour is very transparent, and has on section a netlike structure, the meshes of which are filled with colloid matter. Small hæmorrhages are common, though this is the least vascular form of goitre. This tumour is constantly, or at least generally solid. Under the microscope (Fig. 3) the gland follicles are very large; they are lined with a flattened epithelium, and there are no droplets of clear secretion between the cells and the colloid. Frequently the entire ground substance is composed of colloid matter, and the follicles are only distinguishable as rings of brightly stained nuclei. New follicles are developed from cells which lie between the old ones. Mucous adenoma is soft and fleshy; it is also encapsuled and easily enucleated. It is usually more or less cystic, and frequently contains hæmorrhages. Except in the form of old cysts (bronchocele) it is generally a smaller tumour than colloid

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adenoma; perhaps for the same reason, whatever it may be, that exophthalmic goitre, which it resembles, is smaller than parenchymatous goitre, which resembles colloid adenoma. These soft glandular adenomata, except when very small or almost entirely cystic, are generally associated with neurotic symptoms, palpitation, and debility, and sometimes even slight exophthalmos. Surgical aid is more sought for these reasons than for mechanical trouble, which is significant. Under the microscope these tumours often also present in parts large follicles filled with colloid matter, but the lining epithelium is longer, and there are droplets of clear secretion between the colloid and the cells, as in Fig. 11. In other parts of the tumour smaller follicles may be found with probably still longer epithelium (short columnar) and no colloid at all. (Fig. 2.) Occasionally foetal thyroid tissue is present in abundance. (Fig. 6.) In mucous adenoma the gland elements apparently increase both by the development of new follicles from cells lying between the old ones and by the branching growth of foetal thyroid tissue, but I have seen nothing to suggest that any of the new gland tissue is produced by intrafollicular budding. Fibro-adenoma of the thyroid is a rare tumour, of which I have met with only one example. It occurred as a dense hard tumour, the size of a medium orange, in the thyroid of a woman, aged 47, with a goitrous family history. It had been growing twelve years. Histologically (Fig. 4) it consisted of dense fibrous tissue in which were dispersed gland vesicles, sometimes near and sometimes far apart. The vesicles commenced as single cells lying loose in the tissue, which divided and subdivided until full-sized follicles filled with colloid matter were formed. A similar appearance as regards the isolated vesicles may be seen occasionally in parts of a mucous adenoma, but the intervening tissue is then of a delicate myxomatous nature, and may originally have been a blood-clot. Cavernous growths, whether adenomatous or otherwise, are also rare. The case I met with occurred in a woman, aged 35, as a cyst about two inches in diameter and a second smaller tumour. The latter was entirely composed of fibrous trabeculae containing cavernous spaces and with foetal thyroid tissue between them. (Figs. 5 and 6.) The wall of the cyst was composed of a thick layer of young connective tissue having a decidedly sarcomatous appearance, and directly outside it were patches of foetal thyroid. I shall watch this patient with interest in case it may possibly prove malignant, and related to those rare pulsating tumours of bone occurring in connection with an enlargement of the thyroid gland.²

I cannot pass by the tumours of the thyroid without noticing those of a malignant nature, though they are rarely, if ever, remediable by surgical measures. Once in my wards an attempt was made to excise a cancerous thyroid, but it had to be abandoned as impracticable. At different times I have come across about half-a-dozen cases of malignant disease of the thyroid. All proved to be carcinoma, and of the same type: villous growths culminating in imperfect gland follicles, filled with colloid matter. Large tracts of the tumours may have an indifferent structure consisting of unequal-sized cells (possibly chiefly connective tissue), exactly resembling sarcoma; and I think it is chiefly owing to the imperfect examination of specimens that sarcoma of the thyroid has come to be regarded as a form of tumour, at any rate not excessively rare. The more carefully and thoroughly we examine tumours of glandular organs, the less frequently do we find them to be sarcomata. Carcinoma of the thyroid is generally of the scirrhous type, though sometimes it grows abundantly. It has great penetrating power, and a special liability to cause malignant thrombosis of the internal jugular veins. Its metastases are not numerous; beyond the neighbouring glands small patches in the lungs are all I have met with, but the latter are almost constant.

STRUCTURAL CHANGES IN PARENCHYMATOUS GOITRE.

These, so far as my cases go, resemble the appearances seen in colloid adenoma, though the colloid matter is more limited to the interior of the follicles. The epithelium is flattened, and droplets of clear secretion are absent, or almost absent. (Fig. 7.) The gland, though so large, appears to be functionally quiet. Sometimes the collections of colloid are very large, apparently owing to the coalescence of several follicles.

New follicles are developed between the old ones; I have only once seen intrafollicular growth. Partial thyroidectomy was performed in all the cases, for mechanical reasons only.

STRUCTURAL CHANGES IN EXOPHTHALMIC GOITRE.

These are very different. They are characterised by the evident activity of the gland epithelium. When thyroidectomy has been performed at an early stage of the disease plenty of colloid matter is found in the follicles, and it would seem that the first effect of the increased activity of the gland is to distend the enlarging follicles with colloid matter. (Figs. 9 and 11.) The process however does not rest here at all, for the lining epithelium continues to grow and multiply, being in some instances shed into the follicles till they are full of cells, but generally the growth takes a villous character protruding into the enlarged follicle, and growing, branching, and coalescing again, until what was originally a single vesicle becomes a definite lobule composed of glandular acini lined with columnar epithelium and containing only a clear secretion and no colloid matter. (Figs. 9 and 10.) This latter description is evidently the usual structural expression of the increased activity of the gland, but it is not quite constant, and it is puzzling to meet with different appearances. Some specimens are markedly colloid (Fig. 11), and others have myriads of follicles filled with catarrhal-like cells. (Fig. 12.) Perhaps there are colloid, catarrhal, and villous forms, all mere structural varieties or different stages of a pathological change indicating greater secreting energy. The colloid form is not like colloid but like mucous adenoma. The lining cells are elongated and there are clear droplets of fluid secretion between the cells and the colloid matter. (Fig. 11.) There are also tracts where the follicles are small and contain no colloid. Still I have met with one case in which all the clinical features were most marked, yet the gland was translucent from end to end, and I have had another gland sent to me for examination with almost similar characters. New follicles in exophthalmic goitre are typically produced by intrafollicular budding, but possibly they originate in other ways as well. In regard to the vascularity of the gland in Graves's disease, as I have already stated, I am of opinion that it is decidedly greater than in other forms of goitre, and I have seen some specimens in which the vascularity was in excess of what should be required to meet any increased functional activity sufficient I should say to constitute a condition which might present the clinical features of a vascular tumour. (Fig. 8.) In considering this matter it should be remembered that surgical specimens may differ considerably from *post-mortem* specimens, since the evolutionary changes tend to end in sclerosis, and therefore the more advanced the disease beyond the full development of the affection, the less likely is it to show excessive vascularity.

RELATION OF STRUCTURAL CHANGES TO SYMPTOMS.

The theory that the symptoms in Graves's disease are due to toxic products derived from the abnormally abundant secretion of the gland, receives confirmation from a study of the structural changes in adenoma and parenchymatous goitre. The five cases of the latter presented no constitutional symptoms, and applied for treatment for conditions the result of mechanical interference alone. In all, the epithelium was flattened, the follicles were filled with colloid, and droplets of fluid secretion were absent, or almost entirely absent. Some of the adenoma cases presented symptoms of mechanical obstruction only; these were the colloid cases, with structure, as in the preceding. Others had constitutional symptoms, which resembled the early stages of Graves's disease—nervousness, instability of the vaso-motor centres, with palpitation, quickened pulse, and sometimes slight exophthalmos. In all these cases the epithelium was elongated or greatly multiplied, and large droplets of fluid secretion were visible in the follicles, containing colloid, whilst many small follicles contained no colloid. The symptoms were relieved by the removal of the tumour in most instances, though in some originally neurotic subjects the cure was less complete. The six cases of Graves's disease presented the characteristic symptoms in various stages. They were all seen by physicians—Drs. Caton, Barron, Abram, and others—and there is no question as to the correctness of the diagnosis. If there were on clinical grounds the pathological specimens would decide the

Fig. 1. Cystic Adenoma; $\frac{1}{2}$ in. Fig. 2. Mucous adenoma $\frac{1}{2}$ in. Fig. 3. Colloid Adenoma; $\frac{1}{2}$ in. Fig. 4. Fibro-adenoma; $\frac{1}{2}$ in.

Fig. 5. Cavernous Adenoma; 1 in.

Fig. 6. Foetal tissue in Adenoma; 1 in.

point in all except the colloid case, and that was such an advanced and striking case clinically, that no room was left for doubt as to the correctness of the diagnosis. The conclu-

sion that constitutional symptoms accompany any large increase in the active glandular elements of the thyroid, whether in Graves's disease or adenoma, is, I think, irresistible.

Fig. 7. Parenchymatous Goitre; $\frac{1}{2}$ in.

Fig. 8. Exophthalmic Goitre, excessive vascularity; 2 in.

Fig. 9. Exophthalmic Goitre, intrafollicular growth; $\frac{1}{2}$ in Fig. 10. Exophthalmic Goitre, a stage more advanced than Fig. 9; $\frac{1}{2}$ in. Fig. 11. Exophthalmic Goitre, colloid form; $\frac{1}{2}$ in. Fig. 12. Exophthalmic Goitre, catarrhal form; $\frac{1}{2}$ in.

SURGICAL TREATMENT.

I now come to deal with the surgical treatment. This may be divided into cutting operations and other methods, such

as counter-irritants, setons, drainage, and injections. In regard to these latter it is not necessary, nor does time permit me to go into detail respecting them. They are either

less efficient or more dangerous than the former, and I have not recently made use of them. Of the major operations there are four varieties:—Thyroidectomy, partial and complete; ligature of the thyroid arteries; exothyropexy, or exposure of the gland with the object of inducing atrophy; and enucleation. Complete thyroidectomy is very rarely employed. It may sometimes be used in cancer involving the whole gland, though there are few places in which cancer is less remediable by operation than in the thyroid. In no other affection do I think it either desirable or justifiable to completely extirpate the gland. Partial thyroidectomy, ligature of the arteries, and exothyropexy are employed in Graves's disease, and in some cases of parenchymatous goitre; enucleation only applies to the removal of adenomata. I have only undertaken partial thyroidectomy and enucleation, as these have seemed to be the best means by which to attain the end in view; but I can quite believe that exothyropexy may be usefully employed in some advanced cases of Graves's disease, in which it would be unsafe to attempt excision. Enucleation is the simplest of the operations. It is employed for the removal of all innocent tumours of the thyroid, most of which are encapsuled and shell out easily. In such cases an incision is made, either across the neck in the line of the skin folds as recommended by Kocher, or obliquely as is more usual and generally more convenient. Superficial veins if in the way are divided, the expanded throat muscles displaced or partly divided if necessary, and the surface of the gland exposed. The capsule is now incised and the tumour shelled out, which is generally done without difficulty, and without hæmorrhage. Hæmorrhage is never troublesome in the smaller cases. When the tumour is very large the remains of the gland are lost sight of, and the operation is practically the same as thyroidectomy for parenchymatous goitre. In either, with ordinary skill and care, if the respiration is free, and the tumour is limited to the neck, the operation is fairly simple when you have learnt to deal with the hæmorrhage. By fearing this too much one loses time in trying to secure every vessel, and the end is not gained for more blood is lost also. I like to make a free and convenient incision, fully expose the surface of the tumour and work quickly round it, keeping clear as far as possible of the large vessels running in the capsule. When these must be cut, first clamp them on the distal side, and if convenient do so on the tumour side as well. All large vessels except the main arteries bleed chiefly from the tumour side, but unfortunately the tissues of the capsule are liable to be so delicate that the compression forceps tear away, and then perhaps two or three branches are opened and the trouble is increased. I have found that hæmorrhage from the gland side is best arrested by grasping the tumour, as will be referred to again shortly, pending the securing of the arteries. One has to remember that these large capsular veins are very thin walled, and when dragged on are empty and invisible, and if carelessly cut bleed copiously before they can be secured. On the distal side they may perhaps not bleed until the wound has been closed and the patient put to bed, when coughing or vomiting may cause a sudden or copious hæmorrhage. Hence it is a good thing, when the tumour is large and vascular, if the patient can be made to strain before the sutures are put in, and for this as well as other reasons I have never objected to the use of ether in these operations and have often preferred it in Graves's disease. When dealing with a tumour, one first works beneath which ever side comes out easiest. In goitre the upper and lower horns are first cleared and dislocated out of the wound, the superior and inferior thyroid arteries being secured at the same time. As one gets near the trachea it is necessary to keep close to the tumour in order that the recurrent laryngeal nerve may not be injured. At this stage I sometimes continue to work in the same direction, that is on the under side of the tumour turning it across the neck and dividing the isthmus from beneath, but in other cases it is easier after clearing the outer part of the tumour to replace it, cut the isthmus, and remove it from the trachea in the opposite direction. No doubt, one should be very careful of the recurrent laryngeal nerve, but I very rarely see it during the operation, and have certainly never injured it. As regards the isthmus I used to ligature before dividing it, but this is not often necessary.³ In exophthalmic goitre thyroidectomy is undoubtedly a more

serious operation, and I never undertake any but quite early cases without a feeling of anxiety. There are three reasons for greater difficulty in Graves's disease:—1. The patients are much less fitted to bear a serious operation. 2. The gland usually has no tendency to shell out, but requires dissecting from the neighbouring tissues. 3. The hæmorrhage is much more difficult to control. In the first place patients must be selected with due care, and division or excision of the isthmus, or possibly exothyropexy (of which I have no experience) substituted for thyroidectomy when the latter seems too severe. The close connection of the enlarged thyroid with the surrounding tissues not only prolongs the operation, but is the chief cause of the greater difficulty in controlling hæmorrhage. To recommend the surgeon to keep well outside the capsule is good advice, but in those cases in which the capsule is blended with the surrounding tissues the advice is practically meaningless. To clear the gland the vessels must be cut, and though they are easily controlled on the distal side, neither ligatures nor forceps will stop on the gland side, they often only tear the capsule and make the bleeding worse. The way to deal with it is simply to take the gland in the left hand, squeeze it dry like a sponge, and continue to squeeze it until the thyroid arteries are secured. Of course, this leaves only one hand free to operate with, but that is sufficient when you have, as is always necessary, an assistant. Apart from the greater difficulty in securing vessels in exophthalmic goitre there are many more to secure, and it is well when a surgeon is able to train himself in thyroidectomy for other purposes before he is called upon to undertake the operation in an advanced case of Graves's disease. The other necessary details are not special to thyroidectomy, and, therefore, need not be described. In regard to these cutting operations enucleation is simple and in every way satisfactory. It may always be recommended with the same confidence that we would recommend the excision of an adenoma of the breast. Thyroidectomy is a more severe operation. In small parenchymatous goitres it is quite straightforward, and almost devoid of danger; but it becomes both difficult and dangerous in large or awkwardly situated goitres. In exophthalmic goitre it is certainly dangerous, and is perhaps not to be recommended in advanced cases, at any rate until the milder measures of division or removal of the isthmus or exothyropexy have been tried and failed. It is assumed, though I rather doubt it, that either of them would render a subsequent thyroidectomy more easy and safe.

CASES.

ADENOMA.

- i. Mrs. C., 39, 8 children. No goitre in family. Small lump growing in right lobe of thyroid for four months without symptoms. Enucleated September 1891. Tumour was a cyst the size of a walnut with thin mucous adenomatous wall. (Fig. 1.) No recurrence. Now in excellent health.
- ii. Mrs. H., 36, children. No goitre in family. Noticed lump growing in right lobe of thyroid for two years. Patient of neurotic type; debility; tight sensation in throat. Enucleated May 1895. Mucous adenoma size of small egg, partly cystic. Health improved at first, but neurotic symptoms continued. Recently albuminuria. The only unsatisfactory case of adenoma.⁴
- iii. K. J., 13, born at Cape Town. Delicate type of girl. Swelling in middle line of neck low down coming six months; gradually increasing dyspnoea, general health failing, nervous, excitable, quick pulse. Enucleated May 1895. Mucous adenoma size of an egg, partly cystic. (Fig. 2.) Marked improvement rapidly followed the operation. Health excellent, since become quite a strong girl.
- iv. Mrs. G., 47, goitrous family. Had a swelling in the right lobe of the thyroid since a girl. Growing more rapidly recently and obstructing respiration. General health good. Enucleated September 1895. A dense hard fibro-adenoma size of an orange. (Fig. 4.) Quite well since.
- v. Mrs. C., 37, 12 children. No goitre in family. Lump growing on left side of neck for 12 years, recently more rapidly. Obstructing respiration and circulation, but no constitutional symptoms. Enucleated September 1895. Large solid colloid adenoma 12 inches in circumference. (Fig. 3.) November 1896 writes in best of health.
- vi. M. F., 28, servant. Small adenoma in left lobe of thyroid. Some neurotic symptoms. Enucleated December 1895. Solid, mostly colloid, small follicles with numerous cells between them. Writes been in very good health since the operation.
- vii. L. P., 39. No goitre in family. Soft adenoma in left lobe of thyroid growing 5 or 6 years. Health steadily getting worse, neurotic symptoms, debility. Enucleated January 1896. Solid mucous adenoma size of small egg. Marvellous improvement rapidly followed operation, then health fell off somewhat owing to home trouble, but improved again later.
- viii. Mrs. B., 53. No goitre in family. Lump in middle line of neck 13 years. Increasing last 2 years. Tumour pulsates violently. No constitutional symptoms except some debility, has had home worries lately. Enucleated February 1896. A large cyst with old adenomatous wall partly calcified, measured 5 by 3½ inches. No difficulty with hæmorrhage,

pulsation all communicated. Her doctor writes she has been altogether better since the operation.

IX. J. B., 39. Goitrous family history. Goitre noticed since 12, slowly increasing. During last year grown rapidly and pressed on trachea. No constitutional symptoms. A large parenchymatous goitre with encapsulated adenomata in the middle line. June 1896 enucleated three adenomata, largest size of orange. All colloid type. The goitre was not interfered with. The doctor reports much relieved, general health better, no obstruction to respiration, but not quite gained original health yet.

X. E. L., 25. No goitre in family. Soft tumour growing in left lobe of thyroid last five years. Marked constitutional symptoms, giddiness, palpitation, flushing, headache, general nervousness, and incapacity to attend to her duties. September 1896 enucleated a soft vascular mucous adenoma, size of a large egg, and partly cystic. Doctor writes some symptoms almost completely relieved, in others marked improvement.

XI. M. P., 35. No goitre in family. Adenoma growing in left lobe of thyroid near middle line for five years. Slight constitutional symptoms. Enucleated September 1896. Cyst size of small egg with smaller tumour adjacent. The cyst had sarcoma like wall, outside which were thyroid remains, and small masses of fetal thyroid tissue. (Fig. 6.) The smaller tumour was a soft, spongy, cavernous growth, with fetal thyroid tissue scattered through it. (Fig. 5.) Discharged well in a fortnight, and remains well up to the present.

XII. M. S., 31. No goitre in family. Adenoma growing in left lobe of thyroid near middle line during last 5 years. No constitutional symptoms. Enucleated November 1896. A solid colloid adenoma the size of an orange. Discharged well.

PARENCHYMATOUS GOITRE.

I. E. J., 24. No goitre in family. Good health until four years ago when tonsils enlarged. More recently thyroid has been enlarging with slight dyspnoea, and a sense of fullness in the neck. A small goitre. December 1895 right half removed. Usual colloid type with flattened epithelium. States now that she has been well ever since the operation. Married last April. Looks well. Opposite lobe has atrophied, and is not much larger than normal, just noticeable.

II. A. G., 39. No goitre in family. A very large parenchymatous goitre coming since 14. Increased more rapidly last 12 months. No constitutional symptoms. Difficulty in breathing on exertion, and faintness or rather giddiness on stooping. July 1896 isthmus and right lobe removed. The usual colloid goitre with flattened epithelium. (Fig. 7.) Now health much improved, considers herself quite well, and is able to do all her household work. The opposite lobe, which was also very large, has diminished remarkably in size, being only about one-fifth what it was.

III. M. G., 17. No goitre in family. Had the lump as long as she remembers. Getting larger lately and causing dyspnoea on exertion. No constitutional symptoms. A rather small parenchymatous goitre. October 1896 excised left lobe. Recovered well.

IV. Mrs. S., 26, children. No goitre in family. Tumour in neck coming last 2 years. Recently middle lobe grown considerably; grown upwards as a pyramid. No symptoms. October 1896 excised middle and left lobes each about three inches long. Typical colloid goitre. Opposite lobe underwent atrophy at once, and was only just visible when she left the hospital three weeks after the operation.

V. Mrs. B., 33. A healthy woman with goitrous family history. Tumour coming five or more years. Dyspnoea, no other symptoms. A large goitre, nearly as large as A. G., measured $1\frac{1}{2}$ inches round neck. November 1896 excised right lobe. Usual colloid type. Recovering.

EXOPTHALMIC GOITRE.

I. J. B., 23, school-teacher. A subacute case, symptoms only moderately severe, coming on about two years. Thyroid rather large for Graves's disease, exophthalmos only moderately marked. Getting worse and becoming unfitted for her work. December 1893 a small isthmus was excised. Healed quickly, and at once went back to work. Improvement very slow, but gained instead of losing ground. Has remained at her post ever since, and Dr. Barron who sent her to me states that she is now very much better, nervous symptoms almost gone, and able to do her work quite well.

II. Miss F., 20. An acute case. Symptoms coming on two years, now all very marked. Temperature often 101° , pulse 140° to 160° . October 1895 right lobe excised. Recovered well. Immediate marked improvement in all symptoms. Left lobe rapidly declined in size, and within a week slept with eyes closed. Temperature fallen to normal, and pulse to 100° . This case was the colloid type of exophthalmic goitre previously referred to. (Fig. 11.) She is now considered very fairly well by her friends, and has put on a good deal of flesh, but she is very nervous, and has decided exophthalmos, also there is some suspicious firm oedema of the legs. The left half of the thyroid has remained about the size of a bantam's egg. This case is much the least satisfactory of the six.

III. A. W., 33. A fireman on board a P.S.N.C. steamer. Symptoms coming on three years, started by a great fright owing to the wrecking of his steamer. Symptoms all decidedly marked without being of a very severe type. Had to knock off work three weeks before reaching home, and was told by the doctor that he could not be taken again. February 1896 excised right lobe. Recovered well. Was very pleased with himself, and determined that he would go back to his old work. Seen in November. Has been two voyages and worked as a fireman throughout the whole of each. During the first the work was trying, but managed it easily during the second. Still has slight exophthalmos, but looks strong, and says he is quite well.

IV. Miss R., 36. Symptoms coming on three years. Augmented by influenza a year ago, and again later by the extraction of several teeth. Now a typical case with marked exophthalmos, worse than I. or III. but not as bad as II. February 1896 excised right lobe. Healed rapidly and went home in a fortnight. Seen in July. Much stronger, no palpitation, gaining weight, less exophthalmos. In November writes "I now feel almost my old self again." (Fig. 8.)

V. C. McC., 29. Symptoms coming on two years following an attack of bronchitis. Thyroid large for Graves's disease, especially isthmus. All chief symptoms present including *bruit* over tumour and heart. July

1896 removed the large isthmus size of a walnut. Discharged sixteen days later, general condition improved, left lobe already much smaller, right not much altered. November, seen at her home laid up with feverish cold. Exophthalmos much less. Two lobes of gland separated $1\frac{1}{2}$ inches, both much smaller but several times their normal size. States that her general health has much improved, is able to do house work, and feels that she is gradually getting all right again. (Fig. 9.)

VI. E. W., 22, travelling saleswoman. Always had very good health until six months ago, and looks as though she had been a robust girl. Now becoming unfitted for her work at which she is greatly distressed as she has a good post. All the characteristic symptoms including *bruit*, but not in a severe form. Thyroid moderately enlarged and very hard in parts, the only case in which the gland was hard. July 1896 excised right right lobe. Very little blood lost, report says not an ounce. Discharged on ninth day with wound healed. Seen recently after travelling through South Wales. She has been fully employed in responsible work, is bright and cheerful, and very pleased with the improvement in her health. Left lobe much atrophied, but still visible. Exophthalmos not very noticeable now. Nerves strong. *Bruit* and von Graefe's sign disappeared. (Fig. 10.)

CONCLUSIONS.

To sum up the results of the treatment, we have it first as a fact that in twelve cases, tumours weighing up to $\frac{3}{4}$ lb. were removed, and in eleven cases, portions of the gland, some of considerable size, were removed without a fatality.⁵ Healing was rapid in all, only a few patients being under surgical treatment more than about a fortnight. There were six cases of adenoma in which the patients complained of constitutional symptoms, and in all of them young, active gland tissue was present; and six in which the symptoms were *nil* or of mechanical obstruction only. In these the tumour was very small, colloid, fibrous, or almost entirely cystic, that is to say, they were tumours in which there was little or no active secreting epithelium. The patients suffering from mechanical obstruction only were of course entirely relieved by the operation, whilst those suffering from both mechanical and constitutional symptoms were cured of the former and relieved or very much improved in regard to the latter. I consider the operation for the removal of thyroid adenoma a complete success and worthy to be recommended in all cases. Of the five cases of parenchymatous goitre only two have been operated on sufficiently long to pronounce an opinion. These were a class of cases in which I was not at all disposed to urge operation, unless the mechanical interference was such as to render relief imperative, as there are no constitutional symptoms; but if the result obtained in these two is maintained—that is perfect health and atrophy of the opposite lobe—I shall be willing to go further in parenchymatous goitre than my original position. If a patient can be relieved of the unsightly mass without serious danger, and without risk of myxoedema, why should it not be done to improve appearance? Finally, in regard to exophthalmic goitre, I consider the operation in these cases as still on its trial. At best, perhaps it is only worthy of a position like that we accord to operations for cancer. It is a case of treating symptoms. No doubt a very proper thing to do when nothing better is available, but never altogether satisfactory. In regard to the danger of thyroidectomy in Graves's disease, although my six cases have recovered, I certainly do not shut my eyes to the fact that this element has to be contended with. It is present in every case in which the disease is at all advanced, and, though experience helps us to meet it, I feel sure, from what I have seen, that we may all expect on occasion to have to reckon unsuccessfully with it. In regard to the results, they seem to be satisfactory. This is a new disease to the surgeon, and my previous acquaintance with it is slight. The immediate effect of the operation is a marked amelioration in all the symptoms. In some cases the first improvement is so decided, little short of remarkable, that I think there can be no doubt it is directly due to removal of thyroid tissue. If one only followed such cases for a month one would observe the results as "cures;" but, after the temporary rapid improvement, the progress may be slow, and up to the present the whole of the symptoms have not completely disappeared in a single case. I feel one must wait three or four years before passing a final judgment, both on the score of permanency as to benefits obtained, and as to the possibility of encouraging a tendency to myxoedema. The six cases have all been unquestionably benefited. The teacher has continued her work for three years uninterruptedly since the operation. The fireman has had two three months' voyages without knocking off work for a day, and felt much stronger the second voyage. The saleswoman is also back at

work in a responsible position, and able to acquit herself well. Of the other three, one, in which only a middle lobe or enlarged isthmus was removed, has improved very slowly, and only does housework at home. The other two are young ladies; one, the younger and more delicate type, is quite pleased with herself, but is evidently far from well yet; the older and stronger lady is certainly very much improved, and considers that she has regained her old health. I think this is putting matters at their best; and, although it is not quite as definite and satisfactory as one would like, it is sufficient to encourage me to continue the operation in all suitable cases. In adenoma the success is all one could wish, and I believe one might almost say the same in regard to parenchymatous goitre; but in Graves's disease the circumstances are different, and I should be sorry if, by painting the results in too glowing colours, I encouraged anything like reckless operating in so serious a condition.⁶

NOTES.

¹ These have since been doubled. ² It has not recurred. ³ Have since had reason to believe it to be very necessary. ⁴ Just seen accidentally, looking very well, and says she is very well; so there may be some mistake in regard to the unsatisfactory report. ⁵ Since writing this paper, I have had the misfortune to lose a case of parenchymatous goitre, which I will report later. The case was complicated by advanced idiopathic cirrhosis of the liver. ⁶ Since this was written the improvement has been very marked in all the cases of Graves's disease.

A LECTURE ON YELLOW FEVER,

WITH A DESCRIPTION OF THE BACILLUS
ICTEROIDES.

Delivered before the University of Montevideo on June 16th, 1897.

BY PROFESSOR G. SANARELLI,

Director of the Institute of Experimental Hygiene of the University of Montevideo.

[TRANSLATION.]

[AFTER some preliminary observations on the history of yellow fever and on its clinical symptoms, Professor Sanarelli proceeded to give the results of his own investigations as follows:]

CLINICAL AND ANATOMICAL INVESTIGATIONS.

The material of my studies I procured partly at the lazaretto of the Island of Flores; where during last summer I installed a small laboratory for the investigations on the sick, or on the cadavers of individuals coming from the Brazilian ports, and who were taken ill during the voyage; in part at the hospital of St. Sebastian of Rio Janeiro, where, thanks to the kindness of the excellent director, Dr. C. Seidl, and of his able colleagues, Drs. Fajardo and Couto, I was able to instal myself conveniently, and to devote more than a month to clinical, anatomical, and bacteriological researches.

BACTERIOLOGICAL INVESTIGATIONS.

The bodies of those who die of yellow fever (icteroid typhus) are either altogether sterile, or are entirely invaded, by certain microbic species, such as the streptococcus, the staphylococcus pyogenes, the coli bacillus, the protei, etc., which cannot in any way be considered as the cause of the malady, or by a mixture of microbes, of which the isolation alone, the classification, and the study require such an amount of labour as to render accurate systematic research impossible.

I believe it superfluous, then, to recount the ways by which I arrived at the recognition of the microbe of yellow fever; I owe this good fortune to the second case of yellow fever I met with in the Island of Flores. This case presented, in a state of relative purity, the specific microbe to which I subsequently gave the name, not altogether proper, but sufficiently expressive, of "bacillus icteroides," because yellow fever is also called icteroid typhus.

I have said in a state of relative purity, because yellow fever presents the prototype of diseases with mixed infections. In the eleven necropsies that I made, I have never met with the bacillus icteroides alone; it was at least associated with

the coli bacillus, staphylococci, or the streptococcus. In the second case, at the Island of Flores, it was only associated with a small quantity of coli bacilli, and in the eighth, studied at Rio Janeiro, with staphylococcus aureus.

In all the other cases, I either found it mixed, in a large minority, amongst numerous common microbic species, or I was not able to find it owing to the cadavers being completely invaded by other microbes, which, as we shall subsequently see, after having succeeded, owing to the action of the bacillus icteroides, in invading the organism, eventually injure or cause the total disappearance of the specific microbe.

I would briefly premise that the bacillus icteroides must be sought for in the blood and tissues, and not in the gastrointestinal cavity, where, contrary to what might *a priori* be supposed, it is never found. In fact, in yellow fever the digestive canal becomes the seat, as in typhoid fever, of an exaggerated pullulation of the coli bacillus, which is met with in a state of almost absolute purity.

According to the results of my researches, the isolation of the specific microbe of yellow fever is only possible in 58 per cent. of the cases, and in some rare cases may be effected also during life. The reasons why in every case of yellow fever one cannot isolate the specific agent are easy to understand. In the first place, at the beginning of the disease the bacillus icteroides multiplies very little in the human organism, a small quantity of the toxin, as we shall see later, being sufficient to develop in man the very grave picture of the complete disease. In the second place, the toxin, either by itself, or indirectly by means of the profound lesions that it determines, above all in the digestive mucosa and the liver, facilitates in an exceptional way secondary infections of every kind. Such secondary infections may sometimes assume the type of true and special septicæmiæ, with coli bacillus, streptococcus, staphylococcus, etc., capable of killing the patient by themselves alone. At other times they occur mixed, so that, in the last stages of life, they may transform the individual into a true culture of almost all the intestinal microbic species.

Finally, as the result of my observations, that the bacillus icteroides is found in the circulating blood and in the interior of the tissues, and that it is never found in the gastrointestinal contents, it must be held, contrary to what is at present supposed, that the virus of yellow fever does not reside in the digestive tube, and that therefore its poison, instead of being absorbed through the intestinal walls, is manufactured in the interior of the organs, and in the blood itself.

THE BACILLUS ICTEROIDES.

This bacillus at first sight presents nothing morphologically characteristic. It is a little bacillus with rounded extremities, for the most part united in pairs in the culture, and in small groups in the tissues, from two to four-thousandths of a millimetre in length, and as a rule two or three times longer than broad. It is very pleomorphic. A search for it in the tissues does not give good results, excepting in the cases in which the death of a patient occurs without secondary septicæmiæ. Even in the cases which on bacteriological examination give the purest results, it is not easy to see it in the sections of the tissues owing to the number being sometimes extremely small. Yet, by employing suitable methods, one can find it in the organs, usually united in little groups, always situated in the small capillaries of the liver, kidneys, etc. The best means for demonstrating not only its presence, but also the special tendency it has to be localised in small groups in the blood capillaries, is to place a fragment of liver obtained from the body whilst fresh, in the incubator at 37°C. for twelve hours; this favours the multiplication of the specific microbes.

The bacillus of yellow fever develops sufficiently well on all the ordinary nutritive substances. In plate culture in ordinary gelatine it forms roundish colonies, transparent and granular, which during the first three or four days prevent the appearance of leucocytes. The granulation of the colony becomes continuously more marked, and usually a central or peripheric nucleus, completely opaque, is delineated. With time the entire colony becomes opaque, but does not liquefy gelatine. Streak cultures on gelatine solidified obliquely, forming brilliant opaque little drops similar to drops of milk.