that of Graves's disease, the symptoms being due to excess or change in the character of the thyroidal secretion.

It is also well to remember that if for any reason a patient has been taking large doses of thyroid extract for a long period a condition of thyroidism may be produced in which many of the symptoms of Graves's disease develop—such as tachycardia, tremor, nervousness, sweating, and emaciation.

Time will only permit me to allude very briefly to the treatment of these slight cases of exophthalmic goitre. As in fully developed cases, we must enforce a sufficient amount of mental and bodily rest according to circumstances. A liberal diet, which includes two or three pints of milk, is required to compensate for the increased metabolism. A mild faradic current applied to the neck for two or three hours daily is often most beneficial. A prolonged course of arsenic in small doses, with or without the addition of tincture of convallaria, is also useful in most of the cases. On no account should thyroid extract be given in these cases, as it naturally only aggravates the symptoms.

REFERENCES.

¹ *Edinburgh Medical Journal*, August, 1900. ² *Lancet*, November 11th, 1905.

Remarks

ON

THE NATURE AND TREATMENT

OF

PARENCHYMATOUS GOÏTRE.

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UNDER the term "goitre" several varieties of enlargement of the thyroid gland are embraced, and in classifying them great difficulty is felt at the outset from the fact that the varieties are not very distinct.

Part of the gland may show changes characteristic of one class, while another part may display all the features of a goitre of another class. English pathologists regard parenchymatous goitre as distinct from adenoma of the thyroid, but the German schools do not make this distinction. But there is much to recommend the English classification from the point of view of the practical surgeon.

The normal thyroid gland consists of a vascular fibrous stroma, including in its meshes rounded follicles or acini which either possess a central lumen or are filled entirely with epithelial cells. The acini are lined with a single layer of cubical epithelium without basement membrane, and the lumen may be either clear or filled with colloid material.

PARENCHYMATOUS GOÏTRE.

In parenchymatous goitre there is glandular proliferation which results in the production of clusters of cells or of gland-like acini lined with epithelium, which may be somewhat irregular and flattened compared with the normal gland. Both varieties may be seen in the same specimen. The cut surface of a fresh goitre shows to the naked eye a reddish or dark brown colour; in parts where many of the acini contain masses of colloid material the section has a translucent honey-like appearance. All the tissue elements in these goitres are increased in amount.

The patient presents a smooth, full neck, reminiscent, when present to a small extent, of Burne-Jones's paintings. This condition is more common in females than in males, and generally commences about the age of puberty. It is at first quite painless, giving rise to no discomfort. The consistency of such a gland is rather soft and has a somewhat elastic feeling on palpation. It is movable on swallowing.

It frequently enlarges during the menstrual period, and the patient sometimes complains of a slight sensation of suffocation at that time. The voice is not altered and no laryngoscopic changes are to be seen. In many of these cases I have found great hypertrophy of the tonsils, and removal of these seems to have some influence in producing

diminution in the size of the gland; possibly this may be due to the improvement of the patient's general condition.

This mild variety of parenchymatous goitre, which is exceedingly common in Derby and Derbyshire, often subsides gradually without treatment as the patient develops. It is quite common for people here to say that they had a Derbyshire neck when they were young. The popular treatment in the female is to apply a string of artificial pearls or a black velvet neck band, and I was recently much interested to read in the *BRITISH MEDICAL JOURNAL* that the Abyssinian treatment of goitre is to tattoo a string of beads round the neck.

Besides the enlargement of the gland at the menstrual period I have seen the same occur during pregnancy, and decrease in size after childbirth.

When the goitre enlarges to a further degree, the swelling is unsightly, the feeling of suffocation becomes more marked, especially in the recumbent posture. There is often associated anaemia, and the case demands treatment.

An inquiry into the residential situation of the patient is made, and the water supply and general hygienic surroundings ascertained. The water should be boiled and flavoured with lemon to make it palatable. Internally a mixture containing iodine and potassium iodide is given, and if there is anaemia, iron and arsenic also. Thyroid extract may be tried, commencing with $\frac{1}{2}$ -grain doses every other day, and gradually increasing it up to 1 grain three times daily. But the effect on the pulse should be most carefully watched. In my experience the result of treatment with thyroid extract has been very disappointing. If no diminution occurs with this treatment after a month's trial it is useless to continue. Locally the red iodide of mercury ointment has seemed to have some effect, the patient spreading it over the enlarged gland, and then sitting in bright sunshine or before a hot fire. It is very difficult not to blister the skin, however, and although good results are reported from India, its effect has not been very convincing in my own practice.

If such cases are watched for some time the swelling, instead of being uniform, becomes asymmetrical. The changes producing the asymmetrical enlargement are briefly as follows: The acini undergo great dilatation with colloid, the lining cubical cells become flattened, the intervening stroma is absorbed, and a small cyst is formed. This degenerative cystic formation generally causes the formation not of a single cyst but multiple small ones. Haemorrhage may take place in these, thus increasing their volume. Another cause of asymmetry is the growth of a definite encapsulated adenoma, which in its turn often becomes cystic. There may be one or many adenomata, and all stages of cystic degeneration of these may be seen in one gland. Again, asymmetrical enlargement is seen in carcinoma, primary or secondary, in sarcoma, and in endothelioma of the gland. Suppuration is yet another cause of asymmetrical enlargement, and is due to breaking down of new growths, especially sarcoma, to suppuration in a pre-existing cyst, either due to auto-infection or to the injudicious introduction of a septic needle. Metastatic pyogenic deposits have been seen in pyaemia and very rarely gummata and tuberculous granulomata.

If the parenchymatous goitre is of long standing, other degenerative phenomena are common. Fibrous degeneration, with shrinking of the acini and blood vessels and great increase of the fibrous tissue stroma, may be found. This has been observed to lead to myxoedema, or at any rate patients with myxoedema sometimes give a history of having had previously an enlarged thyroid. Impregnation of the fibrous tissue stroma and colloid substance with lime salts is quite common, and true bone is said to have been observed. Colloid degeneration of the stroma itself is sometimes seen; and in such cases the walls of the blood vessels, becoming softened, may give way and a sudden enlargement of the gland due to haemorrhage take place. Amyloid degeneration is occasionally found, the arteries being the chief seat of change, but circumscribed amyloid deposits have been also seen.

Course.

Many goitres, besides the deformity and slight dyspnoea, give rise to no other symptoms.

Dyspnoea, however, is often urgent, and depends on several factors. The gland being tightly bound round the trachea by the deep cervical fascia causes lateral pressure

on the sides of the trachea, producing the "scabbard-shaped" stenosis. If one lobe only is enlarged the anterolateral aspect of the trachea is pressed inwards. It is extremely rare for the pressure to be exerted in an anteroposterior direction, and I have not seen such a case. Another cause for very urgent dyspnoea is enlargement of one or both lobes in a downward direction and impaction behind the sternum. Dyspnoea due to paralysis of the abductor muscles of the larynx by pressure on the recurrent laryngeal nerves I believe I have seen in one case: it was most urgent; aphonia was present at the same time, but the patient was far too cyanosed when I saw her to warrant a laryngoscopic examination; hemithyroidectomy was performed, and she is now well but has paralysis of the right recurrent laryngeal nerve.

Dyspnoea due to penetration of the trachea may be produced by malignant disease or rupture of a suppurating cyst. Softening of the tracheal rings is supposed to occur, but my experience coincides with that of Berry; in one case in which stridor had been so marked that tracheotomy had been performed I was able to show *post mortem* that the tracheal rings were compressed laterally, but no absorption of cartilage had taken place, and they were in nowise softened.

Besides these cases of dyspnoea, acute oedema of the glottis has been seen, more often in malignant disease of the thyroid than in simple, and swelling of the mucous membrane of the trachea itself may also occur. If there is inflammation of the thyroid gland itself, there may be extension into the lumen of the trachea; but more often the swelling of the tracheal lining is only part of a general catarrhal condition of the air passages due to cold, influenza, etc., and only becomes noticeable from the lumen of the trachea being narrowed by a thyroid tumour. A patient with a parenchymatous goitre often says there is no dyspnoea unless he has a cold, and then it may be very urgent indeed.

Difficulty in swallowing is not a common symptom, but in one case under my care it was the only one. Several cases of intense dysphagia due to goitre have been described, but were mostly due to extensions of the thyroid behind the oesophagus and pharynx.

Pressure on the cardiac nerves and on the large blood vessels has been described, especially in the intrathoracic goitres. Tachycardia and irregular heart-beat and some oedema of the head and face, especially the eyelids, have resulted from such goitres.

The symptoms hitherto detailed have been mechanical or pressure symptoms. If the thyroid gland is removed or atrophies, the train of symptoms known as myxoedema results. Now, when all its elements undergo hypertrophy, are there no physiological symptoms produced other than pressure symptoms?

In order to answer the question properly it is necessary to consider what we know of the secretion of the thyroid gland, which is so necessary to the human body. The thyroid is a ductless gland and the colloid substance which fills its acini is its internal secretion or contains it.

The colloid is formed from the granules which can be seen in the cells of the acinus; these granules discharge themselves into the lumen of the acinus, where the colloid collects until a separation of the cells is produced by pressure and the colloid is emptied into the lymphatic spaces. From these spaces the lymphatic vessels convey the secretion into the blood stream by the thoracic duct, etc. According to some observers the colloid is directly absorbed also by the capillary blood vessels. Chemical examination of the gland shows that it contains two proteids, a nucleo-albumen and the colloid substance. This latter substance is a compound proteid containing iodine, the percentage varying, but forming about 3 per cent. of the dried gland. The colloid is not a nucleo-proteid, as no nuclein is yielded by gastric digestion. When the colloid is subjected to digestion, only those substances which contain iodine possess active properties. The active substance, called iodothyron, produces the same effect on the metabolism of the body as the gland substance itself. It is a brown amorphous substance, almost insoluble in water, but readily soluble in weak alkalis. It contains phosphorus and about 10 per cent. of iodine and gives no proteid reaction.

The nerve supply of the gland is derived from the laryngeal nerves and the sympathetic. Pembrey did

not observe any structural changes in the cells as the result of section or stimulation of these nerves or of the vago-sympathetic trunk, and states that the evidence is all against nervous control of the glandular tissue of the thyroid. Edmunds, experimenting with dogs, comes to much the same conclusion. He says:

The paralysing operation does produce some effect both clinical and pathological, but not a great effect; and it must be inferred that the secretion of the thyroid gland is due mainly to a chemical stimulus acting directly on the secreting cells, or on the nerve endings distributed to them, or through fibres which pass along the blood vessels with the sympathetic fibres.

The present belief appears to be that the thyroid gland is in a constant state of slight activity, which is increased under certain conditions. The stimuli which affect the gland appear to be chemical and arrive by way of the blood stream. Proteid feeding has been thought to produce hyperactivity, in fowls at any rate; but Forsyth¹ controverts this view, which was put forward by Chalmers Watson in 1904. Fordyce² (Edinburgh) has made some interesting observations as to the result of feeding rats with milk only or bread and milk. Increase of colloid was found in the pure milk-fed rats. The fact that symptoms of hyperthyroidism do not occur in all goitres that are hypertrophied cannot be due to diminution of the lymphatic spaces by increased amount of fibrous tissue present and the consequent contraction that would follow. In those cases of parenchymatous goitre in which the colloid is so abnormally increased in amount that the freshly cut surface has a honeylike appearance, one would have expected that the colloid would readily have been absorbed by the lymphatics, which are also increased in number. But as a rule we find no symptoms of hyperthyroidism in such cases, so it is probable that the amount of colloid material is no indication of the amount of active internal secretion, and this enormous increase of colloid is a sign of gland degeneration rather than of increased cell activity.

Exophthalmic Symptoms.

But there are occasionally seen cases—the *formes frustes* of the French—which present clinically in the goitre, and also microscopically, typical parenchymatous glands, and which have also marked general symptoms, especially tachycardia and tremors. It has been attempted to prove that those cases of Graves's disease which have apparently benefited by hemisection came under this category. With this view I disagree, and will relate two cases in justification.

CASE I.

Mrs. C. W. came to the out-patient department of the Derbyshire Royal Infirmary in June, 1905. She had had no children, and gave a history of poor general health. The thyroid was enlarged, especially on the right, where it extended from the right sterno-clavicular joint to the submaxillary region. There was some hoarseness and difficulty in swallowing, but tachycardia, palpitation, and tremors of the hands, faintness and giddiness were the chief symptoms. There was no exophthalmos, and von Graefe's sign was absent. The heart was enlarged, and the pulse-rate 136. There was impaired movement of the right vocal cord.

She was admitted under Dr. Thornton, and as with rest, etc., no improvement followed, I saw the case with him and advised operation. A very large right lobe was removed, and part of the isthmus, the pathological report on which is as follows: "This is a typically parenchymatous goitre. The alveoli of the thyroid are of different sizes, and their lumen is full of colloid substance. There is no small-celled infiltration or epithelial proliferation."

The wound healed by first intention, and she was discharged with a pulse-rate of 80, palpitation and tremor still present; the right vocal cord was still not freely mobile, and the dysphagia had not quite disappeared. For nine months she was kept under observation and the dysphagia became more marked, a swelling in the middle line running up to the thyro-hyoid membrane appeared, and in September, 1906, I removed a lobulated tumour undergoing cystic degeneration. Since then there has been no dysphagia, her general condition is better, and the tachycardia only present on any mental excitement.

This was one of the *formes frustes*, which benefited to a considerable extent by operation.

CASE II.

E. W. had been a domestic servant, but had done no work for two years owing to Graves's disease. The symptoms were increasing swelling of the thyroid gland, pulsation and thrill, very marked exophthalmos, von Graefe's sign, Stellwag's sign, tremors of hands, jerky movements, tachycardia, hot flushes, and wasting diarrhoea. The pulse-rate was 140 when seen in

the out-patient department. She attended for four months and did not improve; she was then admitted under Dr. Thornton, who treated her for six weeks.

As she was getting worse rather rapidly he asked me to operate. I used local anaesthesia, allowing the patient to smell a Skinner's mask flavoured with chloroform. The whole right lobe was removed and the left superior thyroid artery ligatured. The microscopical report was: "This is a thyroid gland showing the characteristic cell proliferation found in exophthalmic goitre."

Although rather excitable for twenty-four hours after the operation, she made a rapid recovery and has now been at work for nearly twelve months. Her pulse-rate is about 80 and all her other symptoms have practically disappeared except the exophthalmos, which I think is much the same, but the patient declares is better.

I think it is not necessary to say more to prove that this was a true case of Graves's disease which had benefited by operation. I have had the opportunity of seeing with Dr. Thornton several other cases of *formes frustes* in which the symptoms have not been so well marked, but the occurrence of hyperthyroidism as the immediate result of surgical interference may be touched upon in this connexion.

In one of my own cases, a girl with a large parenchymatous goitre and a thick short isthmus, there were symptoms of hyperthyroidism, restlessness, rapid pulse (140), flushed face and slight elevation of temperature for forty-eight hours after operation. The wound, which was drained as usual for twenty-four hours, was perfectly aseptic throughout. After forty-eight hours the pulse-rate came down to normal, and the patient was discharged cured in a week. In a case under one of my colleagues I saw the same condition. In the case of a young man, operated on by Mr. C. H. Hough at the Derbyshire Royal Infirmary, the heart, a few hours after operation, became very rapid and irregular, great restlessness and sweating was noticed, together with tremors of the hands. The patient died in thirty-six hours from the time of operation. All these cases were both clinically and microscopically parenchymatous goitres. In all the internal secretion must have been distributed to the body in excess at the time of the operation. This must have been due to the manipulation of the gland forcing the internal secretion into the lymphatic spaces, although, as far as possible, this is reduced to a minimum by retracting the surrounding structures away from the gland and touching it as little as possible with the hand. Another cause must be escape of the internal secretion directly into the wound when the isthmus is divided. To limit this as far as may be, the isthmus is, when possible, crushed in a clamp, ligatured and divided, and the wound is rapidly washed out with hot normal saline to limit the amount of internal secretion left in it. If the isthmus is thick and fleshy, the application of the crushing clamp itself must force an undue amount of internal secretion into the surrounding lymphatic spaces. I have noticed that post-operative hyperthyroidism has not occurred in patients whose thyroids contained enormously dilated acini, but rather in those firm, fleshy glands in which the acini are only moderately distended with colloid; these patients are usually young people—that is to say, post-operative hyperthyroidism is most likely to occur in the actively secreting glands of moderate size, and not in the parenchymatous glands which are enormous and whose contained colloid is more a sign of degeneration than active secretion. I know that certain patients with cystic goitre, when the cyst has ruptured during operation, have exhibited signs of post-operative hyperthyroidism, but as a rule no such manifestation occurs. Enough has been said to warrant the belief that the colloid is the vehicle which contains the active internal secretion, and this may be present in a larger or smaller amount, but the quantity of colloid substance present is no indication of its physiological value.

THE OPERATION.

A sandbag is placed under the neck. The anaesthetist is shut off from the operation area behind a sterilized sheet held over two upright iron supports. The sheet is continued over the body, and there is a slit in it which comes over the goitre, the edges of which can be clipped to the skin incision. In parenchymatous goitre the incision should be transverse. The resulting scar is excellent, and can be concealed by a strip of velvet or a neck-lace. None of my patients have been dissatisfied with the

cosmetic result. The anterior borders of the sternomastoids should be well defined to permit of easy retraction. The infrahyoid muscles and the layer of fascia covering them are divided close to the hyoid bone and dissected off the front of the gland. In this way the nerve supply is not interfered with, and the line of suture at the end of the operation does not coincide with the skin incision. All bleeding is now carefully stopped. The upper pole of the lobe to be removed is cleared first, and the superior thyroid artery and vein clamped between two pairs of forceps and divided, and then tied off in one ligature. In some of my earlier cases I tied the superior thyroid vessels with an aneurysm needle and then divided them. But since the ligature with which the artery was tied once slipped off when I was dividing it, I have given up the aneurysm needle. The next step is to tie the middle thyroid vein, and in doing so to free the outer border of the gland. Then the upper border of the isthmus and the pyramidal lobe is cleared, and then the lower border of the isthmus is defined. The inferior thyroid vein is tied at this stage, and the thyroidea ima if present. The isthmus having been defined is crushed up in a clamp, one blade of which is carefully passed between the trachea and isthmus. The crushed portion is easily tied and divided; if any colloid escapes at this time into the wound it is washed out at once with hot sterile saline solution.

The half gland can now be held downwards and forward, and the attachment is the inferior lateral ligament and inferior thyroid artery. This is the most anxious part of the operation. The artery is in such close relationship to the recurrent laryngeal nerve that several methods have been adopted to protect the latter. Careful isolation of the nerve has been performed, but in one case in which I did this the patient suffered from recurrent laryngeal palsy which did not clear up for several weeks after operation. Another method is to cut obliquely into the tissue of the gland itself and to pick up the points of the inferior thyroid artery inside the capsule. In this way the nerve is not seen and the bleeding arrested easily, but unless the assistant is very careful not to allow the ends of his forceps to more than seize each bleeding point, I conceive it possible that the nerve might be nipped up and included in a ligature just the same. I now prefer to hold the gland well out of the wound, and, cutting absolutely on to the capsule itself, pick up the branches of the artery just as they penetrate the capsule. By this means I often see the nerve, but do not disturb it with instruments, and so have never had any traumatic neuritis. The gland being now free is lifted out of the wound, a hole is made at the lower end of the musculo-fascial sheet, a drainage tube inserted, and the muscles and fascia sutured where divided, the sandbag under the neck being removed at this point and the head raised by the anaesthetist. The skin is now sutured with interrupted finest silkworm gut, the glass drainage tube is left projecting, and the wound carefully dressed with sterile gauze, wool, and bandage. The patient is propped upright in bed, with bed-rest and pillows carefully supporting the head. The wound is dressed in twenty-four hours and the tube removed. The patient is allowed out of bed on the fourth day. Stitches are removed on the sixth or seventh, and a collodion and gauze dressing applied.

Single adenomata may often be shelled out easily, and sometimes multiple ones also by cutting into the gland capsule and dividing the gland substance until the adenoma is reached. But it often happens, if many adenoma are present, that a hemi-extirpation is the only practicable operation possible.

The immediate results of thyroid operations are excellent; healing by first intention is practically always obtained. Amongst nearly forty cases that I have had in hospital and private practice, there has been one case of suppuration, and that occurred after the wound had apparently healed, being due to a spreading infection from the site of the tube.

REFERENCES.

- ¹ *Physiological Journal*, 1907.
- ² *BRITISH MEDICAL JOURNAL*, 1907.

THE late Mr. J. A. D. Shipley, solicitor, of Newcastle-on-Tyne, has directed that after the payment of certain legacies his residuary estate, estimated at £100,000, should be divided amongst various local charities, including the Royal Victoria Infirmary and other medical institutions.