

# The Erasmus Wilson Lectures

ON

## THE PATHOLOGY AND DISEASES OF THE THYROID GLAND.

*Delivered at the Royal College of Surgeons of England on Feb. 18th, 20th, and 22nd, 1901,*

By WALTER EDMUNDS, F.R.C.S. ENG.,

SURGEON TO THE TOTTENHAM HOSPITAL; SURGEON TO OUT-PATIENTS AT THE EVELINA HOSPITAL FOR SICK CHILDREN.

### LECTURE I.

*Delivered on Feb. 18th.*

MR. PRESIDENT AND GENTLEMEN,—The subject of the lectures which the Council has done me the honour to elect me to give is the Pathology and Diseases of the Thyroid Gland. The subject is not new to this theatre, for in 1891 Mr. James Berry selected the pathology, diagnosis, and surgical treatment of goitre for the Hunterian lectures which he gave that year, but in the 10 years which have since elapsed considerable progress has been made in our knowledge of the physiology of the thyroid gland, and it is therefore convenient to reconsider our views as to the nature of its diseases, and more especially of Graves's disease, in the light of these advances.

The thyroid gland consists mainly of closed vesicles lined with epithelial cells which secrete the colloid; it may here be remarked that the normal vesicles are in shape round or square (in some conditions they become branched and stellate), that the secreting cells are cubical (in some conditions they become columnar), and that the colloid readily stains with the usual microscopic agents (in some conditions it does not stain). It may be added that the nerves to the thyroid have been traced into close proximity to, but not actually into, the secreting cells. Besides the thyroid proper there are certain small glands named "parathyroids." Recent researches have shown these to be of much importance in the organism; indeed, their excision generally causes the death of the animal. These glands were no doubt observed from time to time by various anatomists, but the first full account of them was written by Sandström of Sweden in 1880. In this country they were independently described by Cresswell Baber in a paper published in the Philosophical Transactions of the Royal Society in 1881. The parathyroid glands differ from the thyroid gland proper in that they consist wholly of cells and contain no vesicles and no colloid, or at most a minute droplet (Fig. 1 and Fig. 2).

It is not easy to identify the parathyroid glands in the human subject because some of the minute outlying nodules are found to consist of ordinary thyroid tissue and to be therefore accessory thyroid glands; only those that consist exclusively or mainly of cells are to be regarded as parathyroid glands. The anatomy of the parathyroid gland in man has been worked out by Dr. D. A. Welsh of Edinburgh. He finds that there are four of these glands—one anterior and inferior to, one posterior and superior to, each thyroid lobe. The parathyroid glands are said to differ from the thyroid gland proper in another way—developmentally; they develop in advance of the thyroid lobes.

We can study the physiology of the thyroid gland by operations for its removal in whole, in part, or in successive parts; also by the administration of preparations from the thyroid gland or from the parathyroid glands.

The earliest experiments on excision of the thyroid gland were made by Sir Astley Cooper as long ago as 1824.

In 1844 Sir John Simon made an important contribution to the subject. He proceeded by the very Hunterian method of studying the comparative anatomy of the organ, and embodied his results in a monograph on the thyroid gland in vertebrata which was published in the Philosophical Transactions. He came to the conclusion that the thyroid gland is intimately concerned in the nutrition of the central nervous system and in the regulation of the circulation to the brain. It is interesting to note that these views, arrived at more than half a century ago mainly through comparative anatomy, have recently received confirmation from the experimental methods of to-day.

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In 1856 and 1857 Schiff made a series of experiments. He showed clearly the fatal results that usually follow the complete excision of the thyroid gland in dogs and cats. But not much attention was paid to the subject till 1882 and 1883,

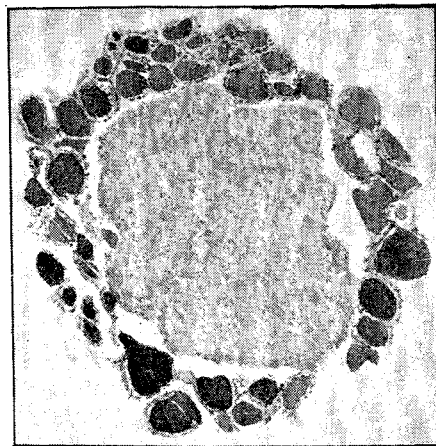
FIG. 1.



Normal parathyroid gland of the dog. A small part of the adjacent thyroid gland proper is shown and can be recognised by its vesicles containing colloid. In the dog the parathyroid gland lies on the surface of the thyroid gland. (x 50.)

when Reverdin and Kocher respectively reported cases of excision of the goitrous thyroid gland in the human subject which was followed by serious, and in some cases fatal, results. Schiff now repeated his experiments, and he has been followed by numerous observers. The subject, however,

FIG. 2.



Normal parathyroid gland of the monkey. The parathyroid gland is completely surrounded by the thyroid gland proper.

has proved rather complicated, as the results apparently differed in different kinds of animals.

Sir Astley Cooper's experiments were made on the dog, and it will be convenient in the first place to consider

the now well-established results which follow the complete extirpation of the thyroid gland and the parathyroid glands in the dog. The symptoms commence generally about 48 hours after the operation. One of the first symptoms noticed, probably the first if the animal is closely observed, is a fibrillar twitching of the muscles; this can be seen, and it can also be distinctly felt by placing the hand on the dog. Within a day or two this is often followed by a severe attack of general convulsions; the animal lies down—in fact, it cannot stand—as its limbs are in a state of spastic paralysis; further, its respirations are hurried, rising to 200 a minute or more. Also during the attack its temperature is raised, sometimes as much as several degrees. These attacks last for an hour more or less and completely pass off, so that the next day the animal appears to be itself again. The convulsive attacks may recur and in a day or two other symptoms may appear; the dog becomes much less lively—in fact, quite listless. Its hair falls out and a peculiarity is noticed in its gait; also it has a difficulty in maintaining its equilibrium, especially when turning round. Later a rigidity is noticed in its limbs, and before long its hind legs may become completely paralysed; trophic symptoms may come on, such as ulcers on the skin, also a conjunctivitis followed by a keratitis leading to destruction of the eye. It may be added that the urine sometimes contains albumin and more rarely sugar; also that between the convulsive attacks the temperature is subnormal. Finally the animal dies on about the fifth day, but death may occur at any time between the second and the eleventh day, or even later.

There is one other point which, considering its bearing on Graves's disease, ought not to be overlooked, and that is whether there is any alteration in the prominence of the eyes. It is much affected; the palpebral fissures become narrower and the eyes less prominent.

The great majority of the dogs submitted to total thyroidectomy die, but a small percentage recover; this result seems to be common to nearly all observers, and cannot therefore be explained away by error of experiment. We must conclude that even in dogs and cats total excision of the thyroid gland and of the parathyroid glands is not necessarily a fatal procedure, while in other less extensive operations we must be prepared for an absence of absolutely conclusive results.

Now, although the operation was followed in dogs and cats with so great a mortality it was found to produce no effect whatever in rabbits. It was soon shown, however, by Gley that the contradiction was only apparent, for he found that two of the parathyroid glands in rabbits lie separate from the thyroid gland proper, and consequently escape removal when the thyroid gland is excised. Gley found that when these were also removed the rabbit, as a rule, died.

In monkeys total excision of the thyroid gland produces symptoms similar to those seen in dogs. The majority of monkeys thus operated on have tremors and convulsions and also passing paresis of the limbs. They have, too, cedema under the eyelids, and occasionally well-marked swellings there. Finally, the monkeys nearly always die, many with acute nerve symptoms similar to those seen in dogs; others have, as was first pointed out by Horsley, symptoms identical with myxedema in man. The hair falls out and swelling occurs in the face which is especially marked under the eyelids. In monkeys, too, enophthalmos and narrowing of the palpebral fissures occur, but exceptionally widening of the palpebral fissures may be seen.

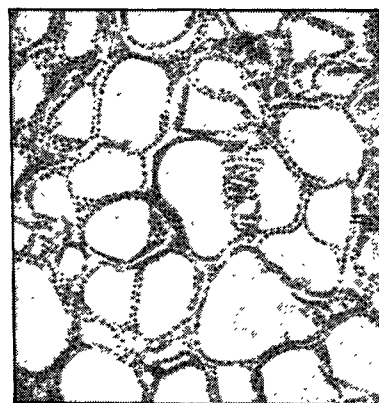
The fatal termination in dogs cannot, as a rule, be prevented by thyroid gland feeding or by the subcutaneous injection of thyroid extract. The conclusions which I arrived at from some experiments on this point were that the symptoms were somewhat modified, the attacks of convulsions with rapid breathing being less frequent; that death occurred on an average a few days later than in untreated cases; and that the small percentage of recoveries was somewhat increased. Cunningham came to similar conclusions: he found that by thyroid gland feeding the lives of thyroidless dogs could be prolonged from an average of from 52 to 54 hours to an average of from eight to 12 days. It has been thought that the lives of the animals might be saved by grafting into them the excised thyroid lobes, and with this view a lobe has been returned to the site from which it has just been excised or it has been placed in the abdomen. The result, however, in most cases at least, has been that the grafted lobe has simply been absorbed (that certainly has been the result in my

experiments on this point) and the dog has died. This treatment, however, is not absolutely without effect, for during the process of absorption the lobe acts as thyroid gland food and the course of the ailment is slightly modified accordingly. In monkeys, too, thyroid gland feeding, although it modifies and prolongs the course of the disease, fails as a rule to save the life of the animal. Such, then, are the results of total excision.

If in a dog one lobe of the thyroid gland, together with its two parathyroid glands, is excised, leaving the opposite lobe with its two parathyroid glands, no obvious effect is produced on the dog; and if the remaining lobe and its parathyroid glands are subsequently removed the dog dies, and this occurs no matter what the interval between the two operations may have been; similarly with piecemeal excision, the dog dies after the removal of one of the later pieces.

Although no symptoms occur in a dog as a consequence of the removal of one lobe of the thyroid gland important changes occur in the lobe which is left; as was pointed out by Wagner, it hypertrophies. The microscopical changes were first described by Horsley; the vesicles enlarge and become branched, the cubical secreting cells become columnar, and the colloid disappears and is replaced by a mucous secretion which takes the staining reagents badly (Fig. 3, Fig. 4, Fig. 5, and Fig. 6).

FIG. 3 AND FIG. 4.



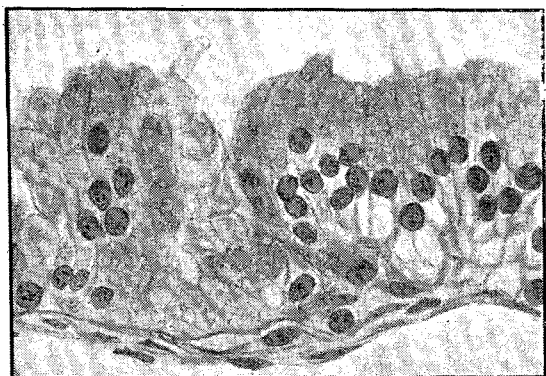
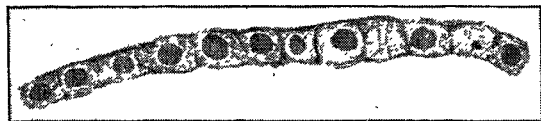
The upper figure shows the normal thyroid gland of the dog. The lower figure shows a portion of the thyroid gland left *in situ* for 41 days after the whole of one lobe and nearly the whole of the other lobe of the thyroid gland had been excised, leaving only one parathyroid gland and a small portion of thyroid gland proper. The vesicles are enlarged and their lining membrane is folded. The colloid has nearly disappeared. The drawings are to the same scale. ( $\times 90$ .)

Whether there is any difference in the physiological action of normal colloid and that of the secretion in compensating hypertrophy we do not yet know, but it is a point worth investigating. In order to ascertain to what extent the symptoms produced by total excision are due to the excision of the thyroid gland proper and to what extent to excision of the parathyroid glands it is necessary to excise them separately. In dogs if one parathyroid gland be dissected free from the thyroid lobe, taking care not to interfere with its blood-supply, and be left in the animal, and the rest of the thyroid gland on that side be excised and also the whole of the thyroid gland with its two parathyroid glands on the opposite side, so that only one parathyroid gland be left in the animal, the dog will live and no obvious effects will ensue; such, at least, is the usual result. If the parathyroid

gland is subsequently excised the dog will die with the usual acute symptoms. The parathyroid glands that are left in these experiments show signs of more active growth than the normal, but they do not develop into thyroid tissue proper. No vesicles form. This it will be noticed, tells against the view that was once held, that the parathyroid glands are undeveloped thyroid tissue.

In rabbits the excision of the thyroid lobes with the two attached parathyroid glands, leaving *in situ* the two other parathyroid glands, produces, as already stated, no immediate effect; but if the animals are kept for several months the

FIG. 5 AND FIG. 6.



The upper figure shows the normal secreting cells lining the vesicles of a dog's thyroid gland. The lower drawing shows the same cells from a small portion of the thyroid gland which had been left together with a parathyroid gland 132 days after the greater portion of the thyroid gland had been excised. The drawings are to the same scale ( $\times 600$ ).

following symptoms may arise. In four experiments I noticed (1) failure of health, (2) hair falling out, and (3) a swelling of the lower part of the face, presumably myxoedematous in nature. Dr. G. R. Murray of Newcastle has also observed myxoedematous changes coming on late in rabbits which have been deprived of their thyroid glands proper. With respect to the condition of the eyes in these animals which have been deprived of their thyroid glands proper, in dogs I have not noticed, as a rule, any change; but in one dog still under observation there have recently come on symptoms—tremors and spastic gait—and for months past it has been noticed that the eyes have appeared sunken and the palpebral fissures narrower; these symptoms are getting worse. In rabbits a series of experiments were made especially to test this point, the result was that there was found a marked tendency for the eyes to become narrow; if eventually the animals died from thyroid symptoms the eyes became very narrow.

**MEMORIAL HOSPITAL COT.**—Dr. W. F. Clarke, as trustee of the estate of the late Mr. James Ewen Maddilove, has forwarded to the treasurer of the City Orthopaedic Hospital, Hatton-garden, London, £1000 to endow a cot in memory of Mr. Maddilove's daughter.

**BRISTOL ROYAL HOSPITAL FOR SICK CHILDREN AND WOMEN.**—On May 1st, in fulfilment of a promise given some few months ago to the Duchess of Beaufort, Earl Roberts visited Bristol for the purpose of opening a bazaar held in Colston Hall on behalf of the funds of the Royal Hospital for Sick Children and Women. Earl Roberts, who was received with great enthusiasm, in the course of his speech alluded to the fact that for some years past the annual expenses of the hospital had exceeded the income by £1300, and that at the present time there remained a deficit balance of £3000. The bazaar, which lasted for four days, was most successful, and it is thought that a substantial sum has been raised for the hospital.

## An Address

ON

### THE IMPORTANCE OF THE TEACHING OF INSANITY TO THE MEDICAL STUDENT AND PRACTITIONER IN RELATION TO THE PREVENTION OF INSANITY.

*Delivered before the South Eastern Division of the Medico-Psychological Association on April 24th, 1901,*

By ROBERT JONES, M.D. M.R.C.P. LOND.,  
RESIDENT PHYSICIAN AND SUPERINTENDENT, LONDON COUNTY ASYLUM, CLAYBURY.

GENTLEMEN,—I venture to take for my subject the teaching of insanity in a somewhat wider sense than that for the medical student only; in part because of the increased public interest which the subject has caused through enormous expenditure necessitated in housing and accommodating the victims of this disease; in part, also, from the loss to the community through the permanent disablement and consequent unproductiveness of those who fail to recover from it. Acres of print are blown on to us daily from the four winds, and some apology may be needed for pinioning these thoughts in manuscript and placing them before you. Mine shall be this—that as we are all members of a great association to which this subject in all its bearings is and ever must be a matter of the very greatest concern I may be permitted to claim your attention upon an aspect which may tend very materially to modify its extension. Such, I take it, is the aspiration of our hearts and the exertion of our hands.

This association, which was established in 1841, can look back upon 60 years' record of lively and unbroken interest in the welfare of the insane. It has ever assisted efforts made for the amelioration of those suffering from this most melancholy and grievous of human afflictions. Its prosperity is in no small measure due to the manner in which its council has adhered to the objects for which the association was established—viz., "the promotion and cultivation of science in relation to mental disorder, the improvement of the treatment of the insane, and the maintenance of the honour and interests of the medical profession generally." How the "medical profession generally" is to become conversant with this particular branch of medicine is the subject of this paper. All of us are agreed that the commencement must be in the proper training of the medical student and many of us recall the difficulties which accompanied our own early efforts in the proper comprehension of this subject.

Within a few years of the foundation of the association a general revival grew up in matters medical. In 1855 an arts examination became necessary as a preliminary to a medical career, for which credit is due to the Society of Apothecaries. In 1858 the Medical Act was passed creating a system of registration and bringing into existence the General Medical Council. Since this year—recognising that the fundamental pathological conception of disease is biological—an infinite addition of subjects favouring in the main the appreciation of natural science has been made to the students' curriculum, and this has greatly influenced not only the intellectual status but also the social standing of the profession. It was not until 1893, however, that the General Medical Council made it compulsory for the student to attend a special course of instruction in mental diseases. Some of our teachers in the medical schools still consider a proper study of this subject to be subsidiary and only likely to distract the student from what they believe to be more urgent and more important departments. I shall endeavour to give reasons why the study of mental diseases is in itself important by pointing out the bearing upon, and the utility of, this subject to the varied duties of a medical practitioner, and finally to suggest methods for its fuller and more complete apprehension.

To-day there are no less than 30,000 medical men (and women) in Great Britain and Ireland out of a population of