Classics in Endocrinology

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This issue’s Classic is George Murray’s brief note in the British Medical Journal (1891; 2: 796) that established the value of treatment of hypothyroidism with thyroid extract. This short paper is one of the founding documents of our discipline of endocrinology. While Murray may not have actually been the first to use this treatment (see this issue’s Historical Note), there is no question about the influence of this paper on others. The therapy spread rapidly and, although the paper describes only a single patient, established a valid and successful endocrine therapy.
healthy. We decided, after anxious deliberation, that it would be useless to attempt removal of the mass, and that to avoid rupture of the uterus the fetus must be speedily removed; and as the disease was limited to the uterus and ovaries, no morphine was used. A suppository was introduced into the cervical canal, and the patient was given a few ounces of alcohol, and was then removed to the operating room.

The operation was performed on the 6th day after the last menstruation, at 10 A.M. By 3 P.M., the patient was in a state of somnolence, and the abdomen was opened by an incision above the pubes to the umbilicus. The peritoneum was carefully incised, and the uterus was found to be adherent to the bladder. The incision was then carried down to the level of the cervix, and the uterus was removed in one piece. The patient did not recover, and died on the 10th day.

Remarke.—The case is, so far as I know, the only case of hysteroectomy performed on the same subject during this year. The patient was a woman of 30, of good health, and had been pregnant seven times. The operation was performed under chloroform, and the patient did not suffer any pain or discomfort. The uterus was removed in one piece, and the patient was allowed to recover.

NOTE ON THE TREATMENT OF MYXEDEMA BY HYPODERMIC INJECTIONS OF AN EXTRACT OF THE THYROID GLAND OF A SHEEP.


Myxœdema has until recently been considered an incurable disease. Since the pathology of this remarkable condition, however, has become more fully understood, hopes of the possibility of greatly relieving the symptoms, if not of curing the disease entirely, have been entertained. The observations of the symptoms which followed the removal of the thyroid gland in man made by Professor Kocher, of Berne, and the results of the experimental removal of the gland in animals obtained by Mr. Victor Horsley have firmly established the view that this disease is due to the loss of function of the thyroid gland. It was found by Dr. von Eiselsberg that if the thyroid gland was successfully transplanted from the neck of an animal to some other part of the body, it was capable of continuing its functions, and of preventing the onset of the symptoms which would otherwise have followed its removal from the neck. Mr. Horsley then arranged that grafting a healthy sheep’s thyroid gland into a patient suffering from myxœdema should be tried as a means of arresting the
progress of the disease. This suggestion has since been carried out. Bettencourt and Serrano, of Lisbon, introduced one half of the thyroid gland of a sheep beneath the skin of the inframammary region on each side in a woman of 36, suffering from myxoedema. The operation was followed by an immediate improvement. Movements became more easy and the speech more natural. The number of red corpuscles in the blood steadily increased till it nearly reached the normal standard in a month. The temperature was raised, the subcutaneous swelling diminished, and the patient began to perspire once more. The period of menstruation, which before had lasted for two and sometimes three weeks, was reduced to four days. These authors considered that as the improvement commenced the day after the operation, it could not be due to the gland becoming vascularised and so functional, but suggested that it was due to the absorption of the juice of the healthy thyroid gland by the tissues of the patient.

Now it seems reasonable to suppose that the same amount of improvement might be obtained by simply injecting the juice or an extract of the thyroid gland of a sheep beneath the skin of the patient.

If we consider that myxoedema and cachexia strumipriva are due to the absence from the body of some substance which is present in the normal thyroid gland, and which is necessary to maintain the body in health, it is at least rational to apply to the patient the missing substance, that is, thyroxine, by injecting the extract of a healthy gland. G. Vesselle has made intravenous injections of an extract of the thyroid gland in dogs after thyrotoxicosis with beneficial results. As far as I am aware, this means of treatment has not before been tried in the human subject. Since suggesting this treatment at the February meeting of the Northumberland and Durham Medical Society, I have been able to carry it out in a well-marked case of myxoedema. Such decided improvement has resulted that the details of the method of treatment employed and the results obtained are worth recording. After trying one or two slightly different methods, the following has been found to be the most convenient, but is probably capable of considerable improvement.

The left half of the thyroid gland of a sheep is removed as soon as possible after the animal has been killed. The surrounding fat and connective tissue are removed from it. All the instruments and glass vessels used in the further preparation of the extract should be either sterilised by heat or thoroughly cleansed with a 1 in 20 solution of carbolic acid. The gland is cut up on a glass dish into small pieces, and then placed in a test tube with 1 cubic centimetre of pure glycerine and 1 cubic centimetre of a 0.5 per cent. solution of carbolic acid. The mouth of the tube is closed with a plug of cotton-wool, and the mixture allowed to stand in a cool place for three days. The gland is then placed in a small handkerchief which has previously been placed for a few minutes in boiling water. It is then firmly squeezed by screwing up the handkerchief so as to express as much juice as possible through the handkerchief. By this means 3 cubic centimetres (50 minims) of a turbid pink liquid are obtained. This preparation, which will keep quite fresh for at least a week, should be kept in a small bottle with a glass stopper. It is best to make the extract fresh each week, so as to avoid any risk of putrefaction taking place. This extract may be given in two equal injections of 1.5 cubic centimetres (50 minims) each during the week, so that at first the patient receives the extract of one lobe of a sheep's thyroid in the course of each week. After a time the injections need not be made so frequently. The injections are made with an ordinary hypodermic syringe, which is carefully washed out with a 1 in 20 solution of carbolic acid both before and after the injection is made. The surface of the skin is also carefully cleansed with the same carbolic solution at the point where the injection is made. The loose skin of the back, between the shoulder-blades, is a convenient situation in which to make the injection.

The following note gives the history and condition of the patient before the commencement of the treatment: 

Age 38, aged 40. For five years ago it was first noticed by her friends that her speech and actions were becoming very slow. She herself began to feel soon after that it required a great effort to do her ordinary housework. Her features gradually became enlarged and thickened. The hands and feet increased in size and became altered in shape. She has not perspired at all during the last four years. Six years ago she had a miscarriage; since then she has only menstruated once, four years ago. At the present time she presents most of the characteristic symptoms of myxoedema. She complains of languor, a disinclination to see strangers, and great sensitiveness to cold. The temperature is sub-normal, and varies between 95.6° and 97.2° in the mouth. The pulse varies between 60 and 70. The face is blank and expressionless, and the features are notably thickened. This change is well seen in the alae nasi and lips. The subcutaneous connective tissue of the eyelids is so swollen that she finds it difficult to look upwards. There is also considerable swelling beneath the eyes and of the cheeks. The hands and feet are both enlarged; the former have that peculiar shape which has been described as "spade-like." The skin is very dry, there is no perspiration, and the superficial layers of the epidermis are continually being shed as a fine white powder. The hair is very fine in texture, and a considerable quantity of it has been lost. She is slow in answering questions; all her actions are slow, and are performed with difficulty. The speech is remarkably slow and drawing, and the memory is impaired. No hair is left on the hand, and no hair is felt in the neck. The urine contains no albumen or sugar.

July 13th. It is now three months since the treatment was commenced; it has not, however, been carried out continuously all the time, and at one period treatment was stopped. The results obtained have been of a much more decided character than that described was used. Extracts of five lobes of sheep's thyroid have been injected, that is altogether equal to the extract of two glands. The patient has been considerably improved since the treatment commenced, and, though three weeks were allowed to elapse between the injection of the last two extracts, she did not lose any of the gained and previously gained. The swelling has gradually diminished, and has practically disappeared from the backs of the hands, the skin over them being now loose and freely movable. The lips are much smaller. The swelling of the upper eyelids has diminished so much that she can look upwards quite easily. The swelling beneath the eyes and of the cheeks has also much diminished. The face consequently, as a whole, has greatly improved in appearance, and has much more expression, as many of the natural wrinkles, especially about the forehead, have returned. The speech has become more rapid and distinct, the drawl being scarcely noticeable at all times. She answers questions much more readily, the mind has become more active, and the memory has improved. She is more active in all her movements, and finds it less effort than formerly to do her housework. She now walks about the streets without any hesitation without a companion.

She has menstruated normally during the last six weeks at the regular interval. For the last four weeks the skin has been much less dry and she perspires when walking. The hair remains as before. She is no longer so sensitive to cold. Unfortunately owing to circumstances a daily record of the temperature has not been kept, but out of four observations that have been made lately, about 11 a.m., three times the temperature has been 98.2° F. and once 97.4°.

Many cases of myxoedema doubtless do improve to a certain extent when untreated, and it is not wise to draw many conclusions from a single case; but the return of perspiration and menstruation when they have not occurred for four years, together with the many other signs of improvement which have followed the treatment, are, I think, sufficient to show that this treatment really has a beneficial effect upon the disease. The improvement, of course, cannot be expected to be continued if the injections are discontinued, but there seems no reason why it should not be maintained if the injections are repeated at intervals of two or three weeks.

This case is published in the hope that others may be induced to give the treatment a fair trial in similar cases. It might also be tried in cases where it is found necessary to remove the whole of the thyroid gland to prevent the onset of, or at least modify, the unpleasant train of symptoms which are cachexia strumipriva, which so often follows thyrotoxicosis.

2 BRITISH MEDICAL JOURNAL, FEBRUARY 8th, 1900, p. 287.
3 La Semaine Médicale, August 18th, 1896.
4 Centralblatt für die medizinischen Wissenschaften, 1891, p. 14.

7 The Endocrinologist