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[Reprinted from St. Bartholomew's Hospital Reports, Vol. XXIX.] 1893.

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SOME RARE CLINICAL POINTS IN GRAVES' DISEASE.

BY

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Having followed with some care for several years a number of cases of this disease, I propose to submit in this paper a few clinical observations which are of rarity. These cases have some of them formed the basis of a paper read by the author before the Medical Society of London in October 1893, but the full clinical details being unsuited to a short paper at such a Society, it has been thought well to store them in the pages of the Reports, which are appropriately open to more minute records.

I.—*Myxœdema and Graves' Disease—Connection by Heredity.*

Mrs. J., a labourer's wife, aged 58.

I have known her for six years, during which time she has exhibited an increasing hebetude and an enormously increasing bulk.

Her family are very neurotic. Her mother was insane; one brother committed suicide, insane; a first cousin is a congenital idiot.

I do not propose to give full details of her case: suffice it to say that the onset of the disease was so gradual that for some years I considered her as affected by huge corpulence, slight osteo-arthritis, and commencing primary dementia; but it was gradually obvious that she had myxœdema in an early stage, the diagnosis being based on the following symptoms:—Continual slow pulse. Marked supra-clavicular swellings. Almost total loss of hair on the scalp. Coarse, dry, scaly skin. Temperature continually sub-normal. A garrulous, inconsequent form of dementia, with continual delusion of grievance. A frequent subjective sense of "smelling something rotten."

Several sudden attacks of semi-coma. Enormous increase in bulk.

The thyroid body deserves special notice; it varied almost from day to day during the periods of attendance, when I have examined it carefully; it has been usually quite impalpable, but at times can be felt very distinctly; it then feels not only slightly enlarged, but of a dense, cartilaginous hardness, quite unlike the feel of an ordinary thyroid.

The speech became markedly drawling in the autumn of 1892.

I have treated her periodically by thyroid feeding, using first raw thyroids, and later on Burroughes & Wellcome's compressed thyroids. She has improved very considerably, but the result was not the magical cure which it has been in some reported cases. Probably this modified improvement is due to the fact that the case is not purely myxœdematous, that she is suffering also from slight early senile dementia, chronic arthritis, and emphysema, and that these factors have impaired her nutrition.

In passing, I may offer these remarks on the treatment:—

First, that no one should employ crude thyroids, now that manufactured preparations are to be obtained, because not only the size of thyroids vary, but also their therapeutical value. I gave this patient weighed quantities (one drachm) at one time, and the dose certainly had very varying effects.

Secondly, that a dose of *two* whole thyroids, which I gave experimentally, rendered her very alarmingly ill; her slow pulse ran up to 130, and she was very faint and collapsed.

Thirdly, a sufficient dose makes them so very uncomfortable and ill that it is cruel to give it continuously, even if there is no actual danger in the continual administration.

Fourthly, that the period of improvement after six weeks' treatment did not exceed two months.

This woman has seven children, all adult.

One son has a slightly enlarged thyroid, and is very anæmic and thin, suffering from constant dyspepsia and palpitation, but I have never had the opportunity of examining him with due care to determine if he has Graves' disease.

One daughter, E. J., aged 35, unmarried, is slightly deficient in intellect. I have known her for six years. She has had a large goitre since puberty. Till the autumn of 1892 I could find no evidence of exophthalmic goitre; the only (doubtful) evidence was retraction of the eyelids, which I noticed first in 1890.

The goitre affects both sides, but the right lobe is larger, contains a large cyst, and a great deal of firm, fibrous tissue.

In December 1892 there was no question that she had Graves' disease in a rather acute form; all the usual symptoms were well marked.

Mr. Berry kindly admitted her to the Royal Free Hospital, and proposed removal of part at least of the thyroid, but at the last moment she refused operation.

The occasional connection between Graves' disease and myxœdema is now well established. There is sufficient evidence that myxœdema is sometimes preceded by exophthalmic goitre, a reduction of the thyroid taking place simultaneously with the development of the symptoms of myxœdema.

"So far most of the observations on myxœdema have been made on well-pronounced cases of some years' duration. As experience grows, there will arise the possibility of recognising cases in early periods, and of determining the existence at such periods of changes in the thyroid body. It is not too much to say that in this aspect all cases of exophthalmic goitre ought to be followed with much care."[1]

Enlargement of the thyroid occurring early in myxœdema was noticed in 1885 by Mr. Hopkins,[2] but the suspicion of pre-existing definite Graves' disease had perhaps not occurred to him, though (with much acumen) he suggests that "perhaps flushing, inordinate sweating . . . will be found to be, in some cases at least, the first symptoms of the disease."

Some of the symptoms in the two conditions are significantly the same—flushing, perspirations, crises of diarrhœa and of vertigo, all pointing to vaso-motor disturbance—while the tremor of Graves' disease and cachexia strumipriva are identical.[3] Moreover, transient bulbar symptoms are common to both diseases—difficulty in swallowing, slight dyspnœa, passing glycosuria.

Several instances of similar transition from the one state to the other have been reported in the last few years, and in these cases considerable variation in the size of the thyroid has been found.[4]

Sollier related two cases[5] of undoubted Graves' disease accompanied by myxœdema, in both of which the thyroid was atrophied. The myxœdema underwent improvement, together with the fellow-disease, by the use of the continued current.

A reversal of this order is described by Kovalevski. A man of epileptic parentage had "suffered from 'petit mal,' beginning

[1] Report of Clin. Soc. of London on Myxœdema, 1888, p. 180.
[2] Clin. Soc. Trans., 1885, xviii. p. 332.
[3] Professor V. Horsley, Brown Lectures, 1885.
[4] W. Ord, Berlin Internat. Cong., 1890. Dr. Ord has kindly helped me with references on this head.
[5] Rev. de Méd., Dec. 10, 1891. Abst. Brit. Med. Journ. Epitome, 1892, i. p. 25.

at about twenty years of age; at forty he showed signs of Basedow's disease, which became aggravated. When he came under observation, the skin of the feet was found swollen, dry, dirty, hairless, and glistening. Pressure with the finger produced pitting; a similar swelling was apparent in the face. The patient was excited and had delusions; later he became stupid, remained lying on his bed, and made no answers or wrong ones; this condition lasted three months, after that only the symptoms of Graves' disease remained." Kovalevski believed that the exophthalmic goitre was incident on a previously existing myxœdema, and that the transitory activity of the diseased thyroid had become discontinued.[1]

Quite recently a case is reported from Nottingham in which myxœdema become evident five years after the recognition of Graves' disease,[2] and I have a note of an unpublished case in which exophthalmic goitre had existed for eight years, but disappeared after an attack of measles, to be succeeded by the slow development of myxœdema.

Bearing in mind the connection between the two diseases, Dr. W. B. Ransom has recently tried the effect of injections of thyroid juice in two cases of exophthalmic goitre in which the symptoms were very marked. The treatment was kept up in one case for six weeks, but in neither experiment was there the least result.[3]

The daughter's condition bears on the question, which I raised at the Medical Society's discussion,[4] whether Graves' disease is apt to occur in previously goitrous persons.

II.—*An Uncommon Form of Cardiac Irregularity.*

In the discussion on Dr. Sansom's paper at the London Medical Society in December 1892, I drew attention to an uncommon form of cardiac irregularity, of which the following are full notes.

Mrs. St., aged 24. Soon after marriage, when just pregnant, she was frightened by an attempted housebreaking. Soon after a goitre appeared. When I first saw her, about eighteen months after, she had a large goitre, affecting the left lobe chiefly. There was marked retraction of the eyelids, but no other signs of the disease. The action of the heart was very rapid (100–120).

[1] Archives de Neurologie, xviii. p. 422, 1889. Schmidt's Jahrb., ccxxvii. S. 147. I have translated from a paper by Möbius; Deutsche Zeitsch. für Nervenheilk., 1891, p. 423.

[2] Henry Williams, Brit. Med. Journ., i. 1893, p. 799.

[3] Trans., Oct. 16, 1893.

[4] Brit. Med. Journ., 1892, ii. p. 451.

There was evidently some hypertrophy, the impulse being very forcible, and felt in the nipple line and outside in the sixth interspace. The pulse presented a rhythmical variation both in rate and volume, quite appreciable by the finger. The beats become gradually feeble and slower for a quarter or half minute, and then as gradually increase in rate and force. This variation has no connection with the respiratory action, as it continues when the breath is held. In addition to this peculiar rhythm, the pulse was somewhat irregular and intermittent. From lack of time I was unable to take a sphygmogram, or indeed to see her again till April, when her general condition was much improved, and the pulse presented no abnormality save a slightly irregular action. In February 1893 she seemed quite well; there were no signs present except the goitre, and this was intermittent, for on May 8th I could find none at all, but three weeks afterwards it had increased again to an appreciable size.

III.—*Rhythmical Jerking, Clonic Spasms, associated with Goitre, Palpitation, and Rapid Pulse.*

Mrs. K., aged 23, married three months. One other sister has a goitre. She has always had fair health, though she is not robust. A distinctly emotional girl. Her menses had been regular since marriage till October 1, 1892, when she got wet through during a fatiguing walk on the eve of a menstrual period. She was seized suddenly with peculiar rhythmical convulsions, which began in the hands, then spread to the neck and arms, keeping her awake all night. Consciousness was not affected.

Next morning her condition was thus:—First, when she lay quietly on her back, there was a regular, sudden jerking forwards of both shoulders, occurring at intervals of about two to four seconds. The movement was very forcible, and affected chiefly the great pectoral muscles. She was perfectly natural and composed in manner, rather amused than frightened at her condition. Secondly, in a few minutes the shoulders became less convulsed, and violent tremor began in the right arm, at first a rapid pronation movement, exactly resembling paralysis agitans, changing in a few minutes to pure flexion and extension tremors of both wrists, so violent that she could hold nothing. Any attempt at voluntary movement increased the tremor. When left quietly by herself the movements cease.

Temperature normal. Pulse 120–130, somewhat irregular. No diminution of field of vision. Sight normal ($V = \frac{6}{6}$). Smell certainly deficient on left side. Slight general anæsthenia.

She has had a uniform soft goitre since childhood. For some years she has been liable to cardiac palpitation, especially when startled. She has also some chronic dyspepsia, but no gastric crises.

October 4.—The character of movements slightly altered. There is a constant, regular, violent shrugging of the shoulders, occurring at intervals of one second almost exactly. This takes place in the upper part of the trapezius. Slight irregular twitching of the platysma.

October 5.—The type of movement changed again; both arms are moved backwards and forwards synchronously, and very rapidly, as if she were polishing a small object lying on her knees. The muscles chiefly affected are the pectorals, infra-spinatus, and trapezius. When the contractions become most violent the legs begin to move also, the movement being a rapid but slight flexion of each thigh and knee, occurring at perfectly regular intervals, one leg being extended when the other is flexed.

These movements continued at frequent intervals for some days, and gradually subsided in intensity and frequency of occurrence. The jerking of the shoulders recurred occasionally for many months.

These convulsive movements are of types often seen in hysterical subjects, though the jerking movements of the pectorals are rare. Dr. Gowers has, however, recorded such a case.[1] An interest, however, attaches to them here on account of their occurrence in a goitrous girl, having also palpitation and a rapid pulse. Though rapid pulse is a common hysterical symptom, and though it may be claimed that the whole attack was merely an hysterical convulsion in a previously goitrous subject, it is not unreasonable, on the other hand, to claim the spasms as an exaggerated form of the tremor of exophthalmic goitre. The resemblance of the movements of the arms to that tremor was exact in kind, though excessive in amplitude and slow in vibration.[2]

IV.—*The Effect of Altitude of Residence.*

Curtin[3] has produced facts in support of the statement that residence at a high altitude is an exciting cause of the neurosis. Obviously, if this be true, patients should not be sent to a mountain climate. I have hills round me rising to 900 feet above

[1] Diseases of the Nervous System, vol. ii. p. 921.
[2] See "Tremor in Graves' Disease," Brain, 1892, p. 424.
[3] Trans. American Climatological Assoc., 1888, p. 89.

sea-level, inhabited at the top, and have had the opportunity of noting the altitude of residence in fifteen cases; in all these instances the patients had inhabited these places for at least a year, and in most cases for many years. The following were the altitudes:—

Under 200 feet above sea-level . . .	4 cases
300 to 400 „ „ „ . . .	5 „
400 to 700 „ „ „ . . .	5 „
Above 800 „ „ „ . . .	1 „

In two instances, notes of which have been sent me by a friend, the symptoms suddenly supervened in English patients suffering from malaria, after removal to the Nilghiri Hills.

Mr. Hutchinson strongly advocates the trial of long-continued residence in mountain air,[1] while Dr. Gowers disbelieves in it.[2]

V.—*A Rare Form of Œdema.*

Mrs. S. has been affected with Graves' disease for about four years. A note on her condition is to be found in the Hospital Reports, xxvii. p. 139, Case ix. She has presented from time to time almost every variety of localised œdema which has been described in this affection, and during May 1893 she suddenly developed swellings in both supraclavicular hollows. I took the trouble to examine these swellings frequently, and found that they varied very much in degree, being sometimes entirely absent, and often present on the left side and not on the right. They were soft, ill-defined, rather irregular in such outline as they possessed, gave no sense of fluctuation, and did not pit. The swellings are sometimes very tender, and sometimes pulsate synchronously with the ventricles of the heart. They are enlargements of the lower part of the external jugular vein, and probably of the internal jugular and subclavians in part. This condition is not uncommon in neurotic subjects (apart from Graves' disease), and I have seen it in a neurotic woman who presented evidence of mitral disease also. The only description I have met of this condition is by Rendu,[3] who thus describes it:—

"Il donne la sensation d'un empâtement diffus d'un œdème dur et resistent, parfaitement indolent, non fluctuant, mat à la

[1] Archives of Surgery, i. p. 167.
[2] Diseases of Nervous System, ii. p. 821.
[3] Nouvelle Dict. Encycl. des Sciences Med., art. "Goitre Exophtalmique."

percussion, et semble être produit par une sorte de fluxion congestive du tissu cellulaire souscutanée."

This description does not apply at all to the condition I describe, but it does apply very well to the supraclavicular pads in myxœdema. It is possible that Rendu had stumbled by accident on some of these rare cases in a transition stage from Graves' disease to myxœdema, the connection between which was unknown when he wrote.