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10.

GRAVES'S DISEASE.

By Arthur Maude.

Mr. President and Gentlemen,—I propose to touch on certain points in exophthalmic goître or Graves's disease.

The first is the importance of the thyroid enlargement.

The belief is an established one, that the disease may exist (and frequently does) without any goître, and there are plenty of statistics of the proportion of cases in which goître occurs. Having for some years taken great interest in this condition, I have had a routine custom of always examining the thyroid in all cases of anæmia or cardiac disturbance at every interview. The result has been that I have detected several cases of Graves's disease in an early stage, and my diagnosis has been verified by the onset of other marked symptoms pertaining to that condition. I have had 15 cases under my care in the last five years: it is not a large number, but the conditions of my work have enabled me to watch them more closely and for a longer period than, probably, any other series of cases has ever been watched, for it is impossible in hospital or consulting practice to follow patients as I have done. My observation is a positive one, and therefore worth many negatives, that every person has presented variations in the size of the thyroid from the earliest complaints of any cardiac symptoms. This variation has been in several very slight at first, no more than many women show, if the neck is carefully examined, when in perfectly good health. I prefer, therefore, to call it a "variation in the size of the thyroid" than a goître. However, in all these 15 cases, if a large goître was not present at first it developed later.

All my patients have been women.

One case I have watched with peculiar care—seeing her con-

stantly for five years, and almost daily for months together. She had for two years constant variations in the size of the thyroid: it was never much enlarged during that time, but was never the same two days running, and occasionally I found it vary almost from hour to hour. Without such continuous observation she might easily have been described as having no goître, for she had not noticed it herself.

I do not press this prevalence of bronchocele as an ætiological factor in the production of Graves's disease in my part of the country, the more so because there are two factors tending to produce neuroses, which are worth attending to, and which are both in full force round me.

1st. In America there is a growing opinion that neuroses are particularly common in parts of the country where a quiet rural life is being rapidly exchanged for a more active, highly competitive civilisation, where frequent trains, posts, and telegrams have been rather suddenly introduced.

2ndly. In country villages the milder imbeciles, the feeble intelligences sprung of neurotic families, always marry with other imbeciles of like lineage, because no other girls will look at them. I know a young man whose father is a drunkard, whose mother and aunt were half-witted, who had one brother a suicidal melancholic, and another epileptic; he must needs marry an hysterical girl whose mother has hystero-epilepsy of a well pronounced type, whose aunts are two of them very hysterical, and a third has Graves's disease, and the latter has several feeble-witted children, one of whom is epileptic. This well-selected pair have children: I could produce dozens of such cases. These feeble-minded neurotic young women in villages get married to the exclusion of better girls, because in many cases they are seduced and the seducer is forced by public opinion to marry them. This factor in the production of neurotic offspring is not at work in towns, for social and economic reasons on which we need not touch here.

It is interesting to enquire whether Graves's disease is on the increase. On this point the opinion of this Society should be of value. The figures of admission to St. Bartholomew's Hospital, as an example, show that from 1870 to 1880 only 17 cases were admitted, but from 1880 to 1890 53 cases came in. This may be due merely to a better recognition of the disease on the parts of house physicians and others.

The Registrar-General, unfortunately, classifies all deaths from affections of the thyroid, except malignant and specific diseases, under the one head of "Bronchocele," but his figures are instructive, for they show that there has been a steady rise from 91 to 152 in the decade beginning with 1881. The increase of deaths has been almost entirely female, the male mortality averaging 22⅓ and increasing from 21 steadily to 26. Now, simple goître rarely kills, except by excessive thyroid enlargement, and such very large goîtres are rare in England. The presumption is, therefore, that the increase in death rate is due to Graves's disease, and this is supported by the increasing preponderance of female deaths. For there is no question that Graves's disease far more largely affects women, and though women are more liable than men to all thyroid affections, I am not aware that there is any evidence that they are becoming increasingly so liable.

Next, does Graves's disease never occur in previously goitrous subjects? Two years ago M. Lasvénes* published in detail three such cases, in which the persons had been goitrous many years. They are the sole records I can find. I have myself met with *seven* instances. I have known them all for years, seen them frequently, and devoted great care to the diagnosis, as the question is, to my mind, of great importance.

Case 1.—Married woman, aged 47. Goîtrous since 18 years of age. Examined carefully and often in 1887—1888, and decided to be a case of simple goître. Not till 1891 did she develop any real signs of Graves's disease, and these were then accompanied by various paralytic conditions of great interest. I have twice published an account of her, and shall allude to some of her symptoms later.

Case 2.—Married woman, 43. Goître first noticed early in 1888, probably due to constant use of water contaminated by cow-dung. A neighbour in the next cottage, using the same water, is also goitrous. Patient miscarried in November, 1891; immediately after she began to have severe palpitation, constant rapid pulse, and typical attacks of diarrhœa, while the goître increased largely.

Case 3.—Mrs. S——, 51. Goitrous for 14 years. Has had, during the last two years, an attack of cystitis, probably secondary to slight cystocele, and two attacks of influenza. For six months she had rapid pulse, severe palpitation, flushing, sweats, and tremor, while for a year afterwards I noticed marked retraction of the eyelids, so great as to expose the upper margin of the corneæ.

* 'Thèse de Paris,' 1891.

Case 4.—Mrs. P——, 54. Goître since marriage at 29 years old. In the last two years it has increased largely, though the water supply she uses is excellent. At the same time, she has developed frequent distressing palpitation, and a rapid and irregular heart. She has some dilatation of the heart; this, however, may be due, as may the other cardiac signs, to emphysema, which is present. But she presents, also, marked and typical tremor of hands and trunk.

Case 5.—Mrs. W. K——, 23, is the daughter of the last patient. One other sister is also goitrous; patient has had a large goître since childhood; for about two years has been subject to distressing palpitation, especially when startled, which she is very easily. Soon after marriage, last autumn, she suddenly developed a form of rhythmic spasms, which I shall describe briefly later on, and on watching her closely for some time I noted extreme palpitation and rapid pulse.

Case 6.—Mrs. A. S——, 52. Goitrous 15 years. For about two years her menses, previously natural, became irregular, prolonged, and profuse, with no objective cause discoverable. During this time she has become increasingly subject to severe palpitation and irregular rapid heart. She also presents marked retraction of the lids.

Case 7.—E. J——, unmarried, 37. Mother myxœdematous patient of weak intellect. Goître has existed since puberty. I have known her nearly seven years, and found no sign of Graves's disease till the autumn of 1892. Since then she has developed every sign of that disorder in an aggravated form.

I may say boldly, here, that in my opinion the value of the eyelid symptoms in Graves's disease has been much over-rated; that I find them common in many people in good health, and particularly common in neurotic subjects.

Next, the disease is said, on all hands, not to occur in districts where bronchocele is common, nor in the subjects of previous bronchocele.

I can find, however, nothing like statistics on either point. In wading through the vast bibliography of this disease, I am struck by the large number of cases reported in certain Western American States, possibly because the medical press is so prolific there; but in 1878 an Illinois physician* (Mr. Earle) asserted that it was very common in that State. Mr. Burton, of Cambridge,† thought it also very common in that county, where bronchocele is comparatively unknown, but where rheumatism and anæmia (the result of malaria) are very rife.

Again, though it is known in India among natives (we have Sir

* 'Brit. Med. Jour.', 1893. II. Epitome—21 (95). Tachycardia.

† Earle: 'Trans. Illinois Med. Soc.', 1878.

Joseph Fayrer's authority for that), it cannot be common, for I have these definite statements from ophthalmic surgeons, who, as we saw in 1886, do stumble across a good many cases. Mr. Drake Brockman,* of Madras, never saw one case during 15 years of practice there: Professor Perry, of Lahore, kindly informs me that he has never seen one in his large *clinique* there, and he adds that Professor Murray, of that city, has had the same experience; though both these gentlemen have huge numbers of goitrous Punjâbis continually in their hands.

Now, what is my own experience?

I live 20 miles from London, on the borders of Kent and Surrey, and I find I have made notes in six years of 55 cases of enlarged thyroid, out of a population which may be roughly estimated at 3,000 souls. When allowance is made for cases which will not have come under my observation this seems a high percentage of goître: but on that point I ask for opinion from some of you who are more widely informed.

Out of these 55 cases of enlarged thyroid, 12 are undoubted cases of Graves's disease, 9 of which I published a few years back, 5 more are ill-marked, "*fruste*," cases, to adopt the name that Professor Charcot's School have given them. The remaining cases are simple goître.

The figures are small, but even if they do not prove that Graves's disease is common among goitrous people, they certainly do not support the opposite assumption.

Now, of these cases, I regard only three as at all doubtful: they may be merely instances of paroxysmal tachycardia coming on in women approaching the menopauses, or under the nervous stress of recent marriage, as in one example, and the fact that they are goitrous may be purely accidental. Kisch has lately shown how common paroxysmal tachycardia is in women at such epochs. But the balance of evidence is in favour of all seven cases being exophthalmic goître.

The other four cases are undoubtedly exophthalmic goître. The only question with them is whether they had not exophthalmic goître all along; to that I can only reply that I have been for years looking for it, and that any special knowledge I may possess on the subject would be more likely to lead me to think that the

* 'Trans. Ophthalm. Soc.', 1886.

disease was present when it was not, than to overlook symptoms which were not well marked.

The last patient brings in another point, the connection of exophthalmic goître with myxœdema. She belongs to a highly neurotic family. Her mother, whose portrait I pass round, is myxœdematous, in an early stage, and the mother's thyroid has exhibited marked variations in size for some years. The two diseases here occur in two generations, but there is plenty of evidence that myxœdema is sometimes preceded by Graves's disease, and a reversal of this order has been described by Kovalevski,* in the case of a man having exophthalmic goître, who developed signs of myxœdema which disappeared after some months, while the symptoms of Graves's disease remained. This sequence of myxœdema to Graves's disease is of great practical importance, for if a surgeon performs extirpation of the thyroid in a case of Graves's disease and myxœdema ensues, it need not necessarily be the result of the operation. But, curiously enough, I can find no record of myxœdema ever having followed such an operation for this disease.

I collected last year† 20 cases of operation on the thyroid for Graves's disease. In 11 the whole gland was extirpated, with great improvement in all, and absolute recovery in several. One case remained well for 10 years. Half the gland was removed in two instances with great improvement, and in three the surgical treatment of cysts was attended by relief, but in one of these the symptoms recovered in a few years. In two cases, however, tetany ensued, and there was no relief.

In my list there was no fatality, but I learn, through the kindness of Dr. Hale White and Mr. Arbuthnot Lane, that a patient has recently died in London during this operation.

In spite of these apparently encouraging results no one could approach the operation of thyroidectomy in this disease without misgivings, and I do not mention the procedure to urge it as a remedy, but to point out that it is significant that surgical treatment of the thyroid does lessen or remove the symptoms.

* Kovalevsky : 'Arch. de Neurologie,' xviii, p. 422, 1889. Möbius : 'Deutsch Zeitschrift für Nervenheilk.', 1891, p. 423.

† 'St. Barth. Hosp. Rep.', vol. xxviii.

Part II.

I propose now, without touching on any of the cardiac or vascular disturbances, to draw attention to the alterations in nervous function, many of them very common, alterations which affect every part of the nervous system.

I shall attempt boldly to group the symptoms according to their probable seat of production, that is, under the three headings of brain, spinal cord, and peripheral nerve trunks, but this grouping must naturally be somewhat rough and experimental. First among the "encephalopathies" come *mental changes*. In only very slight, early cases are mental changes *absent*. In only one instance have I ever seen a uniform, sweet temper, and a natural turn of mind, maintained in established Graves's disease.

Pronounced insanity is rare; in fact quite lately one of the medical officers at Colney Hatch informs me that he thinks it must be very rare, because they have not seen a case there for a long while, and the opportunities at that asylum are large. Still, however, insanity does occasionally ensue, usually in the form of melancholia, and less often acute mania.

Dr. Savage suggested,* many years ago, that the peculiar appearance of the patient, from the staring eyes, may form the starting point of melancholia, by giving her the impression that she is being watched. This may be so occasionally, but I can attach no importance to it, because, as I say, some mental change is almost invariable, and not only exophthalmos, but even sufficient stare to attract constant attention is by no means so common as the name exophthalmic goître would imply.

The usual mind-disturbance is irritability, an excitable, restless turn of mind; and this I have found more than once associated with constant muscular restlessness; the patient is eternally fidgeting, playing with her mouth, her watch, her book; a condition which may persist for years. Besides this irritable state, I find two other mental conditions common—

1st. An over-sensitive notion of duty, which I have seen become

* 'Lancet,' 1890, i, p. 1055.

very marked in the cases of several middle class ladies of religious tendencies, a state of mind scarcely separated from religious melancholia, which would probably easily ensue.

2ndly. An incoherence of ideas, to which Dr. Russell Reynolds has applied the apt name of "chorea of ideas." One lady I know occasionally finds it impossible to pursue a train of thought without other ideas crowding into her mind; if she tries to write a letter, other names, and notions, and words, all real ones, crop up, instead of the one she wants. Another woman, who did a great deal of needlework, found that if she started to cut out a garment, half way she would be cutting out another sort of garment instead of finishing the first one. This differs from the enfeebled power of attention you find in neurasthenia, anæmia, or after acute disease, where the attention (or probably memory) simply strikes work. It resembles rather the mental state of mania or ordinary delirium. The links which connect impressions of memory are lost rather than the impressions themselves. At the same time ordinary loss of memory is very constant in Graves's disease.

Consciousness is rarely affected; I have seen such an instance once. A woman, whose curious paralytic symptoms I shall remark on presently, was fairly well when she received a shock at some accident to her son. She suddenly started out of the house to fetch me, and was running down the road when I accidentally met her; on my stopping her she seemed quite unconscious, did not know where she was, or who I was, and remembered nothing after starting from her house, though several people had spoken to her. Her state quite resembled that of ambulatory epilepsy.

I include tremor as a central symptom. If you ask me what is the feature of the disease next most common to the cardiac symptoms and the goître, I reply *tremor*. It is impossible to say much about it in the limits of this paper. It consists of fine vibrations of muscles, very small in amplitude, and very regular in time, the rate being always about eight or nine per second. The movement is usually most marked in the flexor muscles of the forearm, while the interossei and other muscles of the hand are not affected as they are in alcoholism; but if marked in the hands, it is also present in almost all other muscles of the trunk and limbs. I may

say here, that when I wrote on this subject a year ago,* I had never seen it in the muscles of the face, but, led by an observation of Dr. Sansom's, I have since found it affecting the masseters. This is important, as it negatives the theory that the tremor might be produced by spinal change.

The points on which I would lay stress in reference to this tremor are—

1. That it is almost universal in exophthalmic goître.

2. That it exactly resembles the tremor produced in animals after removal of the thyroid: it is in fact a thyroid tremor.

3. That its character is much more uniform than that of hysterical tremor, for which it might otherwise be taken.

I cannot discuss here the diagnostic differences between this tremor and that due to alcoholism, paralysis agitans, disseminated sclerosis, and various metallic poisonings, but here are some tracings illustrating these distinctions.

Dr. Judson Bury informs me that he has once found marked fibrillation of the interosseus muscles of the hand, in addition to the ordinary tremor, but this he was inclined to ascribe to a peripheral neuritis.

My allusion to a pseudo-epileptic state brings up the question of *eclamptic convulsions*. To this M. Ballet† devoted attention in 1883. He collected many cases, and showed that though the main cardiac signs may supervene in chronic epileptics, in another series of patients the convulsions had a direct relation to the increased heart action and were, perhaps, induced by it.

Clonic spasms of one side of the face, convulsive tic, is described in one instance by Eulenburg, and in another by Dr. Hughlings Jackson, who attributed the convulsion to discharge of facial centres in the pores. Similar spasms have been seen affecting the muscles of one shoulder and the side of the neck.

Chorea‡ is undoubtedly a frequent concomitant, but I dismiss it as probably purely secondary to vasomotor disturbance.

* 'Brain,' LIX and LX, p. 424.

† 'Rev. de Médecine,' 1883, p. 254; Kovalivski: 'Arch. de Neurologie,' xviii, p. 422; 'St. Barth. Hosp. Rep.', 1874, p. 254; R. Reynolds: 'Lancet,' 1890, i, p. 1057.

‡ L. Gros: 'Soc. Méd. de la Seine,' August 19, 1864; Gagnon: 'Gay. Hrbd. de Méd. et de Chir.', 1876; Kelly: 'Med. Press and Circular,' 1878; Ghoyinski, 1880; Jacobi: 'Med. Reæ,' New York, 1879; Patel Gros; Thèse de Paris,' 1884; S. West: 'Trans. Ophth. Soc.', 1886; Guéneau de Mussy:

A form of clonic spasm, as yet undescribed in Graves's disease, is worth noting; it occurred in a patient of mine last year, the Mrs. W. K. mentioned above. She had only been married three months, and got wet and fatigued on the eve of a menstrual period. She was seized suddenly with regular rhythmical convulsions, beginning in the flexors and extensors of the hands, and spreading to the neck and arms. Consciousness was quite unaffected, and she had not the least hysterical manner, and was rather amused than frightened at her condition. The convulsions lasted nearly all night. Next day the form had rather changed, the commonest movements were a perfectly regular jerking forwards of the shoulders, effected by the pectorals, at intervals of about three seconds. After a few minutes this would change, and violent tremor begin in the right arm; at first a rapid pronation movement exactly resembling paralysis agitans, and altering to pure flexion and extension movements. The movements were not induced by attempting voluntary action, and were not modified by it, but they were distinctly increased by watching her, or by any sudden disturbance.

Temperature was normal, but the pulse was continually raised 120—130.

There was no impairment of sight, and the field of vision I took and found good.

I thought there was distinct anæsthesia of the legs. These convulsions recovered at increasing intervals for many weeks, but gradually subsided. They varied much in character, but the usual type was a violent shrugging of the shoulders. Another form resembled the action of polishing something lying on her knees.

This form of convulsions is not uncommon in so called hysterical subjects, though the jerking of the pectorals is rare. The flexion movements of the hands were, however, only an exaggeration in degree of the tremor usual in Graves's disease.*

The vague class of symptoms known as hysteria goes hand in hand with Graves's disease, and pure hysterics may develop the

'Soc. Therap.', November, 1881; 'Acad. de Med.', January, 1882; 'Rev. de Méd.', May, 1890. Three cases are given by Marie: 'Arch. de Neurologie,' 1883, p. 84.

* 'Berl. Klin. Woch,' July 3, 1893. Gowers: 'Diseases of Nervous System,' II, p. 921. v. Maude: 'Brain,' LIX, 1892, p. 424.

cardiovascular condition. M. Charcot used to say that as the cardiac signs increase, so the purely hysterical signs diminish, but I confess I have failed to corroborate this remark.

Leaving untouched the vasocardiac disturbance, there are other bulbar symptoms less widely known.

A slight difficulty in swallowing, not due to any pressure on the trachea, is common enough; it resembles that seen in myxœdema.

The patient, whose other paralyses I shall pass on to, presented on the subsidence of those paralyses a slow drawling speech, like that in insular sclerosis; this disappeared after some weeks, and was succeeded by a marked stammer to which she had not been subject before.*

Stammer, of an ordinary type, is however frequent; some persons, according to Dr. Russell Reynolds, have great difficulty in getting out certain words, or even any words at all. I have seen *three* women who at times had this inability: it was not due, however, to incoordination, and I thought was not an *aphasia*, but a pure *amnesia*.

The *facial nerve* is rarely paralysed completely, but a few instances are recorded, one by myself. But almost all cases show some enfeeblement of the upper division of the facial, with lowered electrical irritability.

I have myself no hesitation in saying that both the eyelid symptoms, Graefe's and Stellwag's signs, are due to paresis of the temporal division of the temporofacial nerve.

Of instances of complete external ophthalmoplegia there are already quite a series, beginning with Dr. Bristowe's classical case, and ending with the example I published last year, the same patient who had facial palsy. I must note that she had catarrh of the external ear. But the lesion was probably central, notwithstanding, as she had consecutive paralysis of the facial, the 6th, the 4th, and, finally, the 3rd nerve, though the last was never completely paralysed.

Isolated paralysis of all the ocular muscles does, though rarely, occur; but paresis of the internal and external recti is comparatively common, though I do not think they have been sufficiently studied in connection with the existence of errors of refraction.

* S. West: 'Ophthalm. Soc. Trans.', 1886.

Intense general muscular feebleness is, so to speak, proper to Graves's disease; a general weak muscular action with readily induced fatigue, a condition similar to that in neurasthenia. But this weakness is usually much more marked in the legs, and we find that tendency to give way at the knees in walking, which the French call *dérobement*, noticeable also in myxœdema and in locomotor ataxy; a similarity to which M. Charcot has drawn frequent attention in his Tuesday lectures.

This paresis of the legs may be so extreme as to constitute a veritable paraplegia, and this paraplegia I have from my own observation separated into two groups.

1. That in which the paralysis is merely an accentuation of the previously existing general paresis, produced by the stress of an acerbation of other symptoms, such as diarrhœa, sickness, or cardiac dilatation and failure: this form is, I think, peripheral.

2. Those cases in which the paralysis comes on suddenly and resembles other so-called hysterical or functional forms of paraplegia, such examples are usually transitory, and like other transitory functional paralyses they *never* produce contractions. No instance of diminished muscular sensibility, with the exception of coincident cases of locomotor ataxy, can I find, and in no case has the rectum or bladder been affected in their functions.

The patellar reflexes are usually diminished and often absent; this fact, first noted, I think, by Marie, I have confirmed in many instances.

Muscular wasting is only pronounced when the paresis has been prolonged, but it has been found, in the case of isolated monoplegia, to be quite out of proportion to the degree of paralysis.

In all these cases of paralysis the observers at the Salpêtrière have found both galvanic and Faradic reactions lowered.

Bed sores are unknown except, as far as my reading goes, in the one instance, our President's patient, Marion.

All this evidence serves to throw this second form of paraplegia into the category of functional paralyses of the flaccid type, that is with no contractures, and spinal in origin. Dr. Cheadle has described the only example of contracture following on such a paralysis, which affected the right arm.

Hemiplegia is known, but is rare. Omitting several cases where the lesion was clearly organic and focal, I can find records of but four, in three of which there was accompanying hæmi-

anæsthenia, and in two of them various ocular paralyses. One of those cases is, of course, Dr. Bristowe's.

Monoplegias of divers groups of muscles of the limbs are recorded. The only instance I have seen was of complete monoplegia of the whole of one arm, lasting for about three days, following the subcutaneous injection of digitalin in that arm.

Among functional alterations in the spinal cord a common one is *astasia-abasia;* that condition which has not long been differentiated, in which, with no intrinsic motor paresis, the patient is yet unable to stand or walk, though the legs can be moved briskly when lying down. I have proved its existence in several cases, since Eulenburg first drew attention to it in this disorder. But it cannot be claimed to have any special significance, as it occurs in neurotic subjects in the debility following various acute diseases.

Various *organic nervous diseases* have been found accompanying or preceding Graves's disease. They are rare, and I will merely enumerate them: general paralysis, progressive muscular atrophy, syringomyelia, and locomotor ataxia. The last is comparatively common, and has attracted great attention in France. There is no question that isolated symptoms suggesting exophthalmic goître, such as permanently rapid pulse, palpitation, and slight exophthalmos may occur in locomotor. Moreover, signs of well-marked Graves's disease have supervened in the course of tabes dorsalis, and the question has been raised whether this is not due to an invasion of the medulla by the sclerosis; but as yet there has been no verification *post mortem.*

Focal lesions of the brain from hæmorrhage or embolism may occur in the subjects of our neurosis, but there is no evidence that they are more frequent than in other people.

Lastly, let me accentuate particularly a group of symptoms all of great frequency, which, when unravelled from others, seem to me to point to *peripheral neuritis.*

Unfortunately the evidence is purely clinical as yet; no neuritis has ever been discovered *post mortem*, but, as far as I can find, no attempt has been made to look for it.

These symptoms are—

1st. Cramp, which has often been observed. Dr. Hector Mackenzie* has shown how common it is, and I can verify the

* 'Lancet,' *loc. cit.*

observation. This cramp may constitute tetany of the ordinary form. Dr. Mackenzie saw several cases, and I have seen one. These painful muscular contractions occur of course in persons with considerable intestinal and gastric disturbance, because such disturbance is very frequent in Graves's disease. They may properly be regarded as due to some toxin developed in the intestinal canal as ordinary tetany is caused.* At the same time we must remember how frequently tetany results from extirpation of the thyroid.

2ndly. General hyperæsthesia is so usual in this disease that quite lately Professor Grainger Stewart† has pronounced that it is the rule rather than the exception. Partial anæsthesia is less common. But varying degrees of numbness, tingling, and pain in the legs, the subjective side of anæsthesia and hyperæsthesia, are common causes of complaint.

3rdly. The symmetrical paresis of the legs which I have described, and the lowered or abolished patellar reflexes.

Surely we have here the symptoms of peripheral neuritis in an early stage; but it seems not to become marked. Conditions indicating complete neuritis are unknown. Struck by this I examined these cases carefully for glycosuria, because slight peripheral neuritis is so common in diabetes, while marked neuritis is unknown; moreover, glycosuria is so often associated with Graves's disease. But I never found sugar present once.

On the other hand, the coincidence of gastro-intestinal crises was so frequent that it is reasonable to attribute these neurotic phenomena to intestinal auto-intoxication.

I would suggest also that those forms of localised œdema, evidently of neuropathic origin, which are now well known in Graves's disease,‡ are manifestations of peripheral neuritis. They are comparable, perhaps, to the cases which our President described last year at Nottingham§ as hysterical neuritis, in which œdema was occasionally a prominent feature.

* Ross and Bury: 'Periph. Neuritis,' p. 403.

† 'Edinb. Hospital Reports,' vol. i.

‡ Maude: 'Practitionem,' December, 1891.

§ Bristowe, 'Brit. Med. Jour.', II, p. 1099, 1892.

I have never seen an instance of beri-beri, but the descriptions of the œdematous form of that disorder seem to bear a strong resemblance to the combination of paralysis and œdema which I describe in Graves's disease; and the pathological condition in beri-beri is known to be a peripheral neuritis.*

This is a very imperfect sketch of a large range of nervous disturbances which affect every area and every level of the nervous system. I find great difficulty in ascribing any of the symptoms I have indicated to variations of blood supply, and we cannot fail, I think, to be struck by the resemblance of the clinical picture to the results of poisoning by alcohol, lead, and, perhaps, beri-beri.

Pathologists have long sought to explain the phenomena of this disease by some focal lesion in the sympathetic or the medulla. But as our clinical knowledge grows, the more unsatisfying such explanations become.

The old sympathetic theory died hard, killed by Filehne and Dr. Hale White, but will any lesion in the medulla do more than explain the cardiovascular symptoms? I think not.

We must regard the neurosis as a nerve poisoning, for the present; the brunt undoubtedly falls on the medulla, but it is felt from the cortex to the periphery. What that poison is we do not know. That there are probably secondary poisons I have indicated. But remember the one feature, so peculiar to the disease, the thyroid change.

To my mind the universal goître, the connection with myxœdema the results of operations on the thyroid, point to that gland as the fountain-head of evil.

This is only a provisional speculation as yet, but, failing surer ground, we must have provisional theories to direct our minds at the bedside.

* Ross and Bury: 'Peripheral Neuritis,' 1893, p. 316.

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