THE PATHOLOGY OF THE

CENTRAL NERVOUS SYSTEM IN EXOPHTHALMIC GOITRE.

By W. HALE WHITE, M.D., F.R.C.P.,

Senior Assistant-Physician to and Lecturer on Materia Medica at Guy's Hospital.

In the JOURNAL for July 24th, 1886, I published a series of cases of exophthalmic goître, none of which, however, helped in any way to explain the pathology of the disease. The following case, I think, throws an important light upon this obscure question.

R. M., aged 31, was admitted into Guy's Hospital on September 18th, 1888. Her mother died of rheumatic fever at the age of 21; the patient was in St. Mary's Hospital with what she calls ulceration of the bowels. In 1886 she was in bed with the same complaint, and since this illness has never felt really strong. She has been wasting, especially during the last nine months. For the last ten days she has suffered from sickness and inability to take her food. She has had cardiac palpitation for many years. At the age of 19 she first noticed enlargement of the thyroid.

On admission, is very thin and weak. Eyeballs slightly prominent. Graefe's sign present. Thyroid much enlarged, with a loud murmur over it. She is often faint and giddy. The optic discs are normal. The cardiac impulse is very diffused and heaving; position of the apex normal. Pulse 150. There is a loud systolic murmur, heard best over the pulmonary area. Bowels regular; menses irregular; urine normal.

September 21st. She is very sick.

September 23rd. This continues, and there is much diarrhœa.

September 25th. Developed signs of pneumonia on the right side, became jaundiced, the sickness and diarrhœa continued, and in spite of treatment she died October 5th.

Necropsy Six Hours after Death.—There is very little fat on the body generally, but there seemed to be quite the normal amount in the orbit. Weight of body 53 lbs. Brain weighed 47 ounces. The capillaries in its interior were everywhere full, and they seemed especially congested on the floor of the fourth ventricle; optic discs normal. Cervical glands slightly enlarged. Thymus easily recognised, but not enlarged. Thyroid extremely enlarged uniformly. Lungs, confluent, lobular, pneumonia at both bases. Heart, 11 ounces; no microscopical evidence of fatty change. Stomach, large and small intestines all intensely congested, with swelling of the mucous membrane; the solitary follicles were prominent, and more so than normal. Liver normal, not fatty. Mesenteric glands all swollen and injected. Suprarenals normal. Kidneys normal.

Histological Examination.—Thyroid vessels enlarged and full of blood. There is no increase in the size of the vesicles, but it is evident that many new ones are in process of formation, for there are several of an extremely irregular shape, and also a number of small ones. The whole organ is full of wandering cells of various sizes. Superior cervical ganglia: the nerve-cells are healthy; the sections are crowded with leucocytes. Cervical sympathetic cord: this is quite healthy. Spinal cord: a great many sections of this were examined, and save for one or two inconspicuous hæmorrhages, which were very small and quite recent, the whole spinal cord was normal. Central nervous system: a series of sections were made, extending from the lowest point of the medulla up to the corpora quadrigemina. At the level of the lower part of the olivary nucleus there was, just under the posterior surface of the medulla, evidence of slight inflammation, as was shown by engorgement of vessels, a little blood in their sheaths, and a few wandering cells in the posterior median nucleus on each side. The next few sections were quite healthy, but those in the neighbourhood of the nucleus of the sixth nerve showed considerable changes. Immediately under the posterior surface of the medulla, extending from the middle line as far out as the restiform bodies, which were slightly implicated, were numerous hæmorrhages. The area occupied by these did not extend deeply, so that, except for a slight implication of the sixth nucleus on one side, the nerve-cells had escaped damage. Also the fibres of the facial nerve, which come so near the surface here, were free. The hæmorrhages seemed almost entirely limited to the posterior superficial part of the reticular formation, but there were two or three small deeper ones. It was at this level that they were most marked, but they existed in all sections up to the lower part of the aqueduct of Sylvius, where, however, only one or two could be seen. They always occupied the posterior part of the reticular formation. The hæmorrhages were not old, but probably they did not take place immediately before death, for some of the corpuscles had altered considerably in shape

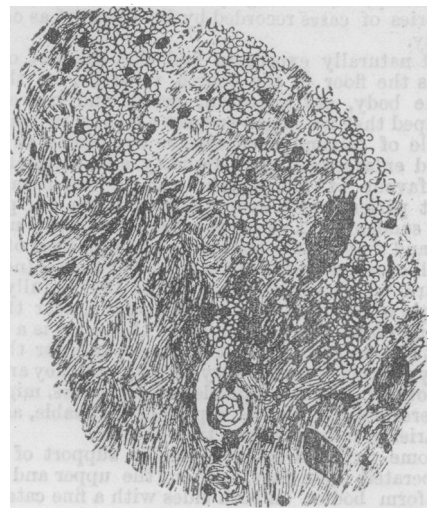

Fig. 1. Shows hæmorrhage close under the floor of the fourth ventricle near to the sixth nucleus.

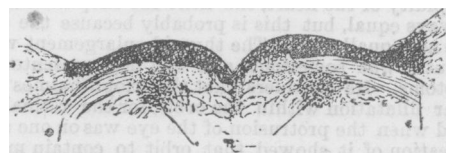

Fig. 2.—Diagram of the floor of the fourth ventricle through the sixth nucleus. The shading shows the area occupied by small hæmorrhages. It extends outwards to the inner part of the restiform bodies.

I should not have brought forward a single case were it not that I believe this to be the first one recorded in which changes have been found in the central nervous system in association with exophthalmic goître, and which could also in any way explain it. For a long while the favourite theory to account for this disorder was that the three cardinal symptoms were due to disease of the cervical sympathetic, but this view is not now held, for often this part of the nervous system has been found to be healthy, or, if changes have been discovered, they have been such as others and myself[1] have shown to be present in many other maladies; and the specimens from this case quite bear out the refutation of this theory, for lymphatic engorgement of the sympathetic ganglia is met with in the most diverse diseases. Then, also, the symptoms of a lesion of the cervical sympathetic and those of exophthalmic goître bear but little resemblance to each other. Möbius[2] has recently put forward the hypothesis that the disorder is a close ally of myxœdema, and that both have for their cause some chemical disturbance due to the alterations in the thyroid; but I think most will agree with me that this is a very far-fetched theory, for, in the first place, the maladies have hardly any points of resemblance; in the second, they present many striking differences; thirdly, the changes in the thyroid are opposite in the two disorders; fourthly, the analogies of exophthalmic goître all bring it into relationship with nervous diseases; and, lastly, no operations on the thyroid ever produce it. Latterly the idea has been more and more gaining ground that the disease is due to alterations in the central nervous system so fine as to escape detection by ordi-

1 "On the Pathological Histology of the Semilunar and Superior Cervical Sympathetic Ganglia," *Trans. of Royal Med. and Chirurg. Soc.*, vol. lxviii, and *Journal of Physiology*, vol. viii, No. 2.

2 "Ueber das Wesen der Basedow'schen Krankheit.," *Centralblatt für Nervenheilkunde*, 1887, No. 8.

nary means of observation, and this is supported by many considerations. Often exophthalmic goître is associated with other nervous disorders. Gowers[3] mentions epilepsy, neuralgia, migraine, and ophthalmoplegia. Savage[4] has shown that it is often connected with mania, general paralysis of the insane, or melancholia. Bristowe[5] has recorded a case of exophthalmic goître in which there were also present external ophthalmoplegia, hemianæsthesia, epileptic fits, and pyrexia. This patient died, but the necropsy revealed nothing. I have recently seen a case associated with a suicidal tendency, and bearing upon this evidence there is the remarkable series of cases recorded by Dr. Cheadle[6] as occurring all in one family.

We should naturally expect to find that the part of the brain diseased was the floor of the fourth ventricle, for there, of all parts of the body, are important nerves and nerve-centres so closely grouped that we might suspect a lesion in this situation to be capable of causing such diverse symptoms as exophthalmos, thyroid enlargement, and rapidity and palpitation of the heart. In favour of placing the seat of the disease there is the fact that patients with exophthalmic goître are particularly liable to die suddenly. A series of cases I published[7] not long ago shows this; and that minute hæmorrhages in the floor of the fourth ventricle will cause sudden death is proved by a case[8] (not of exophthalmic goître) which I have recorded. Sattler[9] is fully of opinion that the origin of the malady is in the medulla, near the origin of the vagus, and points out that probably the lesion is a very slight one, and not always precisely in the same place, for the order in which the symptoms appear is very various, and they are curiously mixed with others. Such a slight lesion, he thinks, might be some vascular alteration, and this is especially probable, as the same symptom varies in intensity from time to time.

Now we come to the direct evidence in support of this view. Filehne[10] operated upon dogs, and cut the upper and inner part of the restiform bodies on both sides with a fine cataract knife. This generally gave rise to one or two of the three cardinal symptoms of exophthalmic goître; the most frequent was the palpitation and rapidity of the heart, the next the exophthalmos, which was not always equal, but this is probably because the restiform bodies were not equally cut. The thyroid enlargement was rarely obtained, but it was sometimes, and one dog presented all the three symptoms. He considers that the exophthalmos is due to the vascular dilatation within the orbit, for the retinal arteries dilated; and when the protrusion of the eye was on one side only, rapid enucleation of it showed that orbit to contain more blood than the other. Also the exophthalmos could not be caused by the action of Müller's muscle, for it occurred even if the cervical sympathetic were cut.

Naumann[11] has recorded a case in which, at the necropsy, the basilar artery was found to be brittle and atheromatous, so that the blood-supply of the medulla might very well have been interfered with, but he gives no histological description. The changes in the brain described by Geigel[12] were clearly those common in general paralysis, which his patient probably had; so mine, I think, is the first case on record showing definite local changes in the medulla oblongata, and they are in exactly the position in which they might be suspected to be, for we have seen there are strong reasons for placing the seat of the disease in the floor of the fourth ventricle, and exophthalmic goître has been attributed to a lesion of the restiform bodies, which were implicated in my case.

No doubt the malady had lasted a long while, and the hæmorrhages were only recent, but I can see no inherent improbability in supposing that a diseased part, even if the lesion is not visible to our means of examination, should be particularly liable to hæmorrhage; for we know that, as a general rule, diseased structures are more prone to hæmorrhage than healthy ones. In connection with this we must remember that Sattler has good reason for thinking the lesion is a vascular alteration, which would usually disappear after death. My interpretation of this case is that the exophthalmic goître was due to changes in certain parts of the floor of the fourth ventricle, which ordinarily escape detection, because they are so fine. We know that in fevers—and this woman had pneumonia—minute hæmorrhages in the brain are particularly liable to take place shortly before death. They occurred in this case in the floor of the fourth ventricle; for, being diseased, it was the weakest part of the brain, and thus we have had revealed to us the seat of a disease that has hitherto evaded discovery. I have, like many others, constantly seen capillary hæmorrhages which took place in the brain shortly before death, especially in fevers, but I never saw anything in the medulla at all comparable to the condition we had here. The punctiform hæmorrhages were visible to the naked eye, and markedly discoloured the floor of the fourth ventricle. No one present at the necropsy had ever seen them so evident in the medulla. Considering it is probable that this is the seat of the disease in exophthalmic goître, it is difficult to believe that the incidence of the hæmorrhages here is the result of chance.

In my article in the JOURNAL in 1886, I called attention to the frequent enlargement of the lymphatic structures in the intestine in exophthalmic goître. I have since seen it two or three times; it was present to a slight degree in this case, and it is interesting in this connection to note that the patient had diarrhœa.

[3] *Diseases of the Nervous System*, vol. ii, p. 814.
[4] *Guy's Hospital Reports*, vol. xli, p. 31.
[5] *Brain*, No. 31.
[6] *St. George's Hosp. Rep.*, 1874.
[7] JOURNAL, July 24th, 1886.
[8] *Path. Trans.*, vol. xxxiii.
[9] Graefe und Saemisch, *Handbuch der Augenheilkunde*, Bd. vi.
[10] Communicated to the Physikalisch-Medicinischen Societät zu Erlangen, Sitzung vom 14 Juli, 1879.
[11] Sattler, *op. cit.*, p. 981.
[12] "Die Basedow'schen Krankeit," *Würzburg Med. Wochenschr.*, vii, S. 70.

A CASE OF CHOREA.

FOLLOWED BY

ERYTHEMA AND ACUTE RHEUMATISM;

WITH REMARKS.[1]

BY SIR PETER EADE, M.D., F.R.C.P.,
Consulting Physician to the Norfolk and Norwich Hospital.

D. G., aged 17, was admitted into the Norfolk and Norwich Hospital, under my care, on May 26th, 1888, suffering from an attack of acute chorea. He was reported to have been a healthy young man, and never previously to have suffered from either chorea or rheumatism. The heart was unaffected; the urine was 1030, acid, and free from albumen; and the chorea was uncomplicated. Its cause was not apparent, but he appeared to be of nervous temperament. There was no rheumatic taint in his family. The twitching involved more or less the muscles of all the limbs and of the face. The tongue was protruded with a jerk. The intellectual power was decidedly diminished, and the attack was manifestly both general and severe. The temperature was normal. He was now treated with 5 minims of liq. arsenicalis three times daily, but he did not improve; indeed, the symptoms, if anything, got worse, whilst he distinctly lost mental power, the nurse reporting to me that she did not consider that he was altogether in a sane or competent state of mind.

Up to June 11th the temperature continued to be either normal or only at times raised one degree; but on this day it suddenly rose to 102.2°. Simultaneously a bright red erythematous rash appeared in broad patches upon the shoulders, chest, wrists, and knees; whilst the twitching of the face and tongue became more severe. There was scarcely any redness of the throat. He was now ordered a mixture containing dilute sulphuric acid and sulphate of magnesia, with a dose of chloral and bromide of potassium at night. On the evening of this day, and by the following morning, some swelling of the knees and ankles had shown itself.

Next day, June 14th, he complained of pain in the præcordial region. There was increased action of the heart, and a murmur, apparently pericardial, was audible. Temperature 104°; some delirium, more marked at night. The choreic movements still severe, both in face and limbs.

June 16th. A distinct systolic murmur audible, and also unquestionable friction sounds all over the cardiac area. Temperature 103.5°. Joints still swelled and painful. No severe sweatings. Erythematous rash fading. Nocturnal delirium increased, and feebleness of mind a marked symptom. Pulse 130. To take

[1] Abstract of paper read before the Norwich Medico-Chirurgical Society.