Nine cases of Graves' disease: ophthalmoplegia : remarks on the lid-symptoms / by Arthur Maude.

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NINE CASES OF GRAVES' DISEASE: OPHTHALMOPLEGIA: REMARKS ON THE LID-SYMPTOMS.

BY

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These cases presented themselves in my practice during the last two years. Some of them I have had under observation for some years, an advantage rarely enjoyed by consulting and Hospital physicians.

CASE I. (simple "fruste"[1] case).—July 1890, born 1869, housemaid; has had rheumatic fever three times, last time when seventeen years old. Has been anæmic some years, but has felt no inconvenience till last few weeks, when she has had much palpitation and short breath. Has lost flesh. She is very chlorotic, very thin, and short of breath. Heart, very heaving irregular impulse, distinct hypertrophy. Pulse 100, irregular. Faint basic murmur, most marked over pulmonary area. Menses regular. Constipation constant. Slight proptosis. Gräfe's sign not present. Distinct uniform goître. Given iron, arsenic, and digitalis; improved rapidly. In March 1891 continues well. There were no other signs; no trembling, sickness, diarrhœa, or psychical changes.

CASE II.—Miss C., born 1870, Board school-mistress. In the spring of 1890 she had epidemic influenza, and has been ever since in a state of great nervous depression, almost melancholic at times. Soon after the influenza she noticed swelling of the neck. This subsided, and by Christmas 1890 it had almost gone. A few weeks after it reappeared, and in March 1891 it increased rapidly. There has been much palpitation all along,

[1] An expression properly meaning "defaced" (of coins), used by French writers of undeveloped cases of Graves' disease.

and occasional otorrhœa from the left ear. The tonsils have been enlarged for some months.

March 20, 1891.—She now comes to be treated for the otorrhœa. There is much purulent discharge from left ear; membrane thickened, depressed, with large perforation. She is a fat, flabby girl, very nervous and hysterical in manner, abrupt and excitable in her answers, slight deafness of both sides, much hypertrophy of tonsils. Thyroid uniform, symmetrical enlargement. No cardiac bruit. Pulse 130, regular. The eyelids swollen in appearance. Gräfe's sign absent. Slight tremor of hands. The tremor has been very marked, so as almost to prevent her writing. No sweats. No diarrhœa. During the last two months she has had two attacks of vomiting. She is very nervous, easily startled, and very irritable with her pupils.

April 21.—Distinct proptosis. This has been noticed from time to time during the last month. The pulse continued very rapid (120–150) whenever I saw her. She improved rapidly under large doses of belladonna.

Case III.—Miss ——, born 1848. No family history or previous history of importance. Had always had good health till 1882, when she was noticed to be getting thin, and proptosis was observed by a relative, a doctor. She saw Dr. Wilks in May 1882, who kindly writes to me that he found "her thin, with palpitation of the heart, the number of beats averaging 150; she often broke out in perspiration. There was no thyroid enlargement, but a doubtful tendency to prominence of the eyeballs; kidneys healthy; appetite good, often very hungry. After sitting down for some time the pulse went down 20 beats. I regarded the case as one of exophthalmic goître without exophthalmos and goître." Dr. Wilks gave her a course of belladonna, and she rapidly improved. In fact, she was regarded by her usual medical attendant as quite well in March 1883. I have kept watch over her for years. She continued in fair health for nearly ten years—in fact, improved; but she remained in a condition of "fruste" Graves' disease. Her principal symptoms were: A great mental restlessness; she was always wanting to do something, and made a great deal of the smallest trifles; her family used to say of her that she was always "fashing" (Scotch for "bothering") herself. At one time she showed a completely morbid sense of "duty." She also had an extreme restlessness of the hands and feet. They were never still; she was always playing with her watch-chain or dress, or the corners of her mouth, and there were constant irregular, almost choreic, movements of the facial muscles—sym-

metrical movements, frowning, drawing down the corners of the mouth, raising the brows, or movements expressive of emotions which were obviously not present. She had a good deal of palpitation from time to time, but was still capable of great muscular exertion without fatigue; took long walks, and was an expert and ardent mountaineer. The appetite is usually ravenous.

In May 1891, after a sudden domestic trouble, the symptoms of palpitation, proptosis, and muscular weakness again asserted themselves. After a period of rest she improved.

Case IV.—Miss L., born 1849. This patient and the next are sisters. Their eldest brother had rheumatic fever. Their mother's brother had a "goître" when a youth, and recovered completely, and his daughter has a goître, and used to get bronzing of the skin from time to time. I never saw the lady, but her relations noticed the discoloration, and the cousins described her to me spontaneously as being the "colour of iodine" (presumably skin painted slightly with iodine).

Both of the sisters have that same restless self-denying "sense of duty," common in many maiden ladies, which we saw in Case III.

The first symptom in these two cases was goître, which appeared when they were twelve and fourteen years old respectively, after a simultaneous attack of measles. But I am informed that it was remarked that Miss L. had very prominent eyes when she was seven years old. She has now (1891) a large goître, much tremor which has been marked for many years, distinct proptosis, with slow movements of upper lids. She is a typical instance of Graves' disease.

In May 1891 there were several cases of influenza in the house, and she suddenly presented the symptoms of extreme depression, muscular debility, a slight rise of temperature, 100°–101° for a week, during which time the pulse was rarely above 80 or 90; and there was at the same time great dyspnœa, due apparently to spasmodic asthma.

She recovered slowly.

During her recovery she presented a well-marked case of a mental condition to which Dr. Russell Reynolds[1] first drew attention, and which he calls "chorea of ideas." If she tried to think of anything in particular, or to write a letter on any subject, something else came up in the mind at once, and she became so bewildered that she had to give up the attempt.

[1] Lancet, May 17, 1890.

Case V.—Miss A., born 1847, sister of the preceding patient. Has had a large goître. Since it first appeared there has certainly been proptosis; a photograph taken in 1876 shows it well. She has never had definite rheumatism, but had bad "growing pains" when a child.

The only remarkable feature in her case is that in 1882 she was treated by a well-known throat specialist[1] for the goître with injections of iodine into the thyroid and hydrofluoric acid internally. The treatment was prolonged, and there was great reduction in the size of the gland, and from that time her general health improved very greatly. She used to suffer much from fatigue and feebleness, but now (May 1891) she regards herself as quite well and strong, though she has still a large goître and very distinct proptosis, and she still has periodic attacks of sickness, lasting three or four days.

Case VI.—Mrs. R., born 1866. Rheumatic family history; patient herself had rheumatic pains some years ago. A brother was subject to fits from five to thirteen years of age. A sister was noticed by Dr. Hector Mackenzie to have very prominent eyes. Her only baby had an intra-ocular glioma. Her illness commenced with a sudden attack of diarrhœa in April 1889, accompanied by slight prolapse of the uterus and distinct recto-cæle. She had had her only labour in August 1888; there was no rupture of perineum. I first noticed a goître in July 1889. There was much palpitation. The eyes were normal then. She has become very thin.

In 1887 she used to have frequent attacks of epistaxis, so severe that she described them as "flooding from the nose."

In December 1890 she began to have frequent attacks of vomiting, at intervals of about a week. This vomiting has no relation to the digestion of food, and is frequently accompanied by hæmatemesis, the blood being arterial blood in small quantities mixed with the fluid contents of the stomach. She is never comfortable without a pessary of some sort. If it is taken out, she has a sense of bearing down and local pain and the palpitation increases, generally followed by an attack of sickness. I find the vaginal walls and perineum extremely thinned, feeling like some fine textile fabric. The uterus is small and healthy. The menses regular in time and quantity since the weaning of her baby.

She has all the typical signs of Graves' disease—goître, pro-

[1] I have written to this gentleman to ask for information about the case, but he vouchsafes no reply; so I am dependent on the statements of my patient, which can, however, be accepted.

ptosis, Gräfe's sign, pigmentation round the orbits and about the axillæ and abdomen, while the marks of her garters are well defined by pigment. There is sickness, dry cough, occasional hæmoptysis, hæmatemesis, and sometimes the passage of bright blood from the rectum. Palpitation and rapid pulse are most marked.

There is great epigastric pain and tenderness at times.

Two facts are remarkable in this case:—

First, a uniform sweet temper, very rare in Graves' disease. Secondly, that sometimes on the pigmented eyelids I notice a number of small oval patches of whiter skin, like "reversed freckles." Patchy leucoderma has been noted in this disease before,[1] but not in this peculiar method of distribution.

I have treated her with a Leiter's coil to the epigastrium for half an hour twice a day, and all the symptoms are improved, but only for an hour or two after each application.

Case VII.—Mrs. E. W., born 1845, laundress. Her mother informed me that she herself had a goître, which came on after her first confinement; this disappeared in later life. Mr. Morrant Baker removed an epithelioma from her labium, and she died afterwards of secondary growths.

The patient first developed goître when eighteen years old. I have known her since 1887, and for some years regarded the goître as a simple one. I made a note in 1887 rejecting the idea of Graves' disease. In fact, there were no other symptoms till 1890, when she began to have frequent attacks of sickness, much tremor, and debility. I saw her from time to time, but could not decide satisfactorily that she had Graves' disease, being of opinion that the tremor, and what I regarded as gastric catarrh, was alcoholic in origin.

But on May 11, 1891, she had a long and severe attack of vomiting. Her condition was then as follows:—She is very weak, and unable to sit up in bed. Vomiting has been almost incessant for some days, the vomit consisting of mucus and a little bile. The hands and arms are very tremulous, with the fine tremor characteristic of Graves' disease. She flushes and sweats very easily, the sweats being much more marked on the left side of the head and chest. Temperature 100° morning and evening; pulse 100, small but regular. Far from there being any exophthalmos, the eyes are rather sunken, and there is

[1] Lucy, Brit. Med. Journ., 1887, ii. p. 624; Reynaud, Thèse de Paris, 1875; Rolland, Thèse de Paris, 1876; Ball, Gaz. des Hôp., 1873, xiii. 14; Bartholow, Chicago Med. Journ., 1875, July.

symmetrical ptosis,[1] but at the same time the movement of the upper lids is markedly slow and arrested, as if they caught in the middle of descent. Movement of lower lids natural. She has always had slight ptosis, and has had as long as I have known her an expression of raised eyebrows, as if to counteract permanent ptosis. Her manner is very hysterical at times. There is some discharge from left ear, with slight earache. There is slight external catarrh; no perforation. The goître, which has not increased since 1887, is of medium size, larger on the right side. There is absolutely no pulsation. Some cardiac hypertrophy; no murmur.

She continued in much the same state till May 22, when facial paralysis of the left side suddenly occurred.[2] It affected the orbicularis, so that the left eye remained permanently open. The ptosis of the right eye became more marked. No paresis of any ocular muscle. Pupils equal, act to light and accommodation.

May 24.—She has been very stupid and inert all day. To-day ophthalmoplegia[3] of left eye appeared; at first it only affected upward and external movement (superior and external rectus). On the 26th it affected all muscles, but not completely; the left eye follows the movements of the right, but very slowly and irregularly, the muscles giving an occasional pause in their action, bringing the eye into position after the other eye has stopped. Then, when the muscular action has been maintained a few seconds, the feeble left-side muscles yield, and the left eye rolls into the antero-posterior position of rest, irrespective of the direction of the right globe, as in ordinary weakness of the recti.

Vision in both eyes $\frac{6}{9}$. Estimated hypermetropia 1 D. Fundi normal. Pupils equal, react to light and accommodation.

By June 9th the facial paralysis and the ophthalmoplegia had gradually disappeared. The aural catarrh disappeared also. Sickness abated, and she improved altogether.

June 13.—She complains of a form of tinnitus, "as if there were carpet-beating in her head." This is very transitory, and she is quite deaf when it is present.

To-day she showed, for the first time, distinct exophthalmos. At the same time Gräfe's sign disappeared, and there was great retraction of both lids.

She continued improving, and by June 23 was able to leave her bed, and even attend to household duties a little. Since she

[1] Ptosis is not uncommon. West noted it in one of his cases in the discussion at Ophthalmological Society (Trans. 1886).

[2] Potain observed facial paralysis in two cases. Rev. de Méd., 1888, July.

[3] Ophthalmoplegia has been noted by Ballet, and by Dr. Bristowe in his well-known case Marion (*vide* Diseases of Nervous System).

began to improve she has stuttered continually in conversation, and has at times a slow scanning speech, like that in disseminated sclerosis. She has had occasionally hæmatemesis. Has never had diarrhœa. She has no pigmentations.

During the height of her illness she was hardly able to move, and could not sit up in bed; but as she improved she showed distinctly the condition lately described as "astasia-abasia;"[1] though she could move her legs briskly in bed, and when sitting, she could not stand without assistance, and could not walk a step. This curious state has been found by Eulenberg in Graves' disease.[2]

Case VIII.—Miss T., born 1843. Strong arthritic family history. Father died of heart-disease; one brother had rheumatic fever and died of heart-disease. One sister is crippled with chronic rheumatoid arthritis.

The disease began in 1871, after an attack of diphtheria, which was followed by paralysis of palate and weakness of the legs, which lasted a year, and she was unable to see properly then, though I could get no history of diplopia. The goître was the first symptom, and rapidly attained great size. All the usual signs of Graves' disease have been developed for years, including frequent attacks of diarrhœa and sickness, occurring usually together. She has slight glycosuria. She is very sallow and very much freckled; she has also numerous moles, supposed to be congenital. Pigmentation of face marked, and "garter marks" are present. The goître is very large, the largest exophthalmic goître I have ever seen; there is great pulsation.

Tremors have been very marked for a year. She never noticed them before. They are most obvious in the hands; but she complains of them most in the upper arms (triceps especially), and in the erector spinæ group of muscles.

Œdema of the feet has been noticed for some years. This lady has the same intense religious sense of duty that we have seen above.

I have never found Gräfe's sign present. Retraction of the upper lid and infrequency of winking are constant.

The menses have always been regular in time but excessive in amount.

Case IX.—Mrs. S., born 1851. Labourer's wife. Neurotic family history. One sister is very hysterical, another has hysteria

[1] Charcot, Leçons du Mardi, 1888-89, *passim*.

[2] Neurologisches Centralblatt, December 1, 1890, abstract in Brit. Med. Journ., Supplem., 1891, i. p. 2.

with attacks of semi-cataleptic nature (which I have witnessed). All Mrs. S.'s children, eight in number, are hypermetropic, one boy having 4 D of hypermetropia, and another boy has mild recurrent mania. She is very hysterical herself. Mrs. S. had in 1887 limited pleuro-pneumonia, and I thought I detected cavity signs in that lung soon after. She had then severe hæmoptysis, and this has recurred slightly ever since. I regarded her as phthisical, and in November 1888 she was an in-patient at Victoria Park. When there, a slight goître was first noticed. It has ever since been very slight, and often disappears entirely. There has never been any proptosis, and the lids have moved always in a natural manner.

Tremor is very well marked, especially in the hands. It has existed for two years at least, is quite typical in character, and at times so excessive as to incapacitate her for needlework or writing.

Hæmoptysis has occurred at short intervals ever since 1887. The blood coughed up is bright, fluid, and mixed with watery sputum. The blood never clots, and there is never any sputum suggesting the presence of a cavity. I have failed to find any physical signs of cavity or of consolidation in the lungs since 1888.

She has frequent attacks of diarrhœa of a typical character, and has several times had hæmorrhage from the bowels. The diarrhœa is usually accompanied by sickness. Only once has she vomited blood; the vomit consisted of nearly half a pint of fluid blood mixed with gastric mucus. The thyroid increased notably during the attack. The vomit was seen by me.

Pulse rate rapid—100 to 150—very irregular and feeble. Great muscular weakness.

She complains frequently of great præcordial pain, which radiates upwards to the neck, probably along the plexus of nerves up the great vessels. Sweating is often very profuse. I saw her once, during the last terrible winter, when she had not been able to have her bed-clothes changed in the morning, enclosed in a sheet stiffened with ice formed of frozen sweat.

Her mental condition is characteristic. She cannot trust her memory at all; if she tries to think of the simple matters which concern her (sewing or cooking, &c.), some other idea crops up, and she fails to carry out any little intention. She used to be a good sempstress, but now spoils all her work by cutting out materials quite wrongly.

During the summer of 1891 thermophobia became marked.

This case is of great practical interest—a case of exophthalmic goître with little goître and no ocular symptoms, but presenting almost every other known sign (except pigmentation).

On comparing the details of these cases, we find that *diarrhœa* was present in four (VI., VII., VIII., IX.). It presented the character so typical in Graves' disease, and described recently by the writer.[1] "The diarrhœa is paroxysmal, so paroxysmal that Charcot has likened it to the gastric crises of locomotor ataxy. The bowels are quite natural and regular perhaps for some weeks, and then suddenly, at any time of day, but usually in the early morning, and with no apparent cause, the patient has an urgent call to the closet, and passes without pain or colic a huge liquid motion. The motions are serous and generally light-coloured. There are three or four motions of the same character each twenty-four hours for several days, and then the attack ceases as suddenly as it began, and there is an interval perhaps for a few days, weeks, or even months." In severe cases I have known as many as fifteen or eighteen actions to take place in the day. The recurrence of these attacks is curiously regular in some cases. There is not necessarily any accompanying sickness, but the two do sometimes coincide. The tongue is not affected, and the appetite is not only unimpaired, but may become ravenous. Naturally the prostration produced by these attacks is very great, but I can find no record of a death directly caused by the diarrhœa.[2]

When an intestinal crisis coincides with a rise of temperature, such as is common in the disease, the occurrence of acute intestinal catarrh may be wrongly suspected, and the accompanying tem-

[1] Practitioner, 1891, September, p. 195, "Crises of the Digestive Tract in Graves' Disease."

[2] [Eva E. M'D., æt. 25, single, was admitted to St. Bartholomew's Hospital under my care on July 9, 1891, having for three months been under the care of a doctor suffering from shortness of breath. She considered that she had been in good health up to that time, and had not noticed any change in her neck or eyes. A week before her admission she had a very serious attack of diarrhœa and vomiting, lasting three days. The catamenia had been irregular for three years. On admission, it was noted that she was a highly neurotic, delicate-looking woman, dark-brown hair and eyes, eyes prominent, eyelids pigmented, pupils equal and not dilated, Von Gräfe's sign present, pulse 136, soft, regular, loud systolic murmur, of varying intensity, conducted into the vessels. The thyroid was much enlarged, marked arterial pulsation; a good deal of brown pigmentation on the neck, with unpigmented areas in its midst; similar pigmentation over the chest and abdomen and in the axillæ. The urine was of an average sp. gr. of 1016 whilst she lived, and always had in it a faint trace of albumen. For a week she went on fairly well, but on July 16 had a very severe attack of vomiting, became drowsy and could be aroused with difficulty. Vomiting occurred at frequent intervals after this, and on August 1 diarrhœa set in, and rapidly increased the asthenia; she sank rapidly, and died somewhat suddenly on August 4. At the post-mortem examination nothing was found explaining the diarrhœa or vomiting.

A good many years ago I had a very similar case. The woman, who had improved considerably under treatment, left the Hospital, and lived for nearly two years, being subject to severe attacks of diarrhœa, and died, so far as I could make out from her friends, of asthenia produced by them. W. S. C., Editor.]

perature may be such as to lead to a diagnosis of typhoid fever. My patient (No. VIII.) was pronounced to have typhoid on one occasion when she was away from home. From the description of her illness I have no doubt it was merely one of the severe attacks of diarrhœa to which she is subject. This mistake has been made by good observers.[1] M. Bertoye has shown that fever of various types does sometimes accompany the diarrhœa, but this is exceptional. I have taken the temperature in three cases through several attacks, and found no rise. I have never found any drug have influence on the diarrhœa, except morphia in one case. The drug coto[2] has been vaunted in these cases; I have given it good trial twice, and found it quite useless.

Swelling of the eyelids[3] was present in Case II. There was no œdema elsewhere. On this point I accept the remark of Vigouroux:[4] "False œdema of the lids is very common. It is a swelling of the lids, which gives them an œdematous appearance, and is probably due to paresis of the orbicularis. In fact, when contraction of the muscle is caused by electricity, the swelling disappears, driven back by the tension of the subcutaneous fascia."

Trembling is, next to palpitation, the commonest sign of Graves' disease, far commoner than exophthalmos or goître, and in only one English book is it even mentioned. Dr. Gowers[5] speaks of it, and describes it rather incorrectly as a "coarse jerky tremor." It was quite typical in six of my cases (II., IV., VI., VII., VIII., IX.). The best descriptions have been given by Marié[6] and Charcot.[7] In all my cases it was comparatively late in appearance. It chiefly affects the hands, and in slight cases is limited to them. It is usually symmetrical.[8] It is generally most marked in repose, but is increased when the patient is agitated. The oscillations are very fine, and have a mean rate of eight or nine vibrations per second. Tracings taken mechanically by Marié show that the movement is very regular, though the amplitude may vary, and the evidence is strong that the greater amplitude coincides with a rise in pulse rate. In the hands the tremor affects the hand as a whole, being produced in the flexor and extensor

[1] Bertoye, Etude clinique sur la Fièvre du Goître exophthalmique, Paris, 1888; and Petre, Clin. Méd.

[2] Practitioner, 1879, ii. 258.

[3] This is mentioned by Gowers, Diseases of Nerv. Syst., vol. ii.; and by Mackenzie, Lancet, 1890, ii. pp. 545, 601.

[4] Progrès Medical, 1887, October 22, p. 319.

[5] Diseases of Nervous System, vol. ii.

[6] *Op. cit.*

[7] Leçons du Mardi, 1888–89, p. 231 *et seq.*

[8] Except in cases where there is unilateral goître or exophthalmos.

muscles only. There is no lateral oscillation of the fingers, as in alcoholic trembling, and no pronation movement, as in paralysis agitans.

Swelling of the feet was found in two cases. This is undoubtedly a common feature.[1] It is generally slight, and confined to the ankles. It does not necessarily indicate any cardiac lesion. Debove[2] ascribes its presence to asystole, but in my cases there was no indication of cardiac weakness; in fact, there was considerable hypertrophy. In neither instance did I find any albuminuria, so that, if present, it was not permanent, and there were no varicose veins or other cause to account for œdema.[3] I should rather ascribe it to a peripheral vaso-motor action.

Aural catarrh was present in II. and VII. This was noted also in Dr. Bristowe's case, Marion.[4] It probably produced the facial paralysis in Case VII. It is not noticed in Potain's cases of facial paralysis. We can scarcely regard it as purely accidental, though Dr. Finlayson did so in his interesting case of paralysis of the third nerve.[5]

Is *chronic arthritis* a common family association with Graves' disease? It is said to be, but I can only find a few instances on record.[6] In Case VIII. the connection was well marked. Dr. Spender remarks in his paper that freckling, which is common in arthritis, is unknown in Graves' disease, but my patient was intensely freckled.

My expression "garter marks" needs the explanation that patients who present pigmentation often have most discoloration where there is constant pressure from tight articles of dress, as garters, stays, &c.[7]

The small leucodermatous patches on the pigmented eyelids of Case VI. have not been described before. Pulsation of the thyroid body was only present in one case. The notion, which ordinary text-books would give, that it is common in Graves' disease, is quite misleading. Taking into account the large number of "fruste" cases, thyroid pulsation is comparatively uncommon in the disease. When apparent it is generally due to conducted pulsation from the carotid arteries.[8]

The question of diagnosis is well illustrated.

[1] Millard, Thèse de Paris, 1888, "Des Œdèmes dans la Maladie de Basedow."
[2] Note sur les Accès d'Asystole dans la Cours du Goitre exophthalmique, Soc. Méd. des Hôp., June 1880.
[3] *Vide* Dr. H. Mackenzie's remarks on the point, *loc. cit.*
[4] Diseases of Nervous System.
[5] Brain, 1890, No. III.
[6] Charcot, Leçons du Mardi, 1887–88, p. 326; J. Spender, Brit. Med. Journ., 1891, vol. i. p. 1169.
[7] *Vide* Burton, Brit. Med. Journ., 1888, ii. p. 764.
[8] I am indebted to Mr. J. Berry for drawing my attention to this point.

Case VII. I had for some time regarded as one of gastric catarrh and tremor of alcoholic origin.

Case IX. had for a year at least all the appearance of ordinary chronic phthisis.

Case VIII. was pronounced to be suffering from typhoid.

Ordinary hysteria and Graves' disease often exist in the same subject. Charcot[1] remarks that as the signs of Graves' disease become established, the hysterical symptoms generally subside; but this has not been my experience.

I have had opportunity of seeing the bloody sputum frequently, and I never have found the blood clotted, either when coughed up or vomited from the stomach; it is always fluid and bright, as if rejected directly it passed from the blood-vessels.

Stuttering and stammering are common.[2] In several of these old-standing cases it has been at one time pronounced, and then become dormant. In these cases the symptoms that remain are either goître or eyelid symptoms, perhaps both; and they may remain for years, during which the patient is apparently well.

Epigastric pain and tenderness was present in Cases VI. and IX. This is common, and is only one of many localised forms of pain.[3] When this form of pain co-exists with paresis of the legs and distinct gastric crises, the case may distinctly resemble locomotor ataxia, though the presence or absence of other signs should make diagnosis clear. But it must be remembered that the two diseases may be present together.[4]

In Case IX. the pain was always described as radiating from the spine to the umbilicus, but it was in no sense a constricting or girdle pain. I consider its seat to be the mesenteric plexus.

Have we any evidence in solution of the problem afforded by the lid symptoms? The rival theories are that the retraction of the lid and impaired descent are caused by, first, irritation of the sympathetic fibres supplying Müller's muscle or the involuntary muscle fibres of the lids; second, paresis of the orbicularis.

Undoubtedly Remak has shown that irritation of the sympathetic can produce raising and retraction of the lid. So also the experiments of Köhn and Mr. Walter Jessop[5] have shown that cocaine will not only produce in healthy persons, and increase in those afflicted with Graves' disease, both the eyelid symptoms (retarded movement and retracted lids), but it will also produce

[1] Leçons du Mardi, 1888–89, p. 240.

[2] Russell Reynolds, *loc. cit.*

[3] Gauthier, Rev. de Méd, May 10, 1890, p. 426.

[4] Charcot, Leçons du Mardi, 1888–89, p. 243; Barrié et Joffroy, Soc. Méd. des Hôpitaux, December 10, 1888; Ballet, *ibid.*, February 8, 1889.

[5] Trans. Ophth. Soc., 1886, p. 123; and Centralblatt für medic. Gewiss., March 14, 1885.

proptosis, and it is proved that these phenomena are caused by irritation of the sympathetic.

These two sets of experiments merely prove that the lid-signs in Graves' disease *can* be produced by stimulation of the sympathetic, but not that they *are* so produced.

Clearly there is a relative over-action of the muscles which raise the lid, either the levator palpebræ (supplied by the third nerve), or the unstriped muscle fibre of the lids themselves (supplied by the sympathetic). We may dismiss the notion that the defect is in the centripetal excitor apparatus; that is to say, that due notice is not afforded to the motor centre for the lids by the retina or external ocular muscles, for the reason that the more delicate movements of accommodation, equally dependent on the retina and ocular muscles, are never affected.

Constant active spasm in any set of muscles very rarely results from irritation; it is almost invariably due to some relative weakness in an opposing group of muscles.[1]

Is there any evidence of such paresis in the orbicularis, which is the muscle in question? Yes, for Vigouroux [2] has shown that the electrical contractility of the upper branch of the facial nerve is almost always impaired: "It is often impossible, even with very strong currents (so strong that the diffusion will cause contraction of the masseter), to make the orbicularis or occipito-frontalis contract." This weakness of the orbicularis is the probable cause of the spurious œdema of the eyelids, which is by no means uncommon in this disease.[3]

Again, if the condition were due to irritation of the sympathetic, as in cocaine poisoning, how is it that dilatation of the pupil is not found in Graves' disease? Gräfe states that the pupils are never dilated, and I have never found them so. All the statistics available on this point, in which the factor of myopia has been properly eliminated, confirm this. The balance of evidence shows that the lid-signs are due not to irritation of the sympathetic, but to paresis of the orbicularis, with relative over-action of the involuntary muscle fibres supplied by the sympathetic. My case (No. VII.) throws valuable light on the point, because she had permanent partial ptosis, probably due to lesion in the centre of the third nerve, and yet she had retarded lid-action. The ptosis disappeared, and then retraction of the lid became marked. This indicates that the ptosis was due to mere gravitation falling of the lid in the presence of a

[1] See the excellent paper of Dr. Sharkey, Brit. Med. Journ., 1890, ii. p. 959; reprint Braithw. Ret., 1891, p. 8. I have merely endeavoured to support and develop his position.

[2] Vigouroux, Prog. Méd., 1887, Oct. 22, p. 319.

[3] Gowers, Dis. Nerv. Syst.; Hector Mackenzie, Lancet, 1890, vol. ii. p. 546.

permanent weakness of the third nerve, and also of the superior branch of the facial. When this patient stares voluntarily, *i.e.*, when she forces the third nerve to act, there is retraction of the lid. In her case there is great irregularity in the occurrence of the symptoms, and the irregularity is very marked in all cases if they are watched frequently.

I have taken observations at frequent interviews of eight cases, and find:—

Case.	Gräfe's Sign.	Stellwag's Sign.
One (fruste) . . .	Absent	Absent.
One (developed) .	,,	,,
Two ,, . .	Present	,,
One ,, . .	Present with ptosis	Appeared when ptosis subsided.
Two ,, . .	Never present	Always marked.
One ,, . .	Always occurred together.	

These discrepancies in evidence I attribute to the fact that the symptoms are due to a disturbed balance between two sets of muscles supplied by three nerves, two of which are under the control of the will, and the third involuntary. The irritability of these muscles must vary in different individuals and at different times in the same individual, and it is impossible absolutely to eliminate the factor of the will from a patient under study. The second case on the above list who has never had any lid-symptoms has for some weeks shown œdema of the cheeks and lower eyelids, and this would appear to oppose the remarks I made above on the causation of this œdema. But she has also much swelling of the feet, and (she asserts, though I have never seen it) some œdema of the hands. The solution of this is that œdema of the lower lids in Graves' disease is not due simply to a paralysed orbicularis, for we do not get facial œdema in ordinary facial paralysis, but that it is caused by the paresis coupled with a vaso-motor disturbance which produces the œdema elsewhere.[2]

High authorities[1] have ascribed the œdema in these cases to asystole, but in two cases I have found œdema of the ankles when there has been distinct cardiac hypertrophy and no indications from the pulse of any systolic failure, and I should rather refer the dropsy to a vaso-motor origin.

The ophthalmoplegia in Case VII. is striking. Let us read the facts briefly.

May 22.—Facial paralysis with no deafness.

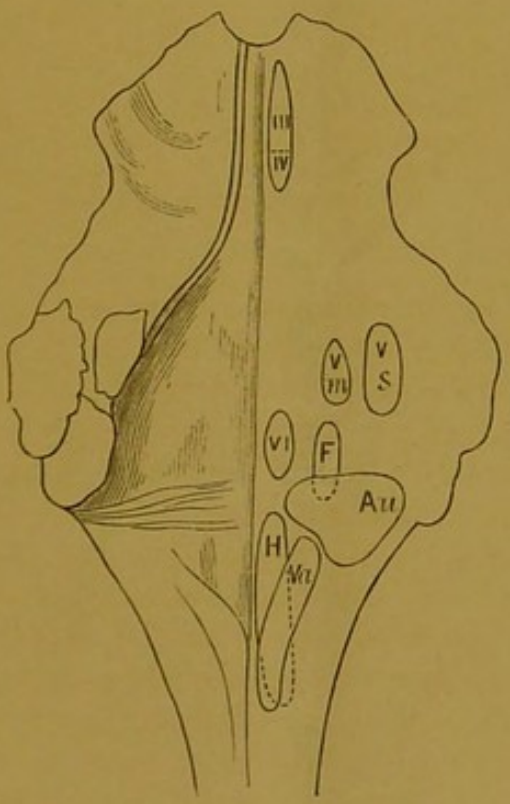
[1] Marié, *op. cit.*; Debove, Soc. Méd. des Hôp., June 1880.

[2] See Practitioner, Dec. 1891, 401, "Œdema in Graves' Disease. Maude."

May 24.—Paresis of external rectus and probably superior oblique.

May 26.—General ophthalmoplegia; pupils unaffected.

We are warranted in assuming the passage of some travelling lesion moving forwards along the floor of the fourth ventricle to the aqueduct of Sylvius, attacking successively the nuclei of the facial, the sixth, the fourth, and third nerves, and passing so close to the middle line as to avoid the auditory nucleus, which lies farther out, and also the two nuclei of the fifth.



AFTER GOWERS.

Diagram of the relative position of the nerve nuclei beneath the floor of the fourth ventricle.

III. Third nerve nucleus; *IV.* fourth; *V.s.* middle sensory nucleus of the fifth; *V.m.* motor nucleus of the fifth; *VI.* sixth; *F.* facial; *Au.* auditory; *H.* hypoglossal; *V.a.* vago-accessorial nucleus, the upper part giving origin to the pneumogastric, the lower to the highest fibres of the spinal accessory.

Where one nucleus lies beneath another, its outline is indicated by a dotted line.

A number of cases of ophthalmoplegia (general) in Graves' disease have been collected,[1] of which Dr. Bristowe's case (Marion) was one.[2] Isolated monoplegia is less common. Mackenzie observed weakness of the external recti producing diplopia in two instances, while Möbius found more than once diplopia due to feeble convergence.[3]

[1] M. Babet, Rev. de Méd., 1888, pp. 337 and 513.

[2] *Op. cit.*

[3] Rev. de Méd., 1888, July.

Dr. Finlayson[1] has recorded an example of paralysis of the third nerve only, and years ago M. Féréol described isolated paralysis of the fourth nerve. In this patient, however, as in mine, other paralyses and nervous disturbances were present in the limbs.[2]

[1] Brain, 1890, No. iii. p. 383.

[2] Soc. Méd. des Hôp., 1874; given *in extenso* by M. Babet, *loc. cit.*, also in Rev. de Méd., 1883, p. 272, and again in M. Marié, "Contribution à l'Etude . . . des Formes fruste de la Maladie de Basedow," Paris, 1883.