On Graves' Disease

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On Grave's Disease

This disease is also called Exophthalmic Goitre and Basedow's disease. The term exophthalmic goitre is not quite satisfactory as it brings into prominence two of the symptoms to the exclusion of others of equal importance. The term Grave's disease is a comprehensive one and includes all the symptoms.

It was first described by Perry in his Collections from unpublished writings, Vol. 1, 1825, p. 110. Graves; however, was the first to point out the symptoms in any definite manner in 1836, see Graves' Clinical Lectures, 1864, p. 387, 2nd Edition, edited by Kellogg, 1871, 195, Vol. 2. Basedow described the disease in 1840, see Cursif, Wachsmuth, 1840, p. 13, W. 14. Since then it has been described by O'the, Charette, Van Graefe and many others.

The disease mostly in females according to the majority of observers but occasionally in men. The proportion between the two has been variously estimated. Brillouin in his Practice of Medicine, 1882, p. 576 says, 'Men are affected much less frequently than women' Cross, Lectures on the Nervous System, Vol. 1, p. 713 says it occurs twice in the female to once in male. Eulenburg in
Trousseau's cyclopædia gives a similar proportion. Trousseau in Clinique Médicale de L'Hôtel Dieu June 1862 p. 618 gives the proportion as 82 females to 8 males. Whilst Hardy says the disease attacks women almost exclusively. Chavel in la Gazette des Hôpitaux 1885 on the other hand says it is little less frequent in men than women. Mackenzie, Lancet Sept. 13, 1890 p. 545 finds it uncommon in men. Russell Reynolds in Lancet May 19, 1890 p. 1055 states the proportion as 48 females to 1 male. Only two cases have all been female, and also those of a fellow practitioner who has a great many cases during the last 10 years. Those cases described as occurring in men are often incomplete.

The disease generally occurs between the age of puberty and middle life; it is extremely rare in childhood but has been seen at 2½ years. Rosenborg saw it at 7 years of age. Goldberg in one at 8 years, Trousseau at 14; it is rarely seen beyond the Climacteric period. Though Stotes had a case at 60. Brianté in his book already quoted says it occurs most commonly above the age of puberty, seldom in younger girls and seldom in advanced life.

The disease is often associated with other, chiefly nervous diseases as Epilepsy, Chorea, Diabetes, and Drowning. There seems to be some association with the condition of Plummer. Mackenzie, op. cit. had in 40 cases of Graves' Disease 5 of acute Chorea.
and Demsey in 9. West as quoted by Mackenzie had 8 cases of rheumatism out of 38 cases of brain disease. Dr. Lowell Sept 22. 1848 p. 573. W. J. W. Burton read a paper on this disease where in he states the prevalence of this in Cambridge which he attributes to the presence also of rheumatism this district is one where rheumatism is very common and may account in the same way for so many cases. Though the connection has not been particularly noticed, Dr. James Esq. in that paper it is stated that Dr. A. has had 8 cases out of 38 of cases which were rheumatic, same as quoted by Mackenzie above.

There seems to be a definite association between nervous disorders, chiefly insanity as will be pointed out later, one either in the subject of brain disease or in the same family.

The cause of the complaint is as yet a mystery but is generally attributed by all observers and the patients themselves to shock or fright. Often to overstepping in labour. In nearly all cases the patient states the illness from some such time.

The symptoms are numerous, no one case showing them all with very few exception. The first to be noticed by the patient is generally.
Jalpitation, and the symptom for which advice is first sought. This is the most constant symptom, and very rarely absent; it is not present, there is very rapid cardiac action. There is often visible pulsation over a large area in the cardiac region, also in the hypochondriac region of the neck and epigastrium. The patient is conscious of pulsation in neck, and head, and in some cases in the eyeball. It may also be seen in the epigastrium region, and over the right lobe of the liver. (Th. Trouseau, as above). He also states that the area of cardiac dulness is increased.

In most cases that have been reported of Sinus disease, mention is made of murmur heard at the base of the heart, systolic in character. Also, I have heard murmurs. In some cases there is dilatation of the heart. The pulse rate in nearly all cases is very much quickened, varying from 90 to 120 or even 160; in some cases it cannot be counted. (Quoted from Bucsi). Bucsi says in his book, "The condition of the palpitating heart varies somewhat. For the most part its action is violent and rapid, and its sounds loud andurring; its area of dulness is often increased. In most cases it is at first structurally healthy, and so it may continue. Often, however, the persistence of palpitation induces hypertrophy and dilatation, especially of the left auricle. A functional systolic murmur is not infrequently audible at the base, and murmurs are often audible, also in the aorta and region of the neck. Occasionally, as has been already intimated,
The phenomena of Graves' disease supervene on actual cardiac disease

The chief symptom in the order of frequency is the enlargement of the thyroid gland. This is one of the most constant symptoms but is occasionally absent. The enlargement is not very great as usually it is noticed to be greater on the right side than the left. MacKenzie of at. attributes this to the thyroid body being larger in the normal state on the right side than the left. She also states that palpation may be felt in the gland. It is generally soft in consistence and may be cystic. The gland may become very large though it is not the usual supraventricular case. In severe cases it becomes no larger as to interfere with the respiration. A case reported in Lancet, Feb. 12, 1891, p. 306, by Hugh Montgomery, of Graves' disease, death took place from bulging in of the cartilage of the trachea which had become softened by pressure of the enlarged thyroid. The base had given way and with the bulging in the cartilages and the thyroid aspiration was stopped. Bullock says in all cases death is caused by pressure on the cartilage of the thyroid at humour. The thyroid has been noticed to vary in size definitely dependent on the cardiac action. Graves, mentions this in his Clinical Lectures.

The third prominent symptom is the prominence of protrusion of the eyeballs. This is very generally present but may be absent in some cases where the nervous symptoms described above are a valuable aid to diagnosis. MacKenzie says the exophthalmos is often un-equal on both sides. Unilateral.
Cases have been recorded in the Lancet April 20, 1887 p. 789 by Felix Semow before The Clinical Society of London read tales of a case in which an operation for removal of nasal polypus caused exophthalmus of the patient's right eye with von Graefe's and Hellwag's signs in addition. This diagnosis being confirmed by Mr. Settle's hip. Associated with the polyposis are the two symptoms just-men- 

tioned von Graefe's symptom is inability of the upper eyelid to move down with the eyeball. 

Hellwag's sign is retraction of the upper lid. 

This may be so marked as to cause a distinct area of sclerotic to show. The polyposis may be so excessive that the lid cannot close over the eyeball by as much as 1/8 or 1/4 of an inch. This has been known to lead to ulceration and sloughing are two cases reported by Swell in the Lancet April 23, 1887 p. 518. one where death occurred and in the other the eyeball was destroyed by sloughing of the cornea. Swell says that these two symptoms 

von Graeae's and Hellwag's are not invariably the first early indication of Graves' disease and reports cases in the same paper one especially where the two symptoms were present and some
slight exophthalmus he was disposed to regard this case as Graves' disease in the absence of other symptoms against the opinion of other. The case developed into a well marked case.

Dr. Hill in his paper that 21 of 22 cases had 20 cases in which 23 were bilateral. He was affected in the right eye and 3 in the left. Dr. Hill had two cases. The first was a well marked case with well treated exophthalmus on the right side. The second case was left sided with von Graefe and Stellwag signs. Eye mydriasis and not improved by glasses.

As a rule the vision in good accommodation unaffected usually although sometimes increased. Diplopia may be developed on looking at near objects. Ophthalmoscope shows generally dilatation and increased tortuosity of retinal veins along with unstable pulsation in the arteries. Pupil unaltered. See also Fig. 1.

In cases of recovery there often remains some degree of exophthalmos.

The next most common symptoms are those affecting the nervous system. The patient is nervous, irritable and conscious of it. Often low spirited and listless.
and fluttered, excitable, and forgetful. The memory is poor. There are trembling and
fine tremors, see Mackenzie et al. If a
patient the subject of this disease told out his
hands, a tremor in them is very perceptible,
consisting of vibratory movements of small
amplitude and with a period of about one-
eighth or one-ninth of a second. The tremor
is a communicated one, affecting all the fingers
individually but the whole extremity, and strange-
ly the whole body so that it may be seen
in the lower extremity as in the upper. It usually
effects both sides of the body; but in some cases
it is limited to one very much more marked
in one extremity. Besides this tremor, which
is more or less presentable the patients generally
suffer from attacks of trembling either with or
without palpitation. Which attacks bear the
same relation to the tremor that the palpitation
does to the rapid cardiac action. The tremor
is generally more obvious when the patient
is fuddled, and sometimes may be reduced
to a mere twinge. Such conditions, Mackenzie
also says he has met with a case or two in which
it is altogether absent. This is a most valuable
aid to diagnosis in absence of other symptoms.
Symptoms such as the Exophthalmos
Russell Reynolds, op. cit. says, "Hysteric symptoms are the most common and troublesome but
least to sever as many others. The highly susceptible nervous temperament is general, but because
hysteric attacks occurred in not more than one
fourth of his cases. He also says, "Maniacal symptoms
present themselves in the form of depression
amounting to melancholia in some cases;
but in the majority alternating with periods of
excitement, irritable temper, melancholy, wandering
 Humbler, capriciousness, mania, delirium,
fluences, delusions, and crazy conduct. That it
is not easy to separate from mania or paroxysmal
attacks or chronic force. There is often a condition
mind which I have been in the habit of
designing as a "choke of ideas" which is peculiar;
trying to the patient and his friends. The patient
tries to think of one thing and another thing
thing else instead, and it is often so discordant
as to give of the attempt to believe". He also
say, There are inverted and sometimes painful feelings.
Cephalalgia is common. Paroxysmic headache
numerous such as vertigo or something short of
sensed as dizziness, confusion, instability in
standing or walking, tremulous attacks of

varying degree of irritability and elevation but no distressing as to induce deafness. Auditory illusions such as spectra of light leading to conversation with imaginary people. Spectra of hearing also. With these paroxysms a sense ofitnessness so distressing as to induce mimicry.

He also says there is dread of impending evil or fear sudden collapse. Muscular disturbances are common but not so much so as the sensorial fluttering and shivering have occurred in some cases. In two of his cases were attacks of aphasia occurring several times a day and lasting from a few minutes to three or four hours. Choreic movements of facial muscles of hands, arms and legs are common and with these disorderly movements of respiratory muscles leading to attacks of dyspnea or a feeling of breathlessness. He also found with the hemorheo- and facilitation of upper extremities, and in some tremulous movements of the head. Clonic-ataxia were present in one case and epilepsy in one. In two cases spasm of left arm and leg, there also difficulty of articulation.

In the Lancet for Jan. 8, 1887, p. 68 is an article by Dr. W. Coleman Collins on "The Relation of Insanity to 'Spectrallus Coelici.'" This is a case of...
well marked Graves disease. Tachypnoea was first complained of, there was exophthalmos and enlarged thyroid gland. Pulse 120. Area of cardiac dulness increased, dilatation with hypertrophy. Palpation visible in neck. Patient was fretful, sleepless and dyspeptic. She also suffered from anorexia nera. Treated by iron, terebinth, nux vomica, choline and bromides. Some relief obtained at first with diet and above treatment, on vincholone disease still further developed. Being tried by domestic trouble her mind gave way, and sheapsed into melancholia. Had to be fed for a month by means of a stomach pump. Belladonna relieved the attack. Constant return of vomiting and mitigated the pulsations of manicde excitement. At end of a month was some improvement which gradually increased and ended in recovery. As far as the melancholia, but the other symptoms, Graves disease remained as before. McLane concludes by stating that "it is not a work of supererogation to inquire into the true cause connection between Graves disease and mental alteration. Emotional disturbance, shock and mental and bodily emotion appear to be active agents in the production of both. The cases are reported by Erance, Trouvé and
Laycock, Beigrie, and Friedreich may be put in evidence to support the one and those by Savage and Brooke to support the other. Athymia, as is so well known, frequently associated with bodily deformity and guilt. D. G. H. Savage in Guys Hosp Med Rep. 19xxvi has drawn particular attention to the fact that patients with athymia frequently become insane and that their insanity is usually acute mania and often proves fatal. Beigrie's patient exhibited grandiosity, mania, and mania; Gesells was attacked by 'maniacal mania de praedens'.

In a case reported by Dr. Arthur Davies in the Lancet on 20/07/1394 there was hereditary insanity on the patient's side. In a case of my own the patient is apparently sound in mind except for the枢纽 of his nervous manner but one of her children is an idiot.

Along with these nervous symptoms are others associated closely. The patient is subject to flushings of head and neck on the slightest provocation. There is also often sweating, particularly above.

The patient, if not the child mentioned above, in a well marked case showing all the symptoms of Gries. Palpitation, Exophthalmos...
Noticeable but not marked, enlargement of the thyroid. She has the flushing, acid sweats, mentioned above. She has also attacks of mastoidea mentioned as occurring in the disease by many observers. Oedema of the legs is present to a slight extent, she also complains of feeling as if about to fall by her knees giving way. Mackenzie noted this in 12 of his cases. Besides the oedema of legs, a distinct swelling of the knees this I suppose to be due to excess of synovial fluid in the joint caused in a similar manner to the oedema.


St. Caiden says this symptom he believes to be present in the majority of cases; he found it in 15 out 20 cases. He noticed that the electrosurgical force necessary to produce at once the desired current strength was very much less under these conditions of the application being the same, than in patients suffering from other diseases. In Graves disease he found an average of 3000 others resistance as against from 30,000 and upwards according to circumstances in other cases. He attributes this marked reduction to excess of moisture on the skin from perspiration, and thinks that this is a symptom of as much value.

Another group of affections or symptoms are more connected with the cutaneous system. The association of cutaneous affections and Graves disease has been pointed out by many observers.

The chief and most common symptom is segmentation of the skin. In these cases there have been well marked basal as urticae. Acne ve Rose quotes Reynaud as bringing attention to presence of Leneoderma in five cases.

"Urtigo et goutte nephithalmine" Paris 1879

Trousseau mentions skin affection. "Clinique
Medical Laws in 1862 p. 638. Bristow in his Practice of Medicine does not mention it, nor does Russell Reynolds in his article quoted. Mackenzie on the other hand draws attention to pigmentary changes, he says Stogrie in his Contributions to Psor. Med. 1862 alluded to the bronzing of the face of one of his patients, and that Trouveaux had a case where the skin became brown and freckled. Two of Mackenzie's patients had the pigmentation and he also mentions Drummond had the cases. He is inclined to think that this condition is not uncommon. The pigmentation is most marked on the face, neck, sides of chest and extima. The abdomen and flexures of arm and thigh. Mackenzie has not seen the patches of leucoderma mentioned by Regnard. The occurrence of pigmentation and other cutaneous had been noticed by many other observers. W. T. W. Burton in the Lancet Sept 22, 1848 p. 573 read a paper before the Cambridge Medical Society on "Pigmentation and other cutaneous affections in Gravel Disease" he mentions that there were two cases in the hospital with symptoms of gravel disease with many of those of Addison's disease there was pigmentation of face neck axilla...
Jack gentnels and below the Ruak. He had also
heard of six other cases with pigmentation. Dr. High
had only one case in 38

Dr. Chandle in St. George's Hosp. Reports mention case of
moles disease with some changes due to congestion of skin from general vascular dilatation.

Dr. Burney too had a case with loss of hair of
eyebrows & eyelashes. I see a case with areola of
hairs of face and back of hands.

In Lancet Dec 6, 1870 Dr. Hackett before the
London Med. Soc read report of a case with pigmentation
of face, armpits, deltoid region, &c.

At a meeting of the Ophthalmological Society
of London reported in Lancet Oct 25/90 & 897
where are three cases with alopecia.

Mackenzie says, 'To cite one of the
rarest cases generally affected, most of his cases
say their hair has become very thin and comes out
very much, and its cleanliness and dryness
have been conspicuous in many of them.

In one of my cases was an acute
attack of Lechen Planus, and in another
no distinct Dr. Ethelbert but blotches on the
face with occasional acne spots.

I think there is some foundation in
assuming a connection between these diseases.
and cutaneous affections, but chiefly in the way of pigmentation. By Burton in case above attempted to show this liability to pigmentation, cutaneous affections was due to sympathetic neurons.

The patients suffering from Graves disease are in many cases anaemic, or if not anaemic there is often some degree of weakness. Even slight cases complain of having lost flesh. In some there is great emaciation. Anaemia has been considered by some to be the cause of the disease e specially by Bigelow. Burton notes the presence of anaemia and cachexia.

There are often digestive troubles with flatulence, constipation alternating with diarhoea. The appetite is often capricious and may be frantic. In most cases the menstrual function is irregular, generally in the way of amenorrhoea but there may be menorrhagia.

Burton says the spleen is enlarged in some cases, in others the pancreas.

Diminished chest expansion is the newest symptom and has been pointed out by Dr. Louise Price-Bryson, accompanied by increased respiration and frequently by cough. In severe cases the chest expansion on
faced inspiration was half an inch or even less. Whilst an expansion on forced inspiration of this
manner was regarded as justifying a favourable prognosis even in the presence of the Cardiac
Symptoms. There was almost always some evidence of previous disease of the Respiratory
tract. Hugon Lays especial stress on the
presence of certain conditions resembling those
which prevail in Angina Pectoris and Asthma, and
a peculiar catching of the Breath at regular intervals
when reading aloud. See Med. Annual 1871,
pp. 225. or New York Med. Jour, Dec 14, 1889

McKenzies has brought forward other symptoms
in addition which I have not found reported by
others. He says that Eruption when extreme
is not bad anything.

Quintes is also not very frequent.
He quotes Troussseau and Chevalle as proving examples. In seven of his cases there was a history of epistaxis. He also states that vomiting unrelieved by the ingestion of food is not infrequent. In eight cases there was lameness. The urine has been stated by some to be affected, in the way of intermittent albuminuria by red blood. Baptist, Ballut, and West Eyre have been recorded by many, among them a case of Dr. Burton's quoted above. MacKenzie has noted the occurrence of painful paroxysm in 13 out of 15 cases. In some only the hands, in others and more frequently the feet and legs are affected. In 12 of these cases he had induced a jumping way at the knees so that there is difficulty to avoid falling.

The connection between epistaxis and other nasal complaints, and Graves has been noticed by others. Dr. Eliz. G. M. S. Lanceet, 1869, 787, reported a case of unilateral Grave disease after removal of nasal polypi. He mentioned 3 other cases in which extra nasal operation for relief of obstruction had unexpectedly led to diminution or even disappearance of symptoms. Graves disease Mr. Geo. Hulcher, mentioned in same paper, had recorded two cases where intra nasal operation had led to diminution of goitres. He says:
"That in these cases the changes in the domain of the sympathetic were actually due to the intra-thoracic operations, and not mere coincidence, appeared from the fact that the diminution or disappearance of the ophthalmoplegia and of the enlargement of the thyroid body in all these cases corresponded to the side operated on."

This concludes the whole list of symptoms, except that Drouet mentions the occurrence of pulmonary, intestinal, meningeal, and central hemorrhages.

The disease is of varying duration; in some improvement is rapid, cases have recorded of sudden recovery in three or five days; in the majority the improvement is only very slow, generally with some enlargement of the thyroid remaining, or some slight ophthalmoplegia. In these again perfect recovery takes place. Drouet also says, "Graves' disease is not usually dangerous to life; it is generally occasionally fatal, recovery entirely; more commonly there is partial amelioration only; and in a large number the disease is slowly progressive, and at last after a while becomes stationary." There are several instances of sudden death recently recorded in Lancet, Mar. 8, 1890. 15445 by Dr. Riggs, Fagge, and Chevalier-Rust. That
Recovery is the rule and death exceptional. MacKenzie in his paper says out of 18 cases there were 10 deaths. Hale White records a similar rate of mortality so that he does not think that recovery is the rule as stated by Trager. Bruceone says death occurs usually from some intercurrent disease, more especially of the lungs. In all cases the thyroïd causes death by pressure on the trachea. Cullen says death occurs from paroxysms and intercurrent disease.

The pathology of Graves disease is very obscure as definite results have been obtained by post-mortem examination. Many theories have been suggested but nearly everyone has his own idea as to the pathology and cause. The parotid is normal or a simple hyperplasia or may be cystic (trag). The arteries have been found considerably developed and the veins dilated.

There is excess of fat in the orbit behind the globe; the ophthalmic artery is often arteriosomatous; advanced fatty degeneration of orbital muscles has been seen. Bruceone says arteries after arteriosomatous alterations have been noticed in cœrebral sympathetic and ganglia, chiefly excess of connective tissue and diminution of nerve elements.
Notes pour servir à l'histoire du goutte Exophthal.

Enlargement of middle and lower cervical ganglia and disease of the cord of sympathetics, by Pecht and Beveridge. Med. Times. and Gazette Vol. 11 1865 p. 521

Obstruction of lower cervical ganglia of both sides by iron on nature and treatment of Exophthalmic goitre, in Dublin Iour. Med. Sc. Vol. 1 1865 p. 344

Atrophy of sympathetic and c, ganglia by Kraehe and Recklinghausen, Deutsche Klinik 1863 p. 286

Increased size and interstitial thickening of upper and lower ganglia by Kirchner, Die Krankheiten Geschwulst. Bd. III 1867 p. 89

And increased envenemng of 10th cervical sympathetics in dense connective tissue Ziegel, Würzburg Med. Zeitschr. Bd. VII 1866 p. 84


These references show nothing definite except a preference for seat of disease in Cervical sympathec's. The superior cervical ganglia appear to be the ones chiefly or exclusively affected (Ross).

Base also attributes the disease to a neurotis.
Grave-like chlorosis, Stokes attributes it to the heart. Laycock and others a nervous
Graves, Awan, Imusaw and others put down the affection to disease of the sympathetic
or cervical part of spinal cord and the medulla
Humphrey, Jackson, Hale White, and Mitchell
Clarke look to the ganglia about the fourth
vertebra as the seat of disease.

MacKenzie in his article has this paragraph "It is
curious that among the many speculations as to
the cause of the disease, that few should have
attributed the disease to the enlargement of the
Thyroid body gland itself" and later on
"It is likely that the alteration of the function of
the thyroid body, whose importance in connection
with nutrition and the transmission of nerve
force has been amply demonstrated, has a good deal
to do with many of the secondary symptoms to which
I have called attention, but the real disease is a
widely distributed derangement of the emotional nervous
system. We also mention the appearance of
our subjects to intense fright, or grief, the appearance
being like a well marked case
of Graves disease—vis. palpitation, staring of the
eyes, trembling, sweating, flushing, and winds.
This fright or shock may have such an
Effect on the nervous system that it is not possible to recover its balance and to lead to a continuation of the symptoms and from Graves Disease.

Ross says the enlargement of the thyroid is due to enlargement of vessels and veins, the soft consistence and rapid growth pointing to the same thing. Paralyses of the vasomotor nerves which run in the central sympathetic is supposed to cause dilatation of the vessels. Benedict thinks the enlargement of the vessels is due to irritation of dilator nerves in the sympathetic and lead to paralyses of vasomotor nerves.

The exophthalmus may be accounted for by the deposition of fat in the orbit and periorbital hyperaemia, but contraction of the muscle of Müller induced by irritation of cervical sympathetic is the main factor in causing protrusion. This is rendered more effective by the ectopic fatty degeneration of the orbit. Benedict mentions in addition to fat in the orbit an increase of connective tissue, and dilatation of orbital vessels.

Connected with the exophthalmus are the lid signs. Several theories have been suggested for these symptoms. Sec in the paper already quoted says the central lesion theory with account for
The symptoms most satisfactorily, thus in a sense of the base motor centre that presides over the base motor nerves of the thyroid gland and orbital tissues and it is inferred from the frequent appearance of these symptoms, goitre and exophthalmos that these centres must be close together. Cardiac symptoms are ascribed to lesion of cardiac inhibitory centre for the vagus and Gräff sign is explained by disconnecting a centre governing the downward movement of the eye and eyelids. The widening of the palpebral opening is due to lesion of afferent centres which are set in motion by stimuli from the upper corneal and conjunctival. The association of diabetes with Graves disease is well known and the diabetic pustule is close to the base of the area. Bell's palsy as the lid begins and often among the earliest begins that the lesion has only affected the centres governing the coordinated downward movement of the globe and eyelid with the lid reflexes generally closely associated, and the other centres may be implicated later on with a further development of symptoms.

Dr. Sharkey read a paper before the Ophthalmological Society of London reported in Lancet 1890, p. 799 on Gräff's test sign. He says many people...
Can voluntarily produce the same by staring
and ask it is also present in cases where there are
no symptoms of Graces disease, he does not consider
it a symptom of very great value as a diagnostic
sign. With regard to its production he says: "It is
clear there is over action of the muscles which raise
the lid. There are two muscles which do this:
The Levator Palpebrae supplied by the Third nerve,
and the orbicular muscle of the lid supplied by the
Sympathetic. Remark showed that relaxation of
the sympathetic produced elevation and relaxation of the
upper lid, and the fact that one can voluntarily
produce this effect shows that it can be produced
through the Third Cranial nerve. Consequent action
spasms however rarely result from irritation through
intermittent spasms may. Prolonged spasms most
frequently result in origin of paralysis or weakening of
the paralysis muscle as is seen in the "Mens en griffe"
with progressive muscular atrophy. Hellvey has shown
that a very constant symptom of the disease
is diminished frequency and incompleteness of
the involuntary closure of the lids which goes
even when continuosly in health. The orbicular
muscles, which affects the movement,
and in the opponent of the muscles which cause
the lid, being weakened in Graces disease.
And losing tone by reaction, the healthy equilibrium of the muscles of the eye is lost. The opening overpowering the closing muscle, and producing attraction of the upper lid and Graefe's sign. Thus, the inequality of working, whichettiwolf refers to disease of the centre spreading over the automatic set, in the primary stage of disease, and which of the lids and Graefe's sign follow as a consequence. This appears to be the most satisfactory explanation. He further states that should Graefe's sign be present when there is no inequality of the palpebral movement of the lid and eyeball is most probably responsible for the lid, but he thinks the above a satisfactory explanation without presupposing such disease.

Fatiguation of accelerator nerves might be supposed to cause palpitation and increased action, but it would be necessary to assume a paralyzing of the sympathetic to account for swelling of the thyroid and the exophthalmos, and it is a strained interpretation to assume that there is
ivitation of our set of fibres and paralysis of another, by the same lesion, but still this is seen in neuritis, though it cannot be a satisfactory explanation. See Rosso, V. C. Al. Friedrich, Traité des Maladies du Coeur, traduit par Loboer et Dayon 1878, p. 367. Prof. Selphalation is due to paralysis of doss motor nerves; according to this theory dilatation of coronary arteries is followed by increased flow of blood to the heart walls and increased excitement of ganglia.

Benedikt places the lesion in the medulla. Seigen in the Cblus spinal region and assumes that one centre the acute purpura is in a state of irritation and the other vas motor centre in a state of paralysis.

In the Medical Annual 1870 p. 259 Dr. Hardland Hall says that the theory of the central sympathetic being the seat of disease is being discarded in favour of the central chiasm theory. The part affected being the floor of the fourth ventricle. Dr. Hale White says that the fact of patients dying suddenly is in favour of this theory. He has published a series of cases showing this. The presence of diabetes with epilepsy. One feature common is a similar theory.
Treatment. Many methods have been adopted and many drugs tried and few only have been found useful. The usual routine has been the administration of Bromides with Quinine, Digitalis. Soon for the Acneema, Digitalis is said by some to have no effect in lessening number of heart-beat. Bostow says Digitalis in large and frequent doses is valuable in preventing contraction of the dilated and pulsatile vessels and in relieving and curing the disease. On the same principle, Ergot or lead may seem to be indicated. Iodine is recommended. Forseacusee contains it, he also along with Von Graepe contains the use of Iron. Belladonna seems to its food in some cases. Cold applications to the Thyroid or parotid region are said to be useful. Mackenzie has found Belladonna very useful while he condemns iron alone, and iodine. Russell Reynolds finds Iodine very useful in connection with Bromine and Iron, giving marked relief when other means fail. Belladonna seems to be very generally used and in case quoted gave relief to the Acneema. Perhaps the most successful method of treatment has been by the application of Electricity.
Either employed after the manner of Eulenburg which is paradisation of the sympathetic, or the electrode being placed on the region of the sympathetic the in the neck and the other to the Cervical vertebrae, or by Charcot’s method to the preceding region. Dr. Hadden see Lancer Feb. 5, 1887 p. 264 applied our pole on back of the neck and the positive pole over the thyroid and also over the epigastrium for 10 minutes at a sitting, in 6 months the patient was practically well. Euphaunthesis is now the drug which seems to give the best results. I have found great benefit from its use in 3 cases.

Dr. Hammond, in New York Med. Jour June 25, 1890 has found this drug beneficial in a few cases referring to the use of Euphaunthesis he speaks of the experiments of Babadurji and Langgaard of Bestel who found that the drug has a marked effect on the vagus, they also report that the aspirations are at first increased but later are slower and weakened. In Euphaunthesis force Dr. Hammond finds aspirations become slower and stronger while power of diaphoresis becomes greater, from which he concludes that the drug acts on the central respiratory centre as well as the vagus centre. Fraser has shown that Euphaunthesis
acts on the base aorta, centre protruding the diastole of the heart and causing the arteries to become contracted. Dr. Hammond concludes from this that the atheroosis has a tendency of great value. The value has been testified by Dr. Joneay in 8 cases. Med. Rec. Aug 10 1859.

Cactus Grandiflorus has been used with good results in doses of 73 to 5 minims of the tincture every four hours, see Med. Annual 1871 p. 225. I have used this drug for ordinary palpitation with marked benefit in two cases.

In some reports onコレ川 is made of Cabraglate of Ammonium as being useful in Graves Disease.

Arsenic is used also in this treatment with some success. One patient with Lißen plasm was under treatment for some time when arsenic was given. At the end of treatment the patient was very much less than it had been for some years.

In addition to the treatment by drugs, there is the treatment of change of air, residence and habits. Patients benefit greatly by recourse to mountain air. The diet should be light, and nourishing. tea, coffee and stimulants...
should be used in moderation. Stages to be withheld. Hydropathy has been advocated. Friedrich's method of treatment—i.e., administration of belladonna. Statler of Bulla Rest obtains remarkable results by sending patients to high altitudes from 1500 to 3000 ft. in the Tyrol and among the Carpathian mountains.

Compression of the thyroid gradually and systematically increased has been known to bring about a marked diminution of all the symptoms. T. C. MacKellar in Lancet—Sept. 27, 1890 p. 703 recommended the use of Martin's bandage—round the thyroid during the day and for thyroidal friction—rubbing the surface with lignum sumbat. Belladonna.

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