Exophthalmic Goitre

A Thesis

I. Tawse Nichol
Exophthalmic Goitre

The subject of Exophthalmic Goitre, that strange malady with its triad of striking symptoms, is one which has given rise to no small degree of controversy in this country and elsewhere, and the steady advance as time goes on towards a more perfect appreciation of its real nature is very remarkable.

The various names which different observers have employed in describing this peculiar affection, are of them selves an indication of the difficulty that has been experienced in recognising its true character, and thus we read of it under the following titles:
Vascular Bronchovcle and Exophthalmos (Buphlie)
Anomie Exophthalmie (MacKenzie)
Anomie protrusion of the Eyeballs (Taylor)
Exophthalmie Bronchocle (De Jager)
Holzangen Cachexie (Bacchus)
Cachexie der Operation Exophthalmique
Stoma Anemomatice
Cardiagmuo Strumosus (Hirsch)
Herzkrankheit Struma + Enz. (Cromberg)
Tachycardia Strumosa Exophthalmica (algm.
Divise three exophthalmingue (Online)
Atopic Cardiovasculaire (Hrél) etc.
and now it is chiefly to be found under the headings of Exophthalmitis
Crotz, Gravis Disease, or Bacchus Disease.

To whom the credit is due of first recognising and associating the
varied and numerous symptoms
is a matter of secondary import-
ance, and it is but natural that
the Germans on their part, and we
on ours, should be desirous of hold-
ing the palm; yet science should
at all times be unprejudiced, and a glance at the earlier history of the subject may therefore not be out of place.

Firstly however let us point out what are the leading characteristics of the disorder:

1. Palpitation of the heart, with increased force and frequency of its action accompanied by pulsation of the great vessels of the neck.

2. Enlargement of the Thyroid Gland

3. Prominence of the Eyeballs.

The term Exophthalmic Goitre refers only to the last two of these symptoms and is therefore imperfect, bear out as it does the first, and as we shall afterwards see, the most important one. Lebert's suggestion of Tachycardia Struma Exophthalmica is more comprehensive, though somewhat unwieldy, but to return...

Flagani appears to have been one of the earliest observers of symptoms which characterise this affection and he gives...
an interesting account of a young Spanish, who had been suffering for three years from a tumour in the front part of the neck, which in the course of four months had so greatly increased in size, as to occupy not only the anterior aspect, but both sides of the neck. It remained under medical treatment for the space of seven months, "not so much on account of the tumour, as by reason of the difficulty he experienced in breathing, and the very great palpitation of the heart." On examining the tumour, he says, "I found it of considerable size, and divided in the middle by a kind of cleft into two parts. Internally the colour was natural except that the superficial veins were swollen and varicose in appearance," and he further states, that the thyroid was evidently the seat of the malady, its substance being occupied, as well as the surrounding cellular tissue, by an exudate tumour." Hajani also
states that he observed two cases close by similar also males, but in none does he appear to have observed any postmorn enlargement of the eyeball. Caleb Parry, whose earliest observations seems to have been made in 1786, records several cases of enlargement of the thyroid gland, in conjunction with affection of the heart, and fully describes one case in which all the leading symptoms were present as follows: "About three months after laying in while she was suckling her child, a lump about the size of a walnut was perceived about the right side of her neck..... the part swelled was the thyroid gland. The carotid arteries on each side were greatly distended; the eyes were protruded from their sockets, and the countenance exhibited an aspect of agitation and distress which I have rarely seen equalled." In this case, the palpitation was so great, that "each systole of the
"heart shook the whole thorax," he
pulse was 156 in the minute, very
full and hard, irregular in strength,
and intermittent at least once in 4
beats. This there is no doubt was
a genuine case of "epithelial
vivre, but doubt has been expressed
as to Flajani's cases being so."
In the "Précis de chirurgie formel
and Précis of 1816" an anonymous
writer describes the case of a young
lady who suffered from palpita-
ation of the heart and a swelling
on each side of the neck as large
as a goose's egg; and whose eyes
were so prominent that they were
like to start from their sockets.
Demouge in 1818 mentions having
observed protrusion of the eyeballs
and enlargement of the thyroid in
a girl of eleven, but makes no
mention of palpitation.
In 1820 a case seems to have
been described in the "New England
Journal" of palpitation with pro-

1. For February 1816.
2. Traité des maladies des yeux, quoted by Bayle.
prominence of the eyeballs, and
Adelmann, in 1828, gives an account
with the results of post mortem ex-
aminations, of two cases of consid-
erable swelling of the thyroid with
enlargement of the heart.
Dr. Graves of Dublin, in his clinic-
at lectures at Dr.ath Hospital in
1835, mentions three cases of "long
continued palpitation in females,
in each of which the same pecu-
larity presented itself, viz.: enlage-
ment of the thyroid gland." At this
time however, he does not appear to
have noticed the affection of the
eyeballs, and it is to R. Stites
that the credit is due of drawing
his attention to that symptom, in
the case of a young lady afterwards
fully described in Stites's admirable
Treatise on Diseases of the Heart
and Aorta. Graves lectures were
afterwards embodied in his cli-
nical Medicine, published in 1843,
and there the triple character of

1. Adelmann: Jahrbuch der philosoph. 1825. 107. 11.
2. Stites, p. 284.
the disease is fully recognised. James Beagle of Edinburgh says: "in the autumn of 1837 my attention was called for the first time to the connection of enlargement of the thyroid gland and eyeballs with disorder of the circulation". But unfortunately his observations were not recorded until 1849, in a paper read before the Med. Chir. Soc. of Edinburgh.

Von Baer also, the German physician, in 1840 mentions cases in which all the leading symptoms were present, and having observed their association with a condition of the general system more or less deplorably described the disease under the by no means distinctive or definite appellation of "cachexia". He regarded the staring appearance of the eyes as the most striking feature, and used the term "holzbauernsche, really goggle eyd cachexia".

Sir Henry Marsh, in addressing...
the Pathological Society of Dublin in 1841. They attacked to several cases he had brought before the members during the previous year, as a singular variety of heart disease with rapid violent and irregular action, co-existing with enlargement and swelling of the thyroid gland, and in the majority of cases he noticed, "a remarkable prominence and protrusion of the eyeballs."

And after this period, the disease having been brought to the notice of the profession, we naturally find the records becoming increasingly more numerous, Dublin especially seeming to be the headquarters of greatest enthusiasm.

It is for von Basedow that Hirsch and other German writers claim priority of observation, and in accordance with a method that finds favour with some, they associated his name with the disease; but...
others, including Trouseau, who in his Clinique Médicale styles it Maladie de Graves, prefer to give the honour to the Dublin physician. So that while the names of Graves and Baudouin are still identified with this disease, it would appear that neither sufficiently grasped the idea of the circulatory, ocular, and glandular phenomena being manifestations of one individual affection. Graves regarded the heart chiefly, and took but little notice of the proptosis, while Baudouin paid greatest attention to the eyes, and only referred incidentally to the other symptoms.

Although we now recognize these cardinal symptoms in the disease, cases are met with where one or other is wanting, but which in other respects correspond to the general manifestations of Encephalomalacic Goitre. There may be palp...
The palpitation and brachycele only, as observed by Trouseau and Chevalier, in the extremity only, and this is not uncommon, but it may safely be said that the cardiac disturbances are invariably present, though sometimes only in a very slight degree; while of the other two symptoms it is the epileptoidism that is most frequently absent.

Sex appears to have a decided influence in the production of the disease, women being much more liable than men, the proportion of the former being very great; thus, Trouseau and Fagge give it as 50 to 90, in Graefe as 6 to 1. Of twenty cases that came under the notice of Austin Flint, only one was a male. Dr. Had this male case in a total of fifty-one. Robert Taylor collected twenty-five published cases up to 1856, and of these 20 were females, 4 were males, and

2. Glaudin's St. George's Hospital Reports, Vol. IV, p. 185, Case VIII.
3. D'Arcy, p. 184, Case VII.
4. Fagge's Principles of Practice of Medicine, p. 1010. 6th ed.
5. Pepper's System of Practical Medicine, p. 784.
in one case the sex was not stated. Of thirty-two cases at Manchester Eye Hospital, quoted by Hill Griffith, only three were males. Romberg found four males in twenty-seven cases; Praër only one in twenty-nine; and so on, suffice it that authority on this point leaves little room for doubt. Eulenberg's observations led him to state it as 2 to 1, but there is weighty evidence against him.

Age also seems to have an influence in the occurrence of this disease, which is rarely seen before puberty or after middle life, and is most frequently met with between the ages of twenty and thirty. Stokes claimed it in a woman of 60; Döbl in a girl of 2½ years; Hawks in a girl of 5; Assenbrück and Silling respectively in a girl of 7, and a boy of 8. Of twenty cases two thirds occurred before the age of 30, and Hill Griffith gives the following analysis of thirty-two cases, showing:

---

3. Pepper, p. 1010.
5. ibid., p. 78.
the ages at the commencement of symptoms:

Under 20 years  3 cases
20 to 30    16
30 to 40    8
40 to 50    6

Fifty per cent lying between 20 and 30.

Besides age and sex, breed,
it in some cases plays a part in its etiology, and a family history
of nervous disease is not unfre-
quently observed; statistics on this
point however are as yet unsatis-
factory. Tazgle mentions the case
of a man aged 26, who had an
uncle and brother with ordinary
goitre; & headle a female (Case
II.IV) whose grandfather died of
arterial softening, one of his sons
being an epileptic and another a
stammerer; also in his second
series of cases, a female and her
two nieces, all similarly affected
with Graves' disease. In Tazgle's
case where all three symptoms

4. Tazgle's, op. cit. p. 579.
came on in one night the father was epileptic, and Hughes's Jackson observed the disease in two sisters, and a third sister was said to suffer in the same way.

But apart from age, family predisposition, and sex, the determining causes are often far to seek, and we have little knowledge concerning them. The so-called nervous diathesis is often observed in those suffering from Graves's disease; disturbances of the uterine function often precede or are associated with it; anemia in some cases doubtless plays an important part, and in some particular instances the onset of the symptoms has been attributed to trauma. Anxiety, prolonged nervous excitement, fright, sexual excesses, extreme fatigue, quinsey, rheumatic fever, are all mentioned as causes, and sometimes the disease has been found associated with hysteria.
epilepsy or mania'. But in the majority of cases the evidence of a causative relation is simply a post-hoc correlation, and etiological speculations in the absence of ascertained facts are not of much advantage.

The association of uterine disorder and disturbances of the menstrual function so often observed has attracted attention and is universally acknowledged. Jayne \(^2\) considers that the causation of the symptoms was in some way connected with the utero-ovarian system, and he directs attention to the enlargement of the thyroid sometimes noticed during menstruation and pregnancy. He argues that as the influence of the uterine and ovaries on the mammae is exerted through the nervous system, the vascular congestion is induced in a like manner, and concludes that "neuro-vascular worms, nat-

---

2) Medical Times, 1864, p. 324.  
3) Williams, Sarop, Reichen.
"naturally of an emotional excitable temperament, or who during uterine activity or sexual excitement have had fright, grief, excessive mental labour, or other causes modifiesly influencing the nervous system, or who are of an age at which the reproductive organs are functionally active, are predisposed to Graves disease; and that emotional and similar mental states are the exciting causes." Cheadle found disordered menstruation or cessation of the catamenia in eight of his first nine cases, and Trousseau observes that hopes of a favorable termination are not to be entertained until this function is fully re-established. It is rare for the disease to come on during pregnancy, but pregnancy may come on during its course, and Trousseau remarks, that the disease occasionally ends in this way.

3. Trousseau, p. 533.
case while the disease occurred during pregnancy, prospectus coming on in the fifth month. Sheadle during his earlier investigations was led to the belief, that the fact of a large proportion of cases occurring in females with disordered menstruation, suggested that the disease in a majority of cases might be dependent on uterine irritation. Later however he saw reason to qualify this statement.

For can the association of rheumatism and rheumatic fever be overlooked, and curiously enough, the very first complete case on record viz: that of Pany, followed closely on an attack of the latter complaint. In 8 of these 38 cases was there a history of this affection; and possibly the severe valvular disease sometimes noted - as by March and Forssman - might be the result of an antecedent rheumatic fever.

The apparent immediately ex-
exciting causes are very various. Thus Somersaul observed all the symptoms come on, with epistaxis, after great grief, as did Lapeck; after severe fright, Fitzgerald; mentions it as occurring in a man after excessive dancing; Brinton in a woman aged 26 after protracted exposure to cold; Bonnilli saw the disease develop under the influence of nervousness, and V. Graife found it attain its maximum intensity within a few days after an unusual amount of exertion; while Bégbie and V. Graife each record a case where the symptoms first appeared after a violent blow.

The disease is essentially a chronic one, being in the great majority of cases of long duration; in a few instances it has been known to develop more or less suddenly, and the symptoms to disappear again in a short time, but as a rule the onset is insid-

incidences and gradual. Of 51 cases the longest lasted nine years, the shortest two months, and in three fatal cases the disease had lasted four years, two years, and 3½ months respectively.

Moll Fracassier mentions the case of a female, who applied to him for treatment of the thyroid, twenty years after it had begun to swell, and four years after her friends had noticed the strange expression of her eyes. Macaroney’s case of John Dr. Keen resulted in a subsidence of all symptoms after seven years, and this in a man aged 48.

Issureau distinguishes an acute and a chronic form, illustrating the former by a boy aged 12, in whose case extreme measures were required to save life during a paroxysm, asphyxia being imminent, three months after the first indication of the disease — bleeding was resorted to with success, and
the symptoms rapidly subsided. The chronic form is illustrated by a case of eleven years standing, but the acute cases, both as regards time and severity, are exceptional, and do not justify such a subdivision.

Palpitation is generally what leads the patient to seek medical advice, and it was so in three out of the four cases that have come under my own notice. Pursing to this it will generally be found that the patient has been out of sorts, irritable, excitable, easily fatigued, while one or other of the functions of the body are interfered with in women chiefly the uterine. Or the patient may have been hysterical, sleepless, or subject to strange fancies. Palpitation, breathlessness and op. pressio are complained of, at first only at intervals and slight, but rapidly increasing to a high degree, becoming more persistent
as it becomes more severe, so that the patient is in a constant state of distress. The pulse rises, and tends to maintain a uniform rate of 80 to 100 in mild cases, but even reaching 120 to 140, and in one case, recorded by Dr. Dornel, as high as 200 beats in the minute.

Besides the rapidity of the heart's action, its impulse may become very marked, and painfully distressing, and be even visible through the clothing, as happened in one of my own cases, and frequently observed by others. The slightest exertion or excitement brings on a paroxysm of palpitation, and Dr. Dornel cites a case where the "beating of the heart could be heard at some distance from the bed."

Most writers are agreed that palpitation is the earliest symptom, though Irenaeus considers that all phenomena which are

due to the same cause should appear simultaneously, and have the same period of duration. Cheadle observed palpitation to be one of the earliest symptoms in his cases, and adds that he finds it to have been so in the great majority of cases recorded; and the observations of Besler Journac, Cattaneo, and others are to the same effect. The evidence of heart is however somewhat in a contrary direction. In his cases palpitation appeared alone and first in 9 cases; thyroid enlargement appeared first in 8 cases; ocular thyro and cardiac symptoms appeared simultaneously in 6 cases; and in 4 cases, ophthalmia first and alone in 4 cases. And as regards the goitre and ophthalmia, Hill in his makes the following notes: 

1. the goitre preceded the ophthalmia by 2 years, 1 year, and 6 months respectively in three cases; goitre and ophthalmia that were synchronous in 4.

---

appearance in 2 cases, and expressed that it was first noted by the patient in one case.

Sooner or later, then, the thyroid gland begins to show signs of enlargement, at first gradual and uniform, and not attracting much attention or causing much distress, till it may reach a considerable size; cases of sudden swelling of the gland, like Inseman's case, being extremely rare. Usually the right lobe is the larger when there is any difference between the two sides, but in a lady aged 32 at present under my care the left lobe is distinctly more swollen, the left half of the neck measuring nearly half an inch more than the right, and this was also noticed two years ago by Dr. Towers when she then consulted.

The tumour has more the character of a fulness of the thyroid region than that kind of tumour we find
Dr. MacDonnell's Case

Recovery after seven years.

Exophthalmos of an unusually large goitre.
in ordinary goitre; sometimes, however, it attains considerable dimensions, so much so as to cause danger from asphyxia, attacks of dyspnea, and stridulous breathing. Occasions surgical interference; pressure on the carotids and internal jugular veins; and headache in one case speaks of the danger of the presence of the goitre.

On the other hand, the swelling may be small, even in an advanced state of the disease, or confined to one side only, or absent altogether. At first it is soft, yielding, and elastic, but afterwards assumes a more solid character, owing to actual increase of the gland substance, and development of connective tissue, and as the disease subsides, and the thymus becomes harder and firmer to the touch, and Thymus is that atrophy—which ensues—may take place. The superficial veins coursing over it are usually vis-

1. Travancor p. 570.
2. p. 525.
visibly distended, and distinct pulsation of the mass may sometimes be seen, owing to the enlarged and dilated arterioles, and pulsation communicated from the carotid arteries. This pulsation of the swelling may be distinctly felt on applying the hand, and is often accompanied by a peculiar thrill, like that of an internal varix—a distinct premonition—and Stokes mentions a case where this condition was actually mistaken for aneurism, and a day appointed for tying the carotid artery; happily however the true nature of the swelling was discovered in time.

It is also worthy of note, that the tumour is liable to increase and subside again, in relation to the force and intensity of the cardiac impulse, and may visibly increase during emotion or excitement. Agitation of the mass in some cases reveals a musical bruit.

1. [Footnote: Paget, p. 69; and Stokes, p. 239.]
2. [Footnote: Calundburg.]
3. [Footnote: Ruge, p. 144.]
or continuous murmur, and this may actually be perceived by the patient. When the tumour is well developed and the gland equally involved it forms a curious horse-shoe shaped swelling as in Ha.

janič case and Besjir mentions that the veins of the neck may be so distended "as to give to the patient a very extraordinary appearance." 2.

Protrusion of the eyeballs sooner or later sets in, and in well marked cases gives the patient a characteristic staring expression, which once seen is not likely to be overlooked, hence the "Oltzénungen Krankheit" of von Riedow. Both eyes may be affected first, but sometimes only one, and often one eye more than the other; the protrusion varies greatly in degree, being sometimes so slight as not to attract attention, except perhaps during excitement.

emotion, or after fatique, while in other cases it is very marked, and a broad line of sclerotic is visible above and below the cornea. Occasionally the eyelids cannot be made to meet over the globe, and this may lead to great irritation from exposure, and even to ulceration of the cornea. The movements of the eyeball is often painful, owing to the great distension, and the ocular muscles may be so stretched that movement of the globe is rendered impossible, and the points of insertion of the recti are sometimes easily visible.

Deviation of the globe may occur, and B. Paskin of Bath mentions one case of a woman in whom the eye was frequently dislocated, slipping in front of the lids on the slightest touch.

In well marked cases the eye have a somewhat lustrous appearance, quite unmistakable, and the con.

1. Franco Clinical Medicine p. 223.
2. Franceau p. 578. Also Ziemssen p. 52.
constructions are often injected and red, sometimes painfully so; or the eyelid may have a bluish appearance, as I have observed in two cases. Pulsation may occasionally be felt on applying the hand over the eye-bell, and the patient may be conscious of it, and suffer much annoyance from the throbbing, and great pain is often complained of. Carington tells us that an assault on the upper lid, a more or less continuous murmur may be heard, but much the loudest at the systole of the heart.

The eyelids also show certain changes, such as a dusky or pigmented appearance, and this may be limited to the region of the bulbar muscle. The upper lid is often noticed to have a wrinkled appearance as if it had once been stretched and afterwards retracted, and this is well brought out in the illustration appended, which in—

indeed conveys a very good idea of the general appearance of the eye in this disease. But the prominence of the eyeball, or proptosis, appears greater than in reality owing to the existence sometimes of a state of retraction of the upper lid, a symptom first alluded to by Stillwag, and consequently associated with his name: it consists of an abnormal widening of the palpebral aperture, due to retraction of the upper lid, and of incompleteness and diminished frequency of the act of involuntary writhing. It is this as much as the protrusion that causes the staring expression, and possibly the wrinkled appearance of the lid is also due to this. Retraction of the lower lid is very rare, but Stillwag observed it in three cases along with the much commoner symptom of the upper lid and it two cases by itself. An abnormal cupping of the lower
lid when the patient looks down has been pointed out by Dr. Jain.

Mr. Traüf was the first observer who drew attention to the fact that in Graves disease the upper lid takes little part in the movements of elevation and depression of the globe, and he regarded this symptom as pathognomonic; it consists in an absence of concomitant movement of the upper eyelid and the globe, so that in looking down, the eyelid does not follow the globe, although the patient can still shut it, the limit of shutting of course being the degree of proptosis.

Eulenburg does not agree with M. Traüf as to the constancy of this symptom, and has seen it absent in a case of great proptosis, and more recent observations show that it is by no means invariably present. West, writing on this point says, as to Mr. Traüf's sign evi-

1 Ziemsm. op. cit. p. 82.
"evidence is not sufficient to justify any conclusion but it seems to occur usually after explatation has existed for some time."

Changes in the pupils are seldom noticed; von Graefe whose experience extended to nearly two hundred cases, states that dilatation never occurs. Eulenburg also never saw it, and he suggests that in those cases in which it is present it is the result of myopia. Instead of dilatation are however recorded by 

† Headle who found slight dilatation with entirely regular action; by and by Brod, who saw it associated with sluggish response to light and accommodation. Eulenburg mentions that Gildemeister, in one case, found the pupils at first much dilated and afterwards contracted, and that Fitzcharles also observed contraction.

Usually there is no impairment of accommodation, though vision is sometimes difficult in consequence

1. Zimmerman, p. 84. 2. p. 84.
2. Fr. op. cit. loc. cit. p. 87.
of the immobility of the globe. Patients sometimes complain of fatigue in using the eyes and are often troubled with lacrimation.

As regards ophthalmoscopic appearances the most common are a dilated and tortuous condition of the retinal veins. Withier and Thenemann both found deposits of pigment around the optic papilla. Other changes in the eye are seen, but they have no particular significance, and quite independent of the disease. Edema of the lids is not uncommon and swelling of the orbital veins may occasionally be observed; in Tawod's case this was so great that when the eyelids were pressed back, voluminous veins were seen to raise the upper lid in masses.

Increased lacrimation is a symptom more or less constantly present, and this has been assigned as a reason for the rarity of occurrence of ulceration of the cornea in cases

1 Tawod. 2 p. 65.
2 Thenemann, p. 573.
where the globe is not covered by the lids; thus cross meetings in the case much secretion of tears with extreme light, or when the eyes down; and Auy and Pringle observed two cases with "frequent attacks of acute pain in the eyeballs, accompanied by profuse wealing, lachrymation".

Ulceration of the cornea is not so frequent as might be expected from the exposure of the globe, to particles of dust, constant light etc.; v. Gaufé noted it in fourteen cases, and considered it more liable to occur in men than in women. Tronsean never observed it at all; Jonathan Hutchinson observed it in three females, but never in a male. Bellering also states it to be more common in men than women and quanto Basechon, Praed and Haumann as evidence; he describes the process as follows: "the cornea first loses its sensibility, on its surface any yellow spots appear which grad.

1. To Q. Optiz Soc. 1747.
2. J. Coompe. p. 84.
4. To Q. Optiz Soc. 1757.
5. S. Rauelf. op. cit. p. 528.
gradually enlarge, and the final result is the formation of an eschar, followed by diffuse destruction, or even perforation.

Besides the three leading symptoms of Erysipelas there are numerous secondary phenomena, many of which are more or less constantly observed, and which are worthy of consideration. And most frequent among these is an elevation of bodily temperature, not always observable, but probably existing in every case at some stage of the disease. Eulenburg, Issier, Guttman, all speak of it so does also Janssen. Who remarks that in other morbid affections, such as diabetes mellitus, the patient often complains of great heat, especially at night and deep sleep, lightly covered, dreaded observed it in all his except me, in that instance however it was tested on one occasion only, in all the others the rise was from one degree to a
degree and a half, equal on each side of the body, and in the normal degree higher under the tongue and in the vagina (when tested there), than in the axilla. The patient also is often aware of a great sense of heat, and feels great uneasiness in consequence, sometimes amounting to an intolerable burning.  

Perspiration often occurs; panic this, and may be general, but is sometimes limited to the upper part of the body, or is unilateral.  

Wilks states that he has seen a woman sitting in a cold room in winter covered with perspiration.

Trousseau pointed out another phenomenon of this disease, viz. that if the epidemics of these patients be slightly initiated, after two or three minutes a most beautiful red stain is seen, which lasts nearly a minute, and this central macula, or clavitated, is by no means an in frequent symptom. Flushing of

1. Dr. Bo. Diph. Rep. vol. VII.  
one side of the face and ear is often noticed.

Another symptom that is of very constant occurrence is marked alteration in the behavior and temper of the patient, who becomes irritable, fretty, fidgety, and fanciful, fretful, irritable, and excited or depressed and lachrymose. Jameson relates a case of one of his patients that "the patient's temper is so altered that the persons about her can hardly put up with her irritability, her want of patient feelings and her exacting ways", and he adds, "I have known a young lady who was usually of a sweet disposition, become disrespectful and quick tempered, almost violent". Russell in one case observed "passionate irritability, great impatience, and hysteric outbursts combined with obstinate sleeplessness.

This last mentioned complication is very common, and often very tormenting. Park mentions a case where there was complete insomnia for three weeks, after which time

the patient felt "very sleepy, but could
not sleep on account of cardiac
irritation". If it lasts for any time
it throws the patient into a state of
perfect despair, she cannot find an
easy posture, but keeps shifting about
in bed, and longs for the return of day; she feels perfectly weak,
yet cannot rest for a moment.
Somnambulism, fits, tremblings,
megrim, insanity, chorea, weakness
of thought and memory, are
among the disturbances of the
general nervous system that occasion-
ally accompany the other symptoms.
Disturbances of digestion are also
very common, and emaciation is
the rule in advanced and long-stand-
ing cases. Vomiting also is a fre-
quent trouble, often very obstinate and
intractable; and sudden attacks of
diarrhea also increase the tendency
to emaciation. The digestive system
also becomes deranged, and the
appetite may be lost, or the patient
become capricious and ravenous, or
have an utter disgust at all food. 4
Ironson says that "when the
complaint seems to improve the dia-
scope diminishes, and stops, the
patient takes advantage of her vor-
acious appetite, and rescues the ap-
parence of good health." 5

Amenorrhcea, Menorrhagia and
leucorrhcea have already been alluded
to as very common symptoms.
Epistaxis often precedes the onset of
the disease, or may come on during
its course. Incisoritis also is frequent,
and many cases are quoted, which
seem to date from an attack of
quinsy. Grippes also has been the
starting point of the disease.

Neuralgia, chiefly facial, is a
very distressing accompaniment, and
Tayrek, in one case which followed
an acute tonsillitis records, "neuralgic
pains shooting down both arms, es-
specially the left and affecting the
fingers of both hands", and "When
"She had attacks of pain in the right temple, severe pain was felt at the same time down the right arm. Sometimes the numbness is in the area of distribution of the trigemini."

Albunminurca and diabetic meli. tus are also met with in this dis. ease. Warburton Befie attached considerable importance to the pres. ence of albumen in such cases, but in those he mentions it only occurred after meals. It is not however very common: Bistone records two cases: west-three, and he states also that polyuria is frequent. Griffith, Parny, West-and others have noted sugar in the urine.

General anaemia has been seen as a complication, and sometimes leads to grave consequences: it has occas. ionally been observed to disappear in a remarkable manner. and this was noticed by Russell in one patient in whom the drowsy was so great that "when she placed her feet on the floor

1. Renal.
2. Ophthalmic Review 1883.
the. Knees were completely obliterated, and three months after, the anaesthesia had entirely disappeared. Sometimes the oedema is local, limited to the extremities, the face, eyelids etc. Pigmentation of the skin may occur, in certain areas, or all over the body; Trousseau observes, "the skin which was formerly transparent is now brown and puckled in some parts," and best noticed browning of the skin not unlike Addison's disease. Also another symptom, "that the hair turns grey sometimes in quite young persons."

The phenomena observed in those who are the subjects of Leucis disease are indeed as remarkable as they are various, and scarcely any two cases are found to be exactly alike. The disease as we have seen may last for months only or may run on for years. It may reach a certain stage and become stationary for a considerable time, after which the
In Schadli's two fatal cases death was more or less sudden, following upon violent vomiting and retching. One of West's cases also died suddenly. She went to bed as usual fairly well, and next morning woke up complaining of great pain in the side over the seat of an old pneumonia. Temperature 105°, respiration 60, and died at mid-day. And in another of his cases the temperature before death rose to 106.2. A suddenly fatal case recorded by Cross was due to cardiac failure. Death may be the result of pulmonary, intestinal, or meningial hemorrhage, and Toussaint had an case fatal from central hemorrhage. Mutter mentions a case where death was preceded by symptoms of softening of the brain, and this condition was found on examining the body after wards. A patient died under the care of March from gangrene of the lower extremities, and disease of the tricuspid...
symptoms may subside, or fresh act.

inity manifest itself. The disease in
itself seems to have no directly
fatal tendency, and cases of recovery
are very common - the recovery in
many cases however is not com-
plete, in so far that the leprousness
and the jaundice do not altogether dis-
appear, nor does the action of the heat
become perfectly normal, and there
is often left in the patient a tendency
to irritability, excitement, or nervou-
sness.

Some cases then do terminate favour-
ably as regards the disease itself, but
even in these cases Linnéian observers,
that the anemia that results from
the disturbed digestion etc is sometimes
so considerable, that hectic fever sur-
pens, or the patient is so weakened
that he becomes susceptible of any
morbid influence, and dies of some
intercurrent affection, which gener-
ally has its seat in the lungs.

Kreul consider that there is a
general tendency to slow and gradual recovery, extending over a period of from one to three or four years, but usually complete in the end; the danger lying in exhaustion from vomiting and diarrhoea. Of his cases twelve recovered and two died.

Jonathan Hutchinson, in his opening address at the special meeting of the Ophthalmic Soc. for the consideration of this disease, said... "it is the most definite and striking example which we can find of a severe and protracted malady, which, despite its severity and persistence, has got a natural tendency to recovery. If the patient can survive for a certain time, apparently the recovery is a matter of course. We have no cases which are indefinitely progressive.

In this feature it differs in a most striking manner from such maladies as ataxia and bulbar paralysis, which are slowly, but surely aggressive, and from which we have no cure.

1. Id. loc. cit. 4th Report, vol II, p. 505.
2. To, 4th Id. loc. cit. vol vii.
and vital values was found. Smith of Dublin took a case by apoplexy, that being hypertrophy of the left-ventricle and disease of the aorta, so that the co-existence of cardiac disease renders the prognosis exceedingly grave.

Enlightening regards the prognosis as "improvable for the most part," the he acknowledges the possibility of spontaneous disappearance, or removal, of the symptoms by medical aid, the prospect of this being greater the more satisfactory is the general health, and the more certainly organic changes in the heart can be excluded, or a neuropathic tendency and severe disturbances of innervation. But the majority of writers take a more hopeful view: even in advanced cases symptomatic treatment often affords benefit, so that a patient who has previously been unable to do any work is enabled to undertake light duties without suffering serious inconvenience. The existence of organic
Heart disease is probably the most serious complication, the access of severe symptoms being almost certain sooner or later, and the diseased heart being unable to stand the long continued and increased activity which goes on; dilatation predominates over hypertrophy, and then occurs the clinical incidental to the inability of the organ to carry on the circulation.

Hoxsey draws particular attention to the danger of choking during a paroxysm, and Huxley records a case where death by asphyxia from pressure was arrested by timely removal of the isthmus of the thyroid.

As regards the actual condition of the heart in cardiac disease physical examination in the majority of cases reveals no sign of organic mischief, and the accounts of post mortem examinations investigated by Marsh, Balfour, and Regbie satisfactorily prove that those changes which result from long
continued functional derangement, are what are met with in this disease, viz.: permanent dilatation, with more or less hypertrophy; and this indeed is what the violent and prolonged cardiac activity would lead us to expect, although even in advanced cases the heart has been found post-mortem to be normal, with the valves healthy, and neither dilatation of the cavities, nor hypertrophy of its walls. There was much controversy among earlier writers regarding the existence of organic heart disease, but now we do not regard it in any way as essential of this malady; and here again the frequent prevalence of rheumatic fever may be mentioned as explaining its existence in some cases.

Stokes held this view, yet he describes separately, "rheothalbmic cachexia complicated with organic disease of the heart," and "rheumatic" expressed him.
himself as favour of such a clinical division. Although "epithelialic gout" he says "is not in my opinion necessarily attended by dilatation of the cavities or alteration in the valves of the heart, yet such lesions may co-exist with it, and perhaps have been instrumental in bringing it on." The intravascular is not infrequently found to be insufficient, probably on account of the dilatation of the ventricle, and the immense strain the valves have to withstand, and the aorta is all infrequently atrophized.

Even when there is no reason to suspect valvular disease, a systolic murmur may often be heard in auscultating over the precordium: the seat of greatest intensity varies, sometimes being most marked at the apex, and sometimes over the auroile, and even in the case of an individual the bruit may vary at times, just as does the hemicraniotomy.

1. Virchow.
murmur in cases of chlorosis, to which indeed Laycock considers it analogous.

But another point worthy of mention, is that notwithstanding the excited rapid action of the heart, the pulse may often be weak and small. Stirling says, "if we compare the pulsations of the carotid with those of the radial artery, the difference is most striking, the former being violent in a high degree, while the latter are small and weak, only corresponding with those of the carotids in their frequency." Wearde notes that the pulse is often jerky.

Irregularity of the heart's action is often marked, and the interval between the contractions so unequal, and their force so slight, that there may be no corresponding beat of the radial pulse. 2.

2. von Breil.
Now what is the nature of this affection? We have seen that not only but several systems of the body are involved; that even the primary symptoms may differ much in individual cases, and that what are looked upon as the essentials of the disease are sometimes wanting; and yet notwithstanding the variety and complexity of the secondary symptoms, it can, I think, be shown with tolerable accuracy, that the several phenomena associated with the name of exophthalmic goitre have all a common origin.

An eminent French physician as recently as 1862 asserted in the Imperial Academy when this subject was under discussion, that there does not exist a morbid unity, called diathesis, cachexia, or neurosis, constituted by a triad, or a tetrad, or a pentad, or a polyad of symptoms, and which merits the name of exophthalmic goitre, but many years previously more correct conclusions had been arrived at by

more than one observer.
It was but natural that, the circulatory symptoms being the most prominent and the most distressing, the explanation of the disease should have been sought for in some morbid condition either of the blood itself, or the centers of the circulation, and hence we find an elaborate theory ably put forward by the late Dr. Regius in a paper termed "Anemia and its Consequences." The opening paragraph of Dr. Regius' paper gives the key to the whole - "impoorishment of the blood, originating in a manifest source, and existing as a primary and chief symptom, associated with enlargement of the thyroid gland, and with a remarkable protrusion of the eyeballs, ... constituting a marked class of features hitherto unrecognized. Anemia then is regarded as the main element of the disease in instances of which he had seen, he adds, "in which the general and physical signs
of anaemia were not more or less com-
pletely developed, and the methods of
treatment he adopted were all di-
rected towards improving the condition
of the blood. The nerves of the head,
he says, are excited by the attenuated
and impoverished blood, which reaches
the centre of the circulation with a ro-
city proportioned to its vitiated con-
dition, producing anaemic palpitation,
and functional disorder of the heart
and blood vessels. Cases that were
reported with no apparent signs of
anaemia—e.g. Withers’s phthisic
patient—he explains, by saying that
anaemia does not always present it.
Self in the same external characters,
and that prolonged indigestion, or
diarrhoea, or leukorrhoea, produce a
condition analogous to it.
So thoroughly indeed had he the
anaemic theory in his mind, that the
very existence of prominent eyes and
a swollen thyroid in a lady who
came to see him, satisfied him.
She was anemic, although she had no erysypohine or pallid look; and he afterwards found that she was suffering from the well-known signs of anemic palpitation.

But Bekbe did not disregard the nervous element so conspicuous in this disorder; he held that such ailments as are calculated to impoverish the blood are also apt to induce a nervous state of the system, as by irregularities and disarrangements of the menstrual function, leucorrhea, child bearing, and so forth, and that women were therefore more liable to the disease than men. And as regards men, he says, the disease is rarely seen in them until a period of life when the system is apt to suffer from impoverishment of blood, arising from diseases of the digestive organs, from diarrhea, from chronic diseases of the liver, the spleen, and the kidney, the organs employed in the elaboration and excretion of
The enlargement of the eyeballs was accordingly regarded by such as held these views, as due to congestion and effusion into the ocular capsules, an increased secretion of the humour of the eye - a true hydrophthalmia - and the goitre is explained by the gland acting as a diverticulum for blood directed to flow into too great a vein to the brain, a view which was also expressed by Parry, and Røhri remarks regarding this, that it still remains to be determined how the eyeball and thyroid gland especially manifest this state of disorder in blood. This theory of a blood disorder is at first sight a very plausible one and was adopted by many, particularly in Edinburgh, including Dr. Christian (afterwards Sir Robert) Professor Ayrton; in a time was one of Røhri's supporters but later on changed his views in favour of
a nervous theory of the disease, and Mr. White Cooper of London gives an interesting account of five cases in the

Cauter. of 1849 under the heading of "Prolapse of the eye in connection with anaemia, palpitation and spire,"

Mr. Babtish held much the same view as Bypee, but hesitated to assign to the condition of the blood such an important role and regarded it as a serofibrin dysperasia or cachexia akin to chrisis.

Brench of Dublin appears to have regarded it as a form of heart disease, but contents himself with a description of the cases, offering no suggestions as to a theory of the disease. Mr. did Graves do much towards the elucidation of this subject, observing that the swelling of the thyroid varied in relation to the intensity of the cardiac action, he was led to suppose the thyroid gland slightly analogous in structure to the tissues properly called erectile. He also

2. Vide Babtish, Argyle's lecture.
draws attention to the connection between the uterine function and the development of the thyroid gland, as palpitation, and to the fact that palpitation is frequent in hysterical and nervous females; he however attempts no explanation of the nature of the disease.

Sir R. took a more advanced view and he says there are strong reasons for holding that the disease is originally a neurism of the heart - the heart being the point of departure of the disease, and the turgescence of the thyroid, the increased action of the arteries of the neck, and the enlargement of the eyeballs, he regards as epi-phenomena.

He points out that the affection of the thyroid gland differs from the ordinary bronchocel on its not being due to the influence of soil or climate, seldom attaining any large size, but becoming stationary at a certain period of its development.
At the same time he considers the two forms of goitre as not perfectly distinct diseases, and this for the following reasons — viz.: that both are more prevalent in females, and that no cases occur before puberty (3); that both swellings are increased by hysterical paroxysms, and finally that both forms have been benefited by iodine.

The enlargement of the thyroid he suggests may have some analogy to that of the liver, in cases of obstruction or weakness of the right side of the heart. With Babcock, he considers the exophthalmos as due to an augmentation of the aqueous and vitreous humors, and observes that notwithstanding the great protrusion of the eye, the power of vision is rarely impaired, and that though the lids do not cover the eyeballs, the patient is not liable to ophthalmia.

Alto together places the starting point of the disease in the heart.
he acknowledges the nervous system as playing an important part in the production of the various circulatory symptoms.

Robert Taylor takes an ingenious view of the phthisis and exophthalmos. While referring the disease as due to anaemia, he considers that a peculiar state of the nervous system exists, which induces spasm of the muscles of the neck, and as a result of this spasm, there is impeded return of the blood from the head, producing hyperemia and hypertrophy of the thyroid gland, and dilatation of the veins of the orbit, causing exophthalmos. Marshall Hall also takes this view.

So far then we have two theories advanced, one that the affection is primarily hemic, the other that it is primarily cardiac, but neither can be regarded as satisfying. Against the former there are many arguments; in the first place the subjects of Gravis' disease are by

Eosophalnic Gastro. Pulse 144, smooth and jerking.

Simple Anaemia.

Eosophalnic Gastro. Pulse 120, full and jerking.

(after Madsen)
is means always anemia, and we find it occurring in full blooded and
even plethoric persons, in healthy looking
men, in young children occasionally,
and in women after the climacteric
period. Anemia again is most pre-
valent between the ages of fifteen and
twenty-five, which is not the period
of greatest occurrence of pneumonia.
Laverack examined the blood
in several of his cases and found
it normal. Moreover, anemia is very
common, while the other effects is
rare, and the pulse of anemia has
not that peculiar character with
a rapid up-stroke so constantly
observed in pneumonia.
No doubt anemia coexists in many
cases, but it is to be regarded rather
as a secondary symptom, common
to many chronic diseases. and the
fact that all the symptoms may come
in some or less suddenly as the re-

cult of fright or accident is not in
any consistent with such an explain.
No means always anemia, and we find it occurring in full blooded and even plutonic persons, in healthy looking men, in young children occasionally, and in women after the climacteric period. Anemia again is most prevalent between the ages of fifteen and twenty-five, which is not the period of greatest occurrence of fevers.

Lapeyre examined the blood in several of his cases and found it normal. Moreover, anemia is very common, while the other affection is rare, and the failure of anemia has not that peculiar character with a rapid up-stroke so constantly observed in fevers.

No doubt anemia coexists in many cases, but it is to be regarded rather as a secondary symptom, common to many chronic diseases. And the fact that all the symptoms may come in more or less suddenly as the result of a fit or accident is not in any consistent with such an explanation.
explanation.

For does not his theory of a primary cardiac neurosis go far toward a satisfactory explanation of the various phenomena.

A theory of the disease, says Eulenburg, to deserve the name, ought to be able to derive all the symptoms, or at least the three cardinal ones, from a common source, and probably we shall find such a source in the nervous system.

The neurotic nature of panic disease is now almost universally admitted, and with the knowledge of the nervous system that has been acquired since the days of those earlier observers, a decided advance has been made, and the sympathetic, the vasomotor, the spinal, and the central nervous system have all found favour.

Thus it much in the disease to lead me to suppose that the sympathetic system of nerves is largely
implicated, either directly or through reflex irritation, and the paresthesia, the flushing of the face, the sense of heat, the actual rise of temperature, the sweating, the diaphoresis, the episcleritis, the frequent instability of temper, so often observed, all point to a neurosis, in which, whatever be the centros involved, there is a persistent condition allied to the transient state produced by emotional excitement, by which all these symptoms may be produced.

Tronson, who studied this disease carefully, speaks of it as a congestive neurasthenia, "a neurasthenia of the sym pathetic, if not a material lesion of the sympathetic nervous system," analogous to hysteria. He regarded the thyroid swelling, the exophthalmus, the heat, and moisture of the skin, the mental disturbances, as phenomena clearly indicating the existence of a congestion. Great convulsions take place physiologically,
as in blushing, pallor from fright, uterine congestion, etc.; in hyposthenia also we find delirium, coma, and protracted convulsions, followed by great hyperemia of the brain; also the globus hypsisticus he suggests, may be due to a sudden congestion of the thyroid gland (as Dr. Grander pointed out), the result of nervous palsy influencing the heart or some peripheral portion of the vascular system. There are then temporary local congestions of nervous origin, which take place phylogenically, and in neurotic affections such as hyposthenia, and asthma, and eph enthalmic purpuric, or, he says, a pathological variety of the great class of neuroses having a paroxysmal course.

Division of the upper cervical ganglion of the cervical sympathetic is followed by hyperemia of the carotids and ultimate paralytic results in relaxation of the coats of the blood vessels and so he argues
the proximate cause of the disease
in a case motor disturbance, originat-
ing in the sympathetic or its ganglia,
and this view was strengthened by
the results of post-mortem examination,
which showed congestion of the lower
cervical ganglia, with proliferation
of the connective tissue, and dimin-
ution in the number and size of
the nerve tubules.

Gayrard lays the seat of the disease
in the olivospinal, or eulo-motor tract
of the spinal cord, stimulation of which,
as demonstrated by Bendor, and Brodie
and Kallier, produces increased rapid-
ity and force of the heart's action and
dilatation of the pupil. The heart is
in direct relation with a special motor
tract of the spinal cord, commencing
and continuing upwards with this
eulo-spinal region. So that, as he
himself puts it, "any sufficient cause
acting mortally upon that portion of
the cord, or upon the cerebral centres
within the cranium," (as doing

emotion) or upon the motor roots of the
two or three first pairs of dorsal nerves,
would tend to induce not only the usual
pupillary changes, but also increased
vascular activity in the region of the
cervical sympathetic, and palpitation of
the heart.

He further considers the pulsations in the
large arteries as also dependent on some
morbid condition of the eido-spiral region.
The cervical sympathetic regulates the
pericardium in the head, consequently
various morbid conditions of the scalp
and brain are purely nervous, such
as throbbings, headaches and the like.
It is chiefly the lower pair of thyroidal
arteries that have been found af-
fected by pulsations and dilatation and
these are innervated by the sympathetic
wheras the upper thyroidal arteries
are supplied from the vagus system
by twigs from the recurrent laryngeal
nerve; Spraque concludes that when
there is nausea, difficulty of breathing,
globus hystericus, etc., the vagus is also
involved.

The theory of the disease being a primary lesion of the cervical sympathetic or of its spinal centres, is one which has been very generally accepted, and physiological experiments along with observed pathological changes have gone far towards strengthening and a cure, but to explain all the complex symptoms which go to form Gran's disease by a reference to the known functions of these nerves, is by no means easy, and "we shall be obliged at the best," says Eulenberg, "to content ourselves with a somewhat unsatisfactory result.

A close relationship between all the symptoms, and the existence of such phenomena as palpitation, loss of sleep, rise of temperature, sweating, diarrhoea, amenorrhoea, pigmentation, etc., suggest a wide disorder of the general nervous system, and the suddenness of the onset of symptoms in some
faces, coupled with the fact, that recovery may take place, points to it being functional rather than organic.

The Esotere is generally admitted to be the result of dilatation of the arteries and veins of the thyroid gland; that great hyperemia of its substance does exist there is no doubt, as evidenced by observations during life, and as has been satisfactorily demonstrated post mortem. Lithium gives the results of several autopsies; in one case, "the thyroid gland was very voluminous in size; it had a fibrous structure, and though it was soft, it contained coagula of variable size; there were no cysts. The arteries supplying the gland were very much dilated, especially the inferior thyroid, the coats of which were hard and fragile, and presented several aneurismal dilatations." And in another case he found
that the thyroid gland was hyper-
triphid and full of cysts and vari-
cose veins. Others have met with the
same results by a great increase
in the general vascularity of the
 gland, along with more or less in-
crease in the glandular tissue, or
true hypertrophy, and especially in
many standing cases the violence
of cysts.

duard* has produced in guinea
birds and rabbits, a considerable
amount of exophthalmus, lasting
several days, by tying the intimal
and internal jugulars in both sides
and simultaneously dividing the
cervical sympathetics to facilitate
dilatation of the vessels; and by
tying the thyroidal vessels in
addition he produced a distinct
enlargement of the thyroid gland.

There are also good reas-
ons for considering that the chief
element in the production of the
exophthalmus is dilatation of the

arteries and veins of the orbit; the amount of protrusion varies with the degree of palpitation and the size of the thyroid; the protrusion can sometimes be lessened by pressure; the eyeballs usually retract after death; then there is dilatation of the central vein of the retina; and Cremers has noticed elongation and tortuosity of the ophthalmic artery. Postmortem examinations show that there is often an increase of the normal fat in the cellular tissue behind the eye, which no doubt assists in the production of the protrusion. Withriizen found the eyeballs (post mortem) "pushed out of their sockets by a considerable quantity of fat"; and again, "the eyeballs which had been very prominent during life had sunk into the orbit after death, although the left orbit contained a sufficiently considerable amount of fat to prevent retrogression of the eye." The hypertrophia however is

1. Reynolds, p. 375. also Duchenne.
2. Cremers, p. 525.
3. EJtenstein.
the chief element, and the deposit of
fat must be considered as the re.
sult of the hyperemia - increased
pallor like the hypoplasia of
the thyroid gland.
Paralysis of the vaso. motor nerves
that run in the cervical sympathetic
is supposed to be the cause of the
hyperemia, and the disturbed action
of the heart is usually explained by
the existence of irritation of the vaso-
motor nerves which run in the cer-
velical sympathetic. So that what we
may term the sympathetic theory
assumes a state of paralysis to
account for the condition of the
eyes and the thyroid, and a state
of irritation to account for the
condition of the heart.
Beneke ascribed the increased
vascularity of the thyroid as due
to irritation of dilator fibres run-
ing in the sympathetic, and not
to paralysis, and this is a much
simpler theory. It assumes a
spasm of the longitudinal muscular fibres in the wall of the arteries, caus-
ing shortening of the vessels over the column of blood, and conse-
quently increase in their calibre.

We know that stimulation of the chorda tympani produces a strik-
ing dilatation of the vessels in the submaxillary gland, and a simi-
lar action of vasodilator fibres takes place in connection with the
neri erigentes of the penis, but it is very doubtful whether an
analogous action is possible, at least in the larger arteries of the
head and neck, as they possess no muscular cells, though the
existence of a thin, thick layer of smooth muscular fibres, lying
between the intima and adventitia and in the latter itself, has been
demonstrated by Müller in the thyroid arteries. But the extreme
 tortuosity of the thyroidial arteries, Fitzgerald suggests, is suf-

1. Ziemssen p. 91.
sufficient to dispose of Benedict's idea, nor is it easy to imagine that a nerve could remain in a state of permanent irritation for any length of time without paralysis supervening. Gügel again attributes the dilatation of the vessels to paralysis of the vaso-motor fibres of the cervical sympathetic, and the protrusion of the eyeball to increased irritation of the oculo-pupillary motor fibres. Which two sets of fibres are each connected with separate centres in the cervical region of the spinal cord, and run together in the sympathetic.
Section of the sympathetic on one side of the neck, as first discovered by Claude Bernard (in 1852), produces a rise of temperature, and dilatation of vessels on the same side of the head and neck, by paralysing the vaso-constrictor fibres; it also produces flattening of the cornea, contraction of the pupil, etc., traction of the eyeball into the orbit,
contraction of the membrana nictitans, drooping of the upper eyelid, and elevation of the lower. Sympathetic action of the peripheral stumps of the divided sympathetic is followed by an opposite set of results, and enlargement of the palpebral fissure, restoration of the corneal convexity, and protrusion of the eyeball from the orbital cavity take place.

Giesel based his theory on these facts, which certainly bear strong evidence as to the origin of certain of the symptoms of strabismic goitre though they do not explain them all. It seems curious however that there should be two contrary conditions existing for years together, in two centres so near each other.

Section of the anterior roots of the two first spinal nerves, according to Bernard, produces only the ocular pupillary symptoms, but section of the ascending cord of the thor...
thoracic sympathetic between the second and fourth ribs produces only the vascular and theminic effects, dilatation of vessels and rise of temperature on the side operated on.

Another theory is that enunciated by Friedrich to the effect that the cardiac disturbance is due to a paralysis of the vaso motor nerves of the sympathetic, which supply the heart, causing dilatation of the coronary and intra-muscular arteries, and consequent increased supply of blood to the substance of the heart; the result is, excitement of its ganglia and consequent overaction and palpitation. We thus get over the difficulty as to permanent irritation existing without subsequent paralysis, as is involved in Benedek's theory.

Halenberg and Euttmann practically hold the double theory, and in regard to this it is worthy of note, that we have an analogy in proch
a condition, as affections of peripheral nerves, as in certain forms of neuritis, do sometimes give rise to symptoms both of paralysis and of irritation in the same nerve; thus we may have spasm and anaesthesia, or paralysis and hyperaesthesia. If however these two conditions of paralysis and irritation exist in Francis disease, the opposing action of the nerves which pass through the sympathetic system must be attributed to irritation of their respective medullary centres.

In connection with this, Fox has pointed out that if the palpitation were due to paralysis, the influence of the cardiac nerves being cut off, the inhibitory action of the vagus would suffice to antagonize the automatic energy of the cardiac ganglia, and syncope would be the result.

As far back as 1860 Handfield Jones throws another light on this

subject; he considers that the funda-
mental malady is dility, especially
of the nervous system, which by its
affecting various eace-motor nerves
gives rise to the general symptoms;
thus, effusion behind the globe would
cause ptosis; hyperemia and
increased action of the cell elements
of the thigh gland would produce
gouty; and paresis of the vagi would
give rise to palpitation and vomiting.
And this appears to be the earliest
endeavour to explain these symptoms
by a reference to the pneumogastric
nerves, and such an explanation
appears to be a very plausible one,
or is at least a step in advance.

That we have to look nearer
the centre of the nervous system than
the sympathetic is probable, but before
going further let us consider certain
other points which have as yet been
only casually mentioned. Besides
an increased vascularity, and con-
sequent increase in the amount of
fat in the orbital cellular tissue cause
ing the protrusion of the eyeball, the
proptosis has in addition been ascribed
to muscular action. The muscle in
question consists of a set of smooth
muscular fibres usually associated
with the name of Müller and known
as the *musculus orbitalis*, but which
no less properly might be associated
with the name of Turner. Professor
Haycock in 1863 says, "Mr. Turner,
assistant to Dr. Godwin, has lately
demonstrated that there is an un
striped muscular structure in the
orbit, hitherto overlooked, which from
its attachments he designates the peri
ostial muscle. If Mr. Turner’s dissec
tions be confirmed, this periostial
muscle must be held to have con
siderable influence in protruding the
globe." And of this muscle Professor
Turner says, "in man it is rudimen
tary, but in the sheep, ox, elephant,
etc., where the osseous wall of the
orbit is deficient, this muscle forms
a well defined structure. It has been suggested that it acts as a protractor muscle of the globe.

This muscle is innervated by the sympathetic, and the upholders of the sympathetic theory make a point of this fact. We have seen that stimulation of the peripheral ends of the divided cervical sympathetic produces esophthalmus, and it is due to contraction of this muscle. These experiments were however performed on animals, where the muscle exists as a definite structure, but Wagner and Müller, by experiments on de-capitated criminals, have shown that stimulation of the sympathetic produces no esophthalmus, simply opening of the eyelids. This is no doubt explained by the rudimentary condition of the muscle in man so that it has no power to protrude the eyeball. It has been said however that the antagonistic muscles, the recti are fattedly degenerated and weak.

and their power much diminished. But such a condition is not always present in the ocular muscles or a bulging found to be healthy and only in a state of fatty degeneration. In some cases of long-standing posture, again, the proptosis as we have seen may come on suddenly and may entirely or nearly disappear, so that there appears to be little in favour of the much accepted theory of the action of the muscular orbitales as a cause of proptosis in Graves' disease.

Müller has also described certain unstripped muscular fibres in the upper and lower lids and it has been thought by some that Graefe's and Stillwag's symptoms were due to permanent irritation of the symp.

pathetic causing spasm in them. Stillwag however did not think so. These eyelid phenomena are tolerably constant, and have a special significance in this disease, being
in ordinary exophthalmos, as from infra-orbital tumour; they are often early noticed, especially in children, even before the protrusion, and one case has been recorded by Groover where the Graefe's symptom was present on both sides although the proptosis was unilateral. On the other hand, Sander Brunton mentions a case in which it existed only on the side on which the proptosis was most marked and E. G. Fitzgerald records four cases of unilateral exophthalmos, as with the Graefe's sign also unilateral.

The absence of pupillary changes in Graves' disease is greatly against the idea of a sympathetic theory, as changes in the diameter of the pupil are constant in lesions of the cervical sympathetic. Cases of the disease have been recorded in which dilatation or contraction have been observed, but in the great majority of cases the pupil is normal. That

a constant state of continuous irritation should exist as hard to believe and there is no physiological analogy for it; and as regards the assumption of other symptoms being the result of a condition of paralysis, there is no experimental evidence that section of the cervical sympathetic has been followed by crephathalmos and goutre.

How do the results of pathological observations support with any certainty a sympathetic explanation of the disease. Post mortem examination has no doubt in a very few instances revealed alterations in the cervical sympathetic, but they have been of an inconsistent nature and were altogether absent in the vast majority of cases which have been microscopically examined. Keith found in one case the middle and lower cervical ganglia of the left side much enlarged and very firm and hard, also the lower connecting cords corves.
correspondingly thickened, and the branch from the middle cervical to the inferior thyroid artery was thickened. In Siegel's case both sympathetic trunks were apparently thickened, and enveloped in a fatty sheath of connective tissue, but microscopically no alteration in the tissue of the nerves and ganglia could be detected except brown pigmentation of the latter.

*Sheehe* examined one case carefully, and as regards the ganglia and the communicating cord found everything "typically normal"; in this case however he found very great dilatation of the vessels of the medulla oblongata and cervical region of the spinal cord, and at certain points it seemed as if the wide vessels must exercise injurious pressure upon the nerve tissue with which they were in close contact, but no degeneration or atrophy could be made out.

A theory that would refer all
or at least the three cardinal symptoms to a common centre, in the medulla or brain itself, would be much more satisfactory, and it is only lately that any definite and precise theory of a central origin of Graves disease has been put forward, and we owe it to Professor Bättler of Erlangen. Graefe's symptom he attributes to lesion of a centre which presides over the associated movements of the lids and eyeball; the goitre and ophthalmoscopy to a lesion of these vaso motor centres that preside over the vaso motor nerves of the thyroid gland and intraorbital tissues; and the cardiac symptoms to a lesion of the cardio inhibitory centre for the pneumogastric. He takes the same view as Stillweg did regarding the retraction of the upper lid, viz: that it is due to a lesion of the reflex centros which are excited by stimuli from the retina and from the sensitive nerves of the cornea.

and conjunctiva. Saltzer's theory is based on the results of important experiments conducted by Fielme. When that observer divided the rectus body in their upper fourth, the incision not being carried so deep as to injure the subjacent roots of the pneumogastric, he produced impairment of the function of these nerves; exophthalmos, usually more pronounced on one side than on the other; and paralytic paralysis of the ears, the thyroid, and the anterior part of the neck. These phenomena were pretty constant, but in some instances swelling of the thyroid also took place, and occasionally Stillwag's symptom was noticed. In one case only did he succeed in producing all three cardinal symptoms in the same animal; and these effects took place even after the sympathetic had been divided, so excluding the possibility of the proptosis of the

eyeball being due to any action of the muscle of Müller. Boez mentions that Brown-Séquard had also produced esophthalmos by injury to the restiform bodies, and had observed the deformity so produced go through four generations.

Now we know that these nuclei in the medulla oblongata and closely situated to one another various centres: a cardial inhibitory centre, a vaso motor centre, a vomiting centre, a diabetic centre, and Satter assumes the existence also of a centre for coordinating the associated movements of the lids and eyeballs, and it is significant that vomiting is often a marked feature in Graves' disease, and that glycosuria has been found associated with it too.

Michael Foster² says if the medulla oblongata be punctured in the region previously described as that of the vaso motor centre, the area marked out by Seckhard as the diabetic area —

---

¹. Because of Brown-Séquard.
². Text Book of Physiology.
agreeing very closely with that defined by Oppenhiem as the case natura-
the urine will be found in an hour
or two to contain a considerable qu-
antity of sugar, and to be increased
in amount; and, as we have seen,
polyuria has also been observed as
an accompaniment of Gravis disease.
Diabetes is also a frequent complic-
ation, and a possible explanation may
be found in the interference with the
function of the pneumogastric, which
supplies the small intestine - it is
an inhibitory nerve, and Moynan
and Bruntin have shown that
the division of all the nerves going
to a portion of intestine is followed
by the secretion of a fluid just
like the rice water stools of cholera.
May not the stimulation of the
inhibitory vagus be followed by re-
ults much the same as if the
sympathetic supplying the small
intestine were paralysed?
This central theory appears to
be a very plausible one, and satisfactory disposed of the various difficulties connected with the so-called sympathetic theory, there being nothing unlikely nor inconsistent in it; and by an assumption of lesions of certain centres, the essential symptoms of sympathetic Eötre can be explained in an uniform manner. Sattar is fully of opinion that the point of origin is in the medulla, near the roots of the pneumogastric, and he points out that probably the lesion is a very slight one, and not always in the same place, for the order in which the symptoms appear is variable and they are curiously mixed with others. Such a slight lesion he thinks might be some vascular alteration, and he adds seems to have entertained a similar idea, as already mentioned, as the same symptoms vary from time to time.

As regards von Tracpe's symptom, Sattar says, "there is no doubt that..."
Whatever that the movements of the lids in association with the raising and lowering of the level of fixation (that is to say, the corneoscleral action of the levator and orbicularis on the one hand, and of the ocular muscles which rotate the eyeball about a horizontal axis in the other) are provided over by a definite coordination centre, just as much as are the associated movements of both eyes.

Fickew, as the result of his experiments came to the conclusion, that Graves disease may be produced by paralysis of certain nerve regions, controlled by the medulla oblongata, and that the points traversed in common by the nerve paths concerned, are, the restiform bodies: that the exophthalmus and goiter depend on dilatation of the blood vessels, and that the increased cardiac action is due to diminution or abolition of tone in the pneumogastric.

Post mortem examinations in
the human subject are necessary in proof of Helvius's theory, though he points out that negative results from some of them would not be fatal to it, as the existence of functional disturbances is admitted. Clarke was not far from it when he found the vessels in the medulla dilated, and Woulfe Mackenzie recorded an interesting case, in which the corpora quadrigemina, and medulla oblongata, particularly in its posterior part, were very soft, and on minute examination displayed the usual appearances of common softening. But a great and valuable addition to the accurate pathology of the disease has been made by Dr. John White, in a paper in the British Medical Journal of March 30th of this year, and which must have a great effect in favouring the general acceptance of this central theory. The patient was a female, aged 31 years, with well-marked symptoms of Graves's

disease; she had suffered from palpitation for many years, and first noticed the thyroid enlargement twelve years ago. Post-mortem examination gave, inter alia, the following results:... 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 the 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 sixth nerve showed considerable changes: immediately under the posterior surface of the medulla, and extending from the middle line as far out as the restiform bodies, which were slightly implicated, were numerous hemorrhages...
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 haemorrhages seemed to be 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.

Here then we have a record of changes in the floor of the fourth ventricle, near the origin of the vasa in the region indicated by Satler and taken in conjunction with the experiments it must be considered of great importance. Had these minute haemorrhages not taken place, the affected
portion of the medulla might have been overlooked; it is discussed part of the brain that are most prone to hemorrhage, and although in this case the extravasations appear to have been recent, yet the patient had suffered for many years, and the lesion may be, as Satir suggests, a vascular one, disappearing after death.

Now that attention has been directed to a definite region, we shall look for the results of future pathological investigations with great interest, and though many negative results may be expected, even a few cases showing changes in this region would be most valuable. In this case it will be observed that the nucleus of the fifth nerve was involved, and it suggests itself to me mind as worthy of note that this nerve communicates with the caudal planes of the sympathetic. 7 The theory of a

Central lesion seems to gain support from certain points of clinical observa-
tion, as for instance its association with hysteria, epilepsy, neuralgia,
migrain, mania, ophthalmoplegia, etc., and Tommasi's taste changes.

Bristow mentions an interesting case, which after a few years, became com-
plicated with ophthalmoplegia, and later in the patient suffered
from ptosis, complete hemianesthesia on the right side, with colour blindness
and loss of taste and smell on the same side; and still later fits,
apparently epileptic, supervened, with rigidity of the right arm and leg.
She also suffered from haemorrhage from the ears. All this suggests a
spreading lesion, and yet the post mortem showed no sign of disease
in the nerve centres.

Anglings Jackson has seen paresthesia, disease complicated with ophthalmic
paralysis, and with right sided facial spasm, a rarity which he

supposed to depend on discharge of facial centers in the pons varolii. Mackenzie reports a case complicated with epileptic convulsions and maniacal paroxysms.

Further support is given also by the observations of Long and Price 3 in a series of six cases, in which uni- lateral "lid phenomenon", without proptosis, was associated with no other evidence of Graves' disease, except slight thyroid enlargement in two of the cases; in four, paroxysms of the orbital muscles were present; and in three, sensory phenomena - pain, scalding, lacrimation, etc.

And with reference to the connection of the pneumogastric with the small intestine and Brunton's experimental production of choleraic diarrhea, already mentioned, Dr. Russell "observes of one case he had,

... the patient was in the habit of pass-
ing from twenty-six to thirty stools
in the twenty-four hours". 4

"describes the evacuations as consisting of a white fluid without fœcal odour, which sometimes sounds from her." Fitzgerald points out that Brown Seignard has produced ophthalmma, or circumscribed tumours of the ear by surrounding the rectiform bodies near the nê of the calamus scriptoris; and that Graves disease is tolerably frequent among lunatics, who are chiefly affected by this disorder; and that it is not unlikely that patients may be found suffering from both diseases. Fitzgerald has also drawn attention to the preponderance of the symptom in the right side of the body. The right side of the thyroid is usually the larger, and if the preptosis is not equal, it is usually more marked on the right side—all this is generally admitted. Fitzgerald suggests that the extreme constancy of the cardiac disturbances affords a clue to the problem of this preference, and so the right vagus is the one that

chiefly inhibits the heart he considers the heart symptoms as right-sided. Arlbing and Trifoli's experiments, as well as those of Fréger and Massin, show that irritation of the right vagus produces marked cardiac inhibition, and Fitzgerald's explanation of this is based on the mode of development of the heart, which soon after its de- velopment in the embryo projects to the right and comes to be innervated by the right vagus. If this be so, we would expect to find that in cases where cardiac symptoms are absent or slight, the other phenomena should be more marked on the left side, and Fitzgerald quotes several recorded cases which tend to uphold such a view.²

A point of interest in connection with Gräve's disease is the remarkable effect that operations in the nasal cavities have had, in diminishing, and even causing disappearance of, the symptoms.³

---

1. Bull. de l'Acad. Roy. de Belg. 3. 3. 3, p. 693.
3. op. cit. p. 395.
In two cases operated on by Mr. George Slater of London for nasal obstruction, the effects produced cannot have been mere coincidences, as the diminution of the thyroidal swelling and of the exophthalmus corresponded in both cases to the side of the nose operated on. But still more interesting is a case reported in the Brit. Med. Journal of April 20th, 1889 by Dr. Hall Simon of London, where operation for removal of nasal polypi by the galvanoelectric loop, had resulted in the production of exophthalmus of the patient's right eye, within a day or two after the operation. Graefe and Stellwag's symptoms were produced too, showing that the operation was of the nature of a disease, not there was neither disturbance of the heart nor alteration in the thyroid. The curious point is that operation was that it cured the patient of another neurotic affection, viz.: asthma, from which he

had begun to suffer shortly after the appearance of the nasal polypi. These results might be taken as roth favoring the theory of a central lesion as they appear to be cases of peripheral irritation, producing the disease, and Russell records a result which seems to have a similar reference, viz. that lancing of the gum has resulted in amelioration of the symptoms of frank's disease, in the case of a boy aged 12 in whom the attack came on while cutting a large tooth. Twelve years afterwards the symptoms returned in a milder form. He also mentions another case where a lady was rapidly cured with the gum lanced.

The conclusion to be drawn from such cases as these seems to be that just as peripheral irritation can affect the cardio-inhibitory centre, so may the neighbouring centres be likewise affected.

In a disease which in itself exhibits so many manifestations, and is attended by such a variety of complications, it is only to be expected that on these grounds alone the treatment adopted should have been both varied and extensive, and the views adopted from time to time by different observers, have led physicians to employ methods of treatment in accordance with theoretical reasoning or individual fancy. And even now, when we flatter ourselves we know something of the real nature of the disease, we are often at a loss to know how we may best assist the patient. Few maladies offer such scope for the exercise of the physician's ingenuity and resource; some have attempted to control or conquer the disease by the employment of powerful drugs; others have had equal success by doing little or nothing, while the assistance of the surgeon has come.
sometimes been found necessary. To attempt to go into the whole subject of treatment would be impossible in a paper of this kind, and it will be sufficient for our present purpose to give a general indication of what has been done and of some of the results obtained.

What applies to the treatment of every form of disease applies more especially to those of nervous origin and to more more so than the one under consideration—viz: putting the patient in the best position for getting well, by careful regulation of the habits, and surroundings; removal of any cause detrimental to the general health, and placing him under the best attainable hygienic conditions. The patient must be kept from all mental annoyance or worry, emotional excitement or sexual irritation; he should have a quiet house, a cheerful room, proper ventilation, change of climate
in some cases, suitable mental occupations and proper injunctions as to the matter of rest. It is not sufficient to tell the patient "to rest or lie down as much as possible" and "fatigue" and "so forth; it must be clearly laid down how many hours for rest, how much indoor or out-of-door exercise, and what he may do and may not do; patients' ideas vary so much on these points that the doctor's orders cannot be too precise. Absolute rest in the recumbent posture is strongly recommended by some, and in many cases is of undoubted advantage.

Diet also must be attended to especially when vomiting or diarrhoea exists, or in cases of famished and inordinate appetite. Milk, fish, and grape curds, are much eatened in Germany. Stimulants should be avoided in most cases, and the patient should
exercise moderation in the use of tea, coffee, etc., and avoid tobacco.
Any disturbance of digestion must be attended, any peripheral irritation removed;
uterine disorders treated, and treatment directed according to the special indications in each case.
Those who uphold the chlorotic theory adapted remedies calculated to improve the condition of the blood and improve the general system, by salts of Iron and other tonics. Bigbie treated his cases with Iron, combined with
Pyretic, Quinine or Belladonna, giving at the same time Murph and Alum for the bowels. Such treatment, combined with Saline plasters to the thyroid and Belladonna plasters to the heart, proved successful in many cases, and White Copper, Pepper, Sandfild's Juncos, all advocate this tonic treatment. Saull recommends Iron and Quinine given alternately, each for three weeks.
Toussan condemns Iron in any form, but the results obtained by
the persistent use of chalybeate, espec.
ially when anaemia is marked, are
certainly remarkable. Feruginous
mineral springs such as those of
Franzbad, Pyrmont, Schwabach and
Thür is are of considerable value in
such cases.

Chinin, in combination with Iron, is
opined (presumably) by J. Brunton,
and with Digitalis by Ruscel and others.
Digitalis is a drug that naturally
suggests itself because of its effect
on the circulation, and most authors
advise its use. Amercan recommends
it for excellence, especially during
a paroxysm, given in 8 to 10 minu-
tose every hour until the pulse drops
to 60 or 70, then diminished or stopped
altogether; and he adds that in both
cases the cumulative effects of the
drugs are not to be feared, and one
patient, aged 16 1/2 years, took 109
drops of the tincture in ten hours
without harm. Ruscel in one case
found it the only remedy which suc.
succeeded in one case in controlling
the excessive cardiac action. Bingel
records the case cured by it and I.
Sometimes however it has a contrary
effect - in one case in which I tried
it, it distinctly increased the cardiac
rate and produced some head-
ache, not once only, but then repeated
after an interval of some months.
Arnica is a drug which appears to
have a good sedative action on the
heart. Pepper found it very beneficial
alone, and combined with Iron, and
Jonathan Hutchinson had excellent
results in one case, given at first in
5 minims doses and gradually increased
to 20 minims every four hours.
Strophantin may perhaps be found
useful in some cases and has the ad-
vantage of being more easily borne
by the stomach and being not cumu-
lative. Lowne recommends it.
Belladonna has been much employed
in cardiac disease - either alone, or
combined with Iron, Strophina, and
Selenium. Walsworth Regis says... "administered in the form of the extract in doses of 1/8 or 1/4 grain, or as Atropia in doses of 1/60 grain, or applied as a plaster over the enlarged thyroid gland, I have found this remedy to produce rapidly a remarkable effect in the eye, in causing its returnment, and in removing the peculiar staring of passion, in the thyroid gland, in leading to the rapid, or at all events, speedy diminution in its bulk, on the heart and blood vessels in modifying and controlling their excited action. Smith has found it beneficial and accelerates the effect of the stimulus it exercises on the sympathetic. Trower strongly recommends it. Ruedl gave it to the extent of 30 minims three daily, but with no good effect.

Veratrum viride and Belladonna have also been employed as cardiae stimulants, and in their effect on the nervous system, the former was much praised by Balian and see, as making the pulse slower.
without increasing the actual tension as digitalis does.

Lodine was suggested because of its effect in ordinary goitre, and has met with varied results, but is not now in much favour. Cheadle has had excellent results with iodine internally in the form of the tincture, in 5 to 10 minim doses three daily, and applied externally to the thyroid; three weeks of such treatment made the goitre softer, and relieved the dyspnoea in one case; in other cases however he did not find it so successful, and considers that it is useful only in those cases where the goitre is large and excerting dangerous pressure. Trouman condemns lodine in any form, although he saw it do good in one case when given by mistake for digitalis, in 15 to 20 minim doses three daily; and it would seem that large quantities can be given—Cheadle says as much as 40 minims daily for some months—without iodine undergoing.
Austin Hunt also condemns iodine and says that experience shows that applied either topically or for its constitutional effects it is useless, if not injurious. Ergot has been employed successfully by William Pepper, given internally, along with injection of a solution of ergotin half an inch into the substance of the thyroid. He employed a solution containing 96 grains of ergotin to the ounce of distilled water and injected 6 to 10 minims weekly.

Iodide of Potassium is admired by Lowers, Romeyn, and others. Fornier saw a man aged 50 whose condition was singularly improved by the prolonged administration of it. Buller had good results in two cases with the iodide given internally, and iodine applied to the gland. Bromide of Potassium acts well sometimes, both as a sedative to the nervous system and in relieving palpitation; a patient of Reggio's found 20 grains taken thrice daily gave great relief.
when aconite and digitalis failed. In some cases he has been found benefi-
tial by bheadle.

The diarrhoea of choleraic disease is often very intractable, though it frequently
gives way to ordinary remedies. Dr.
Hall, who has been a great deal of
cholera in India, has found that the
hypodermic injection of chloral hydrate
has arrested the discharge from the
bowel and prevented collapse, and
his theory for the explanation of this
is based on Warme and Brunton's
experimental production of reit with
stools by division of all the nerves going
to the small intestine, and that the
right vagus supplies that gut. It
seems to me that in cholera we have
a possible remedy for the diarrhoea
of bronchi disease. Bheadle has ob-
tained the best results by the ad-
mintistration of opium digitalis and
tannin in pill form, and ice by
Drinium, given with sulphuric acid
and opium. In both of which he

it observed opium is present.

Insomnia is another distressing, which

takes the physician's skill, and pro-
lably the bromides are the least objection-
able of the remedies given to tran-
quilize the nervous system and promote
sleep. Opiates are sometimes useful, but
Pepper thinks they should be avoided, be-
cause of their effect on the appetite and
digestion, and of the opium habit.

Dr. Robert Park relates how he success-
fully treated a severe case, where there
had been complete insomnia for three
weeks, by the hypodermic injection of
morphia gradually up to 2 grains—
this quieted the heart's action and in-
duced a gentle sleep.

As regards local treatment, ice
cold compresses and pressure to the
thyroid gland are recommended, and
as we have seen, iodine may be applied
sometimes with success. Ice may also
be applied to the pectoral area, as recom-
manded by Aran, and Belladonna
plasters have also been found of benefit.
For the exophthalmos in Nóife re. commands painting with lodine tincture between the eyebrows and the upper lid, or lodide of potassium ointment rubbed in over the lid; cold compresses, local electrification; and in some cases tararoesia, as a protection against malignant afezioni of the cornea. Biegd advises that the eyes should be frequently washed with tepid milk, to prevent the ocular conjunctiva from becoming irritated. Compresses dipped in milk, or astringent o caustic lotions, may ul. time the afezioni of the cornea if it should become troublesome.

Sacrificiation of the cranial sympathistic has been much employed, and in many instances with a wonderful degree of success. Lichtenberg speaks formally of his method, which was to apply the negative pole to the cranial ganglia on each side in turn, or to both at once by means of a divided electrode, in the case where the pulse was habitually 108 to 130, with ab
Abnormal arterial tension—6 to 8 cells of the continued current gradually reduced the pulse to 84 and even to 70, and diminished the tension in the carotid and radial arteries. Pass mentions a case, treated with the negative pole applied to the spine below the 5th cervical vertebra and the positive at different levels in front of the sterno-mastoid, where the pulse was reduced from 130 to 70 or 64, and the systole and diastole diminished. Suttman states that temporary reduction of the frequency of the heart's action is first produced, but by persisting in the electrical treatment the reduction becomes permanent, together with progressive improvement as regards the thyroid and eyes.

Zundorf has employed galvano-puncture to the thyroid, but only doubtful results were obtained.

Whatever form of treatment be adopted, and there are many, one resides besides those mentioned, a
successful result will be more probable if rest and quietude be rigidly enforced, and the central theory of the disease obviously adds force to the necessity for it.

If medicinal remedies there is one more which may be mentioned as being of use, viz. Duboisia, an alkaloid, according to Lademann, identical with pure hyoscine and isotonic with atropine, but possessing more powerful physiological properties than the latter. Great relief has been obtained from the administration of two grains of the sulphate twice or thrice daily, and Diamont has had good results from ingot internally for fifteen days, followed by Duboisia for a similar period to the extent of producing a slight toxic effect.

Murascan strongly recommends mild hydrophatic treatment, because of its known effects in anaemia hypotonia etc. Massage has also its supporters, but with what effect it has been practiced
I have no knowledge.

The question of Surgical inter-
ference in cases of Exophthalmic Goiter
has only been entertained for the
rare cases of immediate danger from ac-
ute phaeochromic or the trachea,
and glands, has successfully removed
the isthmus of the thyroid along
with the adjoining portions of the
lateral lobes; the operation was suc-
cessful in itself, but the patient died
two weeks later of heart disease,
at which time the lobes had greatly
shrunk, and the goitre was incon-
spicuous.

Tracheotomy may be necessary, and
Broman draws attention to the dan-
ger of the operation from the extreme
vasculosity of the thyroid; he has
recounted a case in which death from
hemorrhage occurred during the oper-
ation. He therefore advises that the
isthmus should first be carefully di-
vided by the scissors. He thinks
surgery would also be safer than the
knife.

The question of operative procedure derives additional interest from the results of operations in the nasal cavities, and Hack of Freiburg, in whose hands some of these results occurred, advises careful rhinoscopic examination in all cases of Ethmoidal sinus sofar as are accompanied by nasal symptoms.