

61644

NOTES ON A SERIES OF CASES  
OF EXOPHTHALMIC GOITRE

- by -

JOHN FINDLAY, M.B., Ch.B.  
D.P.H., R.C.P.Eng.

-----  
M.D. 1913



## I. INTRODUCTION.

I have chosen "Exophthalmic Goitre" as the subject for my thesis because in my first post after graduation I found myself in the centre of a district where this disease is of very frequent occurrence.

After graduating in 1908 I went, as an assistant to Dr. Crawford, to Keswick in Cumberland, the centre of the English Lake District where I stayed over a year. In the valleys around the lakes of Derwentwater, Bassenthwaite, Thirlmere, and Ulleswater the large number of cases of diseases involving the ductless glands is a very remarkable fact. During fourteen months practice in that country I had under my observation nineteen cases of exophthalmic goitre, many more cases of simple endemic goitre, several cases of cretinism and myxoedema, two very well marked cases of acromegaly, one of whom had a large goitre and two cases of Addison's disease.

In 1910-1911 I was first house physician, and later house surgeon in the Cumberland Infirmary, Carlisle, where I again had under my observation several cases of exophthalmic goitre, three of whom underwent the operation of partial thyroidectomy.

For the last year I have been practising in Lancashire, where I have been struck with the large

number of cases of exophthalmic goitre, though the cases differ in many respects from the cases I met with in Cumberland.

In several districts of this country, ~~in~~<sup>in</sup> the Highlands of Scotland and several of the manufacturing towns of Yorkshire where I have had considerable experience in general practice the rarity of this disease compared with its frequency in the English Lake District and the Fylde District of Lancashire is very noticeable.

In all, my experience embraces a series of fifty-four cases of this disease and in the present thesis I propose to give my views of this disease based on these cases.

## II. ETIOLOGY & DISTRIBUTION.

Exophthalmic goitre, also known as Graves's, Parry's or Basedow's disease, is an affection characterised by:-

1. Rapid cardiac action (tachycardia)
2. Enlargement of the thyroid gland (goitre)
3. Protrusion of the eyeballs (exophthalmos)
4. Peculiar nervous symptoms, e.g., muscular tremor, general nervousness, flushing, etc.
5. In addition to the above four cardinal symptoms there are frequently associated, emaciation, anaemia and disturbances of the alimentary tract and the uterine functions.

One of the outstanding features of this disease is that females are affected much more frequently than males.

Of the fifty four cases I have had under my care only two were males. This proportion of one male to twenty seven females is rather less than that given by most authorities. Thus Hector Mackenzie states (Allbutt's System, Vol. IV, part 1, p. 359) that in this country the proportion is about one male to thirteen females.

The ages of my patients have varied between sixteen and sixty five. Several cases have been reported in children, a few even under five years of age.

The great majority of cases start before the age of thirty. Over eighty per cent of my cases first showed

symptoms of the disease between eighteen and thirty. Heredity apparently plays a part in the causation of the disease. Many of my cases illustrate this. In one instance two sisters and two of the daughters of one of them suffer from the disease and in another the patient's mother, and her mother's sister died of the disease. In several of my cases in Cumberland different members of the patients' families were suffering or had suffered from ordinary endemic goitre, and in one of my Lancashire cases the sister of the patient is suffering from myxoedema. A patient in Keswick, suffering very severely from the disease, gave birth to a still-born child with a large congenital goitre which appeared to be parenchymatous in character but unfortunately it was not examined microscopically.

This occurrence of the disease in members of the same family does not disprove the possibility of an infective or toxic origin. The fact may be explained by the disease spreading by contagion or infection, or it may indicate that an increased liability to the disease is inherited.

In the Milroy Lectures 1913 (Lancet, Jan. & Feb. 1913). Major McCarrison, I.M.S., states, and I think proves, that endemic goitre is due to a "living excitant" whose habitat is the digestive tract and that the enlargement of the thyroid is caused by a toxin or toxins circulating in the

blood derived from the "contagium vivum" in the intestines.

A living excitant may ultimately be proved to be the cause of exophthalmic goitre also. On careful investigation of each case one usually finds, as in cases of so called pernicious anaemia, that there is somewhere in the body a mucous membrane or other organ showing signs of catarrh or sepsis. As in pernicious anaemia the teeth are very often decayed and septic. Rapid decay of the teeth is often a symptom of the disease when well established, but in several cases I have found that the teeth were decayed before the other signs of the disease manifested themselves, and furthermore that rendering the mouth and throat healthy markedly improved the condition.

Catarrhal conditions of the mucous membranes are very frequently noted in exophthalmic goitre. One of my male cases suffered from simple endemic goitre for six years and then developed chronic catarrh of the nose and naso-pharynx. Several months after the commencement of the catarrh he presented all the cardinal symptoms of exophthalmic goitre. The concurrence in this case of vigorous treatment directed against the catarrh with marked improvement in the symptoms of exophthalmic goitre is probably more than a coincidence. It is well known that a very large percentage of the

female sufferers from exophthalmic goitre have catarrhal or septic affections of the genital organs. Endometritis with or without displacement of the uterus and accompanied by a leucorrhoeal discharge is very commonly found as are also salpingitis and ovaritis. About seventy five per cent of my cases were found to be suffering from leucorrhoea.

The catarrhal or septic condition may be found elsewhere. One of my patients had an operation for appendicitis performed a few months ago. The appendix and neighbouring structures showed signs of old inflammation which had probably been present for years. Several of my patients suffer from asthma with bronchial catarrh. In the first of the Lettsonian Lectures delivered on 3rd February 1913, Mr. James Berry, B.S., Lond., F.R.C.S.Eng. in dealing with "The condition of the thyroid in earlier cases" says, "This patchy or focal distribution of the disease (in the thyroid) is one of the points upon which stress is laid by those who think that the disease is due to some form of septic absorption. Certainly there is something to be said for this view. In many cases a fairly definite source of sepsis can be found, such as carious teeth, a gastric ulcer, appendicitis and so forth. In the above mentioned case there was a history of some uterine sepsis following a confinement some months before the onset of her other symptoms."

The living excitant having gained entrance to the body at one or other of the places indicated above may become generalised, or, as Major McCarrison proves in the case of endemic goitre, it may remain localised and then its toxins enter the blood stream and cause hypertrophy of the thyroid with its increased or modified secretion.

Any sudden nervous shock as a fright or the receipt of bad news has been suggested as the direct cause of the onset of the symptoms. A history of such a shock can be obtained from many of the sufferers <sup>from</sup> ~~of~~ this disease. And this theory has also been supported by the fact that the symptoms, exophthalmos, cardiac palpitation, tremor and perspiration are all induced in a healthy person by a sudden fright. This view of the causation of the disease I think cannot be maintained. Several of my patients have attributed the disease to a nervous shock, e.g., fright, seeing a street accident, accidentally taking an excessive dose of strychnine, etc., but on investigation I have found that before the shock the patients were undoubtedly suffering from the disease though it may have been in a more or less quiescent or indipient state, and the effect of the shock was simply to aggravate the already unstable condition of the patient's nervous system.

Many other theories have been brought forward to explain the causation of the disease, e.g., some affection

of the central nervous system probably around the fourth ventricle, (minute haemorrhages have been observed by Professor Greenfield and Dr. Hale-White), disease of the sympathetic nervous system, altered condition of the blood, etc. As none of these have<sup>s</sup> been constantly found none ~~are~~<sup>is</sup> at present generally accepted.

The almost universally accepted theory regarding the etiology of exophthalmic goitre is that, due to some unknown cause, the thyroid hypertrophies and becomes over-active and then the excessive secretion, most probably also perverted in some unknown manner, causes the disease. Some modification of the normal secretion is necessary, because a simple excess, as can be produced by giving thyroid extract to a healthy individual, does not cause all the symptoms of exophthalmic goitre, e.g., the exophthalmos does not develop. The cause of this hypertrophy and over-action of the thyroid with the perversion of its secretion may probably be found to be some toxin or toxins derived from some living excitant present in some septic condition in the patient's body.

As regards the distribution of exophthalmic goitre, in the introductory section I have already remarked on the large number of cases met with in Cumberland and in

the neighbourhood of Blackpool, and on the comparative rarity of the affection in some other districts.

In Cumberland the cases I saw showed very well the classical signs of the disease. The exophthalmos was very marked, the goitre was large and the tachycardia was severe but the nervous symptoms were not pronounced. On the other hand, in the Lancashire cases, the nervous symptoms as tremor and flushing, are very well marked, and in the majority no exophthalmos and very often no appreciable enlargement of the thyroid can be detected. In none of the Lancashire cases has there been any dyspnoea or dysphagia due to the enlarged thyroid, while in Cumberland these were present in several of the cases. Tachycardia was (~~invariably~~) found in all the cases.

The difference in the size of the thyroid in the two sets of cases may have to do with the fact that in Cumberland ordinary endemic goitre is very common while in the Fylde District of Lancashire it is practically unknown. Mr. Berry in the Lettsomian Lectures, 1913, (Lancet, March 1st 1913, page 585) when considering the question whether ordinary endemic goitre predisposes to the exophthalmic variety states, "It seems impossible to accept this idea, in view of the fact that Graves's disease is no more common in regions of endemic goitre than it is elsewhere. Indeed, it is probably less common." This

is certainly contrary to the opinion of many practitioners in Cumberland and to my own experience. I have seen two cases of simple goitre develop clinically into exophthalmic goitre. And there are many cases reported, where the giving of iodine or its preparations has transformed a case of simple goitre to one of exophthalmic goitre.

Römheld, in the Journal of the A.M.A., vol. 56., No. 2., points out that few realise that iodine and all preparations of iodine are liable to induce exophthalmic goitre in a patient with a personal or family tendency to goitre. He reports in detail eight cases to sustain his assertion.

### III. PATHOLOGY.

Macroscopic changes in the thyroid. "A goitre in the sense of an enlarged thyroid is probably never absent in exophthalmic goitre, although the enlargement may be so slight, or the gland may be so deeply seated that the most skilful palpation may fail to recognise it." (Mr. James Berry in Lettsomian Lectures, No. 1, Lancet, March 1st, p. 583).

The enlargement of the thyroid is usually fairly uniform. The extreme enlargement seen in some cases of endemic goitre is not found in exophthalmic goitre.

The blood vessels going to and coming from the gland are enlarged and tortuous, but the enlargement of the thyroid as has frequently been pointed out, is a true hypertrophy and is not simply due to dilatation of the blood vessels in the gland. The gland itself, in fact, is rather pale and, as has been pointed out by Greenfield, it closely resembles an actively secreting salivary gland or the pancreas in general naked eye appearance (Beattie or Dickson, Special Pathology, p. 321).

On section the thyroid has a uniform appearance, no small cyst-like spaces or vesicles being visible as can be seen in a parenchymatous goitre.

Microscopic changes in the thyroid. The changes in the thyroid structure are absolutely pathognomonic of the

disease.

The microscopic appearances of the thyroid in exophthalmic goitre are well shown in the <sup>microscopic slide</sup> (~~photograph~~). The section is taken from the thyroid of one of my cases in the Cumberland Infirmary. Dr. Lediard of Carlisle, who operated on the case, kindly granted me permission to use it.

The outstanding characteristic is the enormous proliferation of the secreting epithelium lining the spaces or alveoli. The epithelium forms papillary ingrowths into the spaces which therefore become smaller and lose their regularity. The cells instead of being more or less flattened become cubical even columnar, and may show active mitosis and catarrhal and degenerative changes. The colloid disappears and the contents of the spaces become more fluid in consistence and contain the debris of degenerating cells.

The interstitial or interalveolar tissue also shows an infiltration of lymphocytes.

Chemical changes in the thyroid. "The chief interest in the chemical pathology of exophthalmic goitre is centred in the iodine content of the thyroid." (Mr. James Berry, Lettsomian Lectures, No. 1, Lancet, March 1st. P. 586). In normal thyroids the iodine in the gland is combined with the thyreoglobulin as iodothyrin. In exophthalmic goitre the thyreoglobulin is reduced in

amount while the iodine is increased and much of it is free and not combined with thyreoglobulin. This increase in the amount of iodine in the thyroid is an important change and partly explains how a simple goitre may become exophthalmic when iodine or any of its preparations are administered to the patient.

Changes in other organs.

The Thymus Gland is usually found to be persistent and very often enlarged in cases of exophthalmic goitre - in fact Mr. Berry states that it is constantly affected in the more severe forms of the disease. A simple hyperplasia of the thymus is the usual condition found on microscopic examination.

Other parts of the Lymphatic System are often affected. The Spleen is occasionally found to be enlarged as also are the Lymphatic Glands in the neck and elsewhere. Beattie and Dickson have noted enlargement of the Haemolymph Glands in the majority of cases examined by them (Special Pathology, p. 322).

The Blood shows usually a simple anaemia "chlorotic in type." In severe cases of exophthalmic goitre this anaemia I have found to be very marked. There is usually a lymphocytosis.

Beattie and Dickson (in Special Pathology, p. 322 and 323) describe an important change in the Bone Marrow in a series of ten cases. The fatty marrow of the

long bones was found to be usually completely transformed to red marrow and in several very acute cases the marrow resembled in naked eye appearance the condition seen in some cases of pernicious anaemia. After describing the microscopic appearances they say "these changes (in acute cases) point to the action of some toxic agent of great virulence which at first produces a leucoblastic reaction; and later as anaemia is established, a supervening erythroblastic change. In more chronic cases, similar, but as a rule less pronounced changes were found." This evidence of some "toxic agent," to some extent confirms pathologically the hypothesis brought forward in Chapter II that exophthalmic goitre is due to a toxin absorbed from some septic condition found in the body.

#### IV. SYMPTOMATOLOGY.

##### 1. Rapid cardiac action - tachycardia.

I deal with this first because I think it is the sign most frequently found and also probably the most important. It has been present in all the cases I have seen. "Palpitation of the heart" is very often the only symptom complained of.

In the majority of my cases the rate of the heart beat has been between 90 and 120 per minute when the patient was at rest, but on the slightest exertion or excitement on the patient's part the rate was greatly increased, reaching 160 or even more. In several cases the rate has never been below 130 per minute and in these any exertion renders the pulsations uncountable.

The heart, in these severer cases, is dilated, the apex beat being felt in some cases as far out as the anterior axillary line. On auscultation mitral presystolic and systolic murmurs are frequently detected. Mitral murmurs were present in about half of my cases. Several of these had a definite history of rheumatic affections and in these the murmur was no doubt due to organic disease. In others the murmur was undoubtedly functional as, on improvement of the heart and general condition, the murmur disappeared. In severe cases of long standing, degeneration of the heart muscle sets in and the pulse becomes correspondingly weak and irregular.

The throbbing of the carotid arteries in the neck is a prominent feature and is often complained of by the patient. The "pulsation of the thyroid" is really due to the pulsation of the enlarged arteries going to the gland.

The blood pressure I have found to be usually lower than normal though in two cases it was above normal. In six other cases the maximum systolic pressure varied from 104 to 120 millimetres of mercury. The blood pressure I consider to be rather important as indicating the treatment from which the patient will most probably derive the greatest benefit.

2. Enlarged thyroid gland - goitre.

I have already quoted (at the beginning of Chapter III) Mr. James Berry's opinion that in exophthalmic goitre an enlarged thyroid is probably never absent although the enlargement may be so slight or the gland may be so deeply seated that the most skilful palpation may fail to recognise it. I have also noted that the enlargement of the thyroid is never so great as is occasionally met with in endemic goitre.

In nearly one half of my cases no enlarged thyroid could be made out by inspection or palpation. In two fatal cases at the time of death I could detect no enlargement.

Several of the cases in Cumberland suffered from dyspnoea and dysphagia due to pressure of the enlarged thyroid on the trachea <sup>and</sup> ~~of~~ oesophagus.

3. Protrusion of the eyeballs - exophthalmos.

This may be unilateral as in one of my cases.

The protrusion may be so marked that the upper and lower eyelids cannot be made to meet over the eyeball. By depriving the eye of its covering and protection, this not infrequently leads to ulceration of the cornea and sometimes to total destruction of the eye. On the other hand the exophthalmos is frequently very slight or altogether absent.

When the exophthalmos is present several symptoms and signs in connection with the eyes can be detected.

In the downward movement of the eyes the upper eyelid is seen to lag behind the eye (Von Gräfe's sign).

The palpebral fissure is increased in size (Stellwag's sign).

The convergent power of the eyes for near objects is deficient (Moebius's sign).

Other signs are described, but they all depend on the fact that the eyeballs are further forward than normal and that the eyelids are retracted.

In several cases paralysis of one or more of the extrinsic muscles of the eye has been noted. None of my cases exhibited any ophthalmoplegia .

The cause of the exophthalmos is still in doubt. Most authorities support the idea that it is due to an accumulation of fat behind the eyeball. Mr. James Berry (in Lettsomian Lectures, No. 1, The Lancet, March 1st 1913, p. 588) states that "there can be little or no doubt that it is due solely to local accumulation of fat within the orbit. This is the only explanation that is consistent with the actual findings of morbid anatomy." But this is not universally accepted.

Dr. W.P. Herringham in a clinical lecture on exophthalmic goitre (in "The Clinical Journal", March 9th, 1910) says that he has seen cases examined post mortem and could not even then find what it was that made the eyes stick out during life. He also states that to him "the only thing which can explain it is, that it is connected with the congestion of the eye, and that it is probably some enlargement of the vessels at the back of the eye which disappears when death occurs." Spasm or relaxation of the muscular tissue in the orbit has also been suggested as a cause, but there is no proof of this hypothesis.

#### 4. Nervous symptoms.

Tremor. This is best seen on extending the arms. The whole limb shows a fine muscular tremor. The vibrations are small and rapid, about eight or nine occurring in a second. The legs are similarly affected.

One of my cases had the tremor well marked in the left arm but not in the right.

The skin is very frequently affected probably entirely through the nervous system. The patients complain of feeling warm even though they are very lightly clad. They therefore dislike hot weather and many have informed me how much better they feel in winter than in summer. Other vasomotor phenomena are, increased perspiration especially of the hands and feet and flushing of the head, neck and chest. True dermatographia has been present in three of my cases in Lancashire.

Pigmentation is sometimes seen resembling that in Addison's disease.

The hair of the head falls out very rapidly and it is usually very dry. I have already noted the fact that the teeth are very apt to become carious.

General Nervousness is a very frequent and troublesome symptom. The patients become more excitable and irritable and are liable to attacks of trembling associated with violent palpitation.

##### 5. Other Symptoms.

Metabolism is interfered with. General wasting and emaciation occur in practically every case. As a general rule the more severe the case and the longer the disease has lasted, the more marked is the emaciation.

Figures <sup>I</sup>~~II~~ and <sup>II</sup>~~III~~ are photographs of the patient from whose goitre the section was taken. The emaciation was extreme.

Digestive System. Persistent vomiting and diarrhoea are not infrequently present in severe cases and are very apt to prove fatal. The vomiting in two of my cases was very acute, nothing being retained in the stomach. The condition resembled that of acetonaemia though I failed to find acetone in the urine. Anorexia has been in some of my cases the most troublesome symptom from the physician's point of view.

Blood changes I have already dealt with in Section III.

Genito-urinary System.

Albuminuria and glycosuria have occasionally been found.

I have already referred in Section II to the derangements in the catamenial functions and remarked on the frequency of leucorrhoea. I have met with displacements of the uterus, endometritis, salpingitis and ovaritis, and amenorrhoea and menorrhagia.

I also noted in Section II the frequency of Catarrhal Conditions of the nose and pharynx and of the occurrence of asthma and bronchial catarrh.

## V. DIAGNOSIS AND PROGNOSIS.

Diagnosis. When the symptoms are well marked exophthalmic goitre is very easily recognised.

Difficulty in diagnosis only arises in the "incomplete" cases, "formes frustes" in which one or more of the cardinal symptoms do not develop. The tachycardia I have found to be the most constant sign and the disease ought to be suspected in every patient whose pulse rate, when at rest, is found to be above 90 per minute. Tachycardia<sup>and</sup> muscular tremor with general nervousness and excessive perspiration and flushing are quite sufficient on which to found a diagnosis. I have already remarked on the absence of goitre and exophthalmos in the majority of the cases I have seen in Lancashire.

In 1912 I saw a patient who was said to be suffering from "Graves's disease." The thyroid was slightly enlarged, and the pulse rate was 88 per minute. The nervous symptoms were not very pronounced and there was no apparent exophthalmos. She had had amenorrhoea for five months and had put on half a stone in weight during the same time. On examining the abdomen I found the uterus reaching nearly to the umbilicus and the foetal heart sounds were very distinct.

Prognosis. The disease varies in type.

There is an Acute form of exophthalmic goitre which,

fortunately, is rather rare. The symptoms develop quickly and the patient is seriously ill. The heart soon becomes enormously dilated and very irregular in its action - the condition of "delirium cordis." Intractable vomiting and diarrhoea may also be present. A patient suffering from this acute form may recover completely, or the recovery may be partial; - the condition lapsing into the chronic type of the disease. On the other hand, collapse or acute delirium may supervene with oedema, anuria, severe dyspnoea, and a raised temperature, leading to coma and death. I have seen two fatal cases of this type. The duration of the illness in one was three months and in the other eight months.

The Chronic form is more frequently met with. The symptoms may come on insidiously or may appear to set in suddenly after some severe nervous strain or shock. This form of the disease, as stated above, may also develop from the acute type. The patient is more or less an invalid for years. She may be able to go about and perform light household duties, but she is quite unable to undertake any laborious work. Acute exacerbations of the disease are very common and these are frequently brought on by an attack of catarrh or influenza or by any severe nervous strain. The acute attack added to the chronic may prove fatal.

This chronic type of exophthalmic goitre may last for many years and eventually the disease may pass off leaving the patient apparently perfectly healthy. Relapses or recrudescences of the disease are not infrequent.

The statistics given by the different authorities of the number of complete recoveries from the disease differ very widely varying from 30 to 80% of the cases observed.

A guarded prognosis must always be given, and one has to take into account all the signs and symptoms, paying special attention to the condition of the heart, the degree of the tachycardia, and the presence or absence of progressive emaciation, vomiting and diarrhoea.

## VI. TREATMENT.

### 1. General Measures.

Rest is of the greatest importance in the treatment of every case of exophthalmic goitre. When the disease is diagnosed the patient ought to be confined to bed and kept quiet for at least a month. She must be freed as far as possible from all worries and cares. Visitors should be strictly limited in number. The bedroom must be well ventilated.

The diet should be light and nourishing, consisting mainly of milk, cereals, fruit, vegetables, fowl and a little meat. Fish of all kinds must be avoided as it contains a considerable quantity of iodine which aggravates the condition and for the same reason ordinary table salt must be replaced by iodine-free salt or abstained from altogether. Tea and coffee are to be allowed only to a limited extent, while alcohol and tobacco are entirely forbidden. Attention must be paid to the bowels so that the patient may obtain a daily evacuation. (~~which is very necessary~~)

Before the commencement of this treatment the patient must be thoroughly examined. Every system must be carefully investigated and any diseased condition found should be immediately dealt with. Any catarrh of the nose or pharynx must be cured and carious teeth or

unhealthy tonsils should be rendered healthy or removed. Pyorrhoea alveolaris should be examined for and if found it must be thoroughly treated by a dentist and if necessary by vaccines.

Bronchial catarrh if present should receive attention and any sign or symptom of gastric, bowel, appendicular or gall-bladder trouble must be carefully investigated and if any diseased condition be discovered it must as far as possible be rectified. I have already remarked on the frequency of disorders of the genital organs in these cases. Leucorrhoea, vaginitis, endometritis, displacements of the uterus, disease of the ovaries and fallopian tubes and local cellulitis or peritonitis have to be enquired and examined for and when found must receive appropriate treatment.

With the help of drugs the above treatment may greatly alleviate the symptoms and may even cure the disease.

Patients who have undergone the rest treatment and are suffering from a mild type of the disease may be allowed a moderate amount of exercise, but any severe exertion or nervous strain or excitement must as far as possible be prohibited. A visit to some health resort often proves beneficial. The simple regular life with freedom from worry and with change of air and of scene,

sometimes does a great deal towards curing the patient. I have seen two severe cases greatly benefitted by a visit to Nauheim. They received the Bath treatment but did not do the exercises. In both cases the dilated heart became normal in size and the rate of its action was reduced. I have found artificial Nauheim baths carried out by a capable nurse in the patient's own home of considerable benefit when the heart was dilated or irregular in its action.

Local cold applications as Leiter's tubes on the thyroid have been recommended. In several of my severe cases an icebag applied to the praecordia continuously for twenty four or forty eight hours proved efficacious, to a certain extent, in quietening the heart.

## 2. Drugs.

Many drugs are recommended but none are absolutely specific. Apart from organotherapy, belladonna has been of most benefit in my cases. As recommended by Greenfield, large doses have to be given. The initial dose should be ten minims of the tincture three times a day and this is increased in a few days up to twenty or twenty five minims thrice daily. The patient soon complains of dryness of the mouth and the pupils become dilated. Then the dose should be reduced to five minims. Belladonna relieves much of the general nervousness and is often efficacious

in diminishing the excessive perspiration and flushing. In some of my cases while taking belladonna, the heart rate was reduced, but it is difficult to say how much of this reduction was due to the belladonna and how much to rest and general conditions.

Preparations of phosphorus are recommended. Phosphate of soda (twenty to thirty grains three times a day) or the syrups of the phosphate of iron and of the glycerophosphates (half drachm doses three times a day) may be given.

When the nervous symptoms are very pronounced bromide of potassium in doses of from ten to thirty grains is useful.

When the heart is dilated and irregular in its action cardiac tonics are indicated. I have found strophanthus to be the most useful. It is best given as the tincture of the 1885 Pharmacopoeia in five minim doses combined with two and a half minim doses of tincture of capsicum to prevent gastric disturbances. Digitalis is also recommended

Vomiting and diarrhoea if present require their appropriate treatment. In severe cases of vomiting rectal feeding must be resorted to.

Sleeplessness, delirium, etc., have to be treated symptomatically.

On no account must iodine or its preparations be administered to a patient suffering from exophthalmic goitre.

Organotherapy.

Many substances are recommended for exophthalmic goitre.

Extract of the Suprarenal Capsules.

The late Dr. G.A. Gibson at the meeting of the British Medical Association in Liverpool in July 1912 said, "In exophthalmic goitre no remedy approaches, even distantly, suprarenal extract in importance, and it may be regarded almost as a specific for the affection."

Thirty-five of my cases have had suprarenal extract. The preparation I employ is the tablet of dried suprarenal extract made by Parke, Davis & Co. I prescribe one of the two-grain tablets night and morning and then if they are not disagreeing with the patient I increase the number every three or four days till the patient is taking six or eight tablets (i.e., twelve or sixteen grains of the dried extract) daily. This dose is then continued if necessary for months.

A few patients, I find, cannot take the suprarenal extract at all. In some it causes gastric pain and sometimes vomiting and diarrhoea, while in others it aggravates the palpitation and causes severe headache. Many cases improve markedly when under this treatment. The tachycardia and palpitation diminish and the

general condition improves the patient often putting on a stone or more in weight. In the few cases in which I have recorded the blood pressure I have found that the improvement when taking suprarenal extract is much more marked in those whose blood pressure was below normal than in those whose blood pressure was already at or above normal. This of course is what is to be expected as the action of suprarenal extract is to cause "marked contraction of all involuntary non-stripped muscle" and so raise the blood pressure and also to cause slowing of the heart's action (Oliver and Schäfer "On the physiological action of extract of the suprarenal capsules," Journal of Physiology 1894-5).

Extract of the Thymus Gland is also recommended.

Dr. Guthrie Rankin in "The Clinical Journal," March 8th 1911, states that, though he is well aware that it often fails entirely, in his experience "there are patients who derive more benefit from thymus gland than from any other drug." He gives ten grains of the extract three times a day

Extract of the Pituitary Body.

This has not been extensively tried as the extract is very costly. In those cases where it has been tried the results reported have been very variable.

Extract of the Thyroid Gland itself has been given but it, as one would expect, was found to aggravate the symptoms.

The dried blood of animals from which the thyroid has been removed by operation is recommended. "Thyroidectin" is such a preparation and is given in doses of ten grains two or three times a day. One of my patients improved greatly while taking thyroidectin but in several others to whom I prescribed it I could find no alteration.

"Rodagen" is the dried milk of thyrosectomised goats. I have had no experience with it.

Various other sera have been obtained from animals but none have been proved to be reliable.

#### 4. X-Ray Treatment.

Faradisation and Galvarisation; Radium. These are methods of treatment of which I have had little or no experience.

One of my cases was treated by X-Rays and showed little or no improvement. Many cases are recorded in which marked improvement has followed the use of the X-Rays (Dr. Florence Stoney, On the result of treating exophthalmic goitre with X-Rays, B.M.J., August 1912). The great disadvantage of this treatment is the danger of causing dermatitis which appears to be very easily produced.

Faradisation and Galvarisation have been extensively tried but have not proved very satisfactory.

## 5. Surgical Treatment.

Mr. James Berry (in the Lettsomian Lectures No. II in Lancet, March 8th 1913) expresses "the belief that if sufficient care be taken in the selection of cases, and of the time and method of operating, much maybe done by operation for the alleviation of the symptoms, if not for the actual cure of these patients. Anything like indiscriminate operating for Graves' disease is, in my opinion, strongly to be deprecated."

Various operations are performed, viz: Exothyropexy and operations on the sympathetic nerves and ganglia; ligation of thyroid arteries and partial excision of thyroid gland. The last is the one that is usually performed in this country.

When the disease is very severe and of long standing the risks of operation are very great. The heart and other viscera are then in a condition of degeneration. Three of my cases had the operation of partial thyroidectomy performed. The operation was undertaken as a last resort and in each case it proved fatal.

"The dangerous cases in which operation in my opinion should not be undertaken, are those acute ones in which there is much thyroid intoxication as shown by great excitability, mania, or muscular weakness, or who are suffering from any acute inflammatory infection such as bronchitis; secondly, those in which marked degenerative

changes have taken place in the viscera especially the heart and kidneys." (Mr. James Berry, Lettsomian Lectures No. II, Lancet, March 8th 1913).

Dr. T.P. Dunhill in a paper read before the Surgical Section of the Royal Society of Medicine reported in Lancet, Feb. 17th 1912, said "I myself refuse to operate until I know that the patient has had three months' efficient medical treatment, unless there are present other circumstances influencing the case, and one is guided by all the circumstances."

## VII. SUMMARY AND CONCLUSIONS.

Exophthalmic goitre is a disease probably due, as is endemic goitre, to some toxin or toxins derived from some "living excitant" existing in some septic focus in the patient's body. This septic condition is very often some catarrhal affection of the mucous lining of some of the cavities or passages of the body. The toxin or toxins circulating in the blood cause enlargement of the thyroid. This enlargement is due to excessive activity of the gland. The secretion of the gland is not only increased in amount but is perverted in some unknown fashion. The symptoms of the disease are due to this increased and perverted secretion.

The essential symptom of the disease is rapid action of the heart and in every person in whom this is discovered exophthalmic goitre should be suspected. ~~(and looked carefully for)~~ Many cases do not show a thyroid enlarged to any appreciable extent and in many no protrusion of the eyeballs can be made out. The tremor and other nervous symptoms are important in the diagnosis of the disease and often require to be carefully looked for.

An acute form of the disease is found and it is often fatal.

The more usual chronic form may continue for many

years. It is not very fatal . Dr. Hale White in investigating the after-histories of a large number of patients found "that the mortality among sufferers from exophthalmic goitre was about twice that among the general population for the same age and the same time." (Debate at the Royal Medical Society 1912).

In the treatment of the disease an important point is to carefully investigate the case for any septic condition in any of the various systems of the body. Such a condition when found must be dealt with as thoroughly as possible.

The patient must not be given iodine or any of its preparations or any food as fish or common salt which contains in it a considerable amount of iodine.

Suprarenal extract is of value in the treatment especially in those cases in which the blood pressure is found to be below normal. Belladonna in large doses and bromide of potassium are useful in some cases. Strophthanthus is the best cardiac tonic. The Nauheim baths are beneficial when there is much dilatation of the heart with irregularity of its action.

Before advising surgical interference the physician should carefully consider all the special circumstances of the particular case under consideration and also satisfy himself that after at least "three months' efficient medical treatment" there is no improvement in

the patient's condition. An operation should not be performed where the patient is acutely ill or when the heart and other organs show distinct signs of degeneration.

BIBLIOGRAPHY.

Allbutt's System of Medicine, Vol. IV, part 1.

Article by Hector Mackenzie (contains full  
Bibliography up to 1908)

McCarrison, Milroy Lectures on Endemic Goitre,  
Lancet 1913.

Berry, Lettsomian Lectures, Lancet Feb. 3rd 1913.

W. Trotter, Lancet, March 9th 1912.

Proceedings of the Royal Society of Medicine,  
March 1912.

Discussion on Exophthalmic Goitre.

B.M.J., October 1, 1910. Discussion on the Operative  
treatment of Graves's Disease by Kocher and others.

=====



Figure I. Dr. Kellier's patient.

Figure II. Dr. Keliardi's patient.

