

T H E
E T I O L O G Y O F G O I T R E S .

by

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M.D. 1924.



Introduction.

There are many points of interest to the physician, and many facts the knowledge of which would be to his ultimate advantage, which are passed by without either comment or professional notice; the Student of Medicine, whose time and brain power are - if he be of the type which strives to go forward - beset by the necessity of satisfying his teachers and examiners, and, again facing the future with a sufficient knowledge of the Science and Art of Medicine, is too much engrossed with what are really only the foundations of knowledge, and those are admittedly of such an acreage as to leave him in a mental fog as far as many details are concerned. We have, therefore, a body of men of varying mental capacity annually presented for graduation in the junior degrees, who have no immediate tendency to pursue the science of their calling to any of its further ramifications, while many of these are overshadowed with the necessity for earning their daily bread and making a competence for their declining years; that aspect of the question of later years not being improved by the trend of legislation in this country, there are many tired men, dragging through the immediate tasks - though with an honest desire to do their professional and

humane duty - with no energy to spare for pursuing the bypaths lying outside the classical text books dealing with each branch of their subject. Is it then to be wondered at, that many, whose physical and mental equipment is limited, or whose purses are shallow, should pass by many facts and possibilities bristling with promises, and leave them for the investigation of those more suited - as they imagine - for such tasks? But I contend, as is now more freely admitted, that the General Practitioner, the first line of defence against the army of ills that beset the human body, is eminently the person to be encouraged to cut new paths into the forest of comparative ignorance in which it shelters: as the Physician and his colleague the Surgeon with their auxiliaries - Pathologist Radiologist and others - have more and more taken on the role of attackers, it still more behoves the rank and file of the first line to bring their intelligence and observation to bear in watching for counter attacks, and carrying hints to those who are qualified to deal with them: the analogy of the recent war is nowhere more exemplified than in this struggle of the Medical Profession against disease and the unhappiness that it brings: and the value of organisation and combined action, increasing manyfold in my own short experience, have nowhere else been demonstrated more completely than in the two cases; as in the type of

army service in which I had the honour to be placed, there was no more successful or healthy force than that in which the Commander made a point of sympathising with the troubles of his juniors, down to the lowest rank, so also, as one of the rank and file I would appeal to the organisers to go forward in their efforts (increasing in effect every day) - to keep in touch with the General Practitioner and by helping him to meet his difficulties, strengthen the first line of assault. The teaching of medicine is increasing in its scope, and I think I am justified in asserting that the standard - apart from the actual knowledge and literature at the command of the present day practitioner - is improving. Although there is no place in these pages for propaganda I feel called upon to suggest that the one thing at present still lacking (although that also improves rapidly) is an understanding by their teachers of the troubles and worries that afflict the lesser fry of the Medical Profession and hamper them in their progress.

These remarks have been made as a preliminary to the fact that I, as a general practitioner of medicine in this district and among a class of people who are not in a position to allow medical attendants to deal as freely with them as he undoubtedly should, have come across many abnormalities and diseases which would have repaid study - at least,

so I am convinced - which are not more than touched upon in systematic text books, while the further investigation of theories and proved facts dealing with them means time and expense which cannot be given by the average practitioner, unless he run the risk of involving himself in troubles which he does not seek. Among the varieties of abnormalities which have daily met me in my work, one of the most evident and striking is that of disease, actual or apparent, with enlargement of the thyroid gland: many of these cases are hidden, or presumed by me to be - i.e. they are shown not by signs but symptoms, while a vast number are the reverse, inasmuch as the disease has passed on its way and left its traces in the enlargement of the gland.

In the district in which my lot has been cast a large proportion of the populace, - I cannot find figures to show what that proportion is - are disfigured by "goitre" and during my service in a local Hospital where actually hundreds of persons weekly passed - albeit some of them rather rapidly - through my hands, I was daily impressed with the number who showed either the external appearances, or suffered from some of the symptoms, of disease of the thyroid gland. Admitting that my mind was sometimes impressed unduly with the frequency of the signs or symptoms, I was struck with the variations in these

symptoms with the general well-being of the patient, and hoped some day to go further into the matter: of later years I have been further impressed with a certain aspect of the matter which I propose to formulate as a thesis on a subject which I am convinced is too little realised either by the Practitioner of Medicine, or by any but a few of those who have specialised in many of its branches. The points which have impressed me, I have found on further reading, have been investigated by practical and scientific methods by others; if time and opportunity allow I hope to deal more fully with the subject: I propose at present to deal with what I, at present, consider of much importance to the student of medicine, namely the origin and ultimate results of certain abnormalities of the thyroid gland, on the assumption that much the larger proportion of those abnormalities are directly or indirectly due to bacterial infection by various channels.

As the point with which I wish to deal is mainly an etiological one, I do not propose to deal with treatment except in so far as it bears on the subject of the etiology: if there is an acceptance of my point of view the question of treatment is brought down to narrower limits, and the prognosis altered accordingly: the kind of cases which I propose to adduce are a comparatively small number brought

forward to illustrate the probabilities in favour of the thesis, and not picked for any special peculiarity or variation from the common type; circumstances have not permitted me to enter as deeply as I hope to do into the bacteriological question into which I now go superficially - the detailed bacteriology, though germane, is not essential to the point at issue.

The recognised forms of disease of the thyroid gland are to be grouped in the following manner:-

- (1) Simple congestion.
- (2) Inflammation (a) Simple.
 - (b) Acute Suppurative.
- (3) Tumours (a) Benign, "Adenoma" (varying types)
 - (b) Malignant, i Adenocarcinoma) varying types
 - ii Carcinoma) &
 - iii Sarcoma) stages
- (4) Goitre ("Bronchocele")
- (5) Degenerative Stages ("Myxoedema" & "Cretinism")
- (6) Exophthalmic Goitre ("Graves'", "Basedow's" or "Parry's" Disease)

All the above divisions are essentially, as far as the gland alone is concerned, represented in variations of the secreting structure of the gland, even to complete destruction; the gross pathology and external appearances being brought about either directly or more remotely by such variations: it is my object to point out that, possibly, and even

probably, these changes originate from a common cause; and I cannot exclude even the so called "malignant" cases from this category, for it has been for many years firmly believed by many that the malignant diseases are all of bacterial origin.

In the district in which I practise the incidence of diseases of the thyroid gland is heavy: geographically situated close to a hilly district which has given its name to the commonest form of thyroid disease in "Derbyshire Neck" and lying on the most south-westerly spur of the same mountain system, the Pottery Towns of North Staffordshire are peculiarly liable to a high rate of thyroid disturbance; the district is very largely an industrial one; a large proportion of the workers are notoriously ill paid, the proportion of female workers is high, and the housing conditions are in many extensive areas, atrocious.

The water supply is almost entirely Deep well - there is, in the Towns comprising the group known as the Potteries, no supply, at least of any amount, obtained from river or shallow wells.

In General and Institutional practice I have come across a considerable number of cases showing nearly all the recognised characters of all types of thyroid disease; the commonest of the definitely marked cases is the type commonly called "goitre" and with localising place - names added in many cases.

Localised swellings of either lobe or isthmus, or part of any of these divisions are also extremely common: while evidence of different grades of diminution or apparent absence of the essential secretion of the thyroid gland is peculiarly common; as an instance I may mention that out of one day's medical out-patients numbering 28, six showed definite signs of that condition which may be described as "athyrea" varying from slight symptoms to severe myxoedema.

Acute Hyperthyroidism, the condition believed to be produced by excessive secretion of thyroid substance, is also very frequently seen as "exophthalmic goitre", and certain of the adenomatous enlargements: among the 28 out-patients mentioned, there were two severe cases showing these symptoms and appearances, making a total of eight - that is, 28.5% of the people attending one department in one day had (or showed sufficient evidence to presume that they had), some abnormality of thyroid secretion: admitting that this was a coincidence and an extreme case, it sufficiently demonstrates the assumption that faults in thyroid physiology are causing a vast amount of physical and mental deterioration: I contend that diseases of the thyroid gland may justifiably be classed as a very potent group of enemies to human evolution and advance. While we cannot approve of the easy-going method adopted by some physicians of prescribing preparations

of thyroid substance to all and sundry where the diagnosis is incomplete or absent, there is a partial justification for such supervision in the frequency of both slight hypothyroidism and successful results.

Histology.

Before considering the diseases that effect the thyroid gland, it is essential to have a grasp of its normal microscopical anatomy. The thyroid is limited and supported by a firm fibrous capsule from which septa pass in, to divide the contained secreting tissue into lobules, and along which divisions, pass a very free blood supply and lymphatic drainage; the vessels and lymphatics are capable of considerable increase in content, with the requirements of the gland. The essential part of the gland - its secreting mechanism - consists of small cysts lined with epithelium and containing a colloid material. The cystic spaces are, developmentally, the remains of the ultimate branches of a racemose gland, the main duct of which is the thyroglossal duct. The main secreting epithelium in the spaces above referred to is essentially of the type of all secreting epithelium, and changes in the gland function are the result of alterations, mechanical or otherwise, in the capacity of these cells to secrete the colloid material in the enclosed spaces in its correct amount

and character to meet the requirements of the individual.

The colloid material is regarded as, not the essential secretion of the cells, but as the vehicle for it, the active ingredient being mixed with the colloid, and bearing no relation, as far as quantity or potency go, to the total amount of "colloid" in the gland. There may be small sections of the original gland cut off in the course of development as "rests" and incomplete closure or obliteration of the main duct may occur as a thyroglossal cyst or cyst-adenoma in the track of the original duct.

In close relation to the gland lie the parathyroid glands, two on each side close to the lateral lobes and in some animals actually embedded in it.

The Pathological alterations in the secreting epithelium can best be considered with the different macroscopic changes in each type of abnormality of the gland as a whole. A point of interest to the biologist lies in the fact that the thyroid gland is developed in separate sections - two lateral ones from the hypoblast of the fourth visceral cleft (seen in the fully developed gland as the lateral lobes) and a third, centrally developed as an out-growth from the pharynx which eventually forms the isthmus, its duct becoming the duct for the whole gland in some of the lower forms of life where the thyroid continues to exist not as an internal but an alimentary-tract-secreting organ: although the suggestion

may be partly discounted by the fact that, seen in some mammalia, the isthmus (macroscopically) does not exist, it is a possibility - which I have not heard contradicted - that the thyroid is a multiple gland, analogous to the pancreas or pituitary body: the fact that one frequently sees a central enlargement, with very little increase in either ^{of} _A the lateral lobes tends to the impression that we may one day find that we are dealing with a more complicated problem in bio-chemistry than the physiologists have realised, or at least expressed.

The colloid material contained in the enclosed spaces of the thyroid gland is a gluco-protein substance secreted by the epithelial cells lining them, and closely allied in composition to mucin, which is a normal product of many other secreting epithelium cells, and secreted by extrusion from the secreting end of the cell of droplets, formed by the fusion of smaller ones and without much destruction to the structure, or interference with the vitality of, the cell; colloid material differs from mucin both in its manner of formation and its substance, in as much as it is formed from the casting-off of the cell body along with its contents, the cells themselves becoming swollen, degenerated, and cast off into the spaces, and combined as an almost homogeneous mass known as "colloid". In Pathological conditions of the thyroid gland the material contained in the spaces may become either more mucin-like, or a less watery

colloid than normal, according to the rate of its formation, the amount of cell destruction, or the speed at which its watery content is absorbed into the drainage system of the gland: and the process of formation may be demonstrated in abnormal conditions of the gland by the recognisable differences in the centre and periphery of the colloid spaces.

Pathological Changes:

Atrophy. The type of atrophy occurring in old age is a simple fibrosis - a degenerative process of all the gland structure, shown chiefly by an increased formation of the fibrous supporting structure of the gland and its vascular contents, accompanying which, and partly as a result of it, the epithelial cells are altered in appearance and secreting capacity.

The other form of atrophy - that resulting from earlier pathological changes, apart from the degenerative ones accompanying old age, is seen in the type of gland found in persons suffering from abnormal alterations of secretion, in the condition known as myxoedema; here the fibrosis may become extreme and accompanied or hastened by an invasion of the connective tissue by cellular elements, leaving little or no trace of the original structure; these changes may follow on other conditions, inflammatory or degenerative, including Syphilis. Other forms of degeneration found in the thyroid gland are:-

Waxy Degeneration: originating in the same manner and for the same reasons as in other structures.

Cloudy swelling: affects the secreting cells as in other tissues exposed to toxic conditions producing changes in their secretion - alterations in the character and constitution of the contained substance from its normal colloid nature.

Tuberculosis is rare.

Abcess formation sometimes occurs in pyaemia or infected embolism. Direct infection from neighbouring tissue is almost unknown: a wound penetrating the capsule may cause a local abcess in the gland; apart from wounds (including infective needle wounds) the only way that Acute Thyroiditis occurs is via the blood stream: Edwards of Baltimore (1) quotes Kocher as holding that the blood stream was the only possible way by which an acute infection could reach the gland, inferring that therefore no "primary acute inflammation of the gland can occur.

The gross changes in the Thyroid Gland arising from any one or a combination of more than one of the above changes are commonly classified as follows:-

- I. Congestion.
- II. Thyroiditis.
- III. Tumours (a) Benign (b) Malignant.
- IV. Goitre, "Simple" (a) Parenchymatous (b) Colloid
- V. Exophthalmic Goitre.
- VI. Hypothyroid or Degenerative Conditions.

1. Congestion: this may be attributed entirely to temporary vascular changes occurring at times when the need for increased metabolic changes in the gland arises out of the needs of the individual in either of its presumed capacities of dealing with developmental changes or assisting in the arrest of a toxic attack, bacterial or otherwise. The enlargement occurring in woman, at all the crises of her reproductive life is sufficiently definite to have attracted the notice of those outside the profession of medicine: many have remarked on the enlargement that frequently occurs in disease not confined to the organ and one does not require to be on the watch for changes to notice them in febrile conditions, especially in women.

Years ago I was struck by the way in which text books of medicine dismissed what appeared to me to be such a frequent occurrence in febrile states, and the latest edition of Osler's "Principles and Practice of Medicine" remarks that "slight enlargement is common in acute infections". I will have an opportunity of referring to this point as it bears definitely on the subject of my suggested argument.

2. Thyroiditis. This is an inflammatory, infective, state of the gland, which may be "Simple" or Suppurative. It is not a common condition -

I have never seen a case that could not be described as a generalised infection in the whole gland or any considerable part of it although the very common so called "Simple Adenoma" or "Toxic Adenoma" is an apparent inflammatory process limited to a part of the gland: Thyroiditis occurs in various acute infections of which the most commonly reported have been Typhoid Fever, Smallpox, Measles, Rheumatic Fever, Mumps, Diphtheria, Erysipelas and Puerperal Fever, and epidemics without defined sources have been reported.

The whole gland may be swollen and tender, with reddening of the skin over the part, and may break down and become fluctuating and purulent: in cases where actual pus formation has not occurred a spontaneous cure may result or it may have to be opened and drained. These cases are invariably secondary to haematogenous infections: the views of Kocher - as quoted by Edwards - that this is always the case for anatomical reasons are difficult to controvert: the same writer Edwards notes that Croth pointed out that thyroiditis was found in connection with those fevers only in which the organism had been isolated, but this is not the rule - Osler in "The Principles and Practice of Medicine" mentions smallpox, measles and mumps, in none of which has a causal organism been isolated.

There is a particular type of unknown origin mentioned by Riedel, rapidly developing and involving the whole gland and compressing surrounding tissues, the normal gland being replaced by a hard fibrous mass. A case has been reported (2) by Geo. R. Murray and F.A. Southam.

3. Tumours. (a) Benign Tumours: These are exceedingly rare.
1. Actinomycosis is stated to have occurred, although I cannot find a record of a case; in view of the local nature of the growth of the ray fungus it seems probable that the mention of this granuloma in connection with the thyroid gland refers to local erosion, as the commonest sites of actinomycosis in human cases are the jaw or neck.
2. Tuberculosis: This is occasionally seen as miliary tuberculosis: and tuberculous nodules are very occasionally found in children.
3. Syphilis: supposed to be the origin of fibrous overgrowth in some congenital or infantile cases: and occurring very rarely as gummata in the thyroid gland.
4. Simple Adenoma: this is a very common condition and is supposed to be always of an infective origin; it is essentially an epithelial proliferation localised to one part of the gland and surrounded by a more or less dense connective

tissue overgrowth, forming a capsule round it and eventually so restricting the vascular supply as to bring the process to an end.

(b) Malignant Tumours:

1. Malignant Adenoma, in which the abnormal epithelium overgrowth - from some as yet undefined cause - is liable to metastasis.
2. Carcinoma: possibly arising from the squamous epithelial lining of one of the original ducts of the racemose rudimentary thyroid.
3. Sarcoma: the gland, like any other organ whose supporting structure is of mesothelial origin is liable to take on the uncontrollable growth which we call malignancy.

The latter two of these malignant tumours do not frequently originate in the thyroid gland.

Accessory growths of both the normal thyroid tissue and its abnormal variations may occur in other parts of the thorax and in the vestigial track of the rudimentary thyroid duct, aberrant thyroid glands and cysts produced from enclosed portions of the duct: even the "cystic hygroma" of the neck has been ascribed to a degenerated "rest" from the rudimentary lateral lobe.

4. Goitre: the term is applied in this country to a common condition defined by Osler and others

as "a chronic enlargement of the thyroid gland, of unknown origin, occurring sporadically or endemically" and is a general overgrowth which consists histologically of a collection of small cysts which are simply enlargements of the colloid spaces of the thyroid gland containing an altered content and lined by an altered epithelial lining. The alterations in the spaces may be limited to a part or parts of the gland or may be present in every part of it.

The individual cysts may be partly invaded by an overgrowth of the lining epithelium in the form of papillary outgrowths, or the cystic character over-shadows the epithelial one: the enlargement may be largely produced by increase in the fibrous supporting tissue and diminution of the secreting elements.

In many cases the enlargement is caused by an increase in bulk of an apparently normal tissue with all its elements in their approximately correct proportions - this is the type commonly referred to as a parenchymatous goitre.

A special type of thyroid enlargement, first investigated by Chagas, in Brazil, is attributed to a Trypanosome (*Schizotrypanum Cruzi*) found to be conveyed by the bed-bug (*Cimex lectularius*) and a fly (*Conorrhinus megistus*).

Clinically it is a rapid acute condition with severe nervous symptoms, enlargement of spleen, liver, and lymph glands, pain and swelling of thyroid, continued fever and the presence of trypanosomes in the blood-stream during the acute stage; if the disease is not fatal, the common result is an enlarged and degenerated gland with symptoms of athyroidea.

- V. Exophthalmic Goitre: known also as "Graves'", "Basedow's", or "Parry's" Disease. This is the term applied to a group of symptoms, one of which is frequently an alteration in the size of the thyroid gland, and another is an abnormal prominence of the eyeballs: in cases which have reached the stage of showing this ophthalmic sign the gland is generally enlarged to an extent sufficient to be noticeable. In addition to the enlargement of the gland there is a varying degree of softness of the gland as a whole, and the increase in the volume of the blood supply is indicated by the visible pulsation which frequently occurs in it and the veins in its neighbourhood which are often considerably dilated.

Histologically, there is always a change in the secreting tissue peculiar to this disease, which is seen as an increase in the extent of the

secreting cells, not brought about only by an increase in the surface extent of the acini, but an actual proliferation of the epithelium lining them, which may be wrinkled, so as to produce processes projecting into the spaces: while the individual cells show changes in an increase in depth and, often, signs of division; at the same time the amount of the colloid diminishes in amount proportionately to the size of the organ: in the occasional cases in which there are enlarged spaces or cysts the contained medium is of a more fluid consistency than the so called "colloid".

With the above changes there is found, during the active period of the disease, an increase in the cells around the interacinar vessels: the late Professor Greenfield used to impress us with the fact that the pulsation noticed in the gland in Exophthalmic Goitre was due more to the vessels lying behind and around the gland than the distributing branches within.

Along with the macroscopic and histological changes ~~are~~ symptoms referable to other organs, not seen in other thyroid diseases, and mainly affecting the Haemopoietic and nervous systems. In later stages of the disease, when degenerative processes have commenced, the proliferation of the connective tissue elements may be replaced by a fibrosis more like that found in the colloid enlargement. The changes in the

gland in Exophthalmic Goitre are therefore seen to be of the nature of an increase in its secreting activity, but this is found to be not simply an increase of a normal secretion but, in addition, an alteration in the constitution of it.

The alteration or increase in the secretion is caused, or accompanied, by an increase in metabolism, along with alterations in the action of other ductless glands, and of some elements of the nervous system: the actual connection between the thyroid and other ductless glands, and the effect of either or both on the nervous system is a subject which is still one of conjecture only: the superficial nature of our present knowledge of the subject is indicated in a short article (3) in Vol.XII of the Canadian Medical Association Journal where it is suggested that the relationship between the thyroid and adrenal glands is a definite one, and that they have some sensitizing action on each other or the tissues, possibly through sympathetic nerve endings; the theory is so vaguely touched on as to indicate the present state of our knowledge of the matter.

The point that is perhaps more definite, as far as the chemical pathology of thyroid diseases has been investigated, is the alteration from the normal in the content of iodine: this in Exophthalmic

Goitre is always diminished, and it is to be noted that the amount is increased in those conditions of the gland where the normal amount of the true colloid material is increased: whether the explanation which has been given - that the absence of iodine is due to the rapid absorption of the colloid, the iodine - containing body, into the circulation - is the only one, is still a matter for conjecture; it is the case that the exhibition of iodine in absorbable form stimulates the activity of the gland.

Hypothyroid Conditions.

These are seen in various stages, and showing various effects, immediate and remote, in three main groups; but showing the same effects varied only by the difference in the age of the patient at the time of the removal of the thyroid influence.

As the difference in the at thyroid person from the normal individual is most strikingly seen, by comparison, in the condition known as Myxoedema I will refer to that variety first.

1. Adult Myxoedema: a condition seen more commonly in women than in men: the thyroid gland is found to be atrophied and may eventually become a fibrous mass with few traces of secreting tissue except a few ducts surrounded by small round cells.

2. Operative Myxoedema - of which the symptoms are the same as in the degenerative variety, - occurs as a result of removal of all, or part of, the thyroid gland.

3. Congenital Athyrea - in which the thyroid gland is either completely absent or only vestigial, its absence of function resulting in profound alterations in the growth and development of the individual.

Symptoms.

For the purposes of the argument which I wish to evolve, the conditions of the gland which require consideration are those of the two most common types, namely, (a) Simple or toxic adenoma (b) Goitre, endemic or Epidemic, and (c) Exophthalmic Goitre.

- (a) "Simple" Adenoma or "Benign" Adenoma (which may be merged, in classification, with "Toxic Adenoma")

It is to be noted at this point - which demonstrates in a marked degree the stage at which the enquirer finds the literature on the subject - that the classification of pathological conditions of the thyroid gland varies considerably: I have therefore adopted a classification which appears to me to be the simplest, as the result of observation and consideration of recent literature;

admitting perhaps, that such a classification may suit my purpose by corresponding with a possible obsession in a certain direction.

The Benign Adenoma may appear at a comparatively early age, even in children of a few years, and most commonly before the age of 30: it may declare itself as a tumour in the general enlargement of the thyroid seen in growing boys and more frequently, girls.

The simplest form of Benign Adenoma is a nodular enlargement of one part of the gland, single or multiple, frequently confined to the isthmus and causing no symptoms; the enlargement may, however, be so situated, and progress in such a direction, as to cause definite pressure symptoms on the structures of the neck and thorax: the tumour of the gland may pass downwards behind the sternum and may compress and flatten the trachea from in front, either side, or both sides, producing dyspnoea which is liable to periodic and frequent nightly attacks with, some times, alteration of the voice. Both the dyspnoea and voice changes may be produced by pressure affecting the recurrent laryngeal nerve on either side. The veins of the neck may also be compressed and, occasionally, the vagus nerve.

Mr. James Berry (4) has emphasised the frequency of the occurrence of retrosternal enlargement

of the gland from a large operative experience.

The Toxic Adenoma (so called) shews, in addition to the possible pressure symptoms mentioned above, a group of other symptoms which approach those of another group - the Exophthalmic Goitre. The adenoma may be single or multiple and may be a large cystic mass often described as a simple goitre; there may be pulsation in the neck. There is frequently tremor of the hands, restlessness and irritability which sometimes becomes very marked; fairly rapid loss of weight and energy, a moist skin with tendency to sweating and inability to stand heat: in acute cases there is frequently, in my experience, a definite exophthalmos, though I have not seen a case where there was any question of the classification of the condition, as between an adenoma and a true exophthalmic goitre, in which the signs, to be later referred to, associated with exophthalmos, were definitely present.

There is frequently a definite tachycardia, the pulse ranging not so high as is to be found in cases of exophthalmic goitre. At this active stage, the blood pressure is frequently increased. With regard to exophthalmos I cannot agree with the view that this does not occur in cases which can justifiably be classed as toxic adenoma. Sudden or

rapid increase of symptoms, or at least those associated with increase of size of the thyroid tumour, are always suggestive of haemorrhage within the substance or capsule of the growth, or malignancy.

E.M.Eberts (5) in comparing the conditions of Exophthalmic Goitre and toxic adenoma, definitely states that exophthalmos and other signs are conspicuous by their absence: the case of M.J. (case 15) in which the appearance was at first sight more than suggestive of true exophthalmic goitre, and others similar, have convinced me that true exophthalmos can exist in cases where the gross changes, at least, are localised to one part of the gland: the possibility also exists that there may be occasional cases in which there is a general change, of the same nature as that occurring in exophthalmic goitre, in a gland the seat of a localised encapsuled adenoma. The classification of toxic and non-toxic goitre indicated above is purely a clinical one: there has, so far, been no definite differentiation by the pathologist, as the Microscope has not yet shown us where we may draw a line between the actively and potentially toxic gland.

J.M.Blackford (6) expresses the present stage of our information on this point, in his statement that "it is an unsettled question whether all adenomata eventually become toxic" but inclines to the belief that all adenomata are toxic at some stage in their

histories: the result of further investigation of the value of tests of basal metabolism may eventually help us to come to a useful conclusion. Blackford suggests that "the lack, or severity of symptoms is only an expression of the patient's resistance to the toxicity of that particular goitre". I should express it that the symptoms, or lack of them, are an expression of the patient's resistance to the toxicity of the influence producing the goitre, and the identity, virulence, and dose of the causative factor - presuming that the presence of a tumour believed to be associated with a toxæmia is itself produced by that toxæmia, either as a part of the process of resistance, or a pathological accident associated with it.

The symptoms of malignant Tumours of the Thyroid are those produced by pressure on, and destruction of, surrounding structures, and fixation of the tumour - among these are dysphagia, dyspnoea, cough, hoarseness, congestion of the face and the various signs of pressure on afferent, efferent and sympathetic nerves.

The progress of symptoms varies with rapidity of the tumour growth; adenocarcinoma being of slower growth than the uncommon sarcomata which are liable to rapid increase and invasion. Other symptoms are those associated with metastases of the growth in other structures, most commonly bones and lungs.

It is to be noted that the malignant Thyroid tumours are most often found in goitres in which there is already-existing disease.

- (b) Goitre, "Bronchocele," sometimes referred to as "endemic" or "epidemic" goitre is spoken of as "parenchymatous" or "colloid" according to the presumed histological abnormality existing in the enlarged gland. The symptoms associated with this variety, which Osler defines as "a chronic enlargement of the thyroid gland of unknown origin occurring sporadically or endemically" are much the same as those referred to under "adenomata" above - that is, they are all associated with the presence of enlargement of the gland and resulting pressure on neighbouring parts.

One of the first symptoms is commonly produced by pressure, through the enlarged gland on the trachea or veins, of the clothing; it is surprising how, in the working classes, the swelling is overlooked or ignored till the increasing difficulty of fastening a collar forces the sufferer to look for a reason.

As a further (or preliminary) symptom, dyspnoea is common, and paroxysmal attacks, often occurring at night, and sometimes producing an

inspiratory stridor, are sometimes the first evidence of an enlargement.

Along with the symptoms due to pressure there is often an involvement of the heart, and the term "Goitre heart" has been applied to the group of symptoms produced by increased irritability, and recognisable dilation of the heart, often associated with what is looked upon as a harmless chronic enlargement of the thyroid. (I shall take an opportunity of referring to this particular point later).

The cardiac symptoms have sometimes been attributed to pressure on nerves, vagus or sympathetic.

Symptoms may be rapidly increased by the development of cysts and most rapidly by haemorrhages which frequently occur in the more vascular parenchymatous type. Between the two commonly recognised types "Parenchymatous" and "colloid", and the degenerative cystic or fibrous conditions which often result from them, no symptomatic distinctions can be drawn with any attempt at definition, as the symptoms of these types or stages of change in the gland may be combined in various ways.

Prognosis of Goitre: This varies with type and size of the affected area of the gland: but there is frequently complete recovery, while the tumour may

remain as an inert disfigurement.

In relation to the question of prognosis we come back to that of the differentiation of different types of thyroid disease, and find that, omitting cases of malignant disease and uncontrollable cases of Exophthalmic type, there is no mention of mortality "qua" thyroid disease: all of which implies or suggests that the commoner forms of goitre - except where they happen to cause death from pressure, - end in cure, spontaneous, medical or surgical, in myxoedema of various degrees, or develop exophthalmic or malignant characters.

- (c) Exophthalmic Goitre: The Symptomatology of "Exophthalmic Goitre" is largely covered by the definition of the disease as given by Osler - " a disease characterized by goitre, exophthalmos, tachycardia, and tremor, associated with a perverted or hyperactive state of the thyroid gland and increased activity of the vegetative nervous system". Osler goes on to say that a distinction should be made between hyperthyroidism and "Graves" disease, that not all the cases of over-activity of the gland go on to exophthalmic goitre, but that it is probable that the possibility of this progress exists, and that it may be difficult to classify the border line cases. A pronouncement

of this nature, in a recognised standard text book published in 1923, gives a pointer, as it were, to the difficulty that exists in giving a true definition or tabulating the etiological factors in the various "goitres": while the grouping under the same paragraph of "Hyperthyroidism" and "Exophthalmic Goitre" in a text book so given to statistics as "The Principles and Practice of Medicine" is calculated to further increase the effort to acquire an accurate knowledge of the Etiology and symptomatology of the diseases involved.

The onset of symptoms is usually gradual but occasionally rapid: Osler quotes a case in which the patient died on the third day, presumably from the direct effects of the disease.

The characteristic signs and symptoms, which bear no regular relationship to one another as regards either time or degree are

1. Enlargement of the Thyroid Gland is most frequently uniform but may be more marked on one side: I have heard it stated that the right side is most commonly enlarged first but I have not noticed that myself: the enlargement bears no relationship to other symptoms and may be comparatively slight.

On palpation the tumour varies in consistency but it is mostly soft: it is rarely, if ever, tender

and a thrill can be felt in most cases where the tumour is large and the symptoms well developed, and pulsation can mostly be felt and frequently seen, and in auscultation over the gland a loud systolic or "to and fro" murmur can be heard; the enlargement may also produce pressure symptoms, although the soft consistency of the gland makes these comparatively uncommon in relation to the amount of enlargement, unless there is a tendency for the thyroid to push its way behind the sternum.

2. Tachycardia: in which the pulse may become uncountable, and which is aggravated by the slightest external influences. Along with this one finds the cardiac area and the extent of visible or palpable pulsation much increased and forcible, while ^{of} there are mostly loud murmurs to be heard over some [^] or all the cardiac orifices, and the pulsation can be seen in the vessels of the neck; the late Professor Greenfield used to insist that this was the origin of the pulsation ascribed to the intra-Thyroid vessels. When the heart muscle becomes seriously affected irregularity of the pulse occurs.
3. Exophthalmos.

This is the term applied to the prominence of the eyeballs, both real and apparent, the

appearance of prominence being added to by certain changes in the surroundings of the eyeball, the lids being retracted over the upper and lower ophthalmic conjunctiva.

The nervous or mechanical method of production of exophthalmos has never been satisfactorily explained: it is partly accounted for by the deposition of fat within the orbital cavity and also by a supposed spasm of the orbital muscle of Muller.

This exophthalmos is the last symptom to disappear when the hyperthyroid state has regressed for some time and allowed the nervous and vascular system to approach the normal: it has no definite effect on vision, except of course in such cases as those in which it has led to damage to the eyeball by excessive extrusion.

Certain signs looked upon as diagnostic of true "Exophthalmos" are:-

- (i) Von Graefe's: When the eyes are widely opened and the patient looks down or follows a descending object, the sclérotic above the corneal margin is visible below the more slowly-falling upper lid.
- (ii) Stellwag's Sign: along with a wide palpebral fissure there is a spasm of the levator palpebrae superioris, so that the normal act of periodic winking is less frequent & complete.

- (iii) Moebius' Sign - want of optic convergence for near objects unaccompanied by the subjective accompaniment of diplopia.
 - (iv) Joffroy's sign - absence of the wrinkling of the brows seen normally when the individual looks upward.
4. Tremor - rapid and fine, most noticeable in hands but actually affecting the whole limb.
 5. General Nervousness - The patient is easily startled, and, along with this, are, temperamental changes, irritability which in very severe cases goes on to uncontrollable mania and is a common cause of death from exhaustion.
 6. Vasomotor Skin Changes: The patient flushes easily and perspires freely, and does not tolerate external warmth; the skin occasionally becomes pigmented.
 7. Headache of a thumping character.
 8. Nutritional Changes: Loss of weight which may be very severe, and loss of physical energy, with anaemia (chlorotic). There is sometimes pyrexia, severe in very acute cases.
 9. Alimentary: Both vomiting and diarrhoea occur in

rapid cases.

10. With anaemia - there are sometimes alterations in the differential leucocyte count - a lymphocytosis is frequently found, although only relative, the total leucocyte count being little or not increased in many cases showing severe symptoms, and an actual leucopenia does occur.

PROGNOSIS OF EXOPHTHALMIC GOITRE.

This is difficult to gauge as there are undoubtedly many of the milder cases which do not come under continued observation: the fact that there is marked nervousness and shyness as a result, keeps the poorer class of patient away from the medical attendant unless symptoms become unbearable: of the cases which come under systematic treatment and observation - the acute ones - the disease progresses for a period of a year or more, with remissions and relapses, and sometimes ends in degeneration of the gland and myxoedema: death results from general asthenia, cardiac weakness, sudden heart failure or superimposed disease in numbers variously estimated at 10% to 25%: Hale White gives 84 in 214 cases - 39 %.

Prognosis in particular cases depends on the general condition and surroundings of the patient, while the prospect is poor if the stage of emaciation, much cardiac weakness, or severe mental

changes have appeared.

The future of the exophthalmic sufferer has been improved of recent years with the advances in surgery and anaesthesia and with the increased efficiency of hospitals. It is my object to emphasise how further co-operation between the different branches of medicine and surgery, and the team-work which results, may possibly lower the actual and relative mortality, at least in civilised countries.

on

I have proceeded in an unconventional manner with the arrangement of the heads of the subject up to this point, with the definite object of narrowing down the argument in a definite direction: having omitted anything but a passing reference to those varieties of thyroid disease in which the cause of the condition is not in question, and where the classification is as complete as we can make it. I have mentioned the histology, pathology, symptoms, diagnosis and prognosis of the varieties which we so far consider to be produced by external agencies, be they toxic, organic or inorganic, psychic impressions, or any of the previously suspected causes, and may now touch on their clinical differentiation and, later, the recognised methods of treatment leaving the question of Etiology, which is properly the subject of my thesis to be dealt with under a separate section .

Thyroiditis, simple or acute which may be suppurative, is extremely rare, and, if found, the question of its origin would probably not be in doubt, the condition being similar in character and course to acute inflammatory processes in other tissues and always secondary to other infective processes.

There remain (1) Benign adenomata.

(2) Goitre or Bronchocele, Parenchymatous or Colloid.

(3) Exophthalmic Goitre.

Malignant diseases and Hypothyroid conditions may, for the purposes of this paper, be ignored.

1. Benign adenoma may be either single or multiple and can most often be seen as a definite localised swelling in some part of the gland: it is said to be more often found on the right side, though I have not noticed this, and have seen it occupying the isthmus as frequently as either of the lateral lobes; it is discrete and can mostly be distinctly palpated as a globular mass of different consistence from the rest of the gland, which is frequently generally enlarged also: it frequently occurs in a gland the subject of the parenchymatous type of goitre.

The adenoma varies in its consistency as

it does in microscopical histology, in that it may be found to possess all degrees of variation in its secreting epithelium and the amount of contained colloid. It is not easy to distinguish malignant adenomata from benign forms until the characters of malignancy - invasions, fixation or metastasis - declare themselves, while the carcinomata vary in type and character, macroscopically, in a fashion similar to the simple adenoma.

2. Goitre or Bronchocele can be distinguished by its general character, apart from presumptive evidence associated with its endemicity: the whole gland or a lobe may be involved. The terms often applied, "parenchymatous" and "colloid" or "cystic" describe the varieties most commonly found histologically although the peculiarities indicated by these adjectives appear to apply simply to various stages in a degenerative process.
3. Exophthalmic Goitre - is distinguished from the two above partly by physical signs but mainly by symptoms involving the general vascular and nervous systems. There is not always a very great increase in the size of the gland (the largest goitres commonly seen are the cystic types of bronchocele) and the enlargement does not bear

any relation to the number of degrees of the symptoms.

To differentiate exophthalmic or hyperthyroid goitre from others, we have the tachycardia, exophthalmos, and tremor, with the cardio-vascular and nervous accompaniments mentioned under the head of symptoms. It must however be understood, that, if we really attempt to draw a definite line between Adenotomata of the so called Toxic type, and true exophthalmic goitres we cannot help but realise that in several of these characters the difference is one only of degree: in cases which one has eventually to place in the category of adenomata and which regress without developing the marked symptoms which we look upon as those of exophthalmic goitre, it is not uncommon to find a moderate degree of tachycardia, a staring expression suggestive of exophthalmos, and tremor almost as violent as is seen in that condition. It appears to me that, even if we include recent work on metabolism as measured by heat and waste production, these distinctions become a matter of degree alone, and except we classify the different conditions by virtue of their progress or results, or by the amount of the gland involved in each case, we cannot make a distinction which is quite convincing: certainly we find that the adenoma

(so-called "toxic") is a localised condition of the gland, while exophthalmic symptoms are found in those in which the changes in the gland occur through-out the whole extent or greater part of it.

It is, I think, admitted that the differentiation of adenoma or "nodular" goitre and true exophthalmic goitre sometimes presents difficulties which should not exist if some of the distinctions were not inclined to be somewhat arbitrary.

At a meeting of the Royal Society of Medicine in 1912, Dr. A. Kocher (7) dealing with the indications for operative treatment of exophthalmic goitre, classified the "hyperthyroid" goitres as:-

- (1) With symptoms of hyperthyroidism with only occasionally pronounced hyperthyreosis, not progressive or continuous.
- (2) Steadily progressive.
- (3) Periodically progressive.

Dr Kocher pointed out that it was only in the latter two of these groups that marked injurious results to other organs occurred.

TREATMENT.

Reference to the question of treatment of thyroid diseases is made for the reason of what appears to me to be its direction bearing on some of the

probabilities with regard to etiology; but once again the lack of distinction and classification of types introduces difficulties.

The Adenomata "Benign or Simple" by which terms, according to the method of classification I have adopted, I imply nodular enlargements which I am presuming to be toxic in origin, and which are typically encapsuled; there seems at present to be a general concensus of opinion that surgical removal is the only satisfactory method of treatment; it must however be remembered that in those cases in which the process has become stationary or retrogressive, the tumour being well encapsulated and itself fibrous or otherwise degenerated, operative measures are required for three reasons, not connected with the actual present toxicity of the growth but

- (a) as a precaution against the possible development of malignant character.
- (b) To prevent pressure effects.
- (c) To remove unsightly growth.

In the active or toxic state of the toxic adenoma, surgical removal (decapulation) with as little as possible of damage to the unaffected part of the organ, results in a rapid improvement in the patient's

condition and lessening of the symptoms referred to above, the nervous symptoms, the tachycardia, and even the lesser degree of prominence of the eyes sometimes seen in these cases.

As a preliminary to operative treatment, - it is most important to procure an adequate preparation of the patient, by complete rest; and the evidence of rapid improvement shown after such rest must not be looked upon as a reason for postponing the radical treatment longer than necessary on the assumption that the process is about to be arrested: renewed activity will in all probability be the signal for further toxic symptoms to appear, while the preventable damage to the patient's cardiovascular and nervous system will have a chance to progress.

The mortality from operation is low: Berry (8) some years ago gave us his figures in this type of case as 3 out of 276.

Blackford (9) from more recent figures collected, gives 31 deaths as occurring in 4,720 cases of "Simple goitre" the enlargement of the thyroid gland being apparently held responsible for a large proportion of them.

In P. Kocher's (10) clinic at Berne 130 cases of operation in nodular goitre - all with hyperthyroid symptoms, resulted in a cure in all but 2, in which

death was attributed to pneumonia.

Previous to the recognition of the safety and satisfactory results that are credited to partial thyroidectomy it was the custom to give iodides, iodine, or thyroid extract in various of these cases, although the use of such drugs was in many cases founded on such indefinitely empirical bases that it served only to hide the path to the possible benefits that might be discovered. I have so far omitted reference to the question of the iodine content of the healthy or unhealthy gland, chiefly for the reason that I have failed to convince myself that this particular chemical question has any bearing on the etiology of thyroid disease: without having gone deeply into the subject of chemistry and therefore not stressing the point, I have failed to find any evidence that goes definitely to prove that iodine deficiency or excess has any causative effect on the incidence of goitres: the facts that the exhibition of iodine compounds has an effect on abnormal thyroids or that such contain more or less iodine, does not seem to me to go far towards proving that iodine compounds will alter the normal thyroid. I do not remember having heard it stated that iodine administration has produced disease in an already healthy thyroid gland, and surely the number of patients who have been dosed

with iodides in sufficient amount to cause the disappearance of large gummata or actinomycotic masses would have produced sufficient effects to draw attention, provided that any degree of iodism were a causative factor in thyroid disease.

I am called on to introduce the question of iodine in relation to the question of treatment, because iodine and its compounds are often quoted as being drugs that have a beneficial effect on goitres of more than one type, or as I would express it, more than one stage, without a definite line being drawn between the class that will be benefited by the administration of iodine, and the class that will not, and hence one frequently sees iodides being administered to patients who are wholly unsuitable.

The question of iodine treatment leads to the next variety - Bronchocele. Iodine compounds may be given with benefit to those patients in whom the adenoma has ceased to produce any toxic symptoms and become colloid or cystic in type. A.T.Cameron (11) has suggested that in colloid goitres, as more material is formed, we may consider that the globulin contained therein is manufactured at an increased rate and that sufficient iodine is not available, or that it cannot be utilized to the best advantage, to make use of the thyroid radical: and also

suggested that the hypertrophy may be a normal response to thyroid deficiency: in view of the fact that colloid types of goitre are sporadic at times and do not occur regularly in the same areas I cannot understand why iodine, conveyed in ~~the~~ water or otherwise ingested can have any definite effect on the production of goitre, although it may have an effect on abnormal conditions of the gland. It is however undoubted that the administration of iodine in any form often causes diminution and alteration in the consistency of goitres of the colloid type: Osler says "its effect is to stimulate the gland to healthy action" and leaves the matter there.

The prolonged use of iodine by the mouth in the form of the iodide has shown good results: one method is to give it regularly, say, for three times a day for a few weeks with a remission of a week. The Tincture of Iodine has also been given. External applications of Iodine in the form of pigment or ointment are also used; and a weak ointment of Red Iodide of Mercury.

The other form of treatment of this type of goitre that has claimed much attention is that connected with the administration of thyroid substance in some form: this is undoubtedly of benefit in a comparatively small section of the cases where the process of damage to the secreting part of the gland has not progressed far.

X Rays have also been tried and have been credited with some success: I need only refer to the use of this method, as it more concerns the treatment of another variety of goitre: operative treatment is only applicable to degenerative conditions when pressure symptoms are troublesome or where appearances are considered.

The same statement that I have emphasised with regard to adenomata holds good in this case - the method of treatment adopted, and indeed the necessity for treatment of any kind, depends entirely on the stage at which we find the condition: it lies with the physician to fully satisfy himself of the pathological stage, before he makes any move in the direction of treatment. Still another method of treatment which has been recommended in bronchocele is the administration of Thyroid Extract: this also has apparently been successful in checking the degenerative process, but the same applies to this as to other methods; the actual condition of the gland and its secreting mechanism must be known before any line of action is taken: one sees so frequently the harmful effects of the empirical use of drugs in cases in which the simplest means of gauging the pathology of the condition have not been taken, that the necessity for caution cannot

be too much emphasised.

EXOPHTHALMIC GOITRE.

The treatment of Exophthalmic goitre is one of importance in its bearing on the subject of this paper for the reason that certain methods are similar to those frequently directed to the treatment of diseases of bacterial origin.

The first step in treatment of exophthalmic goitre if any degree of severity is concerned with the necessity for diminishing the circulatory activity by complete rest, both physical and mental; the rationale of this appears to me to be the reduction of the rapidity of the output of thyroid products - normal or abnormal. In addition to rest, the diet should be limited, a strict milk diet being given and proteids avoided.

Drug treatment is directed against both the disease and its symptoms, with a view to quietening the patient directly, and, indirectly, by attempting to slow down his thyroid activity.

Belladonna is given as a sedative, presumably for its value in reducing the action of secreting epithelium.

Bromides are given with the object of reducing mental excitement and so aiding the effect of rest: both these drugs have to be used with caution, and

the depressant effect of large doses of bromides has undoubtedly done harm in many cases. Application of the ice bag over the heart, and over the gland, acts usefully as a sedative, and I have seen benefit from continued use of the cold coil over the thyroid.

The use of drugs given with a view to slowing the heart's action is also accompanied by some danger; stophanthus and digitalis, used to stimulate a dilated heart may have to be given with great caution, and their effect on secretion, where the object is to check, at least temporarily, the output of an over-active gland, is not calculated to be beneficial to the patient.

Sodium phosphate has been given to a considerable extent, although I have not found a basis of reason for its use, nor have I observed any benefits coincident with its introduction in dealing with exophthalmic goitre.

Sodium Salicylate may be temporarily useful if given with caution.

Arsenic, in the form of liquor arsenicalis, in increasing doses, with remissions, given over long periods has been found useful; it acts, presumably, by improving the patient's general condition apart from any definite or localised action, but the undoubted benefit derived from its use in many bacterial, plasmodial or other blood infections suggests the possibility that its action may be concerned with its effect on an infective agent.

X Rays have been tried with varying success and where there is sufficient care and measurement of results, much benefit seems to be attainable: indeed Florence Storey in 1912 (12) and again in 1921 (13) went so far as to protest against the neglect of this method in favour of operative procedure: and Hooton (14) about the same time and Seymour (15) in 1916 report considerable success: at the same time H. Mackenzie (16) in a Bradshaw Lecture advocates their use, pointing out as a proof of their efficacy that they sometimes produced myxoedema; which possibly accounts for his later statement (17) that his experience with X rays had been disappointing.

The X ray method of treatment appears to me to be simply an attempt at producing a degenerative fibrosis, permissible in skilled hands and with due caution.

Crile quoting C.H. Mayo (18) says "with Rontgen ray treatment, remissions may occur just as they occur without treatment or with several other methods of treatment; our experience has been failure or but temporary benefit. It is difficult to regulate the dosage and its use adds to the difficulties of operation": Crile points out that the dosage is at best a guess, relapses are common, delay leads to damage to other organs, while the scar tissue etc., are a handicap to future operation.

Operative treatment: undertaken to remove part of the gland (sometimes after ligation of the superior thyroid arteries) and so diminish the amount of the abnormally acting gland, is looked on as the method likely to prove of most permanent good. The adoption of this attitude argues that its exponents are satisfied that the abnormality of secretion is mainly one of quantity more than of quality: it has the advantage that the operation can be repeated on a further part of the gland if there is a return of the symptoms.

Precautions must be taken to select the proper type of case for operation; this is in some degree a question for the physician to settle, but indications for it may be shortly stated as existing when medical treatment is not showing sufficiently good results; operative treatment should not be postponed where the hyperthyroidism is apparently increasing or when it is of such a degree as to produce rapid changes in other organs.

The question of the anaesthetic to be used in thyroidectomy is another question that may well be considered by the physician: these questions were all fully discussed by the late Sir V. Horsley, Dunhill and others (19) in 1912 and have again been considered by some of the same authorities (20) in 1921: the consideration of operative treatment

is outside the scope of this paper.

A method of treatment by the injection of hot water has been tried by Porter (21) and others with limited success.

Preparations of Serum or milk from animals that have had thyroidectomy performed, have been used with doubtful results (22) and the absence of any recent pronouncements on the subject suggests there is little to be gained from such treatment.

Very little has been done in this direction in recent years, and the lack of definite results shown in the work of Edmunds (22) and others has not been improved upon.

Treatment of the symptoms of exophthalmic goitre or Hyperthyroidea is to a great extent covered by the procurement of complete rest: one sees the most distressing symptoms - serious excitement, vomiting and so on - cease as if by magic with rest, physical and mental: the same applies to many conditions showing some similar symptoms - the tachycardia and mental excitement so frequently found in any febrile condition, in which, as I have suggested above, some of the signs or symptoms may be produced indirectly through an alteration in thyroid secretion.



ILLUSTRATIVE CASES

The following short accounts of cases have been selected as illustrating certain points which I wish to bring forward: the accounts of History, Family and personal, and of examination results have been written shortly, leaving out details which are not concerned directly with the question of etiology.

Case 1.

A.J. aet. 22: Colliery Loader: Single.

First seen in 1915, when he consulted me for a "sore throat" which appeared to be due to a follicular tonsillitis; he then had a moderately enlarged thyroid gland which, his Mother since told me, commenced to become noticeable when he was 14. Patient has since been under my care on three occasions, on each of which he has suffered from an acute follicular tonsillitis.

Family History: Father & Mother living and healthy.

Three brothers all living & healthy.

One sister healthy.

One brother is mentioned as Case 2.

Physical Examination: on 23.2.22. his condition was as follows:- complained of sore throat, for two days with pain on swallowing, and headache. Since previous day he had noticed that he could not fasten the stud

of his shirt collar.

On examination he was flushed, temperature 103.

Pulse 110: tongue thickly furred and fauces red. Tonsils large and covered with pus oozing from follicles.

The neck-band of his shirt, which he stated he could usually fasten with comfort, could not be fastened without causing a choking sensation and engorgement of the veins of the neck.

The thyroid gland was very prominent, the lateral lobes being almost symmetrical and distinct: the gland feels firm and resilient and is slightly tender on pressure.

Minimum circumference of neck 17"

Heart and lungs normal.

Blood pressure (systolic) 140 mm.Hg.

Abdomen normal.

Nervous system normal.

Blood: Leucocytes 11,000 per c.m.m.

Differential count	Polymorphs	77%
	Small Lymphocytes	14%
	Large Lymphocytes	5%
	Large Mononuclear	1%
	Eosinophils	2%
	Mast cells	1%

Progress: Instructed to remain in bed: milk diet.

Given a mercurial purgative and sodium salicylate Gr.X. four hourly.

The following morning pulse and temperature reduced.

Neck measurement as before. On the third day the temperature was 98 and pulse 80.

Neck measurement reduced by half an inch ($16\frac{1}{2}$ ").

A week afterwards pulse and temperature were normal and patient well.

The following week he could button his neck-band without discomfort (measurement 16").

Patient appeared again on 27.2.23.

Complaint as before: sore throat came on "last night."

T. 102. P. 116.

Tonsils enlarged and follicles filled with pus.

Patient again complained that his neck had become more swollen and that he could not fasten his neck-band.

Neck measurement $16\frac{1}{4}$ ". After rest in bed and usual diet and treatment the tonsils were clean and patient felt well.

Patient appeared again on 15.9.23. with same complaint, and there was definite increase in circumference of neck - 16".

Next morning the tonsils were less swollen and cleaner.

On 19.9.23 the neck measurement was $15\frac{3}{4}$ ".

and on 2.1.24 measurement was $14\frac{3}{4}$ ".

No further illnesses recorded to date.

Case 2.

F.J. Aet. 19. Colliery Haulage Hand. Single.

First seen on 6.3.23 a week after second appearance of his brother (Case 1).

Complained of sore throat since previous day, and "swelling of neck this morning."

Family History: Vide Case 1.

Personal History: No serious illnesses, but on direct question says he has had "mumps" at times.

Examination: Flushed: T. 102. P. 108
 Tongue furred: Tonsils enlarged with pus oozing from follicles.
 Minimum neck measurement $16\frac{1}{2}$ ".
 Heart and Lungs: normal

Blood. Leucocyte Count 12,000 per c.m.m.

Differential Count	Polymorphs	70%.
	Small Lymphocytes	21%.
	Large do	3.5%.
	Large Mononuclears	2%.
	Eosinophils	2.5%
	Mast Cells	1%

Two days afterwards: Feels well: Temperature and

"Nephritis and heart trouble".

When seen by me on my return from service in December, 1919, complained of shortness of breath and nervousness. He was then drawing full Pension and Allowances for "D.A.H." "attributable to service": I could find no evidence of nephritis or organic disease of the heart and he has improved after my assurance that he had no organic disease, but that his illness was due to worry; he having lost his situation and having an invalid wife and delicate children. Later Mr. G. was granted allowances to start a small business which proved a failure: he then procured employment as a clerk, from which he resigned as his employer wished him to assist in what he considered a dishonest course; he has been on part time employment as a labourer, and is now suffering from the effects of a displaced semilunar cartilage - further source of worry; and his employers, the Municipal Corporation are refusing his claim to compensation on the ground that his disability is due to service.

I give the husband's history at some length in view of the possible suggestion of mental worry as a cause of Exophthalmic goitre.

Patient also had one son who died in infancy. Another adopted son has been under observation at

Tuberculosis Dispensary but does not appear to have any definite signs of tubercular infection.

Two daughters (cases 4 & 5).

Personal History:

Patient has always been delicate and until a few years ago was troubled with annual attacks of tonsillitis. When first seen in 1919 complained as above. She had at that time an enlargement of the thyroid gland, tachycardia, slight exophthalmos, dilated heart, and was losing weight rapidly. During the last four years she has gone through the typical course of exophthalmic goitre of moderate severity, with frequent exacerbations of symptoms and variation in size of the thyroid gland. Satisfactory treatment has been impossible on account of home conditions.

A year ago patient was admitted to the medical wards of a local general hospital with a view to preparation for thyroidectomy, but after a month decided to leave without operation.

Symptoms have since been less marked than during the last four years and exacerbations less frequent, but accompanied by vomiting attacks.

Present condition (7th Jan.1924): complains of nervousness and palpitation.

The thyroid is much enlarged; 3 distinct nodes, no pressure symptoms. The gland is definitely smaller than it was a year ago and nodulation more distinct; there is tachycardia, the pulse varying from 120 to 160: praecordial pulsation; heart enlarged (apex beat in 6th space four inches from mid-line).

Blood pressure (systolic) 160 mm Hg.

Exophthalmos is marked with all classical signs present, tremor, general nervousness, attacks of sweating and wasting, the deep reflexes are all exaggerated, the tongue is furred, the fauces red, tonsils slightly enlarged, flat and scarred. There is no other abnormality.

Case 4.

G.G. Aet. 18. Clerkess. Single (daughter of case 3).

First seen January, 1920.

Complained of breathlessness on exertion, discomfort after food and irregular menstruation.

Family History: Vide Case 3.

Personal History:

Diphtheria at age 7.

"Kidney trouble" at age 10.

Has always been anaemic and pale.

Menstruation twice in last year:
intervals 5 months.

Physical Examination:

June 1922. Pale, looked dull with appearance
of oedema of lower eyelids.
Slight thyroid enlargement, neck
measures 13".

Circulatory System:

Pulse 72, small volume and compressible.
Heart sounds soft, and accompanied
by murmur at apex, conducted towards
axilla.

Nervous System:

Intelligent but slower than normal
mentality.

Blood:

R.B.C.	4,500,000
W.B.C.	6,500
Hb	85%

Differential Leucocyte Count:

Polymorphs	61%
Small Lymphocytes	22%
Large do	9%

Large Mononuclears	6%
Eosinophils.	1%
Mast Cells	1%

Treatment with a mixture containing 1 drachm of Syr. Ferri Iodid T.D.S. varied aperients as required and tablets of a thyroid preparation supposed to contain gr. 1 each of dry thyroid substance, three times a day.

Patient has since had thyroid tablets up till present time. She has improved in general condition and appearance and feels well.

Seen in September 1923 the blood was as follows:-

R.B.C.	5,000,000
Hb.	95%

The periods are now regular; the thyroid gland is less prominent.

Case 5.

M.G. Aet. 15. Apprentice Book-binder; is daughter of Case 3 and sister of Case 4.

First seen in January, 1920. (aet 11).

Complaint: General weakness & headache.

Family History: Vide Case 3.

Personal History:

Has been very irregular in attendance at school; has always been delicate

and has twice been referred by School.M.O. for residence in a Children's Holiday Home for summer months, with very little improvement.

Examination:

January 1920. Pale, listless, but fairly bright, intelligent and cheerful when roused.

Marked thyroid enlargement: the enlargement appears to be confined to a firm mass occupying the middle line.

Pulse: Regular, 108, increased to 120 or 140 with slight exertion.

Heart not enlarged: soft blowing murmurs heard all over praecordia.

Lungs normal.

Tongue slightly furred, teeth carious.

Tonsils enlarged, right greater than left and pitted; constipated.

Blood:

R.B.C.	5,000,000
W.B.C.	6,000
Hb	90%

Subsequent History:

July 1922: had an attack of follicular tonsillitis followed a week afterwards by joint pains which disappeared under full doses of sodium salicylate followed

by Lig. Arsen. m ii three times a day increased to m V and continued for some months.

During attack of Tonsillitis there was $\frac{1}{4}$ " enlargement of neck measurement.

In September 1923; had another attack of Tonsillitis and was then referred to throat department of a local hospital and is now waiting admission for tonsillectomy.

Case 6.

Mrs A.H. Aet. 38. Housewife. Married.

First seen in December, 1919.

Complaint: sore throat for two days.

Family History:

Parents both alive and well.

One brother and one sister, both alive and well.

Husband alive and well.

Three children: one (Case 7.) suffers from Tonsillitis.

Personal History:

Since childhood has suffered from frequent attacks of sore throat which have more than once been diagnosed as

diphtheria. Had excision of tonsils performed when aged 20. No other serious illnesses: swelling of throat first noticed when 16.

Condition in Dec. 1919: convalescent from third confinement (3 weeks) complains of sore throat; looks pale. Patient has considerable enlargement of thyroid gland, enlargement consisting of equal bilateral rounded swellings: there is a slight prominence of the eyeballs; no other recognised signs of exophthalmos present. Temp. 102. P. 120.

Circulatory System:

Nothing to note beyond increase of rate: blood pressure 130 mm. Hg. (systolic).

Respiratory System:

Nothing abnormal found.

Alimentary System:

Tongue furred: throat shows remains of tonsils covered with a grey exudate or growth. Nothing else to note on physical examination.

Swab from throat: No Klebs-Loeffler
Bacilli: long-chain
Streptococci found in great number.

Subsequent History:

Patient has had two later attacks of tonsillitis (Sept. 1922 and August 1923). The remains of partially amputated tonsils are visible in intervals of attacks. The enlargement of thyroid does not increase during attacks.

Case 7.

E.H. Aet 8 Schoolgirl. Daughter of Case 6

First seen professionally Sept. 1922 along with Mother, complaining of sore throat.

Family History: Vide Case 6.

Previous History:

Has always had a troublesome cough and has had several attacks of tonsillitis. Three years ago had throat trouble, diagnosed as diphtheria: has frequently required medical attention.

Examination:

Complains of sore throat, flushed, Temp. 103.4. Pulse 140. Tongue dry and furred, tonsils enlarged and covered with grey exudate extending over anterior faucial pillars.

Swab of throat shows no Klebs-Loeffler Bacilli. but Streptococci similar to

those in Case 6. There is a slight degree of enlargement of the thyroid which is more easily palpable than is the case generally in children of her age.

Circulatory System:

Nothing abnormal.

Respiratory System:

Irritating cough, no expectoration; on physical examination of lungs there are occasional fine sibilant râles to be heard here and there all over lung area.

Progress:

Child was well in a few days, the "membrane" disappearing from the fauces in two days with local treatment, when the temperature became normal and the few signs in the lungs disappeared. The tonsils continued enlarged and pitted. A month after above, in October 1922, Mr. G.A. Carter F.R.C.S enucleated the tonsils under a general anaesthetic and patient had an uninterrupted recovery, since which she has not had a day's indisposition

of any kind (up to March 1924).

Case 8.

Mrs. A.L. Aet. 46. Housewife. Married.

First seen in March 1920.

Complains of cough, shortness of breath and spit,
for a few days.

Family History:

Mother & Father dead, causes
unknown.

One brother living and healthy.

Three sisters living & healthy.

(One sister is Mother of Case 9.)

Husband alive and well.

Three sons, Aet. 15, 11, 5, all
healthy.

Previous History:

Has had frequent attacks of
bronchitis; one miscarriage seven
years ago. Had frequent attacks
of sore throat until marriage
17 years ago.

Swelling in front of neck
appeared at age 14.

Present condition (March 1920).

Stout woman, slightly cyanosed. There is a rounded prominence over situation of thyroid isthmus.

Respiratory System:

Dyspnoea, frequent cough and spit with muco-purulent expectoration.

Loud coarse râles and rhonchi heard all over chest.

Circulatory System:

Pulse 130, small volume and irregular.

Heart not definable, heart sounds faint, weak and short.

Blood pressure 140 mm Hg (systolic).

Urine 1025. trace of albumen, sugar present.

Progress:

Improved slowly, after a fortnight there were still some râles heard all over lungs: the pulse remaining fast, with much dyspnoea on exertion. In April 1921 patient had a profuse vaginal haemorrhage, found to be due to incomplete abortion at about three months, not suspected by patient, who had no amenorrhoea.

Curetage, with uneventful recovery.

In May 1922 profuse menorrhagia (patient sure that there was no pregnancy). No signs of pregnancy but enlargement of uterus with continuous acute pelvic pain, continuing till curettage: no evidence of products of pregnancy: Menorrhagia at intervals till November 1922, with much pain: then pelvis was explored suprapublically and nothing abnormal found. Further curettage in October 1923, following continued pain and menorrhagia. Patient has since been well, but glycosuria continues, diminished, but not abolished, by appropriate dieting. There has been very little loss of weight during period of above history.

Case 9.

A.M. Aet. 16. Apprentice Cup-handler. Single.

First seen October 1920 (aet.13).

Complains of swelling of throat for about four years.

Family History:

Parents alive and healthy.

One brother (aet 18) living and healthy.

Mother (sister of Case 8) has small nodular mass in situation of thyroid

isthmus which she states has been there ever since childhood.

In mother's case there is no history of illness obtainable: no history of sore throats.

Previous History:

Patient has been healthy except for an attack of sore throat some years ago.

Condition: (October 1920): Short stoutly built girl with stupid expression and much subcutaneous fat. There is a thyripid enlargement caused by a nodular swelling confined to the isthmus.

Beyond appearances stated there is nothing abnormal but slow cerebration.

Since being first seen by me the patient has attended the Out-patient's Department of a General Hospital so that she has not been under my observation, but is reported to be altered very little in appearance..

Case 10.

Mrs M.W. Aet. 67. Housewife married.

Mother of Cases 11 & 12.

Grandmother of Case 13.

Foster mother of Case 14.

Under observation by me for eleven years. Attended at intervals on account of obstinate constipation, and recently for what appear to be attacks of biliary colic, but refuses exploratory operation.

Family History:

Father & Mother dead, no history available.

Husband died aet 63, from urethral stricture with urinary fistulae, refusing surgical treatment.

One brother dead: cause unknown.

One sister: died at childbirth.

Sons: two living and healthy.

One died, aet 25, eight years ago from acute diabetes, the first symptom being air-hunger proved to be due to acetonæmia (father of Case 13).

Daughters 5 living 3 healthy

2 vide cases 11&12.

Personal History:

Has always been strong and healthy until last 15 years when she has been troubled with attacks of abdominal pain, diagnosed as appendicitis, biliary colic and constipation.

Has had enlarged neck since girlhood.

Present condition: January 1924.

Stout, pale, & flabby.

Has large bronchocele "cystic goitre"
both lateral lobes enlarged.

Alimentary System:

Tongue furred, throat apparently
normal.

Liver palpable 1" below costal
margin: stomach dilated, colon
distended.

Circulatory System:

Pulse 90, slightly irregular in
time.

Heart: Epigastric pulsation:
enlarged transversely on percussion:
sounds weak, with short rough
murmur preceding and accompanying
first sound heard at xiphⁱsternum.

Lungs normal for age.

Urine - Normal.

Case 11.

Mrs J.R. Aet. 46. Housewife. Married. (daughter of Case 10).

Seen in October 1921.

Complaining of lump in throat, choking sensation and
disturbed sleep; is apprehensive of some kind of cancer

of throat.

Family History: Vide Case 10.

Husband living and healthy.

Two children living and healthy.

Personal History:

Has always been strong until last few months, when she has noticed her neck getting thicker and she has occasionally had a choking sensation.

Physical Examination:

Well nourished; slightly flushed; frightened expression; eyeballs slightly prominent with Von Graefe's exophthalmic sign just obtainable. Temp. 99.2. Pulse 140. On examination, slight general fullness of thyroid gland.

Alimentary System:

History of constipation, tongue clean but slightly furrowed, fauces red, abdomen normal.

Circulatory System:

Epigastric pulsation, heart slightly enlarged to left.

On auscultation, a soft murmur accompanying first sound at apex, not transmitted beyond anterior axillary line.

Nervous System: Apprehensive of impending trouble, easily startled, knee jerks exaggerated: fine tremor of hands.

Respiratory System: Lungs normal.

Reprod. System: Normal.

Urine: Normal.

Progress: Assured regarding question of cancer etc: has since consulted various practitioners, qualified and otherwise, with no immediate improvement, but has since then gradually improved with no further treatment and is now quite reassured:

Menstrual history has apparently ended and patient feels quite well again.

Case 12.

Mrs A.W. now aet 42. Housewife and Shopkeeper. Married.
First seen December 1914.

Then complained of increasing weight for last three or four years and has been getting slightly stouter since birth of only child in 1909.

Family History: Vide Case 10.

Husband and one daughter living

and healthy.

Previous History:

Patient has always been healthy except for occasional colds accompanied by sore throat, and attacks of hoarseness.

Reproductive History: Normal.

Physical Examination:

Stout, weight 16 stone 10lbs, healthy complexion: not recognisable enlargement of thyroid gland.

Alimentary System:

Tongue clean, fauces reddened, tonsils appear normal.

Constipated: abdomen, no recognisable abnormality beyond increased abdominal fat.

Circulatory System:

Pulse 84 regular, small volume, heart sounds soft and distant, other wise normal: Systolic Blood pressure 150 mm Hg.

Advised diminished carbohydrate diet, saline aperients and more open air exercise: prescribed preparation of thyroid gland in increasing dose.

Progress: In 1916 having been under observation periodically since time of above account: general condition has improved and she can exert herself with less distress than previously: weight 14 st. 9lbs. Seen again in December 1919: has had treatment only at long intervals in my absence elsewhere. The weight had increased to 17 stones in spite of limited diet: patient then treated similarly to above with thyroid tablets, the dose increasing to the supposed equivalent of thyroid substance grs 2 T.D.S. reduced to gr 1 T.D.S on account of attack of dyspnoea and sweating. Has improved in general condition: weight reduced to 15 st. 7 lbs in December 1923. Patient has several times been incapacitated from work (grocer's shop) by attacks of coryza, pharyngitis and laryngitis.

Case 13.

A.W. Now aet. 12. Schoolgirl.

First seen 1914. No abnormality then noticed. At age 7 was brought to me on account of sore throat which she had complained of for some days.

Family History: Vide Case 10.

Grandchild of Case 10 and daughter of son of Case 10 mentioned as having died of diabetes mellitus.

Mother died four years ago, acute appendicitis.

Patient was only child.

Personal History:

Beyond attack of tonsillitis mentioned, has had no illnesses requiring attention.

Physical Examination:

Well developed but rather pale complexioned, quiet and listless. There is a general rounded enlargement of thyroid gland with a prominence the size of a small hen-egg in mid-line of neck. Tonsils enlarged: no other signs of disease.

Case 14.

Mrs G.F. Aet.24. Housewife. Married.

Complains of general weakness and cough for last three years.

Family History:

Parents died shortly after her birth - cause unknown.

Husband alive and healthy.

Twin children aet. 6; one is delicate

and had pneumonia 3 years ago.

Personal History:

Has always been thin and pale, but no history of illness before birth of children in 1918, since when she has been thinner and "always tired"; pneumonia two years ago: came home to live with foster mother (Case 10) for convalescence when I found her to be suffering from pleuritic effusion, and she was admitted to hospital.

The origin of the effusion was not established - no tubercle bacilli found in effusion nor sputum.

Now under observation by Tuberculosis Officer.

Seen in Jan. 1922: short, poorly nourished, bow-legged girl with sallow complexion. She had then a general slight enlargement of thyroid gland, more prominent from general emaciation.

Pulse 130. Temp. 101.

Dyspnoea present; on examination signs found of pleuritic effusion on

on left side, some epigastric pulsation, and cardiac dullness displaced to right. Since transfer to hospital has not been under my direct observation.

Case 15.

M.I. Aet. 23. Tailoress. Single.

First seen as Hospital Out-patient 20th July 1923.

Complained of swelling in throat, nervousness, breathlessness and palpitation.

Duration of illness — Three months.

Family History:

Father and Mother living & healthy.

Two sisters both healthy.

Personal History:

Has always been healthy, no illnesses of note except tonsillitis two years ago, and again about a month before commencement of present illness.

Physical Examination:

Well developed but thin, slight malar flush, enlarged thyroid with firm mass over isthmus, the size of a tangerine orange.

Definite exophthalmos with Von Graefe's sign just perceptible.

Temp. 99.4. Pulse 120.

Pulsation visible in vessels of neck and in epigastrium. Heart not enlarged. Systolic Blood pressure 140 mm.Hg. Tongue furred, tonsils enlarged, fauces and posterior pharyngeal wall congested.

Progress:

Admitted to Hospital Aug.10.1923.
Partial thyroidectomy Aug.23.1923.
Discharged Sept.17.1923.
Seen at Out-patient department Oct.5.1923.
States she feels quite well, looks much better and has increased 5 lbs in weight since operation.
Temp. normal. Pulse.90.
Appetite good, tongue clean.
Intends to return to work next week.

Case 16.

Mrs A.M. Aet.55. Charwoman. Married.

First seen on 15th April, 1923.

Complains of discomfort after food and constipation for some weeks.

Family History:

Father died at 78 "old age".

Mother died at 50 "rheumatism and heart trouble"; had a big goitre all her life.

Husband living and healthy.

Two sons and three daughters living and healthy.

One son killed on service.

Personal History:

Has always been strong and healthy; no serious illnesses.

"Has always had a big neck; swelling in front of neck increased rapidly at time of first confinement.

Physical Examination:

Rather squatly built woman with muddy complexion, dry skin and coarse hair, high malar eminences and prominent eyes, and has a large goitre composed of two bilateral masses each the size of her own fist.

Pulse 76 regular small volume.

Heart and lungs normal, other systems nothing to note.

Case 17.

Miss F.C.A. Aet 26. Clerkess. Single.

First seen 15th Oct. 1922.

Complained of swelling of the throat and constipation.

Swelling of throat first noticed two years ago.

Family History: Father died at 55 - pneumonia.
Mother living and healthy.
One brother and one sister both
living and healthy.

Personal History:

Has always been well except for
attack of Chorea in childhood
and usual childish ailments not
defined: during the last three
years has had, besides enlargement
of neck, occasional slight sore
throats and joint stiffness and
pain but no swelling of joints:
has not considered it sufficiently
serious to seek advice.

Physical Examination:

Well nourished, complexion healthy,
lips pale. General enlargement of
thyroid noticeable.

Temp. normal. Pulse 84.

Tongue furred, fauces redder than
normal, tonsils just visible with
irregular free surfaces. Heart,
lungs and abdomen normal.

Advised with regard to regulation
of bowels.

Progress: Seen on 5th Dec. 1922 complaining of abdominal pain and feeling of sickness, admits to return of constipation and rectum and colon found to be loaded with faeces.

The tongue was thickly furred and the throat red. Increase of maximum circumference of neck from 13" to $13\frac{1}{2}$ ".

Advised use of liquid paraffin by mouth regularly, with 2 gr. tabloids of phenol phthalein as required: later given 1 drachm of Syr. Ferri Iodid. T.D.S.

A fortnight later maximum circumference of neck was 13". Patient has twice since above date complained of slight soreness of throat, on each of which occasions the neck measurement has increased by about an inch.

Case 18.

F.R. Female. Aet. 18. Pottery Decorator. Single.
(Known to me for 11 years).

Appeared for treatment 12th Jan. 1922.

Complained of "always feeling tired"; increase of weight and absence of periods for four months.

Family History:

Father alive, aet. 66, suffers from

chronic nephritis with retinitis.

Mother (47) has always been very well but has grown very stout in last ten years.

One brother and two sisters all living and healthy.

Personal History:

No previous illnesses "of any importance" but has had sore throats every few weeks for last year: attended by me for acute tonsillitis in March 1920.

Condition in Jan., 1922: unhealthy looking girl with muddy complexion; stout and heavily built: expression dull and stupid: answers questions very slowly.

Weight 11 st. 2 lbs. There is considerable enlargement of the thyroid.

No signs of pregnancy.

Nervous System:

Mentally dull and slow, otherwise normal.

Circulatory System:

Pulse 72. Nothing to note.

Respiratory System:

Normal.

Reproductive System:

Menstruation commenced at 13 and was regular up to four months ago.

Patient was considered to have a condition of hyperthyroidea: she was given a mixture containing the Sulphates of Iron and Magnesium, and tablets containing dried thyroid substance gr.1 increased later to gr.2 three times a day, and advised to have more open air exercise.

Progress:

On March 10th 1922 patient experienced a normal period, she stated that she felt quite different and "no end better". The weight had decreased steadily by about 2 lb a week and weight on above date was 10 stones. The administration of thyroid substance has been continued.

Seen on the 7th Jan.1924, Miss R. states that she feels well, and has had no illness during the last two years except a slight cold: her weight is 10 st. 5 lbs: complexion healthy: appetite good. Periods have been normal for almost two years.

SUMMARY OF ILLUSTRATIVE CASES.

The cases of which an outline has been given are considered to be illustrative of two points which I put forward as of prime importance in the consideration of the origin of thyroid disease; these points are, firstly, the frequency of the occurrence of disease of the tonsils, and secondly, the fact that many groups of cases not confined to one type, are found among people either nearly related, or otherwise closely associated. It will be noticed that Cases 1 to 14 each have a domestic association with one or more of the others.

Cases 1 and 2 are brothers living in the same house and being within three years of one another in point of age. Cases 3, 4 and 5 are mother and two daughters. Cases 6 and 7 are mother and daughter. Cases 8 and 9 are aunt and niece, the mother of the younger, Case 9, showing evidence of previous thyroid disease. Cases 10 to 14 are respectively, mother, daughter, daughter, grand-daughter and adopted daughter.

A further point which I wish to bring forward relates to the fact that these family groups include persons who show signs of disease of the thyroid gland of varied types.

While Cases 1 and 2 are similar in type, the next group, 3 to 5 contain a mother with Exophthalmic Goitre, a daughter with signs of thyroid degeneration who improves in health after the administration of thyroid gland substance, while another daughter, Case 5, illustrates the case of what may be classed as a mild "toxic adenoma".

Cases 6 and 7 are mother and daughter, their cases illustrating, respectively, the pictures of a toxic adenoma and an indeterminate enlargement of the gland.

Cases 8 and 9, more distantly related, but with a distinct domestic relationship, have similar types of thyroid abnormality.

Cases 10 to 14 are a domestic group, (number 14 being related to the others by residence only) which includes a case of presumably colloid goitre with very slight signs of secretory deficiency, in Case 10.

Case 11 has developed, during the menopause, signs of increased thyroid activity; number 12 may be considered as lacking in thyroid activity; number 13 shows rather a slight evidence of deficiency; and Case 14 has had signs of enlargement of the thyroid with arrested development.

The mother of Case 16 suffered from a similar deformity.

With regard to the questions of possible channels of infection, I think the cases illustrate sufficiently what I wish to emphasise.

Cases 1 and 2 show definite tonsillar disease, and at one time both suffered in the same week from acute follicular tonsillitis, which appeared to affect the thyroid glands of both in such a similar manner as to provide strong presumptive evidence of a common cause.

Cases 3, 4 and 5 all have histories of throat infections.

Numbers 6 and 7 have had a simultaneous throat infection with concurrent evidence of thyroid change.

Case 8 gives a definite history of throat trouble.

Cases 12 and 13 have had "throat trouble".

Number 15 has had tonsillitis.

Case 18, has shown evidence of acute tonsillitis. When I assert that, without the aid of direct or leading questions, I have elicited these histories and similar accounts in dozens of recorded and unrecorded cases, I may claim that there is something more than a basis for the suggestion that infection is a very common cause of thyroid disease of varying type and intensity; when these cases are collected in a district where thyroid disease is exceedingly

common, one may be pardoned for wondering whether environment, apart from the possibility of direct transference of a causal infective agent, has much to do with the matter.

It is my object to show reasons why the view suggested above may eventually be the common one, and that previous theories and investigations may have been promoted on wrong premises.

THE ETIOLOGY OF GOITRE.

In treating of the origin of the commoner diseases of the thyroid gland, the enquirer is faced with the fact, that by far the most frequently occurring type is a degenerative one; and in reviewing the microscopic, apart from the chemical, pathology of the various forms, it is seen that all these forms are essentially variations in the secreting mechanism of the gland; as in all disease affecting any organ with a secreting epithelium, the interference with the function of that organ is effected, first, directly on the secreting structure, and degenerative changes in the connective tissue follow afterwards: even in those cases in which the degenerative process is originated by some primary change in the vessels supplying the part, the disease first affects the secreting mechanism. These remarks do not apply, of course, to connective tissue changes of a malignant nature.

In thyroid diseases the essential change is always seen to affect the secreting epithelium principally, and we may therefore argue that it is possible for one cause to be responsible for all the changes occurring in the epithelium. I have referred to cases in which different types of thyroid disease have appeared in the same family - in people

most intimately related in regard to environment - and am strongly of the opinion that in this direction we may find a clue to the origin of all diseases not classed as malignant: indeed I feel that we may in time find that even the malignant diseases are brought into line with others that until the last few decades have been unexplained, to be at last discovered to be originated by parasites.

In the process of enquiring into the origin of any disease we are assisted by a knowledge of its distribution, and it will be of value to consider the geography of the commonest type of goitre, known as endemic goitre.

In the British Isles there are certain localities in which goitre is endemic; the areas in which cases are most frequent are, in England, Derbyshire and the Yorkshire Dales, Sussex, Hampshire and a great part of the Thames valley; and, in Scotland, the fairly hilly area in the South-west. On the continent of Europe the greater proportion of cases are found in the mountainous regions - Switzerland and the Pyrenees, and mountain parts of Germany and Austria.

In Asia, mountainous regions have again been noticed to be most common situations of centres of thyroid disease, and the great range of the

Himalayas and the spurs extending therefrom have more than one large area where goitre affects a large proportion of the population. This frequent occurrence of the most disfiguring form of abnormality of the thyroid in many mountainous regions has led to great stress being thrown on the question of the association of goitre with hills, but one finds that, perhaps to a lesser extent, river valleys have also their endemic areas.

The great valleys of the Punjab and Ganges in British India, the valleys of the Danube in Austria, others in Italy, and the Thames valley in England are found to have a large incidence; while there are many mountain areas which are almost immune: the West Coast of Scotland and the West Indies are found to be nearly exempt from the condition.

With regard to climate, apart from the special characters of mountain and other climates, the distribution of goitre is not limited to any one variety, as we find it occurring in the Tropics, in lands where the climate is influenced more by altitude and distance from the sea than by latitude; and again within the Arctic Circle.

It will thus be seen, that, as definitely limiting factors, both altitude and latitude may be ignored, and we pass on to other considerations

relating to geography.

Distance from the sea appears also to be of little importance, as the disease occurs in some instances close to the sea coast, and islands, such as Ceylon, have their share of goitre. If we further try to localise the incidence of the disease, we come to the fact that there are closely situated areas, with similar geographical peculiarities, in which the occurrence of goitre among the population varies very markedly as between one and a neighbouring area.

Taking all the above facts into consideration we are bound to admit that there is no reliance to be placed on the geographical factor as a cause, direct or otherwise, of thyroid disease.

The question of Race is another point which may be considered, but we find that endemic goitre is a disease that cannot be proved to be more common in one nation or race than in another: the distribution is so widespread that race cannot be looked upon as incurring a pre-disposition; to go no further we may instance the Himalayas, Switzerland and Derbyshire.

Occupation has been advanced as a deciding factor: Mc Carrison (23) mentions the fact that the greatest incidence of endemic goitre in some areas

Is among the working and agricultural classes; he mentions certain of the rural districts in Lanarkshire where goitres are common: he also draws attention to the history of the endemicity of goitre in Valais in 1818: in this case a flood covered the lower lying country with a deposit of mud, and the number and severity of cases, reduced for some years, rose again when the upper layer of soil had been disturbed.

Geological formation, and along with it the inorganic chemistry of the water supply of an affected area have been looked upon as having an influence on incidence, and so many assertions have been made about the influence of certain rocks and the water supply derived from them, the iodine content of the drinking water and its influence, that the connection between the source of the water supply and the incidence of goitre in any given area has come to be almost an established one; and yet no single character of the earth's surface nor of the water obtained from the area has been proved to be common to districts with a large incidence of goitre.

A writer on this subject has said (24) "looking for a local cause, one does not seem to find one. Some areas are thought to owe their goitrous characteristics to a chalky soil, others to the presence of

limestone. Elsewhere a mountainous district blames its hills, where another of sedimentary basin formation thinks it finds the cause in excess of organic material present in the soil. No two goitrous districts seem alike, and even the same range may vary". The writer goes on to show reasons why the absence of iodine in the water supply should be considered to be the causative factor, and quotes the success of the prophylactic administration of iodine as evidence in that direction. He may be correct in his assumption, but the evidence is purely circumstantial; we have no more right to look on the prophylactic or curative effect of iodine as evidence of the cause of goitre by its scarcity than we have to consider the absence of quinine as the cause of malaria, or the absence of antiseptics as the cause of infection.

A substance may be curative or preventive of any specified disease, but absence of the substance is not the origin of it. The author quoted above goes on to dispose of his own arguments by an admission that he is "well aware that the iodine theory will not fit all cases, as for instance the classic goitrous wells in Styria"; he also mentions the empirical use of iodine ~~compounds~~ before any definite observations on the matter had been recorded, and compares it with the empirical use of ipecacuanha

in amoebic dysentery and the success in more recent times of the active principle in the treatment of that condition: he does not of course, suggest that people who neglect to take Emetine will have dysentery sooner or later, but his argument, taken in a strict sense, seems to infer as much.

I have quoted this writer at some length in an attempt to illustrate how to my mind the theories of the causation of goitre may be fairly considered to be founded on initial errors in observation or reasoning: to go further into the question of iodine, it has not been in any way proved that the absence of iodine alone is a predisposing cause. If we compare goitre with, for instance, rickets, we know that many a child has suffered from prolonged absence of fresh air and sunlight without exhibiting the common signs of that disease, although observers of recent years have proved almost conclusively that such conditions of life predispose to it.

The nervous origin of goitre may next be considered ; the same attitude that I adopt to the theories relating to the iodine causation of thyroid disease, if applied to the theory of causation by previous disease of the nervous system, leads to similar conclusions. It appears to me that in this respect the argument "post hoc propter hoc" has been

introduced into the enquiry of the etiology of goitres at an early stage, in such a way as to obscure many of the facts that might have been elicited. Gordon (25) in a fairly recent article in the New York Medical Journal suggests that the nervous origin of exophthalmic goitre is supported by the increase of nervous symptoms, with emotional disturbance which is such a constant feature in that condition: as well might we say that the very frequent exacerbation of symptoms in a woman with tuberculosis of the lungs, during and after pregnancy, is a proof that childbirth either causes, or predisposes to, tuberculosis.

With reference to the question of mental strain, fright, or anxiety as a possible cause of exophthalmic goitre, I may cite Case 3 of the list herein: it will be seen that the onset of the symptoms was coincident, or was thought to be, with mental worry; it can be easily understood that the casual observer, even with some medical knowledge, might readily accept the mental anxiety as a predisposing, or even the only cause.

It will be noticed that I have transferred my observations from the study of bronchocele to that of exophthalmic goitre; this may seem a peculiar method to adopt, but it will be explained by my conviction that the two diseases, different

as they may seem, are only stages or degrees of one disease.

Gordon, quoted above, refers to the observations of Marie and others in cases of nervous disease and mentions that Marie considered the exophthalmic goitre which he noted in certain cases of Tabes Dorsalis to be due to a lesion of the solitary bundle in connection with the ninth cranial nerve, and that Joffroy noted the condition concurrent with syringomyelia with dilatation of the superior cervical cord; also that the disease had been noted in various central nervous system diseases, Parkinson's disease, myasthenia gravis, encephalitis lethargica, acromegaly and others. I suggest that ⁱⁿ many of such cases the thyroid disease is an incident attributable to the same cause as the nervous disease, or to some concurrent infection: all these diseases may be, and some are known to be, produced by some toxin, organic or inorganic: in this connection a recent article (26) in the Lancet by Crichton Miller includes the description of a case of severe mental disturbance with signs and symptoms of exophthalmic goitre; the patient improved with rest but relapsed when she was allowed to go about again; when a colleague of the writer performed a partial thyroidectomy, the patient improved so much that she has returned to work and seems well: the author goes

on to say "now in this case I am open to conviction that the psychic conflict was the sole cause of the hyperthyroidism, but I suspect that an element of bacterial infection must at one time have been operative. Let us, however, grant that the condition was primarily psychogenic. It remains undeniable that the physiological implications of the emotional conflict had reached a point at which no redress of the emotional equilibrium could effect a remedy. In short, emotion had effected function and function had affected structure to a point at which there was no recovery by the path of the original onset". I may be very far wrong, but I more than suspect that an element of bacterial infection was the beginning of the whole affair.

G.R.Murray (27) agrees with Mc Carrison that during the recent war comparatively few men developed exophthalmic goitre from strain only, but that at least three factors were at work - the nutritional, the psychic and the toxic. Crile (28) says "I have never known a case of Graves' disease to be caused by success or happiness alone, or by hard physical labour unattended by psychic strain, or to be the result of energy voluntarily discharged".

Taking into consideration the views quoted which above with my own small experiences agree, I am, at present, quite convinced that, if any cases of

thyroid disease have originated from a disease of any part of the nervous system they are so scarce as to be negligible. I may here remark that my experience daily confirms me in the impression that too little importance is attached by the average practitioner of medicine to the previous history of a patient in the investigation of his illness: too many diagnoses are at fault which might easily have been correctly attained, with a saving of effort and delay, by care in the compilation of an accurate account of past disease.

The toxic origin of thyroid diseases, of the simple adenomatous, the endemic or epidemic goitrous, or the exophthalmic types has of recent years received more and more attention, and I wish to emphasise this aspect of their etiology, in the belief that the medical profession will eventually come to accept the view that toxic agents are the originators of all, or very nearly all, thyroid disease, and that bacterial toxins are in most cases responsible.

I have, in the course of this paper, attempted to emphasise the fact (or, it may be, presumption) that thyroid diseases are simply variations in the number or secreting capacity of the epithelial secreting cells lining the colloid

spaces of the gland: these variations may all be produced by bacterial toxins; analogies collected from the study of other diseases, affecting various secreting epithelia, could be quoted ad infinitum. All the way down the alimentary canal we have instances of secreting cells which are affected in less or greater degree by the presence of bacteria and their products.

It is an admitted fact that foreign bacteria or ferments in the stomach can produce changes in the fluids secreted by the lining epithelium of the organ; the typhoid bacillus will produce changes amounting to complete destruction in certain groups of secreting cells in the small intestine: again, toxins in the blood-stream produce profound changes in the structure and secreting capacity of other epithelium, of which the albuminuria so frequently found as a result of alterations in the secreting mechanism of the kidney in febrile disturbances is a prominent instance. In short, a postulate might justifiably be stated, without fear of contradiction, in these terms "the toxins of any pathogenic organism, if in sufficient concentration, will alter the function of, or totally destroy, the epithelial cells of a secreting organ exposed to it for any prolonged period".

I may here digress to deal shortly with the supposed relationship of the thyroid gland to other of the internal secreting structures.

It has long been recognised that glycosuria - and true diabetes - is frequently associated with exophthalmic goitres. Dr. F.H.Boyd (29) writing in the Medical Annual for 1913, draws attention to the frequency of this occurrence and points out the fact that the tolerance for glucose is often diminished. A. Kocher mentions it (30) as one of the contraindications to thyroidectomy: the fact of his mention of it is sufficient evidence of its admitted frequency. This frequency suggested to me the inclusion of the case of Mrs L. (Case 8) as I consider the occurrence of glycosuria in a case of her type to be at least circumstantial evidence of the intimacy of the connection between nodular toxic or post-toxic adenoma and exophthalmic goitre: J.M.Blackford (31) states that in his experience glycosuria is not more frequent than in other diseases, although he remarks in the same paragraph that bronzing of the skin occurs in older people the subject of exophthalmic goitre so marked sometimes as to suggest Addison's disease, which is considered due to adrenal disturbance; Case 3 of the series mentioned herein was an example of this bronzing to a moderate degree. Francis A.C.Scrimger

of Montreal (32) suggests that the relationship between the thyroid and the adrenal glands is definite; that they have some sensitizing action on each other or the tissues, possibly through sympathetic nerve endings, so that a vicious circle is established. I am inclined to adopt the explanation - somewhat indefinite, I admit - that certain toxins have the faculty of attacking and altering the secretion of internal secreting gland structure, and that in this way the balance which has been proved to exist between the different internal secretions is interfered with: it may be that the interference with the secretion of one makes the other more liable to the influence of a circulating toxin, and that the second responds with a like effect, to the further disorganisation of the patient's nervous and circulatory systems, but these matters still belong to the realms of theory and experiment. Certain inferences may be drawn; thus, when the thyroid gland is in an unhealthy state of altered secretion, that state is frequently accompanied by changes in the secretion of the pancreas and adrenal bodies; I contend that these facts (if they may be considered such), tend to the belief that the abnormalities of the structures mentioned are due to a common cause and that the weight of evidence is in favour of that cause being

a bacterial toxin.

It has been established that, except in the cases of acute inflammation of the thyroid, (which is an exceedingly rare disease following such cases as puerperal fever or erysipelas) the presence of bacteria in the thyroid gland is unknown. J.J.Gilbride (33) has stated that there are no bacterial growths within the thyroid itself during life, except in the case of a general blood stream infection; and if we accept this, while claiming that goitre is a bacterial disease we have to admit that toxins circulating in the blood are the agents producing changes in the thyroid secretion.

Having advanced the thesis that all the common disorders of the thyroid gland are due to bacterial toxins, I propose to discuss some of the possible origins and routes of entry of such toxins.

I have frequently noticed what I thought to be evidence of early exophthalmic goitres with slight thyroid enlargement in patients who have come to me complaining of general nervousness and weakness, to find in time that they were suffering from some chronic infective disorder: a month ago a patient died from tuberculosis of the lungs; her only symptoms before the last three weeks of her life were palpitation and muscular weakness, and the only abnormal physical signs were

enlargement of the thyroid gland and rapidity of the heart's action. Repeated examinations of the lungs by the local Tuberculosis Officer and myself, at intervals during the last three years, had failed to elicit proof of what the Medical Officer supported me in suspecting. A patient with similar symptoms, seen in the Out-Patient Department of a Hospital twelve years ago, comes to my memory as illustrative of the same point; this girl had a normal temperature and a clean tongue, but such extreme tachycardia and tremor, along with enlarged thyroid, that she was admitted direct to the wards, and was later proved to have typhoid fever. Many similar cases occur, but, personally, I have no recollection of seeing one later develop any abnormality of the thyroid. Leon Berard (34) relates the development of goitres in young men, three cases of which he describes as very acute attacks, following fatigue and exposure, along with dysentery and typhoid fever. Several other diseases have been considered responsible for the origin of hyperthyroidism, not necessarily with any signs of such an advanced condition as to warrant the name of exophthalmic goitre. A.J. Todd (35) dealing with 1500 cases of influenza in an epidemic, found 15 of them with definite hyperthyroid symptoms, and Roeder (36)

had a similar experience, and noted that already existing adenomata were increased in size.

The relationship of increased activity of the thyroid to febrile disturbance may be noted in the increased tissue waste in fevers and the rise of Basal metabolism in hyperthyroid conditions.

Jennings (37) notes the occurrence of two cases of measles, one of which died, and the other recovered after thyroidectomy, in patients the subject of exophthalmic goitre; this to my mind illustrating that an intercurrent infection may impose further strain on an organ already suffering from the effects of a chronic toxæmia. The consideration of endemic or epidemic goitre has been very fully discussed by Mc Carrison in his book on the subject, and as it illustrates one aspect of the infective origin of that condition I propose to go into some of the points raised by him. Before doing so, I may touch on an ~~an~~ Etiological question noticed by H. E. Durham: (38) he states in reference to the city of Hereford, that it is common knowledge that the condition of goitre, from being a common disability in rural districts in Herefordshire, has invaded the city itself; he noticed as many as 1 in 8 on some days at Recruiting Medical Boards held in Hereford in 1918. Durham quotes Dr. C. S. Morrison thus:—"The increase

(in cases of thyroid insufficiency admitted to the County and City Asylum, Hereford, in five year periods in 8th and 10th decades of last century) is sufficiently striking to be recorded, and has, I think, an important bearing on the issues of degeneracy".

Durham points out that, although admittedly the men examined in 1918 were seldom first class lives, the frequency of thyroid disease is less in men than in women as a rule, and that therefore the incidence of the disease as a whole must have then been tremendous.

My reason for introducing Durham's paper on the Hereford figures is that my deductions from the evidence he gives are, that as there is much greater migration of people in rural districts into the larger towns, and that the daily going to and fro of both country and town dwellers is more frequent of recent years, the opportunities for contact between the two classes is greater, while there is a bigger proportion of country-bred people employed in the town: the latter increase is probable of little account when we compare the comparative populations of town and country, but the increased contact from improved travelling facilities is not a matter of conjecture. A further point dealt with in the same paper is this - that the water supply has improved and that thyroid disease has not

diminished but rather increased; in view of the fact that some defect in the water supply has been held responsible for the goitre endemicity in many regions, the remarks of Durham are enlightening.

Mc. Carrison (39) makes a reference to the rapid spread of endemic goitre in Nagar following the opening of the district to trade and intercourse from without, after 1893, and relates the history of a small epidemic of the disease in the house of a priest introduced to the district from outside, most of the infected persons being young; and he states that children introduced in a goitrous district are more prone to develop thyroid enlargement than are adults. It will be agreed that any child with unhealthy and large tonsils and adenoids, if introduced into a fresh neighbourhood is even more liable to contract nasopharygeal trouble than an adult.

Mc. Carrison's further observations on his investigations on troops stationed at Gilgit, in Chitral, and elsewhere, are interesting in that, apart from the probability of an infective agent contained therein, water supplies are to all intents exonerated; the experiments of Marine and others with fish as detailed by Mc Carrison (40) point to nothing more surely than an infected water supply, while deductions from his own experiments with groups

of recruits introduced into a goitre-producing district are not all completely free from the possibility of fallacy.

Mc Carrison (41) compared the effects on young, presumably unaffected recruits, of drinking water filtered and unfiltered, boiled and unboiled, procured from goitrous and non-goitrous districts, containing no sediment, and with sediment in suspension, from the beds of water channels in goitrous villages. I think Mc Carrison allowed room for one fallacy to creep into his experiments with these soldiers, in that the men appeared to have been housed together; and it is presumed that the men were selected for experiment after their arrival in the stations, when opportunities had probably arisen for contact with the inhabitants of the district. Mc Carrison does not state that the men selected were marched across the frontier in a band separate from the rest of their regiment, or put under close guard behind wire till the experiments were over.

The writer (Mc Carrison) has previously mentioned (42) the occurrence of an epidemic in the Bishop Cotton Boys' School at Simla, in which the water supply was held to be innocent: a point of interest to me in this account of the

outbreak mentioned, is the fact of its occurrence in a school of considerable size in a well administered hill station, in circumstances in which it may be presumed that the general environment, as regards cleanliness, ventilation and food supply, was likely to be satisfactory. Mc Carrison (43) proceeds to state ^{that} there are proofs that boiling and filtering of drinking water has not been sufficient to prevent the occurrence of cases of goitre in an area affected by it, but goes on to mention that (44) the prevalence has decreased in certain regions with the improvement in purity of the water supply: and further draws the conclusion (45) from his own observations and those of other investigators, including the Swiss Goitre Commission, that no organism is definitely proved to be at fault, but that there is a common increase in bacterial flora in the water supplies of goitrous areas. I need state but two other statements in Mc Carrison's series of lectures (46) "various chemical and experimental evidence goes to show that there is a definite relationship between the reaction to bacterial toxins and alterations in secretion and histology of the thyroid", and herein, to my mind lies the essence of the matter as far as investigation has gone. When the author again states (47)

"that goitres have been uniformly sterile" he does not infer that the fact in any way removes the blame from the bacteria.

Observations on the blood changes in different varieties of goitre tends towards the view that a bacterial or other parasitic organism is responsible; although variations occur as between these varieties, the blood picture has invariably some similarity to one or other of the diseases known to be produced by bacteria or other living excitant.

The frequency of eosinophilia of a high grade in the general blood stream, the thyroid blood, or bone marrow, and other alterations from normal in the proportions of various leucocytes in the active or progressive varieties of goitre all point in this direction.

A Summary of the points that I have tried to emphasise will simplify the consideration of the conclusions which I propose to draw.

1. The changes in the thyroid in the three most common varieties of thyroid disease with which I have dealt, are all variations of one process, therefore it is justifiable to presume that they all originate from one cause.
2. Thyroid changes are clinically apparent in various febrile conditions known to be caused by

bacteria or other parasites. (I have mentioned the parasitic thyroiditis of Chagas as an example.)

3. The blood picture, although varying in different varieties of goitre are all suggestive of a bacterial excitant.

4. Evidence produced in favour of other causes (than a bacterial or parasitic infection) has been largely discounted; this does not apply to the consideration of predisposing causes. The heavier incidence of hyperthyroid and hypothyroid conditions in the poorer, less educated, and most poorly nourished classes, and those least adequately catered for in a medical sense, is taken as granted: the ready access to the physician and surgeon which is procured by wealth, and the advantage taken by the better educated classes of skilled medical advice, are reflected in the better average health of the rich as compared with the poor, which is not all accounted for by difference in feeding and environment.

Conclusions.

In drawing the following conclusions, I have taken into account the observations of various writers and attempted to reconcile them with my own observations made upon patients, both in

institutional and private practice; the cases of thyroid disease with which I have come in contact have, with very few exceptions, been possibly, and many of them have been probably, attributable to bacterial infection. I have concluded:-

I. That all diseases of the thyroid gland, except those classed as malignant, are caused by the action on the gland of bacterial toxins.

II. That the responsible bacterial infection may be transmitted from one person to another by contact or infection, through the water supply, or otherwise.

III. That the bacterial toxins originate from a variety of organisms.

IV. That some of the bacterial infections are due to organisms, possibly ultra-microscopic, which are capable of prolonged existence outside the human body.

V. That many organisms, when introduced into contact with susceptible persons, may produce abnormal action of the thyroid gland in one individual, without similarly affecting others exposed to the same infection.

VI. That infection may take place through a variety of channels.

VII. That much the commonest locality of infection by goitre-producing organisms is by way of the upper part of the alimentary tract.

VIII. That the most common localities for the entrance of toxins into the circulation are the tonsils.

IX. That, once commenced, the abnormal action of the thyroid gland may proceed without further infection, but is more liable to be increased thereby.

X. That the best means of combating the great amount of thyroid disease, is the adoption of adequate hygienic measures, with the aid of surgery if necessary, calculated to discourage or prevent the ingress of toxins by the tonsils.

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