E N D E M I C G O I T R E

with particular reference
to its occurence in Lanarkshire
and to its Etiology.

THESIS FOR M. D.

BY

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(high commend 1891)

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"LANARKSHIRE":

W. Brown. del.

INTRODUCTORY.

Endemic Goitre has been so long regarded by all who have done any work upon it as a mystery, that it is with a feeling akin to hopelessness that one approaches the subject. Yet the recent discoveries upon the part which the thyroid gland plays in the body make us more hopeful that the solution of this mystery lies closer to our hands than it did.

Perhaps no disease has had so many theories of causation, for almost every possible agency conceivable has, at some time or another in the history of the disease, been assumed as its cause. When we consider the peculiarly definite and circumscribed nature of its distribution over the Earth's surface, this is hardly to be wondered at; for an observer very naturally

Too many "it"s all through
12 in this page alone

ascribes to
blames its prevalence upon whatever happens to be the difference between the natural features of the affected and those of the immune neighbourhood around. As the knowledge of the distribution of the disease has gone on increasing, however, we find one after another of these old theories dropped, and it is very doubtful whether its endemic prevalence is associated with any one constant factor in the physical features of a locality.

In like manner it has run the gauntlet of a host of remedies, all more or less successful. Iodine alone has stood the test of time, although it cannot be looked upon as by any means a specific remedy. Within the last few years treatment by feeding with thyroid gland substance has been tried. This will be dealt with later on.

The limits of its endemic prevalence in Lanarkshire have never before, so far as I am aware, and I have gone over most of the literature, been wrought out. We have no means of stating when it began here. Its prevalence is widespread, probably 1 in 4 women of the working classes being markedly affected, while the majority show a slight enlargement compared with the normal condition of the gland.

where is that?

It is accepted as an irremediable misfortune. A doctor is comparatively seldom consulted, and then only when it produces symptoms interfering with the bodily comfort of the patient. I can only find one death attributed to "Goitre" in the parish records and have seen another fatal case myself. Although I have at present under treatment two cases of cretinism (see P. 79) it cannot be said to be endemic, at least to the extent found in Switzerland etc.,

NOMENCLATURE.

The name
"Goitre," "Goître" or "Gotre" is probably a corruption of "guttur" (the throat).

This name

It is popularly used in Switzerland (1) for enlargement of the thyroid. In England it is often called "Derbyshire Neck" a name first applied to it by Prosser (2) from its frequency in the hilly parts of Derbyshire, and "English Bronchocele". An old synonym "Ivew" has dropped out of use. Heister suggested "tracheocele", obviously a misnomer. "Thyreocele" is occasionally used. Mitchell(3) who first described its occurence in the Lowlands of Scotland, added "Nithsdale Neck" to the list. The German names are "Struma" (from struere" to pile up, and "ruma" a pap or teat)(4) and "Kropf" (the crop of a bird). The word "Goitre" is now applied loosely to all enlargements and tumours of the thyroid body, and is often, on that account, a source of confusion. Thus in a book(5) published on Goitre in 1894, the writer is not always careful to say whether he means "Exophthalmic" or "Endemic goitre" and we are left wondering, often, as to his meaning. "Goitre" will be used to designate the endemic disease throughout this thesis.

"Endemic Goitre" is thus defined in the "Nomenclature of Diseases" (R.C.P. London 1869).- "Enlargement of the thyroid body endemic in certain mountainous districts, but not limited to them".

(1) Hoblyn's Dictionary of Medical Terms, Edited by Price. 1887.
(2) Prosser "Account of Bronchocele". London 1769.
(3) A. Mitchell. M.D. "On the Nithsdale Neck or Goître in Scotland". Brit: & For: Medico-chir: Review LV111. April 1862.
(4) C.A. Ewald "Die Erkrankungen der Schilddrüse, Myxödem und Cretinismus" Wien. 1896.
(5) Edward T. Blake. M.D. "Myxoedema, Cretinism & the Goitres" Bristol, John Wright & Co., 1894.

In Hoblyn's Dicticnary it is thus described, "Goitre consists in an enlargement of the thyroid gland, and is frequently associated with cretinism". In the "Nomenclature of Diseases" issued by the R.C.P. of London in 1896 "Goitre" is divided into seven varieties of which endemic goitre is one. The thyroid gland in endemic goitre may however (as we shall see) present features which would bring it under any of the heads, except "Exophthalmic goitre".

HISTORICAL.

From the prominent position of the unsightly tumour, and from the dangerous and often fatal results which mark its presence in the individual and in the community, goitre has long been recognised as a distinct pathological entity. The cutting at the head of this thesis shows that it was known in very ancient times. It is taken from a terra-cotta cast discovered by Dr Luigi Sambon at the temple of Esculapius on the Island of San Bartolommeo, and was removed from there to Capua. It is evidently a "Donarium" or votive- offering of Etruscan origin, and probably dates from about B.C. 2000.(X).

** An occasional reference to tumours of the neck in the Latin classic writers of Rome (Pliny, Vitruvius, Juvenal etc.,) may be taken as meaning goitre. St. Remi in the 5th century, bestowed the curse of "gutturosa" upon certain female delinquents in the neighbourhood of Rheims (Hinkmar's Life of St Remi. lib: VIII).

(X) I am indebted to Messrs. Oppenheim, Son & Co., Ltd., London, for ~~permission to use~~ this plate, and also for the details of its discovery Etc.

** Birchner (Der Endem. Kropf. p. 2) quotes a few verses from the Atharva Veda, which seem to indicate that Goitre was known to the ancient Hindoos (B.C. 2000-1500)

Paracelsus gave the first description of the disease, as he saw it in the Duchy of Salzburg, and noted the relationship between goitre and cretinism. From the 16th to the 18th century many writers describe the existence of endemic goitre in very much the same localities as it is found at the present day (Styria and the Valais, etc.,) Hirsch(6) to whom I am indebted for most of this information, states, that endemic goitre is proved to have occured as "early as the pre-Christian Era", but that the history of cretinism does not carry us so far back.

Within this century, the greatest work has been done on the Continent, as naturally is to be expected from the great prevalence of the disease there. In Switzerland and Germany at the end of last century, Ackermann(7) led the way. Demme(8), the Sardinian Commission (in Italy) 1845-48, St Lager(9) and a "Commission of Enquiry on Goitre and Cretinism in France" (1873) did most in the middde of the century. Hirsch's Book contains an enormous mass of information upon the subject, brought together from all possible sources.

Our recently acquired knowledge of the functions of the thyroid gland will probably prove the first steps to arriving at a correct conclusion as to the nature of endemic goitre.

(6) Dr August Hirsch's "Handbook of Geographical and Historical Pathology" Translated by C. Creighton, M.D. New Sydenham Society 1885 p.122 & Seq:

(7) Ackermann "Ueber die Cretinen, eine besondere Menschenart in den Alpen". Gotha. 1790.

(8) Demme "Ueber Endemischen Cretinismus" Bern. 1840.

(9) St Lager, J. "Etudes sur les causes du Cretinisme et du goitre endemique". Lyon. 1868. (now out of print.)

Schiff(10) (1856 and again 1882), Sir William Gull "(1874)(11), Ord(12), (1878) who first showed the connection between the thyroid and myxoedema, J. & A. Reverdin(13) (1882), Munk(14), Schäfer(15), Oliver(16), Lorrain Smith(17), and Horsley(18), are honoured names in this connection.

Murray J Mackenzie.

(10) M. Schiff, "Resumé dune serie d' Experiences sur les Effets de l'ablation des corps thyroides" Revue Méd: De la Suisse romande. 1884. No. 2. & 8.

(11) Sir W. Gull, "On a cretinoid state supervening in adult life in women". New Sydenham Soc: collection of Sir W. Gull's writings. Medical Papers. P. 315.

(12) Dr Ord, " On Myxoedema etc.," Medico Churgical Transact: Vol: LX1. 1878

(13) J. & A. Reverdin, " Note sur vingt deux operations du goître Geneva. Rev. Méd de la Suisse romande 1883. No. 4 & 6, etc.,

(14) H. Munk, "Untersuchungen über die Schilddrüse" Sitzungsberichte der preuss: Akademie der Wissensch: Bd. XL1.

(15) Schäfer, "On Internal Secretion" B.M.J. Aug. 10th 1895, etc.

(16) G. Oliver, "A contribution to the study of the blood and circulation." Croonian lecture, B.M.J. June 13th, 1896.

(17) J. Lorrain Smith, "On some effects of Thyroidectomy in animals" and Journal of Physiology, Vol: XV11. P. 378.

(18) Horsley, Many publications; and an address on "The Physiology and Pathology of the Thyroid Gland". B.M.J. December, 5th, 1896.

Of more recent workers on endemic goitre, Rose(19), Birch(20), and Kocher(21), in Switzerland, C.A. Ewald(22), and Mikulicz(23) in Germany, and Wölfler(24), may be mentioned. Berry's(25) valuable articles on the pathology of goitre, must of necessity be read by every one who wishes to become acquainted with this branch of the subject.

GEOGRAPHICAL DISTRIBUTION of GOITRE.

Endemic goitre is found all over the world, in more or less sharply demarcated localities. Within its boundaries it is a typically endemic disease.

(19) Rose. "Der Kropftod u. die Radicalcur der Kröpfe" Arch: f: klin: chir: Bd: XXII. p. 1.

(19) E. Rose, "Ueber die Exstirpation substern: Kröpfe". Arch f. klin: chir: 1878, Bd: XXIII. 2 Heft.

(20) Birch, "Der Endemische Kropf u. seine Beziehungen zur Taubstummheit u. zum Cretinismus" Basel. 1883. &c.

(21) Kocher, T. "Vorkommen u. Vertheilung des Kropfes im Kanton Bern" Bern 1889. etc.,

(22) Ewald C.A." Die Erkrankungen der Schildd:, Meyxödem, u. Cretinismus" Wien. 1896. &c.

(23) Mikulicz. S. "Thymus fütterung bei Kropf u. Basedow'scher krankheit" Berl: klin: Woch: 1895, No. 16. etc.,

(24) Wölfler "Ueber die Entwicklung u. den Bau des Kropfes" Archiv: f: klin: Chir: Bd: XXIX. 1 & 4 Heft.

(25) Berry, Jas. M.B. " On the Pathology of Goitre and some other diseases of the Thyroid" Trans: Path: Soc: Lond: Vol: XLI, 1890. P. 258.

From an examination and survey of its occurrence much has been expected in the way of clearing up the doubt upon its etiology, for, if one common factor could be found common to all affected and absent from unaffected districts, we might safely say that we had laid our finger upon the cause of the disease. Many of the present theories of the etiology depend upon our knowledge of the distribution of the disease for comfirmation or refutation, so an examination of the goitre districts of the world is necessary. Along with goitre, as a rule, goes cretinism.

On the Continent of Europe, the chief centres of goitre and cretinism are found in, and around, the great mountain-chains- in the Western and Southern slopes of the Alps of Italy, Switzerland, and France, along the Eastern continuations of the Alps into Austria, in the neighbourhood of the Jura and Vosges Mountains (France) and in the Pyrenees(26).

In Italy, a table compiled by Hirsch from Sormani's (27) list of rejections of army recruits shows, that goitre and cretinism are most prevalent at the foot of the Alps, particularly & in the Alpine villages of Piedmont in Piedmont and Lombardy, particularly in the river-valleys (of the Dora, Po, Adda, and Chiese).
Although in the province of Venice we find centres in the valleys of Belluno, and Udine, yet the general area of the goitre endemic of Italy is sharply defined towards the East by the boundaries of Lombardy (the Mincio river and the lake of Garda), and southwards by the river Po.

(26) Hirsch. (l.c. P. 124. & seq) is my authority for most of what follows on the geography of goitre.

(27) Sormani, "Geografia nosologica dell' Italia" Roma, 1881.

Thus west of the lake of Garda and the Mincio river the estimated amount of goitre is 112 per 1000 inhabitants, and east of these boundaries only 4 per 1000.

Cretinism occurs in direct ratio to the amount of goitre. From 10·7 per 1000 recruits (in Aosta), to 4·5 per 1000 (in Chiari), were rejected on account of cretinism and idiocy. These numbers are not quite reliable, for they, firstly, refer only to adult males and hence under-estimate the amount of the disease among the general body of the inhabitants, and, secondly, include all forms of idiocy as well as cretinism. The Italian special Commission of 1883, quoted by Ewald(28) gives somewhat similar numbers, thus Lombroso is quoted by Hirsch(29) as giving the number of cretins in Lombardy in 1859 as 1·7 per 1000 inhabitants, and the Commission of 1883 makes it 2·5.

We also find goitre and cretinism centres in the Northern slopes of the Appenines in Piedmont and the Aemilia, but to a less extent. They are uncommon in the rest of Italy and absent from Sicily and Sardinia.

The districts in France(30) most affected with goitre and cretinism are, as in Italy, those bordering on the Alps, together with the Pyrenean Departments.

(28) C.A. Ewald, Die Erkrankungen der Schilddrüse, Myxödem und Cretinismus" P. 54.

(29) Hirsch. l. c. P. 127.

(30) "Rapport de la commission d'enquête sur le goître et la crétinisme en France" Paris. 1873.

From the Commission we find that goitre in the Alpine Departments (Haute Savoie, Aisne, Savoie, Hautes Alpes, Basses Alpes and Alpes Maritimes) affects from 133·7 per 1000 inhabitants, (Savoie) to 50·7 per 1000 (Alpes Maritimes), in the Jura and Vosges (mountainous districts) from 58·9 to 56·8 per 1000, and in the Pyrenean Departments, (Basses Pyrénées, Hautes Pyrénées, Arriège, Pyrénées Orient) from 82·7 per 1000 (Arriège) to 24 per 1000 (PyrénéesOrient). The rest of France is affected more or less according to the distance from these centres. In a very large number of the more remote Departments goitre may be said hardly to exist.

Cretinism is commonest in Savoie and Hautes Alpes where goitre is most prevalent, but in the Jura with a goitrous ratio of 58·9 per 1000 there is very little cretinism (2·5 per 1000). The same is seen in Aisnes, and in the Nièvre we have, as sometimes happens, goitre and no cretinism. Ewald(31) informs us, that the total number of goitrous and cretinoid persons in the whole of France for a period of over 20 years is equal to 10·4 goitre and 3·3 cretins per 1000 inhabitants.

With the exception of a group of four Cantons (St. Gallen, Thurgau, Schaffhausen, and Zurich) in the North-east, Unterwalden in the middde, and Freyburg and Geneva in the South-west, the whole of Switzerland is more or less affected with both goitre and cretinism. Uri, the Vallais, and Bern are the chief seats of both diseases. In the last named Canton Kocher(32) says that in one locality (St. Immerthal) as many as 90.p.c. of the school children have enlarged thyroids, and 40 p.c. undoubted goitres

(31) Ewald. l.c. p. 55.

(32) Kocher, T. " Vorkommen und Vertheilung des Kropfes im Canton Bern" p.7. Bern. 1889.

The river valleys of the Aar (Birch) Reuss, and Rhone, are also

The river valleys of the Aar (Birch) Reuss, and Rhone, are also
strongly affected. Geneva contains a few goitre centres without cretinism.

Austria is affected in the provinces bordering on the Alps, the Tyrol, Salzburg, Upper and Lower Austria, Styria, and Carinthia, particularly along the river valleys. In these regions there are many instances of goitrous centres away from the mountain ranges down on the flat country. Gratz, a town in Styria, is according to Hirsch not very severely affected, but in Bircher's map* it lies in the middle of a large district of numerous goitre centres.

In Germany, the kingdoms of Bavaria and Würtemberg afford us instances of a decrease in the prevalence of the disease within very recent times, although in the latter some considerable centres still exist. In Baden we find goitre in large numbers, in the districts bordering on Schaffhausen (in Switzerland.) (Stühlingen(33) with 105·2 per 1000).

The low lying plains of North Germany, the Netherlands, Belgium, Norway, Sweden, and European Russia, are free from goitre.

In Spain it exists in the valleys of the Pyrenees, in smaller endemics in the Cantabrian mountains, and in Sierra Morena and Sierra Nevada. No numbers are given.

Goitre is comparatively common in England, but cretinism as an endemic disease is unknown. It is found more in the South and Midlands than in the Northern hilly counties.

(33) Weber. Mittheil: des bad: ärztl: Vereins, 1857. 27.

* See end of this Thesis.

We hear of it in and around Horsham, among the chalk hills of Sussex and Hants, in the upland parts of Surrey—particularly Haslemere in the West, in several parts of Monmouth(34), in the Forest of Dean (Gloucestershire), in one district of Cheshire, and several parts of Wales. In the East there is a centre in Norfolk, one in Bedfordshire, and one in Bucks (Hambleden)(35). In the Midlands it is endemic in Warwickshire, in the coal districts of Notts, particularly in Derby, and in the hilly parts of Stafford. In the North it is said to exist at Bolton in Lancashire, in Yorkshire, in some parts of Westmoreland and Durham, in the neighbourhood of the lead mines of Cumberland, and in the West of Northumberland.

It is less frequent in Scotland. In the interior of Perthshire and the East coast of Fife it is present, but the greatest endemic centres are found in the Lowlands. In 1862 Dr A. W. Mitchell(36) describes it as occupying "the greater part of Roxburgh, the upper parts of Selkirk and Peebles(37) the Eastern parts of Ayrshire where it touches Lanark and Dumfries, the upper districts of Lanark, the whole of Kircudbright and Dumfries, the west of Berwick and the East parishes of Wigtown. It

(34) Glover. B. M. J. July 13th 1896.

(35) H. C. L. Morris. B. M. J. July 6th 1895.

(36) A. W. Mitchell, M.D. "On the Nithsdale Neck or Goitre in Scotland" Brit: and for: Medico-chir: Rev: LVIII. Ap, 1862. p. 502.

(37) See also "Discussion on Endemic Goitre". Border counties Branch. B. M. A. in B. M. J. Feb. 27th 1897. Dr Somerville's remarks.

reaches its intensity in the upper valley of the Nith," where Dr Chalmers of Thornhill, reports, it affects half the women. Dr Jackson writes me from Sanquhar, that it is still common in that district, but that the individual goitres are small and cause no trouble. The only part of Lanarkshire where Mitchell knows of its existence is in the extreme south. I can now supplement that. In Lanarkshire, it exists in varying degrees of intensity in the valleys of the Clyde and its tributaries in the upper and middle wards particularly on the west side. It reaches its height in the coal -mining districts of Larkhall, Wishaw, Dalserf, Carluke, and Stonehouse, and in the agricultural districts of Strathaven, Lesmahagow, and Blackwood. It dies off immediately south of Hamilton somewhat abruptly. Drs Goff and Grant inform me that it is quite absent from Bothwell and Blantyre. In Wishaw and Newmains (Coal and Iron centres) it is prevalent, (Dr Millar, Newmains). In Strathaven, it attains proportions as great perhaps as with us in Larkhall, particularly affecting the farming classes there, among whom it is found to the remote western boundaries of the county and to the adjacent parts of Ayrshire. Dr D. Dougal of Strathaven, to whom I am indebted for this information, also states that it is increasing in severity. In Lesmahagow and Blackwood and the surrounding neighbourhood, it exists in considerable numbers and according to Dr John Lindsay of Blackwood, shows no sign of decreasing. From the south of the county conflicting reports reach me; from some sources I am told it is quite absent and again. that it is present to a slight extent. Probably from what we know of its prevalence in the surrounding counties and from what Mitchell says, we may take it, that it does exist, although perhaps, in a mild form, in which case unless it were specially sought for it probably would not be noticed. (X)

7 "it" in 6 lines!!

(X) For most of the information herein contained I beg to express my indebtedness and thanks to the gentlemen mentioned in the text and also to Dr Adams of Lanark, To Dr Lindsay (Blackwood) I am indebted for many hints on the subject in general.

See map of Lanarkshire appended. The affected area is marked by lines.

See also Appendix. Note A. for details &c. p. 1.

In and around the town of Larkhall, it occurs markedly in about 25 p.c. of the female inhabitants, and a much larger percentage show slight enlargement of the gland. Men are rarely affected; children occasionally are. I have seen two congenital cases. Of the whole population perhaps, about 10-15 p.c. are affected, the large majority so slightly as to escape their own notice. At the same time, I have seen some very large tumours (to this I shall return later on). About 98p.c. of the cases occur in the mining and labouring classes. The most severely smitten parts are those in the Avon valley, and the largest goitres are found in those whose forefathers lived here before them.

As I remarked before cretinism in an endemic form does not exist here or anywhere else in Scotland.

Goitre is said to exist endemically in a few places in Ireland.

As in Europe so in Asia, the headquarters of the disease are found in the great mountain chains which form the "back bone" of the Continent. On the northern and southern slopes of the Himalayas, goitre and cretinism are endemic to a high degree. A notable exception to the preference of goitre for hilly districts is found in the great Central Indian plateau, where there is a large amount of it. It seems to be absent from the other mountainous parts of India (Nielgherry and Ghaut mountains). In other Asian countries, particularly in North China, and in Siberia, centres are found.

From the centre of Africa, no reports of endemic goitre have come yet, but it is said to occur in the Atlas mountains (Morocco), and to be quite absent in the great river-deltas and the continent generally along the sea-board.

It is absent from Australasia. In the American continents goitre is largely endemic in and around the Andes chain, from Rio Grande del Norte (New Mexico) in the North, to Chili in the South. Although it appears here and there in the United States, it is more common in South America. The severity

of the desease around the Andes chain is said to be quite as great as the Alpine endemic.

CHARACTERISTICS of the GOITRE ENDEMIC.

Goitre as an endemic disease presents several peculiarities which are of great interest, and as a whole quite unprecedented.

What does "unprecedented" mean here?

First of all, we meet with the remarkable fact that women are more subject to goitre, in the endemic form, than men. Wherever authorities mention the question of the influence of sex they state that it occurs "preponderantly", or "almost exclusively", in the female. According to some, (Morel, Manson), the proportion is 1 man to 11 or 12 women; the French Commission fixes the ratio at 1 to 2 or 3. In 77 cases of goitre, ranging in severity from moderate to very great, which I investigated here, there are 12 cases of goitre in men, a proportion of about 1 to 5½.

Another interesting fact in connection with the disease is, that in the endemic areas, the lower animals are often found goitrous, (St Lager, Bircher)*. Although I have been on the look out for about 5 years, I have not yet seen any instances of this here.

When we are able to obtain a history of goitre and cretinism in any particular place for some lenght of time, a variation in the intensity of the disease will often be found. It may be that it has increased in severity, or a gradual decrease may be experienced or an alternation of increase and decrease, or again, goitre may make its appearance as an endemic disease in localities where it ~~had~~ has hitherto been quite unknown. In Piedmont(39), in many parts

a "if" a/m

(39) Fodéré "Essai sur le goître et le cretinisme" Turin, 1792
The Report of the Sardinian Commission. Etc.,

* Bircher l. c. pp. 10 & 11.

of Switzerland(40), in the Pyrenees, in several French Departments(41), in the Rhine-lands, Bavaria and Würtemberg(see p. 11) the endemic has considerably decreased, particularly within the last ten years(42). Denny(43) reports, the appearance of the disease in Pittsburg, where it was unknown at the time of the first French colony, its growth to a very considerable endemic in 1798, and its subsequent decline after 1806. We have already seen (p 13) that the Lanarkshire endemic, in one place has undergone an increase within the last 30 years, and probably a longer acquaintance with the subject will, as time goes on, provide many more instances.

A striking feature of most goitre endemics is their limitation to definitely demarcated areas. Instances of this are afforded in Lombardy (p. 8) and in Lanarkshire (p. 13).

The bearing of these facts upon the etiology of goitre is evident. It must be due to an agency which is capable of ~~spreading~~ increasing and lessening.

One of the most striking events in the history of this very remarkable disease, is the occurrence of epidemic outbreaks. Most of these have occurred in France, and chiefly amougst the military. Hirsch(44) quotes from Valentin (in Simonin's "Récherch: topograph:" 411.) an account of an epidemic outbreak of goitre in a regiment, which in the year 1783 was moved

(40) Mayer Ahrens in Rösch's Zeitschr: ~~III.~~ 7. 15.

(41) Aguilhon "Gaz: méd: de Paris 1851. 135 etc.,

(42) Ewald. l.c. p.57.

(43) Denny. quoted by Hirsch l.c. p.155.

(44) Hirsch. l.c. p.156.

from Caen, where they had been quartered for five years, to Nancy where endemic goitre previous to this had not occurred. Early in the winter of that year, 38 men of the regiment became goitrous. From that time the numbers gradually increased until 1786, when 425 men were affected. Then it slowly decreased. The epidemic lasted five years and affected in all 1006 soldiers out of 4 battalions(45). Privates alone were affected; corporals sergeants, and officers who shared the same Barracks, and drank the same water(46), remained exempt. The civil inhabitants and soldiers previously in the town were unaffected.

Other epidemics similar to, but perhaps, less severe than this one are recorded in Germany(47), but chiefly in France.

Hirsch sums up the following points as common to all.

1) Except in Nancy and Paris(48) they occured in goitrous localities.

2) The epidemic occurred in detached premises (such as barracks, seminaries, etc.,) and the outside population were unaffected.

3) In the case of military epidemics it has often been confined to one barrack or section.

4) The common soldiers, especially if young, rarely the non-commissioned officers, and almost never the officers, were affected: and it appeared in troops who had just been brought into the neighbourhood.

(45) Leberts account from the same source "Die Krankheiten der Schilddruse " Breslau. 1862.

(46) Idem.

(47) Idem and also Hancke. Hufeland's Journ: der Heilkde. 1838. Bd.86. Heft.5. 77.

(48) See Hirsch. p.158. An epidemic in a Boarding-house near Paris. See also Bircher. p. 12 & seq.

It will occur to most, I think, that this seizure of new comers points to residenters having acquired an immunity which enabled them to resist the poison even when in great strenght; this is supported by the fact that persons newly arrived in a goitrous locality often present a trifling swelling of the thyroid which, after a longer stay, disappears spontaneously. Ewald (49) says, that so common is this in Swiss Pensionaires "that hardly any notice is taken of it".

In the Nancy epidemic it is difficult to explain the escape of the officers, but it is more often the case perhaps, that the only part of their lives which officers and soldiers share in common is their professional duty, in other respects their circumstances are generally widely different.

The removal of a goitrous individual from a goitrous district is usually, particularly if the goitre is young, followed by a disappearance of the tumour. Thus we sometimes hear of servant girls home on a holiday, developing a goitre to lose it again on returning to their work in an immune neighbourhood.

ETIOLOGY of GOITRE.

St Lager can number no fewer than 378 authors and 42 different views on the causation of goitre!

Most of these have been forgotten but there are still a number of different opinions, and the most prominent of these will come up here for discussion. Many of them are of considerable importance but not in the way their originators expected, for in view of the modern theory, those will sink to the rank of predisposing causes. The modern view and the one accepted by the most prominent authors in the branch of medical science is, that endemic goitre is due to a contagium vivum. The occurrence

(49) Ewald. l.c. p.59.

of the disease within well-defined areas, its fluctuations in severity, its occasional epidemic outbreaks, the fact, as we shall see later on, that boiling the water of a "goitre- well" renders it harmless, all point to this explanation. In these respects it bears a general resemblance to the infectious diseases. Opposite opinions are, however, expressed occasionally in the Journals.

But there must be some reason why this contagium vivum occurs only in certain well-marked areas. We know that the virus of yellow fever for instance, requires the temperatures of the tropics for its proper growth, and that the malarial organism flourishes in a combination of heat, moisture and decaying vegetable matter(50). In like manner we ought to be able to postulate the conditions which determine the existence of the goitre poison, and which render one district goitrous and another free from goitre; we ought further to be able to tell how the organism reaches man, and how it produces in the body such a peculiar effect as the enlargement etc., of the thyroid.

With regard to the local peculiarities which are supposed to produce goitre, many diverse opinions are still held.

A glance at Bircher's goitre map(51) and a run over the geography of goitre above, show that the grouping of the most severe goitre centres is in, and around the great mountain chains of Europe, Asia, and America. This has given rise to the opinion that goitre depends upon the elevation of the ground above a certain height.

(50) Laveran. "Paludism". New Syd: Soc: Translation, 1893, Chap. V.

(51) ~~See Ewald, etc., End of Book.~~ See End of This Thesis.

(This and all other older theories of the causation of goitre were at one time held to be the actual causes of goitre and it will therefore be necessary to examine first of all their validity to be so considered, and, secondly, to point out whether they are of any importance as favouring the growth of the goitre organism).

It is impossible to connect these diseases with a definite elevation of the Earth's surface, otherwise we should find all human beings living at, or above that height goitrous; and again we know that goitre occurs in large endemic groups on low lying plains (E.G. the Central Indian Plateau see p.13A).

It is nevertheless undoubted, that nowhere on the Earth's surface do goitre and cretinism attain such a severity as in and around these lofty mountains(52), and therefore it is perhaps, not too much to say, that the configuration of the Earth's surface like what one finds, say among the Alps, is peculiarly favourable to the development and growth of the goitre virus.

Some observers(53) would connect it with the rainfall, holding that it is produced by a high rainfall and excessive moisture, but it occurs in all climates, even in the well-known arid districts of Brazil and Peru, and St Lager (54) points out, that in different valleys of the Alps and Pyrenees identical in rainfall etc., the disease nevertheless varies enormously.

Excessive moisture of the soil has in turn been held by some (55) to be a predisposing factor if not the actual cause

(52) Rösch "Untersuchungen" p.318.
(53) Mitchell. l.c. p.506 etc.,
(54) St Lager "Etudes" p.138.
(55) Wenzel "Ueber den cretinismus" Wien.1802.p.96.

of the disease, and one or two have supposed that goitre occurs chiefly on the older rocks, because of their tendency to the formation of deeply cleft and so damp valleys(56). But from many quarters we hear of goitre endemics upon dry soil. If anything, the evidence from our local centre indicates that dampness of soil has little or nothing to do with it, for it occurs with us as readily upon a sandy subsoil, as on a clayey one. At the same time Fodéré and many others since have reported many instances of the declension of goitre after a district has been well drained. Hirsch(58) thinks that this arises from "a general elevation of the state of health" of the community enabling the inhabitants better to resist the poison. But another explanation might be that the drainage has actually removed the virus from the neighbourhood, for, as we shall see, water is a medium by which it travels readily.

THE GEOLOGICAL FACTOR. Perhaps no question bearing on goitre has given rise to so many diverse opinions than as to whether or not the occurrence of goitre in a locality has some connection with the local geological formations. Since St Lager's time the tide of opinion has fluctuated to and fro, and even yet is not finally settled.

Hirsch(59) gives a "tabular survey of Endemic Goitre and Cretinism as occurring on the several geological formations" and from it concludes, along with Boussingault, the Sardinian

(56) Garbiglietti Giorn: delle sc: med: di Torino. 1845. Guigno.
(57) Fodere "Essai sur le goitre et le cretinisme" Turin. 1702.
(58) Hirsch. l.c. p.174.
(59) l.c. p.168.

Commission etc., 1) that "no geological formation precludes the occurrence of goitre and cretinism," 2) that "the two diseases occur much more frequently (although not exclusively) on the older formation including the trias, than on the newer," and 3) that "the only sedimentary deposits affected are those composed of the detritus of the older rocks e.g. in the plains of the Rhine and Lombardy, and in the valleys of the Arve and Doria(60).

But, as Ewald(61) points out, any conclusions drawn from this table are of very little value, because the geology of the places mentioned is not detailed sufficiently, and a district may be put down as Jurassic, when in reality it is a detached portion of Devonian or Silurian rock insulated amongst Jura, and so, if goitre occurs in such a locality, it would be said, in ignorance of the real fact, that goitre exists on the Jurassic formations, whereas many observers(62) state that the Jura is free from goitre.

A minute and detailed knowledge of the geology of all goitrous regions, not only of the surface but also deeper, is therefore necessary, before one can safely affirm anything regarding it.

Of late years Birch-Hirschfeld(63) has published the results of a series of investigations made by him in the Aar valley and afterwards all over Switzerland. He examined, personally

(60) See also St Lager " Etudes etc., p.443.

(61) l.c. p.63.

(62) Rösch. "Untersuch:" quoted by Hirsch. p.160.

(63) Birch-Hirschfeld "Der Endemische Kropf und seine Beziehungen zur Taubstummheit und zum Cretinismus " Basel 1883. p.14 & Seq.

to a great extent, 3000 school children, and the muster roll of the Swiss recruits, in conjunction with carefully prepared and fully datailed geological maps, and holds, that goitre in Switzerland occurs only on the Trias, Eocene, and marine sedimentary ("Molasse")(X) formations, whilst the fresh water Molasse and Jura rocks, with the crystalline rocks, the chalky formations, and the volcanic rocks are free from the disease. The occurrence of goitre in places on the last named rocks is attributed to the closely underlying marine Molasse, Trias, or Eocene, from which the drinking water comes, or to the presence of islands of Trias etc., among the other rocks. He also states that the presence of a surface layer of fresh water deposits may lessen or nullify the influence of the goitrous rocks (a diagram is given by him to illustrate this.)

A further examination of the geology of goitrous districts leads him further to say, that it also occurs on Silurian Devonian and the Carboniferous rocks.

Berry, also, states that in England goitre occurs only on chalk and sandstone and that the volcanic rocks are free.

Birch[er] sums up his position thus:-##

1. Goitre occurs only on marine deposits, particularly on the marine deposits of the palaeozoic eras(Devonian, Silurian, Carboniferous, and Permian), and of the Trias (secondary), and Tertiary period.

(X)) "Molasse" is the name given to a great series of clays, sands, and conglomerates with some lignitic seams, that occurs in Switzerland. This deposit is for the most part of lacustrine origin (Süsswassermolasse) but it contains intercalated marine beds (marine Molasse). It belongs to the Tertiary formations, Miocene and Oligocene.

Birchu. l. c. p. 5-6.

2. The igneous rocks from the centre of the earth and the solidified eruptive formations of the crystalline rocks on the surface, the Jurassic, Cretaceous and Quaternary sediments as well as all the fresh-water deposits are free from goitre.

In 1889 Kocher(64) after a most painstaking and thorough examination of all the school-children in the Canton of Berne (Switzerland), to the number of 76,606, undertaken by himself, his assistants, and medical students, published his results, illustrated by a geological map of the Canton, upon which he has marked out the goitre centres with a diagrammatic indication of the severity of the disease at each place. After going over his data, I think it is impossible not to agree with most of his conclusions. These are(65).

1. That although at first sight the Jurassic rocks seem less affected, a closer examination shows, that they are not entirely free, although the deeply cleft river valleys are most affected where of course deposits of an irregular nature, Molasse among others, occur.

2. All the districts upon the upper (Miocene), and lower (Oligocene), fresh-water Molasse are affected.

This is diametrically opposite to what Bircher teaches, and indeed it may be said that generally speaking, Kocher's observations do not bear out any of Bircher's conclusions. Kocher thinks that goitre endemics occur more in localities where a "mixing up " of the rocks particularly with organic matter occurs rather than on any particular formation(66).

(64) Kocher" Vorkommen und Vertheilung des Kropfes im Kanton Bern" Bern. 1889.

(65) p.7.

(66) Kocher. l.c. p.9.

Bircher in turn combats these conclusions on the ground that the examinations were made chiefly by students and not by expert medical men, and holds besides, that Kocher's statistics when properly examined do not destroy his views.

Ewald(67) inclines to agree with Bircher and to blame O.Lanz(68), a pupil of Kocher's, for saying, that the geological phenomena are not yet quite disentangled, but most people will, I think, coincide with Lanz.

Larkhall is situated on the southern rim of the great coal-basin of Central Scotland. The thicker coal seams give out just North of the village and about 1 or 2 miles south the transition to Carboniferous limestone occurs. The principal rocks in the neighbourhood are, besides the coal beds, red and grey sandstones, clays, shales and fire-clays. Intrusive basalt is met with here and there. So that I can add nothing to clear up the vexed geological question.

THE VEHICLE BY WHICH THE GOITRE POISON IS CONVEYED TO MAN.

Almost all observers since the time of Paracelsus have noted the connection between the drinking of water from certain wells and the occurence of goitre, and in the whole history of the disease no fact is more universally attested to both by medical men and the laity.

Thus, again and again, e.g., we come across instances of families who, by avoiding the water of suspected wells and using rain or

(67) Ewald. l.c. p.69.

(68) Lanz. "Beitrage zur Schilddrusenfrage". Mittheil: aus klin: und medicin: Institution der Schweiz 111. Reihe: 8 Heft. Basel. 1895.

boiled water instead, remain exempt from the disease, while all their neighbours who neglected such precautions took it(69). And again, many accounts are given of soldiers drinking the water of "goitre-wells" on purpose to escape service, since by this means a goitre was rapidly induced(70). In further support of the theory that the vehicle by which the poison reaches man is the drinking water, we find accounts of goitre endemics disappearing when a new water supply was led into the district. Thus at Saxon(71), in the Vallais (Switzerland), the introduction of a fresh water supply obtained by sinking new wells was followed by the disappearance of goitre, previously endemic. In Geneva, Coindet and others found that after the Rhine water was introduced, goitre died out, save among those inhabitants who continued to use the old wells. A very striking example of this is afforded by the town of Bozel in the Tarentaise(72). The Sardinian Commission in 1848 found here 900 goitrous and 109 cretinoid out of a population of 1472. About 800 metres distant on another valley slope is the village of St Bon which was entirely free from the disease. The water of St Bon was conveyed in pipes to Bozel, and in 1864 the French Commission found the numbers of both diseases reduced to 39 goitres and 58 cretins.

Ewald[73] gives the following account of the decline

(69) Among others, Boussingault. Annal de chimie et de phys: XLVIII.

(70) Among others St Lager " Etudes " etc., p.191.

(71) Bergeret. Compt: rend: Vol:77. No.13. p.15.

(72) Ewald. p.70 and Hirsch. l.c. p.188.

(73) p.71.

of a goitre endemic, (privately cnmmunicated to him by Bircher). Into the district of Rupperswyl, near Aargan (Switzerland), a new water supply was introduced in 1884 from a locality free from goitre on the other side of the river Aar, and the following are the numbers of goitrous school children in the succeeding years:-

In 1885 - - - - - -	59 p.c.	goitrous
1886 - - - - - -	44 p.c.	"
1889 - - - - - -	25 p.c.	"
1895 - - - - - -	11 p.c.	"

In opposition to the idea that the hostile ingredient is in the drinking water Hirsch(74) lodges three objections all of which are probably of less value than he imagined.

Firstly, he states, that "goitre and cretinism have appeared as a new thing in some localities, just as they have disappeared from others, on improvement of hygienic conditions, without any obvious change whatever occurring in the drinking water".

In reply to this it may be generally said, that, in dealing with the origin of disease through drinking water, a negative fact is of much less importance than a positive; & the statement that "no change in the water was obvious" is always open to the objection that the methods of examination were not sufficiently perfect.

Secondly, he says "of a number of villages all in one neighbourhood, some are afflicted with goitre and cretinism whilst others drawing their water from the same source as the former, enjoy an absolute immunity from these diseases, this has been observed by Rösch in Würtemberg, Rudel and others in middle Franconia" etc.,

(74) Hirsch. l.c. p.188.

This seems insuperable, but, as Ewald(75) points out, we are not informed whether the water is exactly the same in one place as in the other, or whether it is weakened by the addition of tributaries between the two places, or whether the subsoil is the same in both districts. For it is plain that a goitre stream may become weakened if not altogether inert by dilution, and that a river may become goitrous in its lower reaches through contamination by the soil etc.,

In the district under my own observation a very important point bearing on this has been found. Larkhall and Bothwell have had the same water supply for about 13 years, viz:- from the Logan burn, a small tributary of the Nethan in Lesmahagow parish. It is conveyed to these two towns in pipes and receives no addition from a fresh source between the two.* Goitre exists in Larkhall and as we saw (p. /3) it is reported that Bothwell is quite free. The water then of itself cannot always be the carrier of the poison, although the instances given above clearly show that on very many occasions it is.

The third objection urged by Hirsch is, "it has been shown also by Gougit, Morelle, Fleury, Viry and Richard Müller and Michaud, that the epidemic outbreaks of goitre in French garrisons cannot be brought into any casual (sic) connexion with the water, inasmuch as those of the troops who were the victims of the epidemic obtained their drinking water from the same spring that supplied the unaffected barracks as well as the civil population, none of the latter having had any part whatsoever in these epidemics".

(75) Ewald. l.c. p.71.

* For Chemical Analysis of this water see Appendix. Note. F. p. 17.

This also like Hirsch's second objection does not indicate whether the water-supply was diluted or changed in any way. In any case it is quite easily explained by the theory that immunity had been acquired by residence (see p. 17.).

Hirsch's further doubts depend upon the negative results of the examinations of the "goitre-well " water, but, as already shown, this is of no importance.

Taking all the facts into account it may be said, that as a rule the drinking water is the vehicle by which the poison of goitre gains access to man, but that other modes of ingress exist. It is possible for the organism to be conveyed by unclean hands, unwashed dishes, etc., etc., Thus we explain the existence of goitre in Larkhall and its absence from Bothwell.

At the same time I must state that, although I cannot give numbers to prove it, since the introduction of the new water supply the number of goitres has probably decreased in proportion to the population, which has grown very much since that event. It is noteworthy that all of the older inhabitants whose conservatism forbids them to forsake the old surface wells are goitrous.

THE HOSTILE INGREDIENT in the WATER

Before the modern theory that goitre is due to an organism, there were many theories in existence, which sought to lay the blame upon some inherent change in the water itself. Even now we occasionally hear of such, and it is necessary to run over them not so much on their own account but rather to discover whether any mineral or other constituent exists favouring the life of the goitre organism.

It used to be, and still is popularly (Hirsch(76)),

(76) l.c. p.189.

believed that drinking snow or glacier water induced goitre(ẋ), but the most superficial run over the geography of the disease shows that it occurs where there never is any snow.

It is still held by many(77) in this country, and I frequently hear it put forward as the popular idea, that the disease arises from the use of hard water. How far this is true may be gathered from the following facts "both positive and negative" as Hirsch says.

Rösch(78) reports that in Würtemberg many of the streams are simply a saturated solution of gypsum in cold water, yet in many places supplied from these sources goitre is absent. On the other hand, he instances places where goitre is endemic and the water free from lime. Maffei(79) and Klebs(80) give similar reports. In the valley of Ridgmont in Bedfordshire there is endemic goitre, and the water is free from lime, whilst all around the water is rich in lime and yet there is no goitre(81). In Switzerland it has been shown that goitre is actually commoner where the water is poor in lime than where it is "hard". In addition to these instances Ewald(82) quotes

(ẋ) Of the many "hints" given in guide books to tourists in Switzerland one is, to avoid "snow or glacier water".

(77) H. C. L. Morris, "Notes on Etiology of Goitre". B.M.J. July 6th 1895.

(78) Rosch, l.c. p.313.

(79) Maffei. "Der Cretinismus in den norischen Alpen". Erlang.1844.

(80) Klebs "Studien über die Verkreitung des Cretinismus in Oesterreich sowie über die Ursache der Kropfbildung" Prag. 1877.

(81) Blower. B.M.J. November 1896. p.924.

(82) Ewald. l.c. p.72.

Tschokke as saying of the highly calcareous "Bibersteinerwasser" and Christener, of the well known hot gypsum springs, that they not only do not cause goitre, but that they actually cure it.

These facts very thoroughly dispose of hard water as the cause of the disease. Nor do we find any grounds for supposing that a high percentage of lime salts favours the life of a goitre organism; otherwise, the reports from Bedfordshire etc., would run differently.

Along with the lime, Magnesia salts are supposed to cause or predispose to goitre, but for this view, as for the last, there is no foundation.

In this connection Kocher(83) publishes in his pamphlet a very interesting account of three families which were non-goitrous in the midst of a generalized goitre endemic. On investigation he found, that all three used water from the same well, while the other inhabitants of the place (a valley in the Bernese Oberland) used water from other wells. He had the water of this, and the neighbouring "goitre-wells", examined and found that chemically there was little or no difference.

St Lager(84) blamed the presence of Sulphate of Iron, and lately L.E. Stevenston(85) has strongly insisted upon this on the ground that goitre is almost universally present where Iron pyrites is found. Hirsch(86) however quotes from Garrigou that not a trace of goitre is found in those very districts of France where

(83) Kocher. l.c. p.15 & seq.
(84) Lager. "Etudes". p.454.
(85) L. E. Stevenston. B.M.J. Oct.3.1896. Feb.27. Mar.13. Sept.18.
(86) l.c. p.178.

Iron Sulphate occurs in largest quantity; while it is endemic in many parts of the country where not a trace of Iron Sulphate or any other metal is found in the soil. These facts certainly do not admit of us looking upon the presence of Iron pyrites in any locality as the "fons et origo mali"(87). Besides, such a theory requires us to admit that an inorganic mineral substance can account for such features as the waxing and waning of an endemic etc.,

Such are the most prominent of the theories which ascribe the disease to the presence of certain ingredients in the water. I have endeavoured, as far as possible, to keep in view the possibility of some of the above mentioned ingredients presenting a favourable locus for a goitre virus; but it cannot be said that any definite conclusion has been reached.

A few observers have been inclined to look upon some deficiency in the usual ingredients of water as being the cause, such e.g. as the want of a proper amount of atmospheric air dissolved in the water (glacier water), of CO_2, common salt(88), phosphates, and particularly of Iodine(89), all of which are open to Virchow's objection(90) that it is hardly possible an active, nay, even an irritative process can be induced by the mere absence of a substance, rather than by a positive substance or combination". A survey of the facts shows that none of these are of any value.

(87) Stevenston. B.M.J. 13th Mar. 1897.

(88) Schwalke. Archiv: f: Klin: med: 1875. XV.

(89) Chatin. compt. rend. 1850-52.etc.,

(90) Virchow. "Geschwülste" III. p.59.

HYPERAEMIA of the THYROID GLAND.

That goitre might be produced by a constantly recurring hyperaemia of the thyroid gland, brought about by such mechanical means as pressure on the vessels of the neck or thyroid from long-continued muscular strain of the neck, or from oft repeated, severe, muscular efforts with held breath, or by a cardice or respiratory disease causing an over-distension (through passive hyperaemia) of the gland, was long believed, and is still put forward in some quarters as the probable cause(91). This view has no doubt some connection with the old idea of the function of the thyroid, viz:- that, when blood pressure became dangerously high, the thyroid swelled up, like a sponge filling with water, and so relieved the cerebral circulation. It is supported by the history given by the patient of the illness. Almost every patient who could give a history told me that the swelling came on after a severe effort, such as raising a heavy weight. A possible explanation of such a story is, that the gland, although previously enlarged, did not attract attention until a sudden raising of blood pressure caused a sudden (and temporary) increase in the tumour. The normal gland, undoubtedly, often undergoes a transient enlargement in this way. I have seen it in children, during the paroxysm of whooping cough. But such a universal physiological phenomenon cannot give rise to a disease one of the chief features of which is its occurrence in definitely mapped out areas. If goitre were due to sudden and oft repeated elevations of blood pressure, we would find buglers, glass-blowers, coal-heavers etc., all goitrous.

Ewald(92) thinks that hyperaemia may account for sporadic

(91) T. A. Glover. B.M.J. July. 13th. 1895.

(92) Ewald. l.c. p.77.

goitre of a mild type, but even this is doubtful.

Ewald and Hirsch(93) both suppose that the transient hyperaemias of menstruation and pregnancy account for the predominance of the disease in the female sex, but other theories to account for this are as worthy of credence, as we shall see later on. Dr Bird's(94) opinion, that women are more affected because women drink more water than men (who presumably imbibe alcohol instead) is somewhat fantastic, although he supports it by saying, that in India the sexes are equally affected. Hirsch however, quotes Bennett as saying the opposite for Ceylon.

We see now, that none of the above mentioned theories of the causation of goitre are tenable as being in themselves the cause, with the exception of that which attributes goitre to the presence of a contagium vivum; and further, all we can safely say regarding the favourite soil of such an organism is, that it prefers the neighbourhood of lofty mountain chains, and that it is favoured by the existence of bad hygienic surroundings.

To this theory of a contagium vivum most modern observers beginning with Humboldt, Hirsch, Lücke etc., have come. Virchow(95) says that it, present in water and mixed with air, "affects the body like a miasma".

The actual demonstration of the goitre organism has yet to be made. By analogy we might suppose it to resemble the parasite of malarial fever (or even cancer). Acting upon these lines I made microscopic examinations of the blood of several goitrous

(93) Hirsch. l.c. p.185.

(94) Discussion on Goitre". B.M.J. Feb: 27th 1897. p.528
Dr Bird's remarks.

(95) Virchow "Geschwülste" III p.60.

patients, treating it as Laveran(96) directs, but without any result.

In order to determine this point a considerable number of experiments upon animals have been made by several men. Bircher fed five young dogs for 5 months on goitre water, and mixed with their food the sediment of a goitre-well, without any goitre appearing, perhaps, as Bircher supposed, because they were too young. Ewald(97) points out that such experiments are of little value unless they are performed outside the goitrous area, and upon animals bred outside. This objection holds good against St Lager's experiments with Iron salts which Stevenston(98) holds to be so important.

The experiments of Lustig(99) and Carle(100), who avoided this error, teach us little, inasmuch as although a horse and a dog became goitrous, the other animals (12 dogs) showed no enlargement.

The examinations of the water of goitre-wells are so far, also, of little value. Klebs(101), after examining several notorious wells in Salzburg, attributed the disease to the presence of infusoria in the water, which he called "naviculae". Bircher, as a result of careful examination of the waters of 30 wells on Molasse, 18 on Jura formations, 6 on Trias, and 6 on Crystalline rocks, was struck

(97) Ewald. l.c. p.74.

(98) Stevenston. B.M.J. Mar.13th 1897. "Goitre and Cretinism".

(99) Lustig. "Ueber die Aetiologie des endemischen Kropfes". Verhand: des internation: Congress zu Berlin.1890.

(100) Carle. "La Reforma med: 1888.p.191. Centrallbl: Physiol: 1888. Nr.9. p.213.

(101) Klebs. "Studien über die Verbreitung des Cretinismus in Oesterreich etc.," Prag.1877.

by the constant appearance of a diatom- the Encyonema- as compared with water from other geological formations. Along with this, he found in the water (in his opinion) goitre-bearing rocks a rod-shaped, or comma, motile organism, and was inclined to blame the disease on this, but no proof is forth-coming. Kocher(102) points out, that even in the clearest and purest well-water a large number of different organisms exist, so that the discovery of a coccus or bacillus more than usual, is of no importance.

From the nature of the endemics we may conjecture a little as to the probable habits of the organism. Sudden epidemics of goitre sweeping over a large part of the world, and completely retiring as suddenly, do not occur, and so we may take it that the organism is of slow growth. Notwithstanding that all evidence hitherto tends to the contrary, its definite confinement to certain districts indicates, that it requires some special conditions (telluric probably) for its growth. We may also say, that when removed from its normal habitat it quickly dies or becomes inert, otherwise the divisions between a goitrous and a non-goitrous locality would be less sharply marked. The water of many goitre-wells must find its way into rivers, and yet we never hear of river-valleys affected with goitre the whole way from the source of the river to the sea, a proof that, although the organism lives in (and generally conveyed to man in) water it is easily destroyed by admixture. As yet we have no knowledge as to whether it spreads from man to man through a medium.

Ewald(103) concludes his remarks on the subject thus:-

(102) Kocher. l.c. p.19.

(103) Ewald. l.c. p.77.

"The infection is produced by a specific organism closely bound up with a certain definite telluric condition, and the disease germ reaches man by means of the drinking-water." Hirsch(104) suggests, that the air or certain plants may contain the organism, and I, (p. 28) that the germ may gain entrance by the food, from the soil where it probably has its habitat, and from which the drinking-water receives it.

THE INFLUENCE of HEREDITY. *

Although Hirsch's statement that "goitre is transmitted by heredity" is, as he says backed up by almost all observers, it is clear that this is a point which must be gone into very carefully. To argue ~~that~~, because a child who is born in a goitrous district of goitrous parents ~~is~~ becomes goitrous sooner or later, that therefore, goitre is hereditary, is of course fallacious. The occurrence of goitre in a family, in which one(or both) parent was goitrous, outside of an endemic area would of course be proof, but I have heard of no such case. For this reason I lay very little stress on the family history of such cases as I see.

The only positive proofs ~~I~~ can obtain of the heredity of goitre are, firstly, that I have seen two cases of congenital goitre, and, secondly, that as a rule the descendants of old residenters and families present the worst cases. This shows that the influence of heredity is generally speaking very slight.

This is, of course, different in the case of Cretinism (See p. 76)

PATHOLOGY of the GOITRE etc.,

The essential change in the thyroid gland when enlarged in endemic goitre, is a parenchymatous enlargement. All the

* For family history &c. of cases observed here, see Appendix. Note D. p.p. 9 & 10.

(104) Hirsch. l.c. p.198.

(105) Hirsch. l.c. p.202.

varieties are but modifications of this, due to degeneration in one or other direction, cystic, fibrous, colloid, etc., I do not find this view expressed by the authors I have read, but I think the facts bear me out.

Various varieties of the disease are described by various authors. Thus Sir Morrell Mackenzie(106) divides "goitres" into seven classes. 1) Simple or adenoid, 2) Fibrous, 3) Cystic, 4) Fibro-cystic, 5) Fibro-nodular, 6) Colloid and 7) Vascular. Ewald(107) describes 1) Parenchymatous, 2) Colloid or Gelatinous, 3) Cystic and 4) Fibrous. Although Mackenzie certainly, and Ewald probably(108), made this classification from goitre as they found it in hospital, and not from observation of cases occurring in an endemic locality, yet either classification may be adopted as describing the cases one sees in an endemic.

They are founded chiefly upon the naked-eye appearances of the gland, otherwise one would expect that all forms would be recognized as varieties of the parenchymatous. Wölfler has adopted a peculiar system founded upon his views as to the origin of the goitre tumour. This will be alluded to later on.

From two specimens of enlarged thyroid of goitrous patients who died here, one of dilated heart following on valvular disease, and the other from a cardiac neurosis, the result probably of the goitre, I cut and stained sections of different parts.* The former of these cases was one of the rare and half questioned(109) form of Vascular Goitre. The other was a case of general enlargement in which fibrous changes had occurred. It presented a tripartite tumour (very large) two parts composed of each lobe, and, the

(106) Lancet. May 4th, 1872.
(107) Ewald. l.c. p.80.
(108) l.c. p.77.
(109) Berry. l.c. p.260.

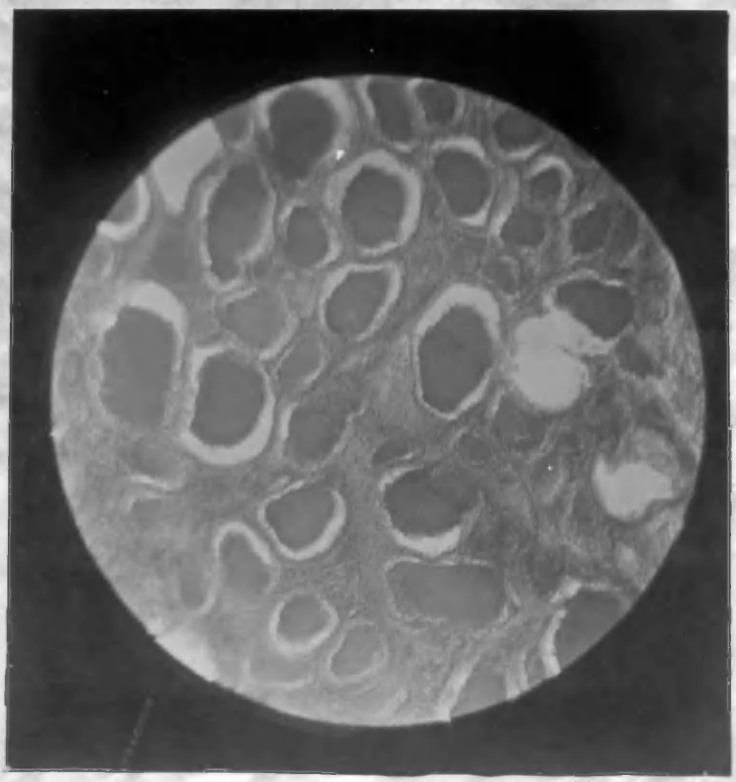
* Further details of these cases will be found in the Appendix. Note. B. pp. 3.

Thyroid enlarged in Endemic Goitre. Showing tripartite tumour. The division between pyramidal tumour and that of left lobe is clearly shown.

the third, as large almost as the others, sprang from the isthmus—the "pyramidal"(110) tumour. The divisions between the three lobes

(110) See Berry. l.c. p.263.

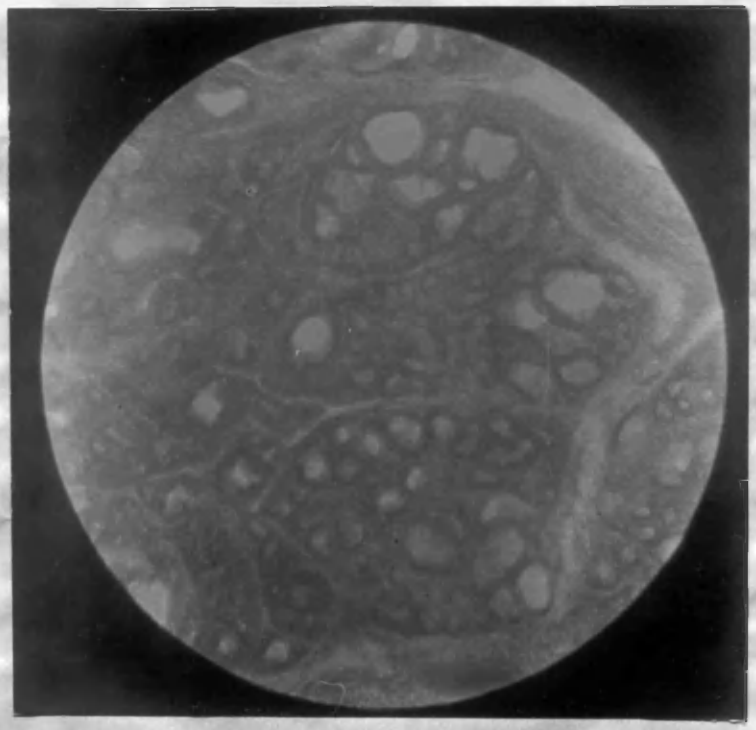
were deep, the pyramidal being isolated by clefts, which extended down to what would have been the level of the normal isthmus. On cutting into the tumour, it was seen to be composed to a great extent of thyroid gland tissue with here and there extensive tracts of white hard fibrous tissue. From both this thyroid and from the vascular one, the sections got show the follicular changes etc., They were cut etc., in the Pathological Institute, Western Infirmary. For purposes of comparison etc., Professor Coats kindly supplied me with two normal adult thyroids, one from a case of Acute Yellow Atrophy of the liver, and the other from a case of Cancer (not in the thyroid). Besides these, I got at home a thyroid from a child of 1½ years, who died of infective pneumonia, and another from a foetus at the 8th month. The specimens were cut in ~~el~~ celloidin, and stained with Carmalum and Picric Alcohol, and with Haemalum and Van Gieson's solution. Sections were taken from as far as possible representative parts of the glands. A general description based on an examination of these sections, follows.



Normal thyroid of Adult.

L.P.

In the normal gland, the follicles are regular in size and shape, almost always round, lined by a single layer of cubical epithelium, and separated from each other by normal connective tissue. They are uniformly packed with colloid (see photo). In the infantile thyroid, the follicles are less regular in size, but are, as before, all more or less round. The cells, under a high power, are seen to be larger, more granular, than the adult and in more than one single layer lining the follicle. Colloid material is entirely absent. (See photo).



Infantile thyroid. Follicles devoid of colloid and filled with cells.

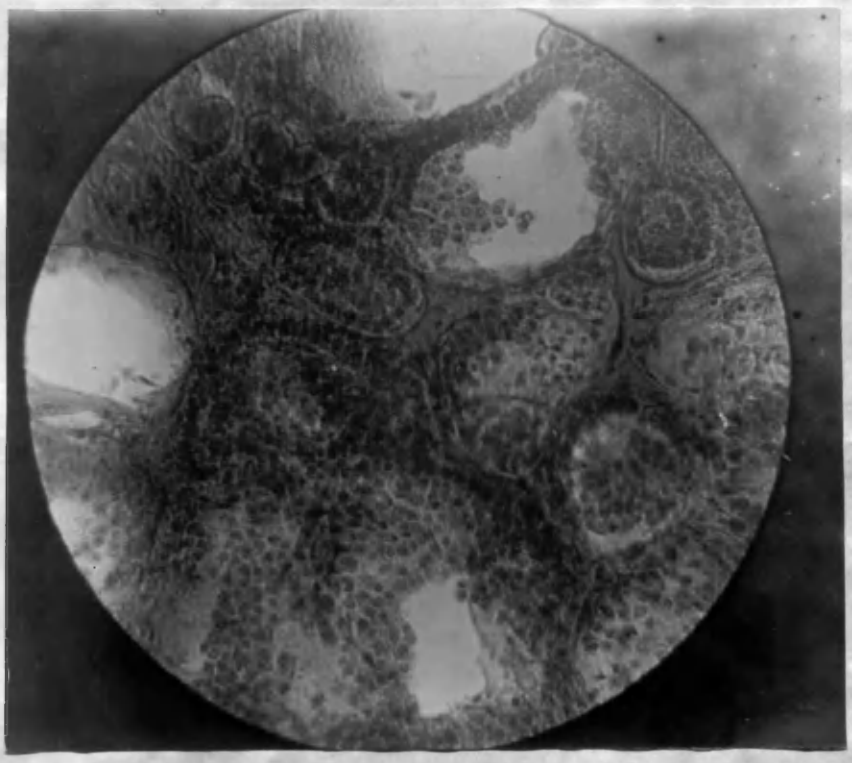
In the foetal thyroid the whole is infinitely more cellular. the cells are larger even than the last. The division into follicles by formed connective tissue is much less marked, and they appear as clumps of cells separated by their newly formed connective tissue. There is no colloid.

In the goitrous gland, the size of the follicles varies enormously, at some places some are only $\frac{1}{6}$th of the size of others. They are no longer uniformly round, but their outline is often wavy. Their cellular contents are not limited to a single layer of cubical cells, but the cells show marked proliferation, and often may be seen in clumps crowding in upon the colloid material (a photomicrograph of this is given). The amount of colloid varies enormously, in the different follicles.

Crowding of cells upon colloid in follicle and general cellular infiltration. H.P. ⅛in.

The inter-follicular connective tissue is very cellular-more or less all over-,-packed with round cells. The follicles are separated by a varying amount of connective tissue.

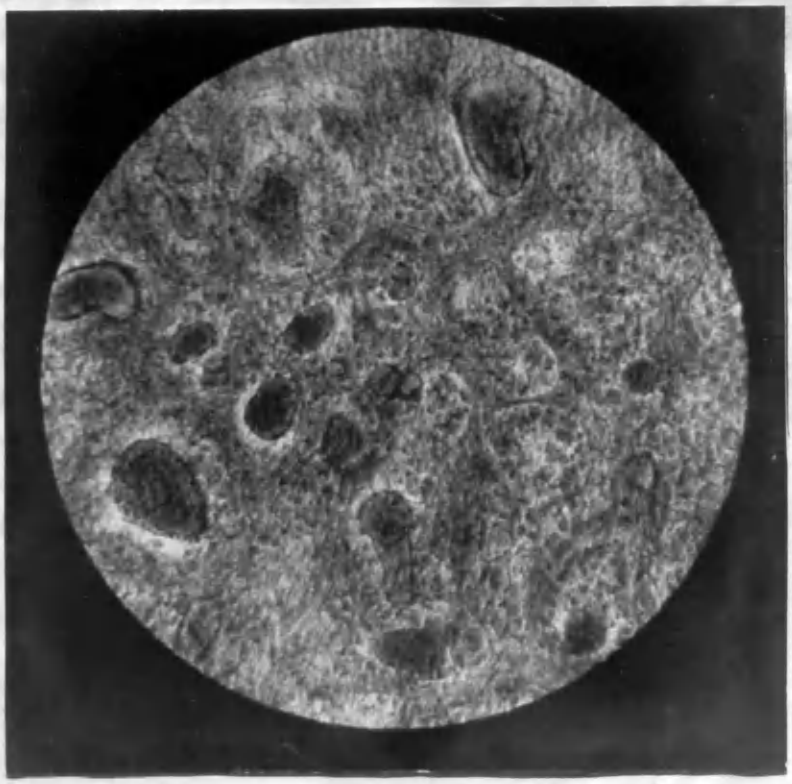
In the normal gland,the cells lining the follicles are cubical and in one single layer, In goitre they are enlarged, irregular,and highly granular, and generally speaking, with the exception of the often present round cell infiltration,the whole appearance markedly resembles the foetal.



Increased proliferation of follicular epithelium in goitre. Approach to foetal condition. H.P.

But a more striking similarity was found in some sections of both glands, viz:- where large areas of hundreds of epithelial cell-groups were found arranged like young follicles. Their cells are large, columnar, and rounded, with a strongly marked granular nucleus; as a rule they occupy the whole follicle, but in some, colloid material is found. The follicles are sharply cut off from one another by connective tissue with many spindle cells. Some follicles are very irregular in outline. In the midst of these, here and there, are dense groups of round cells. This, I take it, is an area of newly-formed follicles. (See photomicrograph.) or the Adenoma of Wölfler Coats, (Pathology. 2nd Edit: p 691) also mention thes "adenoma"

Taken all over, the condition is one of excessive glandular activity, and tallies with the description of parenchymatous goitre as being a hyperplasia of the follicles of the gland with a



New formation of follicles. (Adenoma)

corresponding increase in colloid material(111).

A striking resemblance is noted in many parts, (see especially photomicrograph of increased proliferation of follicular epithelium), to what is described and illustrated by Victor Horsley(112), and Murray(113), as compensatory hypertrophy of the thyroid,* so that I think we are justified from these appearances in looking upon the enlargement of the thyroid in endemic goitre, as first of all an hypertrophy of its glandular elements to meet some demand.

Wölfler(114), arguing from his extensive observations on the development of the thyroid and the formation of goitre, has come to the conclusion that goitre is a new formation. In the normal thyroid of the newly born child and also in older subjects, embryonic masses of thyroid cells are found here and there, particularly towards the periphery of the gland, and at any time these may take on a kind of normal growth, and become fully developed thyroid tissue(115), thus causing parenchymatous enlargement.

* occurring in animals in whom part of the thyroid gland had been removed experimentally (See Appendix note C.) p. 6.

(111) Berry. l.c. p.260.

(112) Victor Horsley. "Physiology and Pathology of the Thyroid Gland." B.M.J. Dec. 5th 1896. p.1623.

(113) Geo. R. Murray. "Discussion on the Pathology of exophthalmic Goitre." B.M.J. Oct. 3rd 1896. p.894.

(114) Wölfler. "Ueber die Entwicklung und den Bau der Schilddrüse mit Rücksicht auf die Entwickl: der Kröpfe". Berlin 1880. and "Ueber die Entwicklung und den Bau des Kropfes" Archiv. fur Klin: Chirurg: Bd. XX1X. 1 & 4 Heft.

(115) Wölfler. " Ueber die Entwick: etc., der Schildd. etc., p. 46 & 47.

He compares it with Cohnheim's theory of the formation of tumours. The thyroid seems, in this way, to be prepared for such an eventuality as an increased demand for its secretion.

If we assume that the organism of goitre when introduced into the system necessitates in some way an increase in thyroid secretion, in my opinion we obtain an answer to most of the questions put by endemic goitre. Firstly, as I have already indicated, this view accounts for the increased glandular activity and hypertrophy. Secondly, it accounts for (as we shall see when speaking of symptoms), the absence of all constitutional disturbance apart from that caused mechanically by the bulk of the tumour. Thirdly, it explains endemic cretinism. If a child is born in a goitrous locality and comes under the influence of the goitre poison, it will become cretinoid if the thyroid gland, subjected to the increased demands for its secretion is incapable of supplying it, either partially or wholly. Three fourths of cretins are also goitrous; this indicates that the hypertrophied gland is in these cases incapable of coping with demand for thyroid secretion. Fourthly, we shall see when speaking of treatment, that the administration of Iodine is sometimes followed by a set of symptoms which have been found to be due not to the Iodine but to the withdrawal of thyroid secretion, that is to say, that a gland of the usual size is too small for a person under the influence of the goitre poison. Fifthly, the facts that thyroid feeding reduces a goitre, and that on stopping this treatment the gland reverts to its original size, are also in favour of this hypothesis.

The only point against it is, that in adults immigrating into an endemic area, myxoedema ought to result in cases in which the increase of the gland is not great enough, and in cases where secondary (cystic, fibroid etc.,) changes have appeared of sufficient bulk to cause atrophy by pressure on the true thyroid tissue. So far as I have observed or read, there is no evidence of myxoedema being common in goitrous localities.*

To sum up, a possible explanation of goitre is, that

* The only case I know of occurred in Dr Mackenzie's practice (Abington). In this there was both goitre & myxoedema. See Appendix Note A. Dr. M's. letter. Perhaps as our knowledge of myxoedema increases other cases will come to light, as has happened in the case of Cretinism.

requires

it is due to an organism which prefers some unknown telluric conditions for its growth, and which, being conveyed to man by drinking-water and sometimes in other ways, induces an increased demand for thyroid secretion in the body, which the gland hypertrophies to supply.

The conclusion here stated is agreed to by most modern observers as far as the means by which it is conveyed. The theory of the method in which it effects goitre, and the reasons stated for believing it, are the result of my own observations and reasoning.

Waters ("Notes on endemic goitre in North-East Bengal" B.M.J. Sept. 11th 1897) arguing from the general features of the disease, and its resemblance (in some degree) to malaria has come to the same conculsion; he does not give any microscopical data etc., to support it. #

Secondary changes in the parenchymatous goitre lead to the other varieties.

1) The "Gelatinous" goitre of Ewald is the "Colloid" goitre of Mackenzie. It is so named from the super-abundance of colloid material in the dilated follicles. By gradual enlargement of the follicles and atrophy of the intrafollicular septa through pressure of the increasing colloid, small colloid cysts are formed, and from them larger cysts, until the whole thyroid gland may be packed with small round cysts filled with colloid material. From Professor Coats I obtained and have in my possession a specimen which shows this, (whether of endemic goitre I do not know). Subsequently, union of all these little cysts with one another may result, and the whole gland be converted into a huge sac filled with colloid debris. Gutknecht (116) describes another method by

(116) Gutknecht. "Die Histologie der Struma". Virchow's Archiv: 1885. Bd: XC1. 2 & 3 Heft.

For further consideration of this question, & details &c of some of the authors & articles referred to, see Appendix. Notes B. &c.

Cystic dilatation of the follicles. (Low Power).

which the gland may become cystic, viz:- by "Colloid" degeneration of the normal gland stroma and connective tissues. The sac of a goitre cyst is formed of the connective tissue of the gland and may contain broken down and compressed follicles. The contents of the cyst are colloid débris and altered blood, which often gives to the fluid a brownish-red or green colour. Occasionally crystals of oxalate of lime, cholestearin, ammonio-magnesian phosphates, and so on, may be found. The presence of blood colouring matter indicates the rupture of some blood vessel into the cyst. As the

cyst becomes older further changes may set in. Thus the wall has been found in some instances hard and calcified, or even ossified, to such an extent, that after opening the cyst and evacuating the contents, the walls did not collapse. The cyst may continue to enlarge from bleeding, or the by secretion of a serous fluid until a very large tumour may be found- the so-called "Giant goitre", when the whole tumour has been converted into a single cyst it is usually very vascular with tortuous dilated veins(117).

The "fibrous" and "fibro-nodular" of Mackenzie are the "fibrous" of Ewald. It arises by increased formation of connective tissue. Almost all parenchymatous goitres undergo secondary changes after a certain time, and of all these, fibrous changes are the commonest. Evidence of this clinically is got by a feeling of hardness in the tumour (see symptoms). This hyperplasia of connective tissue forms generally all over the gland, but in one or two or more places in particular, great tracts or nodes of old hard connective tissue are found with here and there a group of broken down and atrophied follicles, some still retaining their cellular contents, others completely devoid of them. Here and there also we come across islets of round celled tissue where active cell-division is evidently still going on. As we leave the node we find follicles in gradually increasing numbers, and the inter-follicular connective tissue lessening until we come to proper gland tissue. (See photomicrograph). Sometimes however, such a node is encapsuled.

(117) Most of this account of large cystic goitres is taken from Berry's and Ewald's descriptions. I have not myself seen such a case. p. m.

Follicles at edge of connective tissue node, small, compressed and widely separated. Hard, old, connective tissue in upper half. Broken down follicle at right edge. H.P.

There is in other parts a sort of cirrhosis of the thyroid. These fibrous nobules seldom attain to such a size as to occupy the whole gland.

One of the goitres I examined was composed to a very large extent of cavernous tissue formed of large vascular spaces freely communicating. The septa were formed of hard fibrous tissue. The gland parenchyma was quite dwarfed by the enormous developement of cavernous tissue. In these vascular spaces besides blood there were found large round colloid masses stained red, lying free in, or only very slightly attached to, the vessel wall(118).

(118) Dr G. Auld. B.M.J. 25th Jan: 1896. found colloid material similarly in diseased supra- renal capsules.

Gutknecht(119) also reports similar appearances in the vascular goitres he examined, and supposes that the same agent which produces colloid degeneration in the contents of the follicles(see p. 46.) also affects the vessel walls. Some of the vessel walls in my specimen were affected with a sort of hyaline degeneration.* Gutknecht describes a hyaline degeneration of the gland in which a colloid metamorphosis of the interstitial tissue occurs which fuses with the pre-existing colloid of the follicles to form a homogeneous structure. In these cases the vessels also are found degenerated. The capillaries and smallest arteries dilate; the endothelium atrophies and the other parts of the vessel wall undergo hyaline degeneration, ~~whereby~~ and thus cavernous tumours form. Gutknecht and Zielinska(120) think that the blood in these vessels also degenerates, and the final products correspond with the colloid masses which ~~is~~ are found in them.*

The "vascular" form of endemic goitre is, of course, as the above description shows, quite different from the increased vascularity of the gland in exophthalmic goitre(121).

Most goitrous thyroids are not entirely one thing or another, but present at different parts of the gland different forms of degeneration, and while we may call a goitrous thyroid "cystic", or "colloid", according to its most prominent character, it may exhibit in addition, changes in some other direction, and so in the same gland side by side cysts, fibrous nodes, etc., etc., are found.

(119) Gutknecht. ~~Capsules~~. l.c.

(120) Zielinska, "Beiträge zur Kenntniss der normalen und strumösen Schilddrüse des Menschen und des Hundes". Virchows Archiv: Bd: CXXXV1. p.170. 1894.

(121) See Berry. l.c. p.260.

* For fuller description of this, see Appendix. Note B.

The blood vessels in front of and around the enlarged gland are often found dilated and tortuous. This was the case in both of mine.

In rare cases Amyloid disease of the gland vessels may occur producing a pale greyish-red appearance in the cut gland. It was first described by von Friedreich(122) Beckmann(123) and Virchow. There was no evidence of it in the glands I examined.

Wölfler's researches already alluded to (p. 44) have led him to construct a new system of classification. He divides goitres into. 1) Hyperthophic- the "parenchymatous" of the authors.— 2) Vascular. 3) Foetal features. It may overrun the normal gland tissue. and 4) Gelatinous Adenoma the same as the last with colloid superadded.

The enlarged gland is subject to such secondary changes as inflammation, cancerous changes etc., It is in fact more liable to these than the normal gland (Ewald). Inflammatory changes going on to formation of pus have often been reported. They are generally secondary, occurring in the course of the fevers, pneumonia, acute gastro- enteritis, the puerperium, osteo-myelitis, pyaemia etc. An examination of the pus shows the presence of one or many pyogenic microbes.

Calcification or ossification of the tumour may occur in old cases. It has already been described as occurring in the capsule of a cyst, but it is also found in fibrous and other goitres.

(122) Friedreich. "Die Krankheiten der Schilddrüse" Virchow's Handb: der spec: Patholog: und Therapie: Bd. V. Erlangen. 1858.

(123) Beckmann. Virchows Archiv: Bd: X111. p.35.

In one of mine there was a point of calcification. It affects only small nodules of the tumour and may be so hard as to require a saw to cut it(124).

The pressure effects of the tumour are, as we shall see, the cause of all the symptoms.

The manner in which it exercises pressure on the trachea has been the subject of much research. The different varieties of tracheal compression described, depend upon the mode of growth of the goitrous gland. In cases where the growth of the goitre has exerted a uniform pressure on both sides of the trachea, viz:- in general uniform enlargement, the trachea always presents the same appearance- bilateral flattening(125), without any deviation to either side. If the lobes quite surround it however, and meet behind, a bend forward may be found. In all instances where one lobe of the gland is larger than the other, (this occurs in the majority of cases), the trachea undergoes lateral deviation. The excessive growth on one side pushing the windpipe over to the other, may cause an angular bend, which is sometimes very acute. At the same time lateral compression may exist. In many the trachea undergoes some degree of twisting. Of course in all these distortions the calibre of the trachea is reduced, often to a serious extent. (See photograph). The extreme forms of lateral compression and angular deviation produce what Demme(126) has termed the "scabbard form" of trachea.

(124) Ewald. l.c. p.89.

(125(Berry. l.c. p.265.

(126) Demme. "Beiträge zur Kenntniss der Tracheostenosen per compressionem" Würzburger med: Zeitschr: Bd. 11.1861 BD:.111.1863.

A.

B

A. Larynx and upper part of trachea from case photographed (p.38 showing lateral compression and deviation to the right, with narrowing of calibre and slight twisting.

B. Posterior aspect of same.

Ewald(127) describes a dilatation of the trachea below the narrowed part, produced by the air during expiration forcing its way through the constriction. The tracheal wall being in a softened condition tends to collapse with inspiration, and to distend with expiration. This " flaccid softening" of the trachea was first described by Rose(128) of Zurich. Cohnheim(129) says that if the larynx and trachea of a goitrous (especially one-sided) person, be removed post mortem, and made to stand on a table with the larynx as base, the "trachea usually bends over almost at a right angle to one side, at the level of the first cartilaginous ring, while a normal trachea remains straight and perpendicular". This loss of rigidity, he supposes, is due to some chemical change in the cartilaginous substance. The "kinking" of the trachea described may happen during life and is the explanation offered by Rose for the sudden deaths which occasionally occur in goitre—the so-called "goitre — death". Rose thinks the softening is due to atrophy of the cartilaginous rings. In Berry's(130) opinion there is no actual atrophy in the tracheal rings; the softening is only apparent, and the tendency to collapse is due to lessened resisting power produced by the alteration in shape of the tracheal rings. Most authors agree with Rose. This tendency to collapse has been found, after the surgical removal of the goitre, to lead once or

(127) Ewald. l.c. p.93.

(128) Rose. E. "Der Kropftod und die Radicalcur der Kröpfe" Archiv: für Klin: Chirurgie: 1878. Bd: XX11. p.1.

(129) Cohnheim. "Lectures on General Pathology" New Sydea: Soc: 1890. Vol. III. p.993.

(130) Berry. l.c. p.267.

twice to some difficulty and danger. Kocher(131) on one occasion had to hold apart the walls of the trachea with sharp hooks.

Cases are on record in which the ordinary goitre tumour actually penetrated the walls of the trachea(132).

SYMPTOMATOLOGY.

All the symptoms of goitre are produced by enlargement of the thyroid. It is remarkable that a morbid change occurring in a gland in such intimate connection with the economy as the thyroid should not be accompanied by constitutional disturbances apart from those set up mechanically by the tumour.
That grave constitutional change has some connection with the occurrence of endemic goitre is shown by the existence of endemic cretinism in goithous localities, but in the goitrous individual no such obvious constitutional disturbance occurs. The bearing of this upon the pathology etc., of goitre has already been alluded to (p. 45). The symptoms then are local, and consist, firstly, in the enlargement of the thyroid gland, and, secondly, in the results of the pressure exerted by the enlargement.

(1). THE BRONCHOCELE. The tumour begins in most cases about puberty in those who are, before that period, resident in the endemic area. Outsiders who remove into the affected district tend to

(131) Kocher "Ueber die Behandlung der Compressionsstenosen der Trachea nach Kropfexcision" Centralblatt: für Chirurgie: 1883. p.649.

(132) Paltauf. "Zur Kenntniss der Schilddrüse. Strumosa im Innern des Kehlkopfes und der Luftröhre" Beiträge zur Patholog: Anatomie und allgemein. Patholog: X1. 1891.

become goitrous no matter their age, after a period of residence varying from a few months onwards.

I have seen only two cases of congenital goitre; three other patients informed me that they were born with it. Those I saw conformed to the general rule of being children of goitrous mothers. In one of them there was so much fullness in the front of the neck that the hollow between the chin and the chest could hardly be said to exist. The breathing was stertorous, and the child half cyanosed. The lobes of the gland were so much enlarged that they could be felt up under the mastoid processes at the level of the angles of the jaw. The right side was larger than the left. The swelling was soft and spongy. The trachea could be felt working up and down with each breath as we sometimes see it in croup. Breathing was easiest when the child lay on its back, with its head bent back. Pressure by the finger on the trachea induced a temporary cessation of breathing. The mother said there was some difficulty in swallowing. Crying was normal, there was no cough, and the child was in every other way healthy and well-nourished. It was a male. It was 9 hours old when I first saw it. Notwithstanding the large size of the tumour and the severity of the symptoms the case did very well, and the goitre was reduced almost completely to the normal by the time the child was 3 months old. All the other symptoms disappeared. The boy is now about 4 years old and is ~~still~~ slightly goitrous. This history is a common one in congenital goitres. Sometimes they increase rapidly after birth, and may lead to stenosis of the trachea and even death in this way. (133)

We sometimes meet with enlarged thyroids here in children

(133) Ewald. l.c. p.89.

before puberty but not so often as seems to be the case in Switzerland, judging from Kocher's pamphlet etc.; with us it never grows to any great size in childhood.

Bircher* has made calculations from the statistics published by the French Commission of 1861, and according to this, the period when goitre is commonest is between 40 and 60 years of age. Of course a calculation of this kind is open to serious error. According to 77 cases which I have detailed,** I find 15 between 20 and 30 years of age, and 18 between 30 and 40. But almost all who can give a clear history date its commencement to about puberty.

Occasionally one sees instances of the so-called "acute" goitre. One case under my notice was in a man aged 31 years. He came to me complaining of a constant feeling of chokiness and difficulty in swallowing. There was slight hoarseness and a continual tendency to cough. He also suffered from general muscular weakness and slight dyspnoea on exertion. Some swelling of the face was also present. On examination I found a uniform soft enlargement of the whole thyroid which, he said, had been in existence only about a week. He had had a previous attack just like this 8 years ago. Otherwise he was perfectly sound. Under treatment the goitre and its attendant chokiness etc., completely disappeared in a month. This may be taken as a fairly typical case of Acute goitre, although many rise and fall within a shorter period. This is said to be the thyroid of epidemic goitre. Probably the enlargement of the thyroid spoken of at p. 17 F as occurring in incomers to a goitrous district is of this nature. Sometimes, however, after receding to some extent, the gland remains permanently enlarged. Ewald(134) says that the haemic murmur

(134) Ewald. l.c. p.90.

* l.c. p. 5.

** See note D. appendix.

audible over such a goitre is indicative of its vascular origin.

In chronic goitre the gland undergoes a slow enlargement at first affecting both lobes and isthmus uniformly, and forms a soft cushiony rounded fullness in the lower part of the neck more obvious to the palpating finger than to sight.

The accompanying photographs are of a lad of 19 in whom the first enlargement of the thyroid has taken place as described.

In most cases at this stage it causes at the most occasional "flushes of heat" in the face, but one of my cases complained of dry cough etc.,

From the time of its onset it gradually increases in size, in men steadily, in women more irregularly, under the influence of menstruation and particularly of pregnancy, which are associated with a rapid increase of the goitre. During these periods the normal thyroid gland undergoes slight increase in size, which subsides to the normal on a return to the usual

condition(135) but in goitrous women although the gland becomes smaller after parturition than it was during pregnancy it almost never returns to the size it has been before. So marked is this effect upon the tumour that I might almost say, that of two goitrous women, one barren and the other having a family, the latter caeteris paribus will have the larger goitre.

The rate of growth apart from pregnancy is often irregular, so that a thyroid that has been slowly enlarging for years may in the course of a few months take on a very rapid growth and then become semi-quiescent again. The size of the gland varies enormously in different cases. One may exhibit a swelling no greater than that shown in the first photograph while another of the same age shows an enormous tumour. Here for instance are two photographs of a woman 46 years of age in whom the tumour when unsupported hangs down in front of the chest, and Ewald(136) talks of goitres which reach even to the abdomen and the thigh. These cases, and the one photographed, are of course extreme. As a rule, the goitre is no larger than "a big man's fist or a child's head". (Ewald).

As a general rule the subjects of the larger tumours are natives of the district. The most grievous cases are, as has been said, "of the soil", that is, descendants of families which have been in the neighbourhood for generations.

(135) Spiegelberg's "Midwifery". New Syd: Soc: Translat: Vol 1. p. 85 and Lawson Tait "Enlargement of the thyroid body during pregnancy." Obstetrical Journ: of Grt: Britain. June 1875 p.203

(136) Ewald. l.c. p.79.

"Giant goitre" (in a woman, ~~48 years old.~~)

Goitres vary in shape. All observers agree that in most cases the right lobe is more affected than the left. I found it so in 3 out of every ~~four~~ 4. According to Brunet this is due to the difficult venous return from the right lobe to the heart as compared with the left. It is more likely due to some developmental circumstance. In a large number (20 out of 77) I found the isthmus chiefly affected. As a rule only in smaller goitres do we find no disparity in the various parts of the gland. From these features goitres are called "unilateral", "bilateral" and "median" as the case may be. Median goitres tend to grow in a downward direction, in some cases in behind the sternum-"Substernal goitre"- where it may become adherent, and being quite out of sight may give

rise to considerable diagnostic difficulty. I have at present two cases, one in a woman of 24, the other in a woman of 61 years, in whom the usual signs of obstructed tracheal breathing, (and in one of them obstruction to swallowing), and disturbance of laryngeal innervation associated with slight dullness over the Manubrium Sterni, together with (in the other case) improvement on treatment, point out to substernal goitre. This form is called "Goître plongeant" by the French.

The shape of the congenital goitre I described (p. 56) entitles it to be included under the term "sub-maxillary goitre", in which the lobes enlarge upwards under the lower jaw, and, as in the case narrated, may induce serious symptoms(137).

Wölfler(138) describes a pedunculated form of goitre which he termed " wandering goitre" from the facts that the tumour was found to be sometimes retrosternal, and at other times in the usual place, quite independent of respiration. I have not yet seen any instance of this.

After the menopause the tumour, unless cystic, seldom increases in size. It usually becomes stationary but may get smaller and harder. In older goitres the degenerative changes may often be diagnosed during life (see under).

The influence of the blood-pressure upon the size of the gland has already been alluded to (p.32.). I remember one case of death from cardiac valvular disease etc., in an old woman, in whom the goitre, originally about the size of a small orange (pyramidal), gradually decreased as death approached, until it was hard-

(137) Ewald. l.c. p.78.

(138) Wölfler. "Ueber den wandernden Kropf" Wiener klin: Wochenschr: 1889. No.14.

ly visible. The normal increase of the thyroid during menstruation and pregnancy is probably due to the rise of blood-pressure at those times.

(2) The pressure-effects of the bronchocele are exercised upon the trachea and larynx, upon the oesophagus, upon the muscles, blood-vessels, and nerves in the neighbourhood, especially upon the recurrent laryngeal nerve.

Although it is a rule that the pressure-symptoms increase with the size of the tumour, yet I find many exceptions. There is often seen a moderately enlarged thyroid with pressure effects,- dyspnoea, dysphonia etc.,- out of all proportion to the size of the tumour, while, on the other hand, large goitres are often met with, where there is little or no complaint of any symptoms. This apparently unaccountable circumstance I attribute to the condition of the muscles binding in the tumour. In the case of a slight enlargement the muscles are stretched, and hold the goitre tightly against the trachea, in large goitres, on the other hand, the resistance of the muscles has been overcome, and they are atrophied, so that the pressure of the goitre against the trachea is so far relieved.

In the majority of small and middle sized goitres the pressure causes only circulatory disturbances, such as dilatation of the superficial veins of the neck and slight cyanosis of the face, indicative of obstruction to the venous return in the deeper veins; occassionally one finds the patient suffering from neuralgic pains in the head. But it often happens at this stage, that all symptoms of this kind are absent. As time goes on and symptoms of tracheal obstruction appear, all these vascular symptoms are of course exaggerated until it may be, as Ewald(139) says

(139) Ewald. l.c. p.916

the venous blood pressure is so elevated that a vein when cut spouts like an artery. The Jugular vein in the larger goitres is drawn towards the middle line, and the common carotid Artery is often felt beating at the posterior edge of the sternomastoid m., behind a line drawn from the auricle directly downwards. This displacement produced in one of my cases constant tinnitus aurium of a blowing character. Palpitation of the heart, and in one or two cases increased frequency and irregularity of the heart's action, were noticed and are probably due to pressure on the vagus. Wölfler reports a fatal case of this sort, in which the p.m. showed compression of ~~the~~ that nerve.

From what we saw when dealing with the pathology of goitre (p. 52.) it is obvious that the trachea can seldom escape compression, and sometimes indeed it suffers therefrom very severely. In almost every case of goitre of any standing symptoms of embarrassed respiration exist. It makes it first appearance as shortness of breath on climbing a hill, lifting heavy weights etc., I have seen it first complained of, when the patient was suffering from Bronchial Catarrh. After a time, permanent interference is shown by rapid, noisy, stridulous breathing. The patient whose photograph was given, suffers from this. When bronchitis or other pulmonary or cardiac mischief sets in upon such a patient we have to deal with a very troublesome and dangerous combination. Ewald(140) describes how moveable substernal goitres may cause a peculiar form of dyspnoea. When the tumour is fixed between sternum and spine severe dyspnoea of course results, but is at once relieved by the ascent of the tumour into the neck. In another form where it has made a convenient resting place for itself in the thorax a

(140) l.c. p.92.

cough etc., may force it up into the bony ring of the first cortal arch and severe dyspnoea results, which, in a case reported by Kronlein(141), the patient relieved by pushing back the tumour into the chest.

The larynx, from its position and bony structure, is seldom interfered with directly, but the tracheal distortion may be accompanied by some displacement of the larynx. Pyramidal (mesial) goitres even when large, are, I find, often free from severe dyspnoea, probably because they have plenty of room to enlarge forward.

Constant cough at first dry, later on hard and "brassy," and a rough grating hoarseness, indicate implication of the recurrent laryngeal nerves, reminding one of aortic aneurysms. These symptoms along with the noisy snoring respiration, before mentioned, form a clinical picture common in this and every other goitrous locality. According to various anthorities from 7-10 p.c. of those affected with goitre suffer from paresis or paralysis of the vocal cords. The concurrence of this with stenosis of the windpipe gives rise to the very serious group of symptoms just alluded to. As a rule however, the patients manage to get along not so badly.

Severe attacks of paroxysmal dyspnoea coming on generally during the night, and lasting for about 5 or 10 minutes are common in goitre. There is usually also great distress and a feeling of oppression during the attack, so much so that the sufferer tosses about in great agony for a little while. It usually

(141) v. Krönlein. "Ueber Struma intrathoracica retrotrachealis " Deutsch zeitschr: für Chirurg: Bd. XX. 1 and 2 Heft.

comes on and passes off very suddenly, but it sometimes causes sudden death, and is in this way one of the causes of "goitre death", which as we saw is attributed by some to softening of the tracheal cartilages. In many of these cases of paroxysmal dyspnoea there are said to be no laryngeal symptoms whatever, and Krönlein (142) on that account thinks, that it has no connection whatever with the larynx but is due to a kind of softening of the trachea coupled with the goitre and hypertrophied muscles. An unusually strong contraction of the muscles is supposed to compress the goitre against the yielding trachea, the feeling of suffocation thus induced stimulates the muscles to get stronger contractions and so on in a vicious circle, until unconsciousness relaxes the muscles, or death ensues. The chief objection to this explanation is, that the muscles are far oftener atrophied than hypertrophied. Wölfler thinks it arises from sudden increase in the bulk of the tumour, by effusion of blood into a cyst, or into the gland tissue. But this cannot be supposed to happen every time the patient has an attack of paroxysmal dyspnoea. A third explanation connects it with the larynx and attributes it to spasm of the adductors of the Chordae Vocales. This irritation might be induced, I might suggest, by any sudden increase in the contents of the blood-vessels of the gland exerting pressure on recurrent nerves, resembling in this way the paroxysmal dyspnoea of aortic aneurysm. The objection that in many cases no other laryngeal disturbance exists is, I think, not of much importance, for, when the momentary increase in the gland pressure on the recurrent laryngeals has passed off, there will be no permanent change in the larynx. This view does not demand softening of the trachea, or hypertrophy of the muscles.

(142) l.c.

Lücke(143) supposes that it is not due to any gross nervous lesion "but is caused by a general neurosis, such as hysteria etc.,"

The auriculo-posterior nerve, the sympathetic, or the spinal accessory may also be implicated, causing pains behind the ears, hemicrania or exophthalmos, and clonic spasms of the sterno-mastoid, respectively(144). I have not seen any instances.

Several of the cases seen here complained of difficulty in swallowing, but only to the extent of causing some inconvenience, never so far as to require surgical interference. Ewald states that when passing the constricted part the food may give rise to a temporary intensification of the dyspnoea. This symptom, particularly in concealed goitres, may give rise to diagnostic difficulty.

Patients, in whom the goitre is fairly large, assume for the sake of comfort a peculiar carriage of the head, this, and the influence of a large goitre on the facial expression, are well illustrated in the photograph. *(p. 60)*.

In introducing this section attention was drawn to the remarkable absence of constitutional changes apart from those resulting mechanically from the tumour, but there is one feature which I have observed in many goitrous women and which does not semm to have been noticed, judging from the literature. That is, a peculiar sallowness of the complexion, present, often, even in comparatively young women. This is a well-known feature of cretinism.

From first to last the progress of an ordinary goitre is exceedingly slow. Most of the cases have been goitrous for many years, and most of those under observation for five years have during that time, undergone very slight change. Aggravation of the symptoms, following a slow increase in size, is the rule. Removal

(143) Quoted by Ewald. p.96.

(144) Ewald. l.c. p.96.

from the locality, and, as we shall see, often treatment has a favourable influence on the tumour, the growth ceasing or actually retrogressing. We sometimes find that a person with moderate thyroid enlargement leads in other respects quite a normal life, and dies from something quite distinct from the goitre. On the other hand, as we saw, a goitre often proves an awkward complication in the course of an illness, particularly in the case of heart or lung disease etc., Death may be directly due to the goitre. There are two ways in which it may occur. Firstly, it may result after slow growth of a large goitre with serious sequelae which lead suddenly to death from suffocation or more slowly from chronic Co_2 poisoning and so on. The second occurs as a sequel to the suddenly set up paroxysmal dyspnoea referred to above.

Separation of goitres into the various varieties already described is often possible clinically, and is of great importance in guiding us as to treatment, as we shall see.

PARENCHYMATOUS GOITRE is a general increase in the size of the gland. It maintains its shape unaltered, unless it may be that one lobe is slightly larger than the other. It remains like this for a period longer or shorter according to circumstances. As its age increases, it tends to degenerative changes already described (p.46 & 49). Ewald's description of parenchymatous goitre(145) quite differs from mine, and probably the general(146). He seems to place under this heading simple adenoma of the thyroid, for he talks of it as a "single, distinct, sharply-defined, nodular formation in the gland" developing by preference in one lobe. Parenchymatous goitre differs from simple hyperaemia of the thyroid

(145) Ewald. l.c. p.79.

(146) See Berry. l.c. p.260 and Cohnheim's "Pathology" Vol. 11 p. 779.

(which is found in young anaemic girls-Ewald), by being constant and by its firmer consistence.

FIBROUS GOITRE is distinguished by its hardness and irregularity. The nodes of fibrous tissue can be felt by the palpating finger as rounded, clearly-defined, hard nodules. Occasionally one can make out single fibrous nodes in the midst of a parenchymatous goitre. Almost all goitres of some age give evidence in their hardness apart from nodular formation of having undergone general increase in connective tissue which, as we saw, is of a cirrhotic nature.

. COLLOID GOITRE is soft, doughy, and pulpy, to the feel. Nodules are absent.

CYSTIC GOITRE forms the very large tumours(147) we sometinmes see. The cysts are smooth, rounded and tense. Fluctuation is sometimes present, but may be absent if the sac is very fully distended. A large unilocular cyst is diagnosed from a multilocular cyst by the character of the fluctuation wave.

VASCULAR GOITRE is the rarest form. It is compressible like a sponge. Vascular murmurs etc., are present.

In a case of doubt it may be necessary to puncture the tumour. This ought always to be done with the most careful avoidance of any possible sepsis..

It may be gathered from the foregoing description of the goitrous tumour that it is not often liable to be confounded with other cervical tumours. The difference, also, between a case of endemic goitre and one of exophthalmic goitre is so marked that one would suppose it almost impossible to confuse them. Simple hyperaemia of the thyroid is distinguished from goitrous enlargement by its disappearing with the cause, pregnancy etc.,

(147) Berry. l.c. p.262.

In Adenoma of the thyroid, the growth is strictly localized(148), and malignant tumours are differentiated by their rapid growth and metastasis.

Inflammation, going on to abcess, is, as we saw, common in goitre. Its symptoms are unmistakable. Its course is usually very acute. Its occurrence in an already enlarged gland, as may be expected, is productive of great danger from suffocation etc., I have not seen any cases of it.

TREATMENT of GOITRE.

The prophylactic treatment of goitre is a subject which is engaging the attention of many communities on the Continent and elsewhere, where its prevalence is most severely felt. It is in this direction, perhaps, we must look for the most effectual method of dealing with the disease. The avoidance of well-known "goitre wells" in a goitrous neighbourhood is of course necessary, and many large communities have as we saw (p.25-26) of recent years reduced the endemic by introducing fresh water-supplies.

Where this cannot be, or has not been, done, immunity may be obtained as experience shows, by boiling or even filtering the water. Where the latter is used, the Pasteur-Chamberland filter is to be preferred.

The comparative immunity of the better classes in a goitrous district proves that improved hygienic surroundings, good drainage etc., are very important factors, and we are given many examples where improved hygienic surroundings brought about a lessening of the endemic(149).

(148) See Cohnheim's "Pathology." New. Syd. Soc: Vol. II. p.779 & Seq:

(149) Hirsch. l.c. p.180.

In this connection one may insist upon the importance of personal cleanliness, for as we saw (p.28) probably the endemic here is to some extent dependent upon neglect of this.

That method of prophylaxis which we even yet occassionally hear of,—the avoidance of any efforts which tend to increase the blood pressure in the thyroid—will not commend itself, seeing that we no longer look upon this event as causing goitre, to say nothing of the impossibility of applying such treatment.

Once the enlargement has made its appearance the sooner treatment is commenced the better, but at the best it will only confer a temporary benefit if at the same time the rules for prevention above mentioned are not enforced.

The treatment resolves itself into two branches.
1) Treatment of goitre proper- the follicular or parenchymatous goitre, which includes all recent enlargements,—
2) Treatment of goitre which has undergone secondary changes- fibrous, cystic etc.— Thousands of remedies have been suggested, tried, and abandoned; the Iodine treatment alone remains. The introduction within recent years of Thyroid gland feeding for other diseases connected with the gland has led to its application in endemic goitre, with as we shall see later on, some measure of success.

Iodine is an ancient remedy. It was the chief ingredient of "Spongia usta" - Burnt sponge-which was long used in treating enlarged glands. Jean François Coindet(150) a Genevan Physician first used Iodine in goitre, and it has been in use ever since.

(150) "Déconverte d'un nouveau remède contre le goître"
Bibl: univ: de Genève. 1820.

The use of Iodine andthe consequent reduction of the goitrous tumour may be followed by a remarkable train of symptoms which have some bearing on the pathology of the disease (see p.45) These consist in a general loss of weight and fat, general weakness, palpitation of the heart, ultimately fever, going on, if the remedy is not stopped, and even sometimes when it is, to a dangerous wasting, and decline of vital powers. These symptoms were at first attributed to Iodism, but it was noticed that they occurred oftener with small doses than with large (probably because the former was accompanied by a rapid disappearance of the goitre, and the latter was used in cases where the gland was unaffected by small doses). This and the discovery of Cachexia Strumipriva following the removal of the thyroid gland by operation etc., led to the belief(151) that these symptoms were not due to the Iodine but to the withdrawal of the thyroid, and this, as we saw, is important to the idea that goitre is a physiological hypertrophy of the thyroid, and its reduction is in some cases followed by symptoms induced by the unneutralized poison of the goitre-producing miasma.

These symptoms, however, do not often appear, and seldom interfere with the treatment of a case by Iodine.

Every practitioner in a goitrous district can testify to the efficacy of Iodine in suitable cases. Of course no internal medication is of any service in cases where cystic, colloid or vascular changes have appeared to any extent. But parenchymatous enlargement,—the first group,—and very often fibrous goitres yield in great part and to the relief of the symptoms. Dr Arnd(152)

(151) Lebert. "Die Krankheiten der Schilddrüse". Breslau 1862 p.143.

(152) Kocher. Schweiz: Correspondenz: Blatt. Nr.1. 1895.

considers that 90 p.c. of all goitres become so much improved by Iodine that surgical interference is unnecessary, and that those which resist the treatment are cystic or colloid. So that the earlier a goitre is treated the better, and all the cases I have treated with Iodine about puberty or whenever the fullness is first noticed have proved amenable.

There are many methods by which Iodine may be administered. Spongia usta is of course now entirely superseded by the more constant Iodide of Potassium, used in doses from 3 grains thrice daily, upwards. To this we are generally recommended to add a few grains of pure Iodine or of its Tincture, as the presence of free Iodine is necessary. Iodide of Potassium which has become yellow answers this requirement. This makes it all the more important, for us to be on guard for gastric disorder. Iodide of Iron may be used if a tonic effect is, at the same time, desired.

Perhaps the most convenient method is the inunction of Iodide of Mercury ointment, as it is employed in India. The B.P. Unguentum is not used in full strength for it blisters the skin, and the counter-irritant effect is not desired. In India ʒiii of Iodide of Mercury is added to 1 lb: of lard and is well rubbed in for about 10 minutes in the morning and the patient sits as long as he can with his neck exposed to the hays of the sun. A second inunction is made in the afternoon of the same day, and the patient lets it alone for 3 days. This is enough to cure most cases, but a second course is sometimes necessary 6 months afterwards(153). Here, we generally use ℈i or ℈ii Ungt: Hydrarg: Iodid: to ℥i of Vaseline, and direct a piece the size of a large bean to be rubbed

(153) Ringer's "Handbook of Therapeutics" 9th Edition. p.268.

into the skin of the neck, before a hot fire, once daily. It may be kept up for a considerable time. This method is easily applied and is very effectual.

The Tc: or Lin. Iodi are also commonly used, painted over the tumour once or twice daily, but this has to be stopped periodically on account of the cutaneous irritation. Some tender skins will not stand any more than one application.

Ewald(154) recommends, that the patient should not go to bed immediately after applying Iodine because the calm atmosphere enables him to inhale the Iodine vapour and thereby (true) Iodism may be induced.

In 1842 Velpeau introduced the injection of Tc: Iodi into the tissues of the enlarged gland. It did not come into general use until Luton (1865) and Lücke (1868) re-introduced it. They recognized its limitations, and pointed out that, although, like other methods, it is of great service in young follicular, and early colloid and fibrous goitres, yet it is apt to be followed by dangerous inflammatory mischief going on to pus, sometimes also by bleeding, in fully formed colloid, soft gelatinous, cystic goitres, and one might add, vascular goitres. In old hard dense goitres it is of no service whatever. In a vascular goitre one can readily understand how easily such an injection might find its way into a blood-vessel and lead to disastrous results. Ewald(155) directs that a Pravaz syringe should be used and that the needle should be inserted without the syringe and watched if blood drops from it and only when this is not the case, is the injection to be made. Schwalbe (156) estimates that death occurs from injection into a blood-vessel

(154) Ewald. l.c. p.110.

(155) l.c. p.111.

(156) Schwalbe. "Die Ursachen und die geographische Verbreitung des Kropfes" 1879.

in 1 out of every 1000 injections. Several fatal cases are also reported by Heymann(157) and Rose(158). In view of these one would be chary of performing and of recommending this method unless all other means had proved futile. In the hands of Sir M. Mackenzie(159), however, it met with considerable success. Two grains of Iodine dissolved in 25 m. of pure Alcohol are injected twice weekly for 6 or 8 weeks at least, often longer; or 20-30 m. Tc: Iodi may be used. It is also recommended(160) that a tape be tied firmly round the base of the neck below the tumour in order to compress the superficial veins.

Many other injections have been used; Iodoform in Ether and Olive Oil; Perchloride of Iron (particularly for large cystic goitres. Mackenzie); Arsenic; Alcohol, etc.,

Iodine has been used in epidemic goitre, but opinions vary as to its success.

Fluoric Acid in ½ p.c. solution, 20-50 m. upwards (by the month), has been used with success(161). The same author has lately employed Chromic Acid.(162).

(157) P. Heymann "Zur Jodbehandlung der Struma" Verhandlungen der LXI1 Versammlung deutscher Naturforscher und Aerzte. 1889.

(158) Rose. l.c.

(159) Mackenzie. l.c.

(160) Whitla. "Dictionary of Treatment". 1892. p.191.

(161) Woakes, E. "Pathogeny and Treatment of Bronchocle or goitre". Lancet March, 19th 1881.

(162) Woakes, E. Lancet, June. 1890.

TREATMENT by THYROID FEEDING. Reinhold(163) while treating lunatics with thyroid substance first observed that enlarged thyroids were reduced, in some instances as much as 4 cm. ($1\frac{3}{5}$ in.).

Bruns (164), Kocher, and Ewald(165), have published results of this method of treatment. I have treated 12 cases of endemic goitre by this means. The first was begun in April 1894. It was an old goitre in a woman 60 years of age. It had produced paroxysmal dry cough, dyspnoea, and crowing respiration. The enlargement was chiefly confined to the isthmus (pyramidal), and the tumour was very large, smooth, hard, and firmly adherent. Her neck measured 19½ inches round the thickest part. She was given a half thyroid tabloid (Burroughs Wellcome & Co.,), daily and this was quickly increased to one, two, three and finally four tabloids daily. This is a large dose, but she did not show any signs of thyroidism. The treatment was continued for 3 months. From the first she felt an improvement in her symptoms, but there was no diminution in the circumference of her neck for about 2 months, when it was found to measure 17¾ inches, a reduction of 1¾ in: No further improvement was got, and the treatment was discontinued. It has been resumed once or twice since.

Another case, also a woman, aged 36 years, was put upon thyroid tabloids in March 1894. In this case there was geueral enlargement of the thyroid beginning at puberty. Iodine had been tried in her case without success. The neck measured 16½ in: at its thickest part. Dyspnoea on exertion and hoarseness were present. I tried

(163) Reinhold "Ueber Schilddrüsentherapie bei Kropfleidenden Geisteskranken". München med: Wochenschr: 1894. Nr. 21.

(164) Bruns.. B.M.J. Epitome. 30th May. 1896. from Berlin: klin: Woch: p. 406.

(165) Ewald. l.c. p.114.

painting with Tc: Iodi at first but without success and she was put on tabloid daily, increasing in a month to 5 daily, when the appearance of muscular weakness, malaise, disinclination for exertion, with a rapid small pulse, made me reduce the dose to 4 which she could stand easily. By this time the size of the neck was reduced 1 inch measuring 15½ inches. The tumour felt much softer, and there was a great amelioration in her symptoms. The treatment was continued for several months and then stopped. Since then the goitre has gone on slowly enlarging.

I would draw attention to the fact, that both these cases could stand a larger daily dose than people in normal circumstances.

Three cases I saw lately, of early goitre in young people, were treated in this way with complete success, the tumour entirely disappearing. (one of these was the patient whose photograph will be found in the "Symptomalotogy" section) (p. 58)

The rest were cases of older goitre, and in these a result better than in those two just fully described was got. In one or two, however, I combined thyroid feeding with inunction of Iodide of Mercury, and I attribute the success to the combination.

My results coincide as far as they go with those recorded by Bruns etc., In the article by Bruns, as quoted in the Journal we are not told whether his cases are endemic goitre or not. He never gives more than one tabloid daily, and found an improvement in three-fourths of his cases (350 in all). There was complete retrogression in a few (8.p.8.) In one third, the goitre was slightly reduced, in another third, the diminution was not great. He thought the best results were got in childhood and in young tumours. He found, as I did, that even when there was a very slight reduction, there was almost always a relief of pressure symptoms. According to Ewald and Kocher, cystic, colloid, and fibrous goitres, "react little or not at all" (166). In going over the measurements given by Ewald

(166) Ewald. l.c. p.113.

we find that the reductions vary from 4½ c.m. (1¾ in:) in a girl of 13, to 1½ c.m. (⅗ in:) in a woman of 33, a much smaller reduction than I got even in old goitres. Ewald's goitres were, he says, cases of hyperaemie goitre in young chlorotic girls, a very different thing from the follicular enlargement etc., of endemic goitre.

Speaking generally, most seem to agree with Kocher when he says, that the same results may be got from occassional Iodine treatment and total abstinence from unboiled goitre water, and Ewald concludes that the thyroid treatment should be reserved for cases which resist Iodine.

Lately Mikulicz(167) has been treating goitre by thymus feeding on the following highly theoretical grounds. He explains the success of thyroid feeding in goitre by saying, that it relieves the increased activity of the hyperplastic gland. The thyroid secretes a material from the blood which has an antitoxic effect on the toxic products of tissue change. Certain circumstances may cause an increased activity of the gland and so enlargement. If gland material is supplied from elsewhere the enlargement subsides. Mukulicz thinks, also, that the thyroid has a double function to perform, one against myxoedema and one against the goitre poison, and that the latter is also partaken in by the thymus, which is related embryologically to the thyroid. With this reasoning I, of course, am very much in sympathy. The results of his treatment seem rather to support this hypothesis, for a result similar to thyroid feeding was got.

The fresh raw thymus of a sheep is given in doses of from 10-25gm. (from about 150 to 380 grains), thrice weekly, increasing until the patient is taking 300 gm. (~~six~~ ℥ij) weekly. In one case thyroid feeding had failed and this new treatment was followed by a great reduction. Ewald got similar results.

(167) Mikulicz. s. "Thymus fütterung bei Kropf und Basedow'scherkrankheit" Berl: med: Woch: 1895. Nr. 16.

If the increased activity and hypertrophy theory of goitre be correct, thyroid feeding ought always to be followed by a reduction in the tumour unless there are great secondary changes and there ought to be a return of the gland to its former size on stopping the treatment. This last, Mikulicz says, does not occur but Bruns (168) says, that it does in more than ½ of the cases, 1, 2, 3, or 4 months after cessation of the treatment, and my cases, and probably all cases which happen to be treated within an endemic area, when prophylaxis is not attended to tell the same tale.

Colloid material has been shown(169) to be the only active part of the gland therapeutically, and it might be used in goitre instead of the ordinary thyroid material.

In cases coming under the second heading of treatment, cases of old goitres where secondary changes have occurred to a great extent, any hope of benefit by ordinary medication is out of the question. In such, relief can only be obtained by surgical means. Removal of the whole gland is now out of the question as a rule, but the pressure symptoms may be eased by removing part of the gland, by tapping cysts etc., Into the various surgical methods I do not propose to enter.

ENDEMIC CRETINISM.

That endemic goitre and endemic cretinism are two manifestations of one & the same poison, no one now denies.

The relationship was first expressed by Fodéré(170)

(168) Bruns. l.c.

(169) R. Hutchison. M.D. B.M.J. 21st March. 1896 & 21st Jan: 1897 "On the active constituent of the Thyroid gland.

(170) Fodéré F.E. "Traité du goître et du cretinisme" etc., Paris. an. VIII. (1800).

who wrote " Goitre is the first, cretinism the last, step in a series of degenerations". He was led to this position by observing that wherever there is endemic cretinism, there also, and to a much greater extent is endemic goitre, and that by far the greater number of cretins are the offspring of goitrous parents (and grandparents). Lombroso(171) goes further, when he says, "wherever goitre is, there sooner or later cretinism will appear". There are however, as we know many centres of endemic goitre where cretinism is not found.

I do not intend to enter fully into the subject of cretinism, but will describe two cases at present under my care which exhibit some cretincid features.

Case.1. H.Q. aet: 5 years, male. The height of this child when seen on Sept: 11th 1897 was 2 feet 6' inches. The head is somewhat square in shape and seems too large for the body. It measures 19 in: round. The fontanelles are still open and are very large. The eyelids are decidedly puffy; the nose is flat and turned up; the face is full, sallow in colour, and bears an idiotic expression. The lips are large and loose. The tongue is too large and often protrudes over the teeth. The abdomen is protruberant. There is no protrusion of the umbilicus. The legs are short, the femora bent forward at the upper part of the shaft; the tibiae are normal; there is no enlargement of the epiphyses anywhere. He sweats a good deal during the night. The milk teeth were cut late but are now being shed. The hair is dry and scanty, the eyebrows are normal. Hearing and sight are normal. His mother is an immigrant is not goitrous. His speech, actions, and understanding, are those of a child about 2 years old. He is not yet walking. He was put

(171) Lombroso c. "Ricerche sul cretinismo in Lombardia" Gaz: med: Ital: Lomb: Milans. 1859.

on gr. 2½ thyroid extract (Burroughs, Wellcome & Co.,). daily. 3 weeks later. He is brighter, and more active in movements, speech etc., He has started to walk. There has been a considerable loss of flesh, the face in particular being thinner, the eye Case. W.2. from puffiness. He weighs 1 stone 10½ lbs.*

Case. W.2. J. T. aet: 16 months, male, examined Oct. 19th 1897. Face broad, nose flat, turned up at point, and drawn in where bridge meets brow. Eyes oblique, Mongolian; eyelids puffy; brow high and prominent; neck short and thick; hair plentiful; subcutaneous tissue of neck and face pulpy and doughy; tongue too large, often protruding; cheeks large, full, and flabby; complexion pale; fontanelles open; the eyes, the bridge of the nose, the cheek-bones and eyebrows are all on one plane; the abdomen is not markedly prominent; legs short and thick; muscles soft; there are no teeth yet; the movements are active, but creeping, walking, and independent movements, generally, have not been attempted; no attempts at speaking; the child is very cross; cries incessantly; can recognise parents; the swelling of the face led me to examine the urine which was found normal. The child has had several attacks of bronchopneumonia; and muco-crepetant râles were found on the day the report was made, all over the lower and middle lobes of the right lung. Thyroid treatment was begun*. Here are two cases which, while not typical cretins, exhibit in a considerable degree cretinoid features; these are, in one at least, cessation of growth, in both, a low grade of intelligence, in both, evidence of a degree of myxoedema in the subcutaneous tissue, and in both the Mongolian face. Thyroid treatment had improved one in the short space of 3 weeks; in the other it is only just begun. In neither are parents goitrous.

The question which interests us, is, whether these cases are true endemic cretinism or only sporadic cretinism. Clinically Ewald(172) says, it is possible to distinguish between

(172) Ewald. l.c. p.140 & Seq:

* For most recent reports on these cases showing progress under treatment see Appendix. Note. E.

these two forms and gives the following differences. In endemic cretinism premature synostosis of different skull-bones (oftenest the occipitosphenoidal) is particularly marked; in sporadic cretinism, the long open fontanelles, and the efficient ossification of the sutures point more to delay in ossification, than to an arrest in growth. In endemic ~~goitre~~ cretinism the changes, after a time, tend to become stationary, and life is consequently longer; in sporadic cretinism the disease is progressive and death early; in the true cretin myxoedema is not strongly marked, in sporadic cases it is; lastly in endemic cretinism a specific therapeutics has, up till now, proved useless. Ewald puts forward these points, admitting at the same time, that other opinions exist, and that many consider sporadic cretins and endemic cretins of the same age to be indistinguishable. The difference is probably more one in degree than of kind.

If we are content that these distinguishing features really are existent, then the above narrated cases must be looked upon as cases of sporadic cretinism; on the other hand if we doubt Ewald, then ~~in~~ existence in a goitre endemic area is primâ facie evidence in favour of their being endemic cretins.

The End.

Appendix

Appendix to Thesis

ON

E N D E M I C G O I T R E

by

D. M'KENZIE M.B.

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NOTE. A. Extracts of letters from medical men in the county of Lanark, to whom I wrote on the subject of the occurrence of endemic goitre in their neighbourhood.

Dr Adams, Lanark, July 27th 1897.

"Goitre is not endemic in this district ---. Many years ago in a small village near here, Nemphlar, high up on the banks of the Clyde, there were a few (cases) but I think they must be all dead by this time and I do not know that any of the rising generation are afflicted therewith.

I have had no cases of Cretinism."

Dr R. Meikle. p. Dr Macfeat. Douglas, May 28th 1897.

Goitre "has never been endemic in this district at least for the last sixty years. I recollect only two cases occurring in the West division of the parish and only three in the East division and all occurring in the same family and including a male member. In this case the tumour was very large and produced marked confinement of breathing, but under treatment it entirely disappeared."

Dr T. H. Jackson, Sanquhar. Oct: 15th 1897.

"Endemic Goitre is still common in this district ---. Most of the goitres are small and do not seem to cause troub-

le as I have very seldom been consulted about them, and have only noticed them occasionally when examining patients with other complaints. I have seen no cretins."

Dr J. Millar, Newmains. Dec. 12th 1897.

"Goitre 30 years ago was endemic in Carluke. I saw many cases in Wishaw and Newmains but they generally were traced to Carluke, coming to this district on trade developing. To my certain knowledge goitre is decreasing both in the number of cases and in its severity.

I have one case of Cretinism at present born in Camnethan. -------

A new water supply was introduced into Carluke. That is given as the reason for the decrease. In early days their supply was from wells, the water being hard from lime formation."

Dr J. A. Mackenzie, Abington. 13th Dec. 1897.

During 3½ years residence he has "come across seven cases in all," which he details. He notes one as "bordering on myxoedema." # This case quite recovered under thyroid treatment. From his observations he concludes that Goitre is endemic "to a very slight extent" in Abington, and that the endemic is not increasing. He has seen no Cretinism."

Dr D. Dougal, Strathaven per Dr Mason, writes,

"Goitre is endemic in Avondale and has been for many years. It is commonest in the country places towards the west, where the farming classes are chiefly affected." He thinks that it is increasing in severity.

There is no Cretinism."

Dr John Lindsay, Lesmahagow. (25-12-97) writes.

"In this district --- which includes most of

Attention is directed to this case, as of import-ance bearing on my Goitre-Theory.

Lesmahagow, part of Dalserf, Stonehouse and Carluke, and a small part of Lanark and Douglas, the disease is endemic in a mild form. --- The worst district by far is Clydeside --- as we go South the disease decreases. --- I believe the disease is dying out.

I have seen no cases of Cretinism."

NOTE B.

Details of cases and P.M.'s. from which the two instances of goitrous tumour described in the text were taken.

Mrs G: aet 72. born in Wanlockhead, Sanquhar Parish. Her mother who was also goitrous belonged to Leadhills. This patient had been goitrous for 40 years. At her marriage 30 years ago the tumour was the size of a small marble. She had had one son who is free from goitre.

For several years before her death, the thyroid was visible as a rounded tumour situated in the middle line, about the size of a Tangerine orange. It was fairly hard to the touch and did not at all suggest its being a vascular goitre. From the history it appears, that the tumour increased in size after coming here. She had been resident here about 20 years prior to her death, which resulted from dilatation of the heart consequent upon Mitral Incompetence. She suffered a great deal from Anginous attacks during her final illness.

I confined myself to the thyroid gland at the p.m. There was slight enlargement of both lobes. The tumour in the isthmus (pyramidal goitre) was as large as a hen's egg. The superficial veins and those around the thyroid were enlarged and tortuous. The capsule was loose. There were no obvious nodules in the tumour. The spongy tissue of which it was composed was formed of venous spaces with fibrous walls, freely communicating. This occupied the great bulk of both lobes and pyramid. The arterial walls were thickened. The lining of the artery walls was in some places thickened to form little bud-like masses. There was Colloid material, - hard, round, reddish bodies -

lying free, or only very slightly attached to the vessel wall. Many of the blood vessels showed hyaline changes in the vessel-wall; but colloid material was found in both healthy and degenerated blood vessels.

MICROSCOPIC DETAILS of MRS G'S. GOITRE.

Sections were taken including follicles, areas of fibrous tissue, and of cavernous tissue. In many sections all three are present together.

The follicular changes are just as has been described in the text. In this gland there is great infiltration of round cells crowding the interstitial tissue. In the capsules etc., of connective tissue ~~nodules~~ areas, groups of round cells are met with here and there, merging into connective tissue and spindle cells. There is a great variety in size and shape of the follicles in this gland. Many are very much distorted. In sections through cavernous spaces, the large number of blood vessels is very evident, lying side by side. In some sections the homogeneity of part of the surrounding tissue shows that it has undergone transformation into colloid material, and as this abuts on the blood in the spaces, it represents the "hyaline" changes noted in the vessel walls in the fresh gland. see text

Follicular new formation (Adenoma) was observed here and there in the various sections.

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11. Mrs S: aet 63. has been goitrous since puberty. She was born here and had never resided any other where. The tripartite tumour and the cleft between left lobe and pyramid were clearly made out during life. The right lobe was smaller than the left. There was a history of recent increase in the size of the tumour with aggravation of the symptoms. Dysphagia, causing obstruction to every bite ^Swallowed was present. Dyspnoea was present, with hoarseness, and occasional paroxysmal dyspnoeic attacks. The recent increase was accompanied with some pain and tenderness over the right side of the tumour and shooting up the neck. The Carotid on the left side was displaced backwards. The pulse was regular at the beginning. There is no goitre in any of her children.

Under treatment first with Hydrarg: Iod: Ungt: and later with thyroid (one tabloid daily) she improved somewhat; but the latter had to be stopped owing to an increase of cardiac weakness - a symptom which had long troubled her - manifesting itself in "weak turns" (angina sine dolore). Notwithstanding treatment this last condition became more and more grave, with weak and fluttering pulse, sighing respirations, vague distress and feeling of uneasiness. The first heart sound was muffled and soft. Death occurred somewhat suddenly one day after the appearance of symptoms referrible to embolism of the right popliteal artery.

The occurrence of sudden death from heart neurosis is not uncommon in goitre, and is attributed by some to pressure on the vagus, by others to constitutional results of goitre.

The thyroid gland, trachea, and oesophagus were removed. p.m. The trachea was closely embraced by the tumour all round, so as to compress the oasophagus lying behind. The gland when cut into was soft and very free from connective tissue nodules. The capsule was adherent.

MICROSCOPICALLY. The follicles were much the same as in the last. But there was a very much larger amount of follicular new-formation (adenoma) and fibrous changes were, in proportion to the bulk of the gland, much less. The great mass of the enlarged gland was therefore composed of true glandular elements. Beginning Cystic changes were not discovered; the transformation of tissue into Colloid material, and vascular changes were absent. So that in this gland a true numerical increase of follicles was present, and this, together with the appearance of the follicular cells and new formed tissue, laid the foundation of my remarks upon goitrous enlargement as an hypertrophy.

Another theory suggested by Wölfler's theories and followed up by Blake (l.c. p. 59.) is, that goitrous enlargement like cancerous new growths, is the result of a parasite which inhabiting the soil along certain water tracts etc., and gaining an entrance by the drinking water, sets up in the thyroid gland a series of changes in the same way in which the parasite of cancer is suppos-

ed to act, viz:- by finding its way into the normal gland cell and stimulating it to increased growth, sharing its life with the cells as against the organism as a whole. The occurrence of the atypical ademona described (and photographed) in the text favours this theory. As against that I would suggest that it does not explain how the thyroid is selected by this organism in preference to any other tissue, and although a cancer of the thyroid spreads along the usual lines of netastasis, (X) the ordinary endemic goitre tumour does not develope secondary tumours elsewhere. The fact that the parasite is in the cell has not been discovered is of course an objection of little import.

NOTE. C. Extracts etc., from Articles in the Journals, on Goitre, especially on the microscopic appearances.

In Dr George Murray's paper in "a Discussion on the Pathology of Exophthalmic goitre " the compensatory hypertrophic changes are described.

Thyroidectomy had been performed upon a monkey and accidentally a portion of the thyroid gland was left. After the death of the animal which took plaxe 15 months later, the piece of the thyroid gland left was found hyperthophied and a drawing is given of the microscopic appearances. The drawing I append. p 7. Appendix The changes found were " 1) The formation of new alveoli. 2) Folding of the wall of the alveoli in some places so that the internal surface of the epithelium is increased in extent. 3) A change of the epithelial cells from a cubical into a columnar form. Compared with the normal gland of the monkey, we have here clearly the appearances presented by a gland which is working at high pressure somewhat in the same manner that the mammary gland shows signs of unusual activity during lactation."

This description is of a condition almost identical with what we find in endemic goitre.

(X) See Coats. Pathol: Trans: XXXV111 1887.

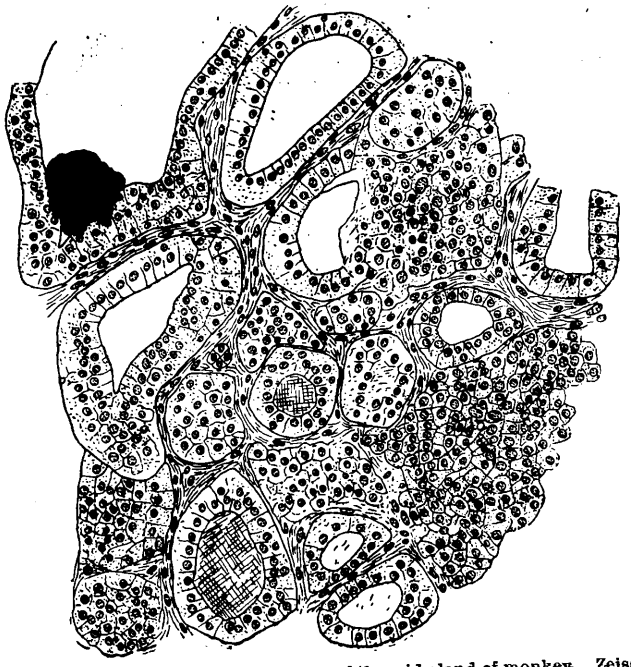

Fig. 3.—Compensatory hypertrophy of thyroid gland of monkey. Zeiss Obj. D. Oc. 4, camera lucida.

This illustration looks almost as if it had been taken from the specimen photographed at p: 42 in the text.

It might be urged that the appearance photographed and described in the text as the compensatory hypertrophy of endemic goitre is an effort on the part of the gland to make up for other parts of the gland rendered inert by the goitre poison; but we know that the follicular increase is much greater than any follicular loss produced by fibrous or other degeneration and further that all such degenerations are second in point of time to the increase of follicles.

Dr Murray in his paper refers to the resemblance between the hypertrophied gland and the gland of exophthalmic goitre.

Dr Victor Horsley. (B.M.J. Dec. 5th 1896) has more to say on this point. After running over the history and alluding more particularly ho Wölfler's and Edmund's researches, he alludes to the appearances in compensatory hypertrophy and says "This compensatory hypertrophy will be recognised to be parallel to what we observe clinically in a human being under circumstances of parenchymatous

Dr. V. Horsley's Plates

Dr. Paul's photos

Fig. 1. Cystic Adenoma; ⅓ in.

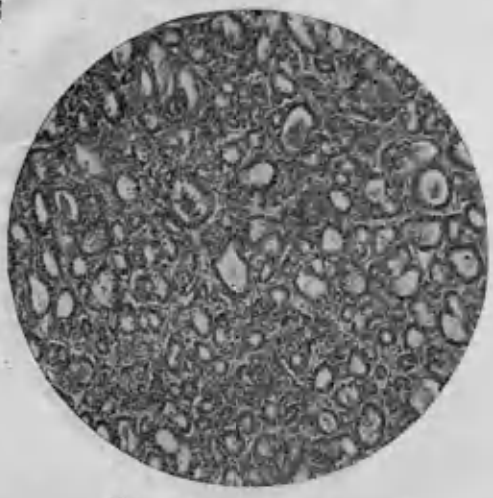

Fig. 2. Mucous adenoma in.

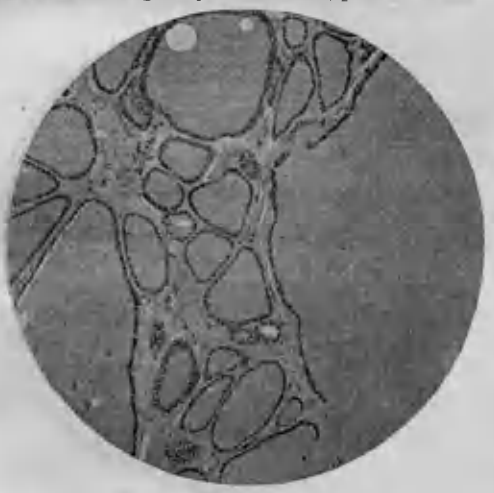

Fig. 3. Colloid Adenoma; ⅓ in.

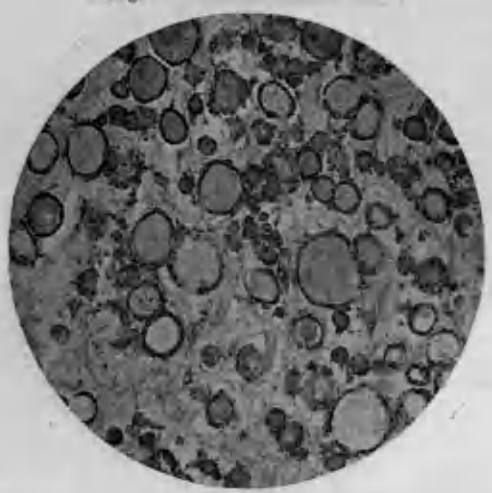

Fig. 4. Fibro-adenoma; ⅓ in.

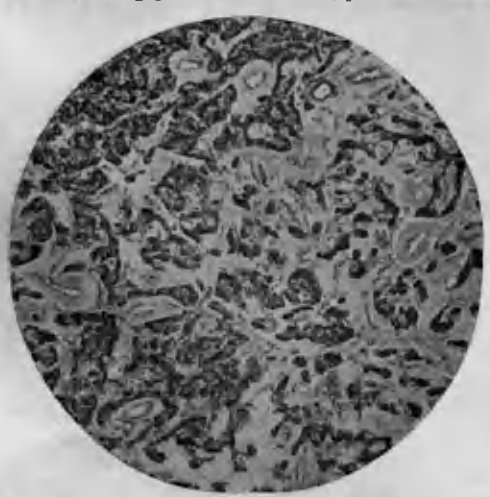

Fig. 5. Cavernous Adenoma; 1 in.

Fig. 6. Fœtal tissue in Adenoma; 1 in.

Fig. 5.—Compensating hypertrophy. (Low power.)

Fig. 6.—Compensating hypertrophy. (High power.)

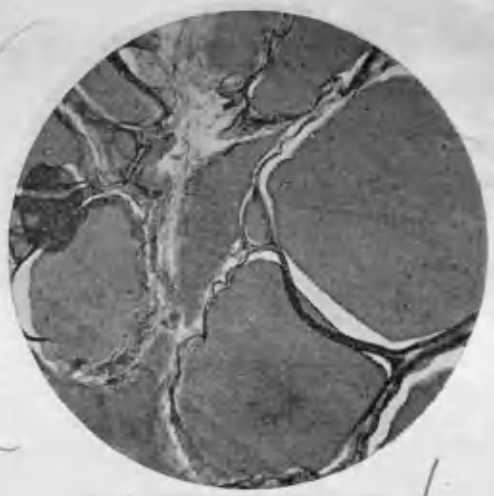

Fig. 7. Parenchymatous Goitre; ½ in.

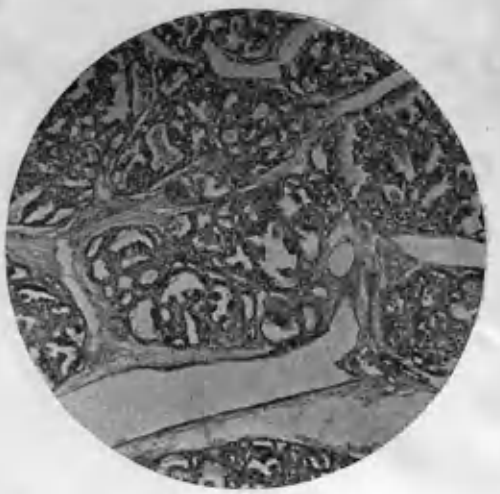

Fig. 8. Exophthalmic Goitre, excessive vascularity; 2 in.

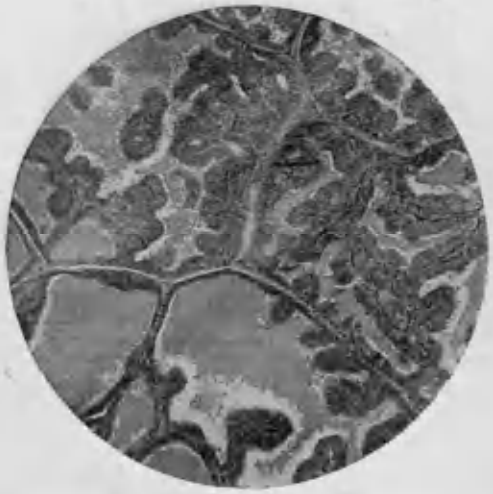

Fig. 9. Exophthalmic Goitre, intrafollicular growth; ½ in

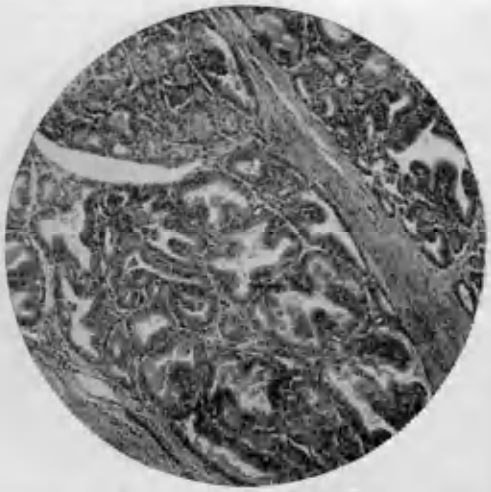

Fig. 10. Exophthalmic Goitre, a stage more advanced than Fig. 9; ½ in.

Fig. 11. Exophthalmic Goitre, colloid form; ½ in.

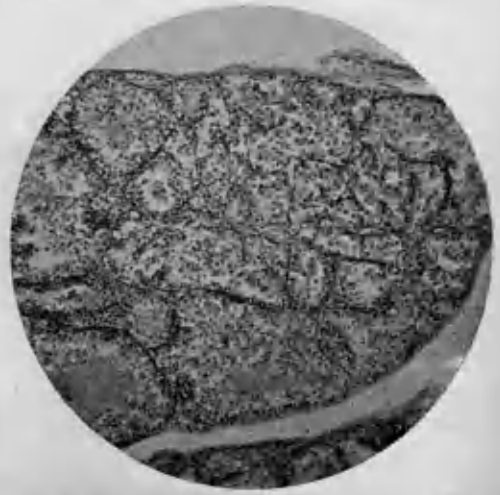

Fig. 12. Exophthalmic Goitre, catarrhal form; ½ in.

Dr. V. Horsley's Plates

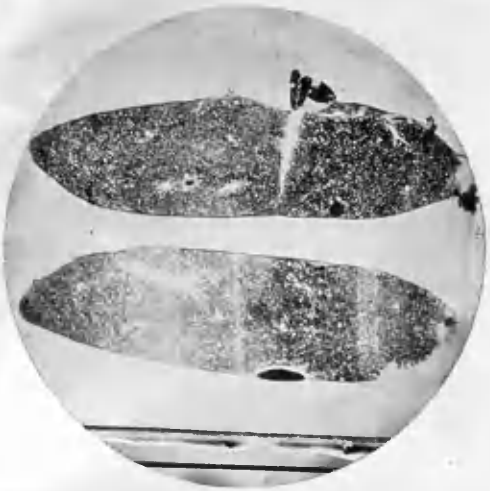

Fig. 1.—Sections of entire thyroid of dog. The darkly-stained lateral masses are the parathyroids.

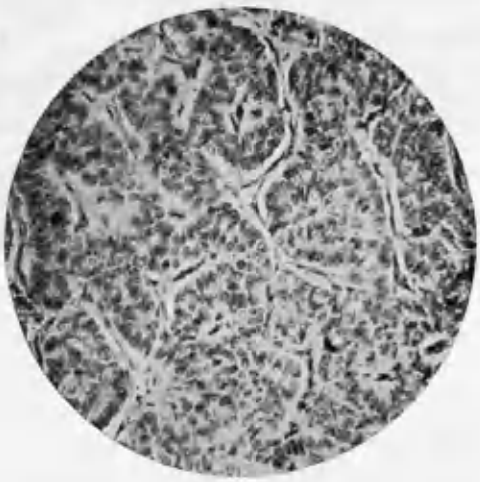

Fig. 2.—Adenoma, resembling parathyroid tissue.

Fig. 3.—Injected thyroid.

Fig. 4.—Commencing compensatory hypertrophy.

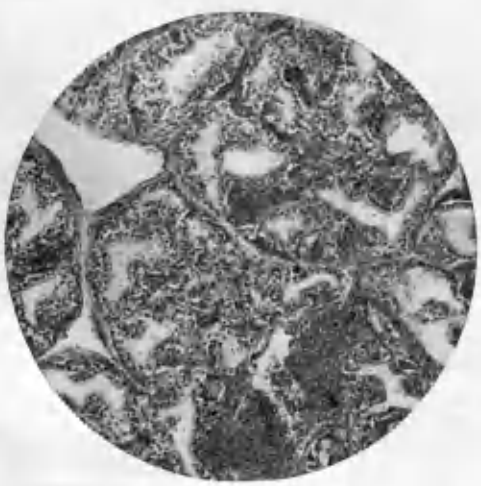

Fig. 5.—Compensating hypertrophy. (Low power.)

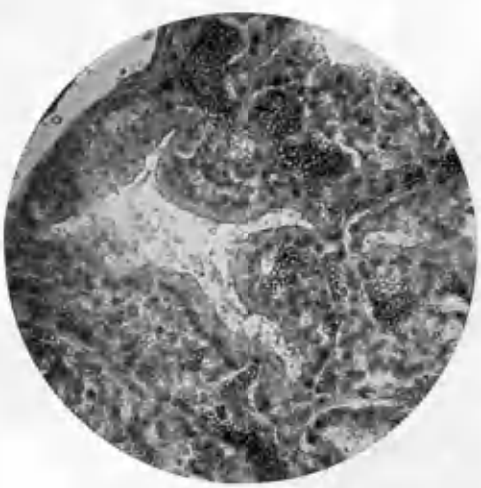

Fig. 6.—Compensating hypertrophy. (High power.)

Fig. 7.—Normal thyroid. (*Cf.* Figs 8, 9, 10.)

Fig. 8.—Commencing disappearance of colloid material, and proliferation of epithelium

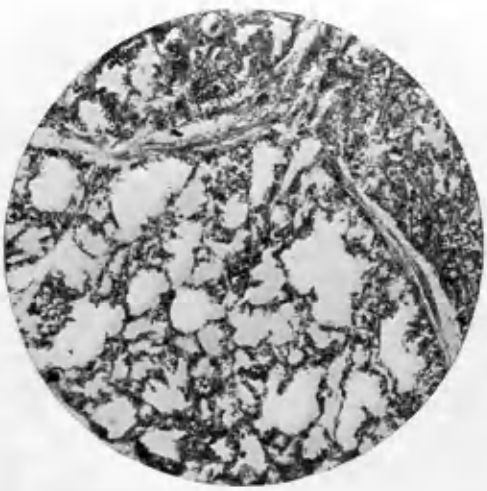

Fig. 9.—Exophthalmic goitre. (Low power.) Conversion of contents of acini into watery fluid.

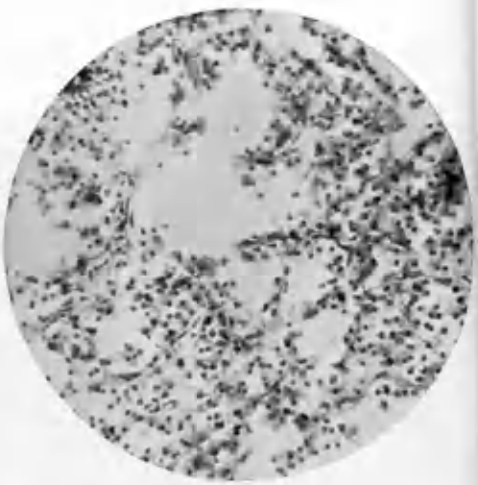

Fig. 10.—Exophthalmic goitre. (High power.)

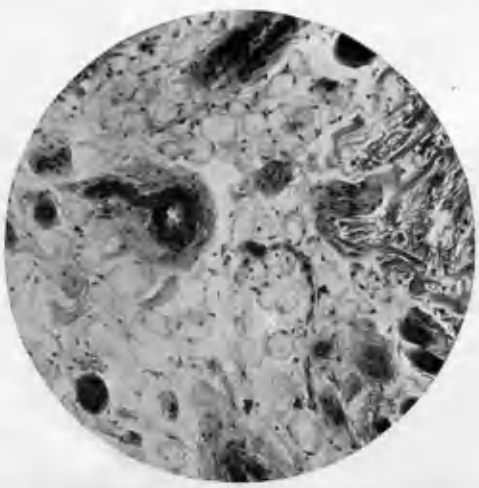

Fig. 11.—The cross is placed immediately below a fat cell, the nucleus of which is vacuolated. Many other nuclei in the preparation can be seen with a lens to be vacuolated.

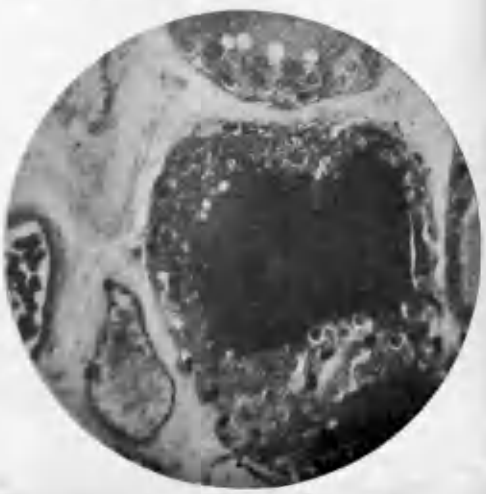

Fig. 12.

enlargement, thus in the so-called parenchymatous goitre the acini are not enlarged "(this I beg to question as inaccurate description) but their outlines become irregular and the epithelium increases in height."

Horsley, however, supports the generally accepted theory that parenchymatous goitre is really a disease of the thyroid, hindering, and in some cases (cretinism), preventing the exercise of the proper function of the gland.

This however does not explain the hypertrophic changes running along such definite and well-marked lines.

Horsley's photographs are also appended. Attention is called to fig. 2. Adenoma resembling parathyroid tissue (see Adenoma photo in text (p. 41)

F. T. Paul, B.M.J. July 0rd 1897 "Tumours of the Thyroid Gland treated Surgically" comes to a conclusion diametrically opposed to mine.

He finds the structural changes in parenchymatous goitre "resemble the appearances seen in colloid adenoma, though the colloid is more limited to the interior of the follicles". The microscopic appearances of colloid adenoma he describes (His photograph appended fig. 3.) are lined with a flattened epithelium and there are no droplets of clear secretion between the cells and the colloid. Frequently the entire ground substance is composed of colloid matter and the follicles are only distinguishable as rings of brightly stained nuclei. New follicles are developed from cells which lie between the old ones" etc., He goes on to say that " the gland, though so large, appears to be functionally quiet. Sometimes the collections of colloid are very large, apparently owing to coalescence of several follicles. New follicles are developed between the old ones: I have only once seen intrafollicular growth." (The italics are mine).

From this I conclude that Mr Paul has got hold of several colloid goitres. At any rate this is most certainly not the par-

enchymatous thyroid of endemic goitre.

NOTE. D. Details of cases observed by me in and around Larkhall.

No. Age. etc.	Birthplace	Length of time resident here.	Character of Goitre	Remarks.
1. Mrs. M. aet 59	Larkhall	----------	Slight fullness	Sallow complexion.
2. Mrs F. aet 33.	Larkhall	here always	very slight fullness	mother goitrous.
3. Mrs R. aet 62	Larkhall	here always	large round smooth pyramidal goitre	treated by Thyroid feeding.
4. Mrs H.M. aet 36	Larkhall	all life	very large child, congenital goitre	Thyroid treatment
5. Miss R. aet 18.	Larkhall	all life save 3 yrs. Glasgow.	slight fullness	anaemic.
6. Mrs H. aet 21.	Stonehouse	3 years	General enlargement Chiefly isthmic.	
7. Mrs R. aet 45.	Larkhall	all life save 4-5 years service.	Moderate general enlargement.	
8. Mrs B. aet 32.	Campbeltown	17 years in Carluke. 2 years here	Moderate isthmic enlargement	Improved by Hg.I_2
9. Mrs A. aet 58.	Larkhall	all life	Large Very goitre	
10. Miss A. aet 28.	Larkhall	All life	Slight mesial fullness	On Thyroid treatment.
11. Mrs D. aet 56.	Ireland	23 years	General slight enlargement	
12. Mrs R. aet 79.	Airdrie	30 years	Pyramidal goitre size & shape of a hen's egg.	
13. Mrs P. aet 35.		18 years	Moderate enlargement chiefly right sided.	Sallow complexion.
14. W.W. male aet 70.		5 years	Slight general	
15. M.C. (male) aet 33.	Larkhall	all life	Slight general	Died of Cardiac valvular disease.

No. Age. etc.	Birthplace	Length of time resident here.	Character of Goitre	Remarks.
16. Mrs A. aet 22.	Quarter near Larkhall.		Moderate Goitre	Slight exophthalmos. No other sign of Grave's Disease.
17. Mrs D. aet 62.	Ireland.	20 years	Very large right sided.	Began in Ireland. Increased rapidly after coming here.
18. Mrs B. aet 61.	Lesmahagow.	15 years	Slight general.	Dates from puberty.
19. Mrs M. aet 28.	Larkhall.	All life.	Moderate general.	Pale not sallow complexion.
20. Miss C. aet 69.	Larkhall.	All life	General moderate enlargement.	Sallow.
21. Mrs L. aet 30.	Dalziel.	20 years	Large Mesial enenlargement.	She has one sister goitrous in Motherwell.
22. W.P. Male aet 15.	Larkhall	Whole life.	Slight general fullness.	
23. Mrs S. aet 51.	Hamilton.	10 years.	Large left sided goitre.	History of disappearing when she left this locality
24. C.H. female aet 10.	Larkhall.	All life.	Slight isthmic lump.	Mother an Auchenheath (Blackwood) woman is goitrous.
25. Mrs P. aet 29.	Rutherglen.	27 years.	Right sided, slight.	Of sudden onset.
26. N.M. (female)	Stonehouse (Parish)		Slight goitre.	Mother slightly affected.
27. - D. (male) aet41	Galston.	14 months.	Slight fullness.	
28. Miss R. aet 35.	Larkhall.	All life.	Slight goitre. Left sided.	Thyroid treatment.
29. Mrs McC. aet 28.	Larkhall.	Whole life.	General moderate enlargement.	
30. Mrs D. aet 48.	Larkhall.		Isthmic.	Scar over front of goitre from an old abces
31. M.W. (female) aet 10.	Larkhall.	All life.	Slight general enlargement.	

No. Age. etc.	Birthplace	Length of time resident here.	Character of Goitre	Remarks.
32. Mrs M. aet 31.	Galston.	7 years.	Moderate general.	Complexion sallow.
33. Mrs G. aet 72.	Wanlockhead.	19 years.	Small mesial goitre.	Case from Wh. sections were made.
34. Mrs L. aet 65	Ireland.	26 years.	Large mesial goitre	Trachea tilted forward. Sallow complexion.
35. Mrs B. aet 70.	Larkhall.	All life.	Large right sided	Sallow complexion.
36. Mrs M. aet 39.	Larkhall.	All life.	Moderate mesial slight lateral.	Pressure symptoms out of all proportion to size of tumour.
37. G.C. (male) aet 17.	Larkhall.	All life.	Large goitre.	of 3 mos. duration.
38. J.C. (male) aet 44.	Quarter.	Quarter. all life.	Moderately large.	Treated. To Iodi.
39. Mrs T. aet 36.	Larkhall.	All life.	Small Isthmic	
40. Mrs P. aet 60.			Moderate general.	
41. J.P. (female) aet 21.	Larkhall.	All life	Moderate.	Daughter of Mrs P. enlarged since puberty.
42. A.P. (female) aet 19.	Larkhall.	All life.	Moderate.	do.
43. Mrs A. aet 44.	Larkhall.	Left & returned 27 years ago.	Large pyramidal.	Many remedies tried in vain
44. A.D. (female) aet 6.	Larkhall.	All life.	Slight general.	
45. J.C. (female) aet 15.	Quarter	1 year.	General fullness.	Began 2 years ago. Exophthalmos since birth no other sign of Graves
46. J.C. (male) aet 31.	Stonehaven.	3 years.	Acute goitre	See text, P. 57.

No. Age. etc.	Birthplace	Length of time resident here.	Character of Goitre	Remarks.
47.-P. aet 14 nos.	Larkhall.	All life.	Slight mesial fullness.	Mother goitrous
48. Mrs L. aet 48.	Larkhall.	All life.	Very large (photographed.) p. 60.	Mother had even a larger goitre
49. M.C. (female) aet 68.	Larkhall.	All life.	Moderate general.	Sallow complexion.
50. A.C. (female) aet 66.	Larkhall.	All life.	Moderate.	Sister of last. This & last stick to old well water.
51. Mrs W. aet 35.	Larkhall.	All life	Moderately large Mesial.	Sallow complexion.
52. Mrs S. aet 70.	Kilbirnie.	30 years.	Giant goitre Pyramidal.	Sallow. Goitre began after removal here. i.e. at age of 40.
53. Mrs F. aet 25.		3¾ years.	Moderate.	Goitrous since childhood.
54. Mrs D. aet 44.	near Shotts.	29 years, 8 years in Newmains.	Right sided, fairly large.	States goitre has always been there.
55. Mrs N. aet 68.	Londonderry.	28 years.	Very large right right sided.	Severe pressure symptoms Sallow. Began in Bellshill.
56. C.A. (male) aet 34.			Slight mesial.	No symptoms.
57. Mrs S. aet 46	Carluke.	7 years.	Slight fullness.	Goitre 7 years old. Iodine treatment beneficial.
58. A.G. (female) aet 18.	Larkhall.	left for Quarter.	Large Goitre right sided & Mesial.	Since childhood irregular pulse. Lessened at puberty Brother goitrous pain present Thyroid treatment.
59. Mrs S. aet 63	Larkhall	All life	Large goitre (p.m. photographed) p. 34 &c.	Case described. Thyroid treatment.
60. A.F. (male) aet 19.	Larkhall	All life	Goitre beginning.	Thyroid treatment Goitre disappeared.
61. Mrs D. aet 52.	Kirkmuirhill.	30 years	Slight fullness.	Sallow.

No. Age. etc.	Birthplace	Length of time resident here.	Character of Goitre	Remarks.
62. Mrs J. aet 35			Small isthmic	Asthmatic attacks.
63. Mrs P. aet 31.	Larkhall	All life.	Moderate fullness.	Sallow.
64. Mrs M. aet 28.	Wishaw.	8 years	Large Goitre	Began 5 years ago. Sudden recent increas Severe pressure symptoms.
65. Mrs M. aet 41.			Moderate Isthmic	Severe pressure symptoms. Giddiness "nervousness" etc.,
66. Mrs P. aet 24	Larkhall	All life.	Concealed Goitre	HgI_2 Ungt: and Thyroid.
67. Mrs B. aet 29	Larkhall	All life.	Large general.	Since childhood. No pressure symptoms
68. Mrs B. aet 34.	Near Lanark	6 years.	Large mesial & left sided.	Pulse rapid and small.
69. W.S. (male) aet 32	Carluke	6 years	Large general	
70. Mrs L. aet 28.			Isthmic-size of hen's egg.	First noticed 1 week before I saw her. Much cough. Pain.
71. J. B. female aet 4.	Larkhall	All life	Slight enlargement	
72. J.T. (male) aet 17.	Coatbridge	9 years	Moderate	Intelligence defective. No Cretinoid signs save small stature height 5 ft. 4".
73. J. B. aet 27.	Canonbie	24 years	Large general node on isthmus.	Thyroid. & HgI_2 Ungt.
74. Mrs M. aet	Lesmahagow.	17 years	General fullness.	Since coming here.
75. Mrs R. aet 38.	Larkhall	All life	Moderate General	
76. Mrs P. aet 33.	Larkhall	6 years away.	Moderate General	Since first child 14 years ago.

No. Age. etc.	Birthplace	Length of time resident here.	Character of Goitre	Remarks.
77. Mrs F. aet 42	Larkhall	All life	Right sided	Ungt: HgI_2 & Thyroid.
78. J.G. (male) aet 16	Quarter	All life	Very large neck 16" round.	Growing quickly. Rt Carotid displaced. Thyroid tabloid HgI_2 Ungt
79. Mrs S. aet 60.			Concealed Goitre	(See text) Thyroid tre treatment.

Where a goitre is characterized as "Moderate General" it means that the gland as a whole is enlarged and although one side may be larger than the other, it is not so stated unless it is much larger.

Male and Female. 64 of these are female and 15 male.

Family History.

Of the cases detailed.
29 gave a history of Goitre in the family.
21. gave a history of no Goitre, and in
29. data on this are absent.

The following is a detailed account of relatives affected in those in whom there is a family history of Goitre.

Mother.	Goitrous.	17.
Father	"	2
Paternal Aunt	Goitrous	2
Maternal Aunt	"	0
Sister or Brother	"	11
Grandmother	"	1
Children.	"	5

Of course these are only very approximate and are probably very erroneous, for I have found goitre in members of a family after I had been told tha. it did not exist in the family.

In the above table the symptoms are not fully detailed; but wherever they are present, this is indicated as far as possible under "Remarks."

NOTE. F.

FURTHER DETAILS of CRETINOID CASES.

H. O. 5th Jan. 1898. There is a great improvement in this case since the thyroid feeding was begun. He is much brighter and more intelligent. He speaks more, and now walks very well. At first he used to grip chairs etc. to help himself along but now he can manage unaided. The sallowness and flabbiness of the face have given place to a better colour and firmer features. The mouth in particular is changed, the lips now being thinner and firmer. The tongue is still too large. His hair is much thicker and is growing faster.
During the first weeks of the treatment he grew very thin, but since then has put on firm healthy flesh. During the first 3 weeks he urinated much more than formerly, now that also is less. The legs are longer and more muscular. The arms are still flabby and soft. There is some slight knock knee.

RECORD of GROWTH.

Oct: 11th 1897.	2 feet 6"
Dec. 13th 1897.	2 feet 7"
Jan. 3rd 1898.	2 feet 7¾"

An increase of 1¾" in about 11 weeks.

WEIGHT.

Oct. 31st 1897.	1 Stone 10¾ lbs.

WEIGHT.

Oct: 31st 1897. 1 Stone 10¾ lbs.

Jan: 3rd 1898. 2 stones 2¾ lbs.

An increase of 6 lbs. in 11 weeks.

CASE 11. J.T. No change in shape of face and features. Eyelids however are less puffy and the general subcutaneous infiltration of flabbiness have given place to firmer and healthier tissue. There are no teeth yet. The general mental condition is much improved. His movements are more active, his expression brighter anf his mother says he is much "cleverer". His general condition is masked by the presence of a small abcess in the neck which has brought him down a bit. The abundant muco-crepitant rales are now absent.

NOTE F.

Analysis of Gravitation Water,
Larkhall 11-6-96.

	Grs: per Gallon.
Total Solids.	9.10
Ignition Loss.	3.5.
Calcium Carbonate	.980.
Magnesium "	.520
Calcium Sulphate	.950
Magnesium "	1.50
Sodium Chloride	.98.
" Nitrate	none.
Ignition Loss	3.50
Al_2O_3, Fe_2O_3, & SO_2 etc.,	.42
	8.850

Alb: Ammonia	.009.
Free Ammonia	.001.

(Signed) Thomas M. McKenzie.

Thus, this water is quite free from any considerable Degree of "hardness."

The End.