

Th. Sect.

On the Etiology of Endemic Goitre

With Special Reference to the

URBAN DISTRICT OF HEANOR IN THE COUNTY

OF D E R B Y

by,
P. H. J. Sutton. M. B. (Edin.).

From the Laboratory of the County M. O. H.,

For DERBYSHIRE - DERBY



M. D. 1925-

I n t r o d u c t i o n

Endemic Goitre is a disease, the etiology of which has not yet reached any finality. Indeed there is scarcely any subject within the ever-increasing domains of medicine, whereof we may say that final and and conclusive opinions have been reached: of many things we know much, of others little; and of those things in which we pride ourselves with overweening vanity, our knowledge frequently amounts to little. Perfection is not of this world.

The etiology of this disease, which, in this country has for one of its best known habitats, the County of Derbyshire, and which has received the name of "Derbyshire Neck", has exercised in my mind an absorbing and increasing interest. The question is intimately associated with the physiology and pathology of the thyroid gland. A study of the literature of the internal secretions leaves one almost dazed. The outpouring of papers on disorders of the thyroid gland itself is enormous, year by year, as a casual perusal of the Index Medicus will show, Biedl's Internal Secretion contains a huge number of references - as does L. F. Baker's Endocrinology. If one were to make a close study of all the literature on the subject of Endemic Goitre alone I fear one would do nothing else. Life would be too short - Forcibly indeed is the

truth of the Latin Quip brought home, "Ars longa, vita brevis." From the days of Hippocrates to the present time the subject has had its champions, numerous as an army with almost as many theories of the essential cause. Nevertheless there are certain facts emphasised by our forefathers which remain true and unshaken to the present day.

I have done this work whilst actively engaged in general practice, without any special facilities except those of being in daily contact with an endemic locality for the past four years. The cases illustrated are those which have occurred in my practice, but they by no means include all of them.

"Let some time be given," said John Chiene in his Introductory Lecture to the Course of Surgery on October 24th 1882, "to the culture of the reasoning faculties, devote a certain portion of each day to self-instruction, self-questioning. Let each of us do a little piece of truthful individual work - Make a start: begin at once, get into the habit of doing some special work and like any habit - good as well as bad - it will grow upon you. If of a practical turn, you will work by experience and observation; if of a scientific turn, you will work by experiment. Both have their value, and even if you

only take up the role of an overturner of false doctrine you will have your use. As Marcus Aurelius says :- 'Men co-operate after different fashions and even those co-operate abundantly who find fault with what happens, and those who try to oppose it and to hinder it, for the universe hath need even of such men as these.' "

The experimental work has been done in the laboratory of the County Medical Officer for Derbyshire. I am much indebted to many for their help, advice and criticism. Specially would I mention the late Dr. Barwise, who was County M. O. H. for so many years and who died in harness, for permission to use the laboratory. To Dr. W.M. Ash, the present County M. O. H., for his assistance and interest; to Dr. Ross and Mr. C. F. Peckham, the County Bacteriologists; to Sir James Berry for his advice and help regarding the literature and to Dr. J. H. Watt for his continued interest. Also to Mr. B. Hunt of Heanor, who has taken the photographs of cases and also the micro-photographs of the thyroid sections.

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Chemistry of the Thyroid Gland

Baumann (i), thought that iodothyronin was the active principle of the thyroid gland, but this is a mixture of peptides containing iodine and is not ^{the} specific substance of the thyroid gland. Cushny(ii), states that Baumann in 1895 was the first to detect iodine in the substance of the thyroid gland. But, according to this author, the iodine compound is not the only active principle of the gland, for Hunt found that thyroid glands containing no iodine were active, though the activity is inferior. Cushny also states that the active principle was thyreo-globulin, which gives the usual protein reactions and contains small quantities of iodine. In 1914, ^{E.C.} Kendall (iii), isolated from the thyroid a substance containing 65.1% of iodine and which possessed the majority of the properties of the thyroid secretion - This substance he named Thyroxin. There are several forms of it - a ring form, a keto form, an enol form, and an amino-hydrate form, and it is closely related to tyrosine, adrenaline and tryptophane. Thyroxin is tri-hydro-tri-iodo oxyindol propionic acid - thus :-

- (i) Quoted by Cushny. A.R., Pharmacol & Therapeutics 7th Ed. p.531
(ii) Loc.cit. p.531.
(iii) Journal of Biol.Chem.xx.1915. pp.501-9 Proc.Amer. Physiol.Soc.xiv.1918. pp. Endocrinology i. 1917.pp.153-169 and iii.1919.pp.156-163.

JOURN. OF BIOL. CHEM. 1914, vol XIX pp. 251-256.

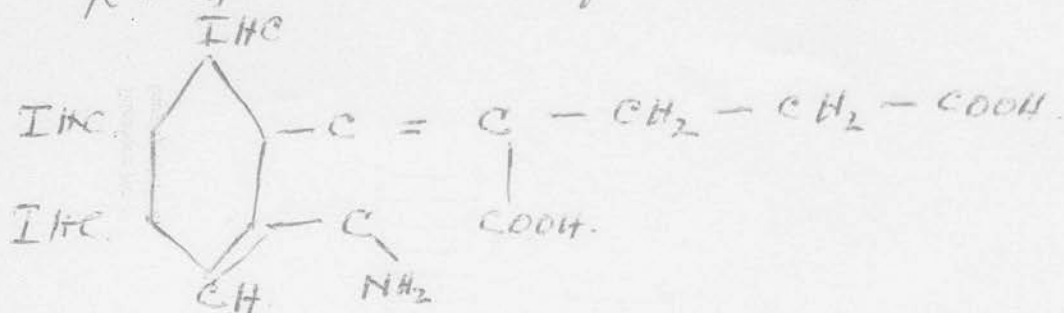
TRANS. ASS. AMER. PHYS. PHILADELPHIA. 1916, XXXI, pp 134-145.

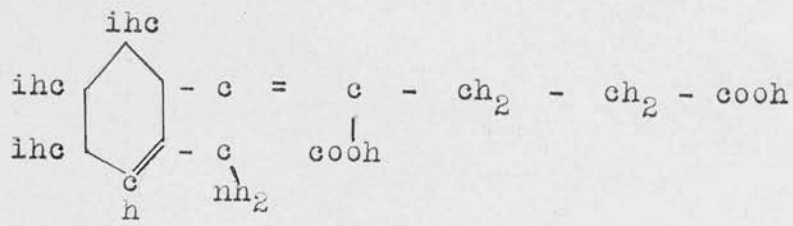
PROC. AMER. SOC. BIOL. CHEM. 1916, XI, p. XXXIX.

JOURN. AMER. MED. ASS. CHICAGO. 1918, LXXI pp. 871-873.

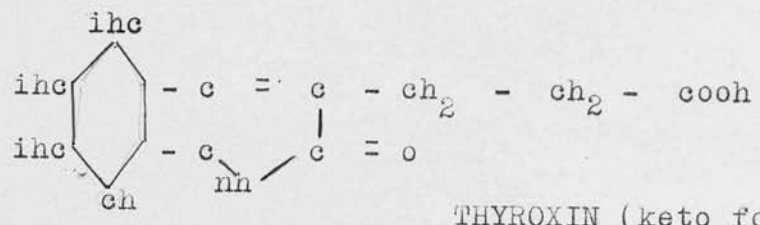
ENDOCRINOLOGY, 1915, II, pp81-93. JOURN-LANCET, 1917, XXXVII, 764-771

Letters should be Capital, the



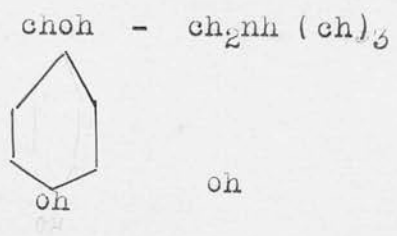
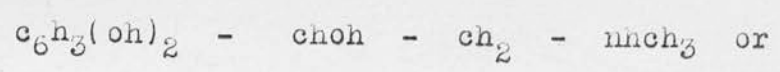


THYROXIN (open ring form)

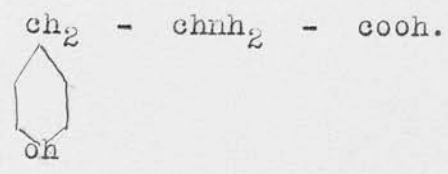


THYROXIN (keto form)

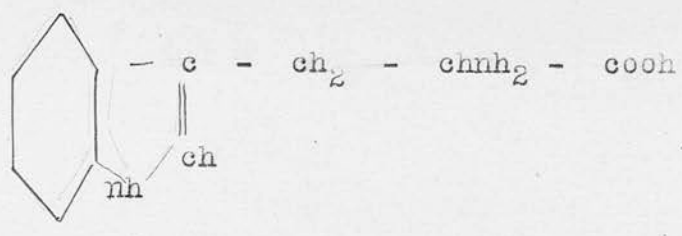
The formula of Adrenaline is :-



The formula of Tyrosine is :-



and that of Tryptophane is :-



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Kendall(i), states that "the entire activity of the thyroid is manifested by the administration of a-iodine, a crystalline compound, alone. There appears to be no other substance in the thyroid secretion which acts directly. This substance given even in very small amounts will supplant thyroid activity, relieving the conditions of myxoedema and cretinism and, in excess, will produce symptoms simulating exophthalmic goitre. It appears to have no direct action on the pulse rate. The extent to which the pulse rate is affected depends, not on the administration of the thyroid hormone, but on the simultaneous ingestion of food and in particular of amino acids. This effect may be outlined as follows:

"After administration of the compound there is no apparent effect for many hours. There is no increased pulse rate or drop in the blood pressure. However, if thyroid hormone and amino acids are injected simultaneously the pulse rate is enormously affected and even death may result, due to the apparently great increase in metabolism going on in the animal. It appears very probable that the thyroid hormone manifests its activity in some way with amino acids."

(i) Kendall, E. C., Boston Medical & Surgical Journal. cixxv. October 19th 1916. No.16. pp. 557-562.

According to Cameron (i), iodine is contained in all marine algae to the extent of .001-0.7% of the dried substance. In human subjects the maximum amount of iodine is found in persons between 40-60 years of age and the lowest in subjects under 15 years of age. The iodine content of the gland has a seasonal variation, being at its height between June and November and at its lowest between December and May. Vincent thinks that this difference may be explained by metabolic changes due to temperature. The iodine in marine algae is in soluble organic combination of a non-protein nature, sponges are said to contain iodo-phenyl alanine and dibrom - tyrosin. (Vincent) (2).

Amongst other constituents of the thyroid gland are, albumose, leucin, xanthin, hypoxanthin, paralactic acid and succinic acid, sodium chloride and calcium oxalate (ii).

Biedl (iii), states that the foetal thyroid gland contains no iodine and that the thyroid is not the only organ containing iodine as it is found also in the hypophysis, the liver, kidneys and ovaries. He quoted Baldi as stating that bromine and arsenic are also contained in the thyroid. (Gautier & Bertrand). The average amount of iodine in the human thyroid he gives as 8.5 m.g.(Jolin) and that the proportion of

(i) Cameron quoted by S.vincent.Intern:Secretion & Ductless Glands. 1914. p.327.
(ii) loc.cit p.327.
(iii) Biedl. Intern: Secret: Organs. 1912 pp.28-29.

Iodine is lowest in localities where endemic goitre prevails while the gland weighs very heavily and, in places where goitre is absent, the iodine content is high and the weight of the gland is low (Baumann). Biedl, further states that in time parenchymatous goitre and in fibrous goitre there is little or no iodine, whilst colloid goitre contains it in quantity (ii). It has been stated above that Hunt found that thyroids containing no iodine were still active. McCarrison states that "iodine is essential to the functional activity of the thyroid gland, but it does not appear that it is essential to the functional activity of thyroxin in so far as mammalian metabolism is concerned". He quotes Kendall as saying - "The function of iodine within the molecule is to increase the reactivity and sensitiveness of the functioning groups present, viz.- carboxyl and imino; any other function of iodine is highly problematical." (iii) and again that Kendall has obtained a substance which has no effect on metabolism, containing half the iodine of thyroid proteins and which controls the nutrition of skin and hair, etc.

(i) *Biedl. Subst. Secret. Organs. 1912. pp 28-29.*
(ii) Schafer, A.S. *The Endocrine-Organs 1924. p.40*
(iii) *Brit:Med: Journ: i.1925. p.1065. Kendall quoted by McCarrison. loc.cit. p.1065.*

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THE FUNCTIONS OF THE THYROID GLAND

The functions of the thyroid gland are manifold,

(i), and Vincent summarises them as follows :-

(a) Produces substances which aid growth and metabolic processes of the body. Thyroxin is one of these and Kendall has isolated another which controls nutrition of the skin and hair.

(b) The antitoxic power of the thyroid secretion depends on its metabolic function and its action may be regarded as that of a catalytic agent.

As McCarrison puts it (ii), the thyroid secretion is "what the draught is to the fire". After Thyroidectomy the changes in the body are damped down and this diminishes the amount of alexins and opsonins.

(c) The activity of the thyroid is chiefly concerned in the direction of katabolism but it may also produce anabolic substances as well.

As regards the effects of the thyroid secretions upon metabolism these have been summarised by Schafer (iii),

(a) The thyroid controls nitrogenous metabolism.

The administration of thyroid substance increases

(i) Vincent, S. Int:Secret: and Ductless Glands 1924 - p.337.

(ii) McCarrison, R. The Thyroid Gland-1918, p.22.

(iii) Schafer, A.S., The Endocrine Organs-1924. p.44

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(a) the nitrogen in the urine, it causes fat to be lost. Schafer quotes Herring(i) that animals fed on thyroid substance developed an increase in the size of the pancreas, ovaries, testes, suprarenal glands, heart and kidneys.

(b) The thyroid has a great effect on growth. Skumway(ii), showed that the thyroid secretion increased the growth and number of paramoecium in hay infusion.

Now all these effects of the thyroid secretion may be observed in the course of clinical experience. The first to note the connection between the thyroid and the nutrition was Sir William Gull in a paper, (iii) "On a Cretinoid State Supervening in Adult Life in women." wherein he describes the first published cases of myxoedema. "In the cretinoid condition in adults which I have seen the thyroid was not enlarged; but from the general fulness of the cutaneous tissues and from the folds of the skin about the neck I am not able to state what the exact condition of it was." (Gull - loc.cit. p.319.)

Both myxoedema and cretinism are a direct result of disease of the thyroid gland, in which the secre-

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- (i) Herring. Quart: Journ: Exp: Physiol. xi. 1917 pp 231-255
and pp 47-57.
(ii) Journ: Exp: Zool: .1917. xxii.
(iii) Published Writings of Sir W. Gull. New Syd Soc. Pub.
vol. cxlvii. pp. 315 - 321.

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tion is deficient differing in this respect only that myxoedema arises in later life whilst cretinism is congenital.

In myxoedema, when it is typically developed, we see and are able to tell how greatly the body depends upon the thyroid for its nutrition. The thickened skin turning yellow and wrinkled, the coarse brittle nails, the scanty falling hair, brittle and rough, the "spade-like" hands, the broadened features, the languid manner, the slow speech and monotonous intonation, the slow pulse, the anaemia, the suppression of the menses and the increased tolerance for sugar all denote what are the functions of the thyroid gland. In myxoedema we have a disease also in which the victims are particularly susceptible to infections.

The effect of the thyroid secretion upon growth is well illustrated in cretinism, where the thyroid secretion is deficient - these children refuse to grow up. They are stunted, pot-bellied, ugly and hideous but when fed upon thyroid extract in a judicious manner become normal subjects.

In the opposite condition - that of hyperthyroidism we see the opposite effect. Instead of a dull heavy lethargic individual the sufferer is restless feckless and capricious, excitable - so much so that

this excitation may amount to mania. All the processes of metabolism are quickened and there is a loss of weight, a rapid pulse and stimulation of the vasomotor nervous system. (Sympathetic). Everything is speeded up.

The secretion of the thyroid gland is the colloid material which is enclosed in the vesicles and is secreted by the cells lining those vesicles. It is of a protein nature and gives the usual protein reactions. It finds its way into the circulation through the lymphatics (i), by rupture through the acinal wall and also through minute intercellular channels. According to Murray (ii), the secretion of colloid is not affected by the stimulation of the sympathetic or, of the laryngeal, nerves but Schafer(iii), states that the activity of the thyroid appears to be increased by quinine and strychnine and that the action is probably produced through the sympathetic nervous system; although the thyroid can be stimulated through the nervous system, it may also function when it(the thyroid)is transplanted so that the nervous impulses are not essential to the production of secretion. Rogers (iv), found that the feeding by mouth of derivatives of the entire adrenal gland - especially of

- (i) Hurthle quoted by G.R.Murray - Diseases of Thy: Gland-1900 p.8 R.M.Horne, Journ: of Anat: and Physiol: vol xxvii.pp.161-168.
- (ii) Loc.cit p.8.
- (iii) Schafer.A.S., The Endocrine Organs-1924 p.25
- (iv) Rogers, J. Endocrinology, vi.1922 pp.7384
Adrenal Feeding in Conditions of Hyperthyroidism

adrenalinucleo-proteins and a slightly hydrolysed aqueous extract, known as the adrenal residue, caused the thyroid to gain 50 - 75% or more in its iodine content within a few weeks. Feeding with adrenalin crystals alone had no effect on the thyroid.

In 1888, Halstead (i), showed that after partial thyroidectomy the remainder hypertrophied. He states that in 1886 Horsley & Wagner observed the same fact, but these observations were not taken up and no notice was taken of them. Halstead noticed in his experimental thyroidectomies that the compensatory hypertrophy commenced as early as the seventh day in some cases, was undoubted by the tenth day and by the fifteenth it was quite evident.

Kimball (ii), states that Marine & Lenhart showed that compensatory hyperplasia could be prevented by giving iodine as long as one-sixth of the total gland was left - but if more than five-sixths was removed a compensatory hyperplasia followed even if iodine was given. Marine & Lenhart (iii), found that the more marked the hyperplasia the greater was the amount of iodine taken up and, in normal dogs, they state, that large amounts of iodine may be given without

- (i) Halstead, W.S., Johns Hopkins Hosp:Rep:-1896 pp.373-408. Exp:Study of Thyroid Gland in Dogs,&c.
(ii) Kimball, O.P., Amer:Journ: Med:Sc:-1922. vol v. p.634.
(iii) Arch:Int:Med: vol iv - 1909. pp 253-270.
Effects of the administration or withholding of iodine containing compounds in normal colloid on actively hyperplastic thyroids of dogs.
See also. pp. 440-493. Relation of Iodine to the Structure of Human Thyroids. Arch. Int. Med. 1909, IV. pp.440-493.

raising the iodine contents of the glands. They also found that iodine administered to dogs with hyperplastic thyroids had an action like that of thyroid extract. They explained this fact as follows :- "In the hyperplastic glands their ability to take up iodine is greatly increased owing to the much increased blood supply and the increased epithelial surface of the glands and the discharge of secretion through the lymph channels is also greatly increased to practically the same extent as is the ability to take up iodine from the blood and, until this secretion can be lessened, the organism is receiving in effect excessive doses of the physiological active substances."

But we are not sure that it is the physiological active substance which is at work here, for as Schafer(i), remarks that in cases of endemic goitre, (which means hyperplasia) where symptoms of hyperthyroidism are often present, the cases show unmistakeable signs of hypothyroidism and that the secretion of the enlarged thyroid is abnormal.(Dysthroidism).

The thyroid gland is intimately associated with the other organs of the body, viz:- the pituitary, the adrenals, the ovaries, the testes, the liver

(i) Schafer, A.S., The Endocrine Organs -1924 p.40

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pancreas, thymus and also the tonsils. It is also intimately concerned in the power of neutralising certain toxic products of normal metabolism. Quervain (i), says - "If such a function really exists, the blood of an athyroidic subject should be loaded with injurious substances which have not been utilised. The experiments performed in our laboratory by Messrs. Hara & Branovacki suggest that this is the case." Gley, (ii), showed that the urine of thyroidectomised bitches was toxic, and when injected into animals caused convulsions. De Luca and d'Angelo showed that thyroid extract removed the toxicity.

RELATION TO PITUITARY GLANDS & ADRENALS

According to Schafer (iii), when the thyroid is removed or atrophied, there is a definite increase in ^{the} anterior pituitary and Larson (iv), showed that thyroidectomised rats fed with anterior pituitary were kept alive longer than control rats which did not receive such treatment and were thyroidectomised.

- (i) Quervain, F.de. Goitre, London-1924 p.15
- (ii) McCarrison. Etiology of Endemic Goitre 1913
pp.141-2.
- (iii) Ibid - p.62
- (iv) Larson, J.A., Amer: Journ: Physiol: xlix 1919 -
pp. 55-89. and Liii 1920 pp 89-100.

"On the functional correlation between the hypophysis and the thyroid", and "Further evidence on the functional correlation between the hypophysis and the thyroid."

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Sajous (i), has stated that one of the functions of the thyroid gland is to sustain the efficiency of the anterior pituitary, but that by stimulating the anterior pituitary, the secretory activity of the adrenal glands is also sustained and therefore the metabolic activity of tissues. "The cardinal role of the pituitary (anterior) as the governing centre of the adrenals being to regulate oxygenation, diminution of its functional activity must entail a corresponding reduction of the oxygen supplied to the body at large and, therefore, a reduction of the general temperature,(i), and if the adrenals and the anterior pituitary are removed we get a lowered temperature. This we see in Addison's Disease where the adrenal glands function in a deficient manner.

"On the other hand" says Sajous(ii), "I have shown that the anterior pituitary body is the general heat centre, and that it raised the general temperature by stimulating the adrenals and, therefore, the oxygen of the body at large. Under these conditions if, as I hold, the functional activity of the anterior pituitary body is sustained by the thyroid secretion over activity of this organ or thyroid extract should

(i) Sajous, C.E. de M. The Intern:Secret: & Prin: of Med: ii, 1907 - pp.1072 and 1073.

(ii) Ibid. p. 1073.

cause a rise of temperature; whilst conversely removal of the gland should cause a fall of temperature.

It is doubtful if the thyroid by itself controls metabolism for, as McCarrison (1), states, "the thyroid gland is to the human body what the draught is to the fire; nay more, its iodine content by its chemical interaction with certain unknown constituents of the cells, is the match which kindles it."

RELATION TO THE GENERATIVE ORGANS.

The fact is well illustrated by clinical observation for one may constantly observe a close association between the thyroid gland and the generative organs, specially in women. Goitre is a disease which frequently arises at puberty :- thus amongst the school children I examined one of the first things I noticed was the sudden increase in the incidence of goitre in girls at puberty, and the same fact obtained amongst boys, though not to the same extent. One of the reasons I think why goitre is more prone to affect women is not the old idea that women drink more water than men but the fact that the generative organs in women (ovaries) are during their active sexual life subjected to far greater activity than is the case with men, and this is specially so during pregnancy and lactation. Women, too, suffer commonly from various ovarian disorders whilst men are not affected to the same extent with disturbances of the Interstitial Glands of the Testes. Another fact which can be

(1) McCarrison - Thyroid Gland 1918- p. 22

gleaned from the harvest of one's clinical experience is that where menstruation fails to appear at its proper time and there being present often simultaneously symptoms of mild hypothyroidism, the administration of thyroid extract frequently will bring about the commencement of this normal function. One has had experience of many of these cases. Why should thyroid extract act so well when introduced into the stomach? Andriezen (i), showed that in Amphioxus the thyroid is a hypobr^aonchial organ and pours its secretion into the pharynx direct. Murray(ii), states that the gland is thus descended from a secretory gland which originally had a duct and that this fact explains why we, the descendents of our ancient vertebrate ancestors, possess a secretion which, when administered orally, the stomach does not destroy.

Robinson, (iii) stated that Low & Lawson Tait found that in pregnant women there was a leucocytosis and that in goitre this was diminished and that in parturient women with goitre there was a tendency to haemorrhage. Such a case I well remember, a woman who herself was somewhat inclined to myxoedema, and who gave birth to a child which was afterwards found to be a cretin, had at her confinement a very severe post-partum haemorrhage. Gudernatsch,(iv) states that when thyroid extract is administered to animals

(i) Quoted by Murray. Diseases of Thyroid Gland 1900 p.2
(ii) Ibid. p. 2
(iii) Robinson, W. Endemic Goitre (1885) - p.29.
(iv) Amer: Journ: of Physiol xxxvi - 1915. pp370-379.

there is a tendency for fertilisation to be prevented and abortion is liable to be produced. This fact again may be observed in practice for there is undoubted tendency for women suffering from hyperthyroidism to abort, and at the same time for them to remain barren. The strong relation of the thyroid to the sexual glands is borne out by the fact that exophthalmic goitre may frequently be traced to pregnancy, and exophthalmic goitre is a disease most common in women. The natural deduction is this - that exophthalmic goitre is a disease closely associated with the sexual glands.

"But things are not always what they seem" said Leonard Williams (i), and this is even more abundantly true in the domain of the ductless glands than elsewhere. These glands constitute a hierarchy of interdependent entities. I am fond of comparing them to the eight rowers in an out-rigger boat, all are pulling in the same direction yet some of them antagonise certain others. If you reinforce one his antagonist will immediately be stimulated to retort so that, unless you have experience to guide you, especially in the dose of the original reinforcement, you may bring about a result which is the exact reverse of what you desire. The more you study the endocrine glands the more deeply do you become impressed by this element of strife within the body. And so we come to the question as to what these toxins are,

(i) Brit: Med: Journ: i - 1922. pp.853-4. The Interstitial Gland.

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which the endocrine system is at such pains to neutralise and nullify. The answer is altogether outside the terms of my present reference but to indicate the sanction of the views, which I hold very strongly, let me remind you that man is the only animal who has lost the instinct of physiologically selecting his food - that man is the only animal who cooks his food and that the Almighty no more invented the kitchen than he ordained the gin palace or the opium den. Cooking destroys the vitamins and vitamins are to endocrines what endocrines are to the economy. The kindly fruits of the earth to which we do lip service in the Litany are ruthlessly relegated to a back seat in our everyday lives and, until we see reason in this respect while it is yet day, we shall continue to poison our endocrines and to pass ignobly into nothingness with our allotted tasks but partially accomplished."

"There is war between the male elements and the female in the product of conception; there is war between ^{the} thyroid and the pancreas, there is an armed neutrality between the thyroid and the suprarenals, it is pull devil, pull baker between the pituitary and the gonads."

The relation of the thyroid to the pancreas is seen in cases of exophthalmic goitre where sugar is of frequent occurrence in the urine and this association of the thyroid with the pancreas may well be also associated with the liver for "that the liver plays an

important part in diabetes is certain and, while this is generally a secondary phenomenon, there is no proof that the primary defect (diabetes) may not occasionally reside in the liver or other organs." (i)

I have observed, too, that the excessive ingestion of thyroid extract may cause sugar to appear in the urine. In diabetes we have a condition where there is a disturbance of metabolism of sugar, fat, ^{and} protein.

"Fat does not give rise to sugar directly, but indirectly it may cause the appearance of sugar in diabetes, specially when large amounts are taken. Fat is the most important source of the acetone bodies, for an increase of fat in^a diabetic diet will frequently give rise to large amounts of these Ketone bodies in the urine." (ii) McCarrison, (iii) has found that an excess of fat in the form of butter and also oleic acid may give rise to goitre in pigeons to a considerable extent and, considering the relation of the pancreas to the thyroid, this may well be due to an excessive stimulation of the pancreas producing its reaction on the thyroid and increasing its burden.

That there is a relation between thymus and the thyroid gland is seen from the fact that this gland is frequently persistent in cases of exophthalmic goitre.

(i) Maclean, H. Modern Methods in the Diagnosis & Treatment of Glycosuria & Diabetes 1924 p.10.

(ii) Maclean. Ibid p.11 & 12.

(iii) Brit: Med: Journ: - 1922 i. pp. 178-181.

RELATION OF THYROID GLAND TO TONSILS

Dr. Margaret Purce(i). has noted that after tonsil enucleation, goitres have undergone acute exacerbation and remarks that it is a subject worth investigating. One does not need to seek far for an explanation. The observation, in itself an important one, is sufficient to condemn, and condemn strongly, the keen tendency amongst some Ear, Nose & Throat Surgeons to whip out tonsils on every and all pretexts. The tonsils are one of the first lines of defence against bacterial infections and the close association of the thyroid with the tonsils is easily grasped when it is remembered that developmentally both are closely related. They are cousins in the first degree. Rupert Farrant, (ii) has drawn attention to this in a paper discussing the effect of toxins upon the thyroid gland.

Leonard Williams (iii), has some remarks upon this subject as follows :- "Adenoids and enlarged tonsils occur in children who have an inadequate supply of thyroid secretion. The hypertrophic condition in each case is apparently the result on the part of the organism to supply an internal secretion as nearly allied as possible to the one which is lacking. If the hypertrophy is not very pronounced

- (i) Report of Sch: Med. Officer, Derbyshire Ed: Com: 1924 - p. 19.
(ii) Farrant R., Proc: Royal Soc: Med: - 1913 vol VII
Part III Path. Sect. p. 21.
(iii) Quoted by McCarrison - The Thyroid Gland - 1918 p. 139.

and if it has not been very long in existence - great enough and protracted enough that is to produce complications such as disease in the tonsils themselves or in the ears - then the exhibition of thyroid extract will cause their regression. It is only when medicinal means have failed that operative interference is justified. " For the year in question, some 1,120 children were operated upon for tonsils and adenoids, (p.10. Report S.M.O. Derby Ed:Com: 1924). The percentage of school children in the county of Derby with enlarged tonsils and adenoids is stated to be 60% and even this does not include all, ^{while} ~~which~~ the percentage of cases with middle ear catarrh was only 4.5% and all cases occurred between the ages of 10-14 years (i). The number of school children referred to for observation or treatment with these conditions was as under:-

Enlarged Tonsils	4,721	(1,592 for treatment)
Adenoids	162	
Tonsils and Adenoids ...	764	
Other conditions	44	

RELATION OF THYROID TO NERVOUS SYSTEM

Edmunds (ii), quoted Simon's (1844) observation that by comparative anatomical research he (Simon) came to the conclusion that the thyroid gland was associated with the nutrition of the nervous system and the regulation of the circulation of the blood to

(i) Ibid p. 18.
(ii) Edmunds, W. Path: and Diseases of Thyroid Gland 1901 - p. 8.

the brain. Von Cyon (i), suggested that the thyroid secretion stimulated the nerves to the heart which regulate pressure and by this means the blood pressure was lowered and circulation was retarded.

The effect of the thyroid secretion upon the nutrition of the nervous system probably depends upon the action it has upon metabolism in general, hence the slow lethargic mentality of the myxoedemic, and the constant excitability and restlessness amounting to mania in some cases of the subject of exophthalmic goitre.

RELATION OF THYROID TO BLOOD

If the thyroid secretion has any antitoxic power and if it is intimately concerned with the resistance to bacterial and toxic invasion, one would expect that the blood would show some changed characteristic of those conditions and this appears to be the case both in endemic goitre and in other conditions where the thyroid secretion is deficient. Neale (ii), in 1854 noticed changes in the blood in goitre and compared them to a "Leukaemia". He found that there was a leucocytosis but did not differentiate the leucocytes.

In thyroidectomised animals Falta & Berterelli, (iii), found certain changes in the blood, viz:- a lessened number of red cells and a leucocytosis,

(i) E. Von Cyon, quoted by Biedl. Intern: Secret: etc 1912 - p. 36.
(ii) Neale, R. Med: Times & Gazette - 1854. vol viii pp. 430 - 32.
(iii) Quoted by Biedl. ibid. p. 66.

specially eosinophiles and mononuclears. McCarrison (i), found in cases of endemic goitre that, from a study of seventy-three cases, the polymorphonuclear leucocytes may form as little as 30% of the total, the average was 46.5%. There was an increase in the small mononuclears in all except six cases and their percentage reached as high as 45%, the average being 32.2%. Eosinophilia was present in all but light cases and in some cases eosinophiles were as high as 20%, the average being 10%. Thus there was an increase in eosinophiles in 88% of cases, of small mononuclears in 92.5% of cases, of large mononuclears in 23% of cases and the polymorphonuclears were below normal in 98.9% of cases. McCarrison was careful to note that the eosinophilia could not in all cases be accounted for by the presence of intestinal worms.

The characteristic changes there in the blood in endemic goitre appear to be a lymphocytosis with eosinophilia both of which are, to my mind, evidence of a toxæmia lymphocytosis, specially the small variety, is characteristic of certain diseases of which typhoid fever is one, and in malaria we have an increase of the large mononuclears. Eosinophilia occurs in parasitic diseases - Trichina, Hydatids and Helminthiasis, also in certain skin diseases and asthma. As a rule an excess of polymorphonuclears

(i) Etiology of Endemic Goitre - 1913, p. 123.

accompanies a coccal infection, of lymphocytes a bacillary infection and of uninuclears a protozoal infection, (i).

Many attempts have been made to isolate an organism from the thyroid itself. Helen Chambers, (ii) examined a large number of cases of goitre, removed for surgical reasons, by serial sections and she found them invariably sterile. In a few cases animal inoculation was made without result. She also states that the sections histologically suggested a toxic substance present in the thyroid gland, of a diffuse nature in some cases, in others localised.

The same observer has described an organism occurring in the blood of cases of exophthalmic goitre (iii). Mc.Carrison (iv), was of the opinion that many of the cases of organisms, described as occurring in the thyroid in endemic goitre, were accidental inclusions and he records Tavel as saying that no method of staining or of illumination had resulted in demonstrating any parasite.

(i) Taylor, F. Practice of Med: Eleventh Ed: p.825
(ii) Brit: Med: Journ: ii - 1909. pp. 855-59.
(iii) Proc: Royal Soc: Med: 1912-1913 val. vi ^{PATH. SECT} pp. 136-142.
(iv) McCarrison - Etiology of Endemic Goitre - 1913, p. 137.

SOME HISTORICAL ALLUSIONS TO GOITRE

The Rev: Mr. Davies in Davies' View of Derbyshire, thus describes the complaint in the early part of last century. "It is a swelling seated on the forepart of the throat occasioned by the enlargement of the thyroid gland; but not infrequently the gland becomes subdivided into several fleshy portions connected closely to each other by cellular membranes. The form and contour of this tumour are very various; during the first years of its existence it is reddish and moderately compressible, endowed with little sensibility, highly vascular in its texture not readily going into suppuration and leaving the external skin of its natural colour. It is generally believed that the swelling, in the greater number of cases, is truly sarcomatous or fleshy; while some have said the bronchocoele consists of a honey like matter; others that it contains little portions of bone or hair; others that it is inflated with air, and some that it is distended by a watery or puriform fluid - all these opinions may be occasionally true. Females, children and persons of relaxed and delicate constitutions are more subject to this affection than males, adults and persons whose habits are rigid and vigorous; but some persons of apparently good constitutions, of

either sex, are afflicted by it."

Thomas Prosser, in 1782, wrote "An Account & Method of Cure of the Bronchocoele, or Derby-Neck." He mentions that "Goitre was frequent in Duffield (close by to Derby) where 50 poor girls were afflicted by it." Duffield at that time would only be a small village. It was common in other parts of Derbyshire as well as elsewhere in certain parts of England.

Thomas White, in a "Treatise on the Struma", London MDCCLXXXIV. p. 15., mentions that bronchocoele was common in Derbyshire. St. Lager gives a reference to goitre in England under "Struma" by Clowes, London, 1602. I have read this little work through but, from his account, I believe that the old authors included other tumours of the neck under this name as well as goitre. "For", says Clowes, "It, (Struma), may appear in the armpits, in the groins, under the chin, on the sides of the cheeks as well as the forepart of the neck."

Hirsch, in his Hand-Book of Geographical & Historical Pathology, (New Syd: Soc: London 1885, vol 11 - p.121.), states that, "it may safely be inferred however from the statement of Pliny, Vitruvius, Juvenal and Ulpian that there were already endemics of goitre in the Alps of their day."

"Guttur homini tantum et suis intumescit, aquarum quae potantur plerumque vitio." (Pliny, "Hist:

Naturae", Lib: ix. cap 37, pp. 68.). Thus very early references have been made by many observers of the occurrence of goitre in Europe, from the day of Hippocrates downwards. According to Hirsch, (ibid p.122), Paracelsus in Salsburg was the first to note the relation between endemic goitre and crettinism.

In the Tempest, Act 3, Scene 3, Shakespeare alludes to goitre as follows :-

"Who would believe that there were
 mountaineers,

Dew lapped like bulls, whose throats
 had hanging at ' em wallets of flesh ?"

TOPOGRAPHY OF HEANOR URBAN DISTRICT

The Urban District of Heanor comprises the town of Heanor, with the parishes of Langley Mill, Aldercar, Stoneyford, Loscoe and Codnor and the hamlets of Milnhay, Langley and Marlpool and has a population of 22,000. The parishes of Heanor, Langley Mill, with Milnhay, Langley & Marlpool are closely associated together. Stoneyford, Loscoe & Codnor lie on the northern portion. Langley Mill is one mile from Heanor, whilst Codnor is two miles distant with Loscoe intervening. The district is hilly in all its parts. Heanor, itself, lies on the top of a hill 400 feet above sea level, (O. D. Line). Langley Mill, with Milnhay and Aldercar, lies at the bottom of this of this hill along the R. Erewash - in the Erewash Valley. The Valley is broad and wide, and the stream running through it marks the boundary between Nottingham^{SHIRE} and Derbyshire.

Codnor lies quite apart from Heanor, upon a hill nearly as high as that on which Heanor stands; and here goitre is pretty evident, but Codnor is on the whole a poorer locality. Its houses are ancient and its sanitation not good and the evidence of its social conditions is likewise reflected in its incidence of goitre (especially in certain schools). In this case the boys show an inclination to have goitre more frequently and of a larger size than in Heanor. All these places have the same water supply

as Heanor itself.

SITUATION - The Urban District of Heanor is situated in the south eastern part of Derbyshire, midway between Derby and Nottingham and is about ten miles distant from each of these places.

OCCUPATIONS - The whole district lies on the coal measures and coal mining is the chief occupation. Other industrial undertakings are Hosiery and Lace Manufacturing, Pottery, Iron and Steel Works. Agriculture plays a very small part as a source of occupation.

SANITARY CONDITIONS - The district is semi-urban and semi-rural; those parts which are inhabited are thickly populated. There is considerable overcrowding of people in many houses, (some 400 new houses are badly needed), and a large number of inhabited houses are very bad, insanitary and ancient. There are no back-to-back houses but the streets are undesirably dusty, unkempt and never watered except when it rains. The back gardens, attached to many houses, are undescribably bad, privy middens abound as also do pail closets. The method of disposal of sewage is faulty and the effluents in many cases worse than the affluents. The R. Erewash is grossly polluted - once upon a time it was a trout stream but now does not contain a stickleback. The method of emptying privy middens is most objectionable. The faecal matter is dumped on to the gardens and then removed piecemeal

to a cart. Soil contamination of a gross character in the close vicinity of dwellings is the result. Unpaved back yards are fairly common. As a result of the unsanitary conditions, the contamination of soil, the prevalence of pail closets and privy middens, the careless habits of the people, the prevalence of bad housing, abundance of flies in summer there is a high infantile mortality rate and, I shall show later that, there is a relationship between^a high infantile mortality rate and endemic goitre in Derbyshire as a whole. However things may be at the present time, they were infinitely worse thirty years ago, and the same may be said for the other districts in Derbyshire and since that time, owing to the labours of the medical officers and sanitary inspectors headed by that enthusiastic pioneer, Dr. Barwise, a vast improvement has taken place in the whole of the county. Water schemes, of which the Derwent Valley Scheme is the chief, sewage schemes, housing and welfare schemes have all contributed towards the general improvement of the health of the people and there is no doubt that, not only in Heanor, but in other parts as well, goitre is diminishing both in the severity of its endemicity and in its amount. Sir James Berry informed me that there was no doubt that goitre in England was likewise diminishing. At Langley Mill, where goitre is specially

prevalent, the sewer in one of the main roads had for years given trouble specially in storms. This was recently opened and the eighteen inch sewer pipe was nearly choked with inspissated sewage so that the internal diameter was reduced to nine inches. In this case sewage during storms found its way into the street.

PREVALENCE OF GOITRE IN THE URBAN DISTRICT
OF HEANOR

During the months of February and March 1925, I examined the elementary school children in this district in order to make a survey of the incidence of goitre. The standard adopted was to include as goitrous all those who showed on inspection a visible enlargement of the thyroid gland. Those having palpable glands only, were not included as goitrous but counted as normal. A large number of people in this district have palpable thyroid glands. The thyroid gland of normal people is not a palpable organ but in endemic localities many people - a great majority - have thyroids larger than is usual. One cannot include such cases as goitrous. They may be considered as pre-goitrous or, as potentially goitrous if the stimulus becomes strong enough from various causes and the resistance of the individual inadequate. Nevertheless, such thyroids are hyperplastic in a minor degree.

Incidence of Goitre amongst Female Employees of
Messrs. I. & R. Morley's Hosiery Factory - Hleanor.

<u>Age</u>	<u>No.Examined</u>	<u>No.Goitrous</u>	<u>% Goitrous</u>
14	39	24	61.5
15	69	39	56.5
16	70	40	57.1
17	66	40	60.6
18	48	23	27.9
19	43	22	51.1
20	38	13	34.2
21	29	17	58.5
22	31	16	51.6
23	21	7	33.3
24	16	9	56.2
25	12	7	58.3
26	8	4	50.0
27	13	6	46.1
28	4	1	25.0
29	8	2	25.0
30	6	2	33.3
31	1	1	100.0
32	3	0	0.0
33	0	0	0.0
34	1	0	0.0
35	6	1	16.0
36	4	1	25.0
37	4	1	25.0
38	4	0	0.0
39	0	0	0.0
40	3	1	33.3
	547	277	50.6%

Tables showing the prevalence of Goitre in the Elementary Schools in the Urban District of Heanor

G i r l s

<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
5	140	43	30.7
6	126	39	30.9
7	164	55	33.5
8	177	66	37.2
9	211	78	36.9
10	217	67	30.8
11	195	72	36.1
12	174	73	41.9
13	140	67	47.8
14	21	13	61.9
	1565	573	36.6%

B o y s

5	176	49	27.8
6	123	32	26.0
7	157	46	29.2
8	116	47	40.5
9	140	38	27.6
10	148	46	31.0
11	140	47	33.5
12	139	56	40.3
13	123	53	43.0
14	34	11	32.3
	1296	425	32.7%

Tables showing the incidence of Goitre in the Elementary Schools in Heanor Urban District.

B o y s - Commonside School, H e a n o r

<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
5	24	6	25.0
6	22	2	9.0
7	13	3	23.0
	59	11	18.6%

B o y s - Mundy St. School, H e a n o r

7	33	5	15.1
8	9	4	44.4
9	27	6	22.2
10	40	10	25.0
11	26	7	26.9
12	32	12	37.5
13	28	10	35.7
14	6	3	50.0
	201	57	28.3

B o y s - Loscoe School, H e a n o r

5	55	16	29.0
6	43	11	25.5
7	31	8	25.8
8	5	3	60.0
9	1	0	0.0
	135	38	20.7%

Boys - Elnor St. School, LANGLEY MILL.

<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
5	19	5	26.0
6	13	6	46.0
7	34	16	47.0
8	21	10	48.0
9	7	2	29.0
	94	39	41.4

Boys - Church School, LANGLEY MILL

7	4	0	0.0
8	22	7	31.8
9	55	19	34.5
10	63	18	28.5
11	62	21	33.8
12	53	22	41.5
13	48	19	39.5
14	17	5	29.4
	324	111	34.2%

Boys - Church School (Infants) LANGLEY

5	10	0	00.0
6	13	4	30.0
7	6	3	50.0
8	6	5	83.0
	35	12	34.2%

<u>B o y s</u> - <u>Clara Mount School, MARLPOOL</u>			
<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
8	27	7	25.9
9	32	7	21.8
10	33	11	33.3
11	30	15	50.0
12	31	12	38.7
13	30	14	46.6
14	7	1	14.2
	<hr/>	<hr/>	<hr/>
	190	67	35.2%

<u>B o y s</u> - <u>Prospect Road School, MARLPOOL</u>			
5	23	15	65.2
6	2	0	00.0
7	20	8	40.0
8	10	6	60.0
9	1	1	100.0
	<hr/>	<hr/>	<hr/>
	56	30	53.5

<u>B o y s</u> - <u>C. of E. Infants School, LOSGOE</u>			
5	17	0	00.0
6	12	4	33.3
7	1	0	00.0
	<hr/>	<hr/>	<hr/>
	30	4	13.3

<u>B o y s</u> - <u>Council School, CODNOR - (Mill Lane)</u>			
5	14	3	21.4
6	10	2	20.0
7	5	1	20.0
8	1	0	00.0
	<hr/>	<hr/>	<hr/>
	30	6	20.6%

<u>Boys</u> - Council School, CODNOR - (Mill Lane)			
<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>%Goitrous</u>
7	3	0	00.0
8	9	2	22.2
9	17	3	17.5
10	12	7	58.3
11	22	4	18.1
12	23	10	43.4
13	17	10	58.8
14	4	2	50.0
	107	38	35.5%

<u>Boys</u> - Jessop St. School, CODNOR.			
5	14	4	28.5
6	8	3	37.5
7	7	2	28.5
8	6	3	50.0
	35	12	34.2%

<u>Girls</u> - Commonsides School, HEANOR.			
5	15	4	26.6
6	17	4	23.5
7	30	8	26.6
8	29	9	31.0
9	14	5	35.7
10	3	2	66.6
	108	32	29.6%

<u>G i r l s</u> - <u>Loscoe Road School, HEANOR.</u>			
<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
9	36	5	13.9
10	70	10	14.2
11	67	13	19.4
12	83	29	34.9
13	46	16	34.7
14	4	2	50.0
	306	75	24.5%

<u>G i r l s</u> - <u>Loscoe Rd.School(Infants) HEANOR</u>			
5	35	13	37.1
6	26	8	30.7
7	42	12	28.5
8	47	18	38.2
9	24	10	41.6
	174	61	35.0%

<u>G i r l s</u> - <u>Elnor St.School, LANGLEY MILL</u>			
5	24	7	29.0
6	22	5	23.0
7	28	12	43.0
8	14	6	43.0
9	1	1	100.0
	89	31	34.8%

G i r l s - Sedgewick Street School, LANGLEY MILL.

<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
7	3	1	33.3
8	13	4	30.7
9	55	21	38.1
10	62	21	33.8
11	56	30	53.5
12	32	18	56.2
13	46	30	65.2
14	4	2	50.0
	271	127	46.8%

G i r l s - Church School, LANGLEY.

5	18	9	50.0
6	18	7	39.0
7	13	9	69.0
8	20	13	65.0
9	31	17	55.0
10	44	20	46.0
11	33	16	48.0
12	27	14	52.0
13	21	14	66.6
14	5	4	80.0
	230	123	53.4

G i r l s - Prospect Road School, MARLPOOL.

<u>Age</u>	<u>No Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
5	12	5	41.6
6	10	6	60.0
7	10	4	40.0
8	14	5	35.7
9	1	1	100.0
10	1	0	00.0
11	1	0	00.0
	<hr/> 49	21	42.8

G i r l s - C. of E. School, LOSCOE

7	12	2	16.6
8	16	6	37.5
9	16	5	31.2
10	8	4	50.0
11	18	4	22.2
12	11	4	36.3
13	13	2	15.3
14	1	0	00.0
	<hr/> 95	27	28.4%

G i r l s - C. of E. School (Infants) LOSCOE

5	17	3	17.6
6	12	3	25.0
7	3	1	33.3
	<hr/> 32	7	21.8%

G i r l s - Council School (Infants) CODNOR, (Mill Lane)

<u>Age</u>	<u>No. Examined</u>	<u>No. Goitrous</u>	<u>% Goitrous</u>
5	10	1	10
6	14	2	14.2
7	7	1	14.2
	31	4	12.9%

G i r l s - Council School, CODNOR, (Mill Lane)

7	7	2	28.5
8	16	3	18.7
9	19	7	36.8
10	19	5	26.3
11	10	2	20.0
12	9	4	44.4
13	12	4	33.3
14	2	0	00.0
	94	27	27.6

G i r l s - Jessop Street School, CODNOR.

5	9	1	11.1
6	7	4	57.1
7	9	3	33.3
8	8	2	25.0
9	14	6	42.8
10	10	5	50.0
11	10	7	70.0
12	12	4	33.3
13	2	1	50.0
14	5	5	100.0
	86	38	44.1%

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The growth is, at its commencement, soft and of a uniform nature. In later life small adenomata are very prone to develop, as are cysts. Colloid goitres are in my experience rare. I fail entirely to understand how anyone is able to distinguish between a diffuse colloid goitre and a diffuse parenchymatous goitre by palpation alone. In my opinion, there is no essential difference between the two conditions. Where there is a diffuse hypertrophy with colloid storage this is merely the final result of the first - a return to the normal condition following the hyperplasia. If these hyperplasias are recurrent, then we get a step like increase of that thyroid following the attack. Too much has been made, I believe, of classification of types. All these so called types are nothing more than different stages of exactly the same process. Virchow, (1), has expressed himself on this subject as follows :- "With reference to true goitre, the opinion has long been held that it comprises a series of different varieties, (Struma Lymphatica; Cystica; Ossea; Vasculosa, etc.) which can develop independently of each other. This is wrong. All these so called varieties are only different modes of development of essentially the same form of goitre. They, (the so called varieties) mean only different forms

(1) Die Krankhaff. Geschwülste - 1863 iii 4.
quoted by Marine & Lenhart. Arch: Int: Med: 1911 -
pp.506 - 535.

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of terminal conditions or metamorphoses which can be combined with one another in the same tumour and a very large and striking variety of these metamorphoses may exist in the same tumour (goitre)."

McCarrison (i), classifies endemic goitre arising in man as of three types - hypertrophic, adeno-parenchymatous and diffuse colloid. The first may be physiological, or pathological, when it represents the commencement of the second type (adeno-parenchymatous). The adeno-parenchymatous variety is, he says, associated with mountainous regions and the third variety, he states, is that associated with lowland areas, and that this type in animals arises when there is excess of calcium in the food but, (p.1068), he states, that he is not prepared to state that, in man, this type is due to excess of lime.

McCarrison(ii), states that both the diffuse colloid goitre and adeno-parenchymatous goitre may arise either sporadically or endmically. Berry, (iii) speaking of goitre in this country says, "Probably in this country most goitres may fairly be considered to belong to the endemic class, but the endemicity is so widely spread over the country while, at the same time, it is so slight that it easily escapes notice and cases of goitre are often considered to be sporadic, which should more correctly be classed as endemic."

(i) Brit: Med: Journ: 1925 - (p.1067) June 13th.
(ii) loc.cit. p.1067 (iii) Berry.J. Dis: of Thyroid Gland 1901. p.49.

It will be seen from the tables that goitre is apparent both in girls and boys at the age of 5 yrs. At this age, or thereabouts, the size of these goitres is not large in the majority, though here and there it may be marked. The influence of puberty upon the incidence of goitre, both in boys and girls, is well seen but is most marked in girls. Examination of women reveals the fact that this increase is maintained. I examined some of the women of Messrs. I & R. Morley's Hosiery Factory, through the courtesy of Mr. F. Parker, and the average percentage of women with goitre was 50.6%. One cannot rely entirely upon the percentage in the age groups over about 27 or 28 years of age for so few were seen. Observations in the course of practice reveal that goitre is much more common over this age than this table shows. In the case of men, however, my observations from examination of coal miners show that goitre decreases after the age of puberty and that the average percentage of goitre amongst them was 12% (total examined 431). I examined the men coming up from the day shift as they arrived at the pit head. This was only possible by the courtesy of the Shipley Collieries Company Limited. I selected the Coppice Pit because practically all the workers at this coal mine are resident in Heanor. The circumstances of the examination were such that one could only obtain a fleeting glance at the men's necks as they filed past one in all their grime but, as it is their habit to keep

their necks bare coming from work, one obtained a very fair, if lightning-like, view of the absence or presence of enlargement of the thyroid gland. Now, if the theory of absence of sunlight, or its lack, or its paucity were the true explanation of goitre then one would expect to find that men who work for a portion of the day in almost total darkness - for no one who has never been down a coal mine can realise the inky blackness, even the more modern electric lamps give comparatively poor light - then one would expect a heavier incidence of goitre amongst such class of workers than is actually the case, whilst the women, who work under better conditions as regards light, suffer more greatly. Then again the difference between the two sexes has been alleged to be due to the fact that women drink more water than men. Well, one knows of the partiality which coal miners have for beer but it is their habit very largely, at least in the locality I am writing of, for the coal miners to drink very large quantities of water, for in some of the deeper pits the work is gruelling on account of the heat which compels them to work nearly stripped. The probable explanation is that, in women, the sexual glands during their actual life have a greater influence upon the thyroid gland than obtains in men; menstruation and ovarian disorders both combine to put the

gland to a greater strain and render it more susceptible to the influences which are the cause of endemic goitre.

Another fact which presents itself from the examination of the school children is, that in the lowlying parts of the district, goitre appears to be more prevalent. This is particularly so in the case of Langley Mill and it seems to me that this can only be explained by a difference in social conditions. Undoubtedly endemic goitre is a place disease, and the agents "which are capable of causing it live in the soil of infected localities and particularly in the soil which contains a high proportion of organic matter of human or animal origin. They are present specially in and around unclean human and animal habitations; they cling to certain houses, rooms, stables, byres, animal cages or fish tanks in which the excrement of the inhabitant is allowed to accumulate. They are capable of life in waters which are grossly polluted and show a high bacterial content but, in pure water or water exposed to the purifying influence of sedimentation, oxygenation and sunlight, their life is comparatively short and their powers of multiplication very limited." (i)

The Langley Mill district is in many parts of it a very poor one socially, and there run through it two streams - The Bailey Brook and the R. Erewash, both

(i) McCarrison - The Thyroid Gland 1918 - p.100

of them grossly polluted streams and their presence gives rise to more dampness of the soil which contains a greater proportion of organic matter than obtains in Heanor itself. The hamlet of Langley is a poor locality socially, the houses there are amongst the most ancient in the whole district, as one may discover from such names as Odessa Yard. Many houses have certainly been in existence long before the days of the Crimean War. Langley is a fairly extensive goitrous locality, and it lies on the hillside, midway between Heanor and Langley Mill. Any contamination of the soil from either Heanor or Marlpool will drain into the Langley district and this added with that of Langley drains into the Langley Mill area, the stream absorbing it being the Bailey Brook. Now as regards adverse social and sanitary conditions, I am not suggesting that they are the essential causes of goitre. By no means, for one may discover endemic goitre amongst people in the best circumstances of life as regards worldly wealth; but adverse social conditions, with poor sanitary conditions as well, undoubtedly do have a considerable influence upon the production of the disease and it is this, I believe, which in part explains the higher incidence of goitre in different parts of this area.

Dr. Watt (i), the Assistant M. O. H. for the County of Derby, speaking of Wirksworth has said :-

(i) Derbyshire Ed: Com: Report of SMO on the Medical Inspection of School Children 1924.p.29

"The town of Wirksworth was found to be among the most goitrous and it was decided to examine it more closely. I made a detailed examination of the whole of the elementary school children in the town schools. A striking difference is brought out in both sexes, between children attending the Church School and those attending the Council School, which can only be explained by different social and sanitary conditions. Children from the poorer homes generally attended the Church School. At the Church School 57% of the girls have goitres and 50% of the boys; at the Council School, 35% of the girls and 21% of the boys had goitres.

Notes on the Relation of Endemic Goitre to Exophthalmic Goitre in Heanor

True exophthalmic goitre, in my experience in Heanor, is one of the rarest diseases one meets with. I have seen extremely few cases of this complaint. I did not see a single case amongst all the school children I examined. At Morley's Factory I saw one case which had been operated upon three years ago and none amongst the coal miners examined. The Registrar of Births and Deaths for this district, which also includes Ilkeston and the outlying districts, informed me that during the last five years only one case had been certified as having died from exophthalmic Goitre.

J. M. H. Campbell (i), concluded that in the British Isles exophthalmic goitre is more likely to occur in regions where goitre is endemic. This is all wrong. Exophthalmic goitre is not an endemic disease and, observers in the field in highly goitrous localities, have concluded that in localities where endemic goitre is common exophthalmic goitre is rare.

Berry (ii), concluded after an extensive enquiry both in England and abroad that where endemic goitre was common exophthalmic goitre was rare.

McCarrison, (iii) who based his observations on personal experience of one of the worst endemic areas in the world, stated very definitely that, "amongst the indigenous inhabitants of the Himalayas I have seen only comparatively few cases in ten years, though cases occur not infrequently amongst European residents in such localities", and he stated that Bircher's experience in Aarau in Switzerland was similar to his own in the Himalayas.

These findings of Campbell's are based upon the returns of the Registrar General, of deaths occurring as certified to have died of exophthalmic goitre. Now there appears to be a good deal of confusion as to what is meant by exophthalmic goitre. In endemic localities cases of endemic goitre not uncommonly are

(i) Quart: Journr: Med: Vol.xviii.No.70.1925 pp.191-223
(ii) Berry, J. Diseases of Thyroid Gland 1901. p.177
(iii)McCarrison, R. Thyroid Gland 1918. p.195 & 196.



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associated with toxic symptoms - a rapid pulse, some tremor, and, maybe exophthalmos. Such cases are very frequently the subject of some adenomatous degeneration as well; the enlargement is nearly always - I should say invariably so - a one sided enlargement, and such cases are particularly suited for vaccine treatment. Now this class of case is commonly regarded as exophthalmic goitre. It is nothing of the kind. "I have had referred to me", said Sir V. Horsley, (i) " and so must other surgeons interested in the subject, numerous cases of parenchymatous goitre with toxæmic symptoms, as Exophthalmic goitres. These form a definite class in which practically the whole gland is enlarged but the enlargement is always greater on one side than the other. The symptoms are sometimes extremely severe, - tachycardia, exophthalmos, a myxoedematous state of the tissues, etc., and these cases are, I say, constantly described as cases of exophthalmic goitre."

Berry, (ii) during the same discussion remarked, "we find that some surgeons include under this term (exophthalmic goitre) only the ordinary typical cases with the classical exophthalmos, rapid pulse, tremor and other well known symptoms; other surgeons embrace under the same heading a large number of cases in which one or more of these symptoms and especially

(i) Clinical Journ: 1909. p.265.

(ii) Clinical Journ: 1909 p.268. Diseases of Thyroid,

exophthalmos is wanting. Most of these are cases, which I personally and I think most of us, would not put into this category at all. The inclusion, or exclusion, of such cases, "formes frustes", as they are called make a very great difference to the statistics of the results of operation for exophthalmic goitre."

Berry, (i) quoted Knocker as defining exophthalmic goitre thus :- "What I mean, to sum up under the name Grave's Disease, or Basedow's Disease, includes the affection in which the symptoms, including the most constant goitre and heart trouble, are dependent directly on the alteration of thyroid tissue and thyroid functions." Knocker stated that exophthalmos is frequently absent at the commencement of the disease and may be absent for a long period. Berry stated that by exophthalmic goitre he meant a case with exophthalmos and goitre. Palpitation without exophthalmos he often saw and such cases were often completely cured by operation. Such cases were not exophthalmic goitre. Berry's, (ii) view was that the primary cause was in the thyroid and that it was a perverted secretion. If the gland were simply over-active then partial removal would cure many more cases than was actually the case.

(i) Clin: Journr: 1909. p.268. Diseases of Thyroid
(ii) loc.cit. p. 269.

McClendon & Hathaway, (1), in America in a paper on the Inverse Relation between Iodine in Food and Drink and Goitre, argue that both endemic goitre and exophthalmic goitre are due to iodine starvation. But the material for their statistics was drawn from Draft Board statistics. In this paper they illustrate their argument with maps showing the distribution of endemic and exophthalmic goitre almost exactly corresponding. This is not in accord with observers in other parts of the world where the endemicity is more severe than obtains in America, and to make comparisons of the distribution of the two conditions from statistics of this nature can only lead to false conclusions when we bear in mind the laxity with which cases of parenchymatous goitre with toxic symptoms are classed as cases of true exophthalmic goitre. One cannot, therefore, accept the conclusions of Campbell or McClendon & Hathaway for if one does one must accept the view that exophthalmic goitre is an endemic disease and against that there is an overwhelming mass of evidence. My own experience confirms me in the opinion that the views of Horsley, Berry, McCarrison, etc., were right; and I believe that the same obtains in other parts of Derbyshire besides Heanor and Ilkeston.

Berry, (ii) states - "Exophthalmic goitre does

(i) McClendon, J.F. and Hathaway, J.C. Journ: Amer: Med: Assocn: 1924. pp. 1668 - 1672. Vol. LXXIV
(ii) Berry, J. Diseases of Thyroid Gland, 1901 - pp. 176-177.

not arise as an endemic disease and is not specially common in districts where ordinary goitre is endemic. Among a thousand cases of goitre, seen by Dr. Savage in a goitrous district in the North of England, there was not a single case of Grave's Disease. Dr. Montoya y Florez, Professor of Clinical Surgery at Medellin, Columbia tells me, "that, although endemic goitre is extremely common in that country, he has never seen a case of exophthalmic goitre."

Berry stated that he came to his conclusion after extensive enquiries in England and abroad. I had recently the privilege of conversing with Sir James Berry on this subject and he informed me that in his experience, and it is a very wide one, what he wrote 25 years ago is as true to-day as then.

The Heanor and Ilkeston Water Supply.

Previously to the year 1902, the water supply of the urban district of Heanor was obtained from wells which were very frequently in close proximity to privy middens, and also from a small water works at Smalley in the rural district of Belper, about 2½ miles distant.

At that time and for a long time before 1902, the water supply was of an unsatisfactory nature; and it was a common matter for the well waters to be polluted in a very gross manner. Typhoid existed, to a large extent at the same time, and more than once was traced to polluted well water. The source of

pollution being adjoining privy middens.

Goitre has been endemic in this locality for an unknown period and it seems that it used to be of a severe nature affecting large numbers of the inhabitants, whilst the goitre frequently attained a large size. Large cystic and fibrous goitres abounded and there are still to be seen, though they are disappearing, examples of the "Dew-laps" amongst the older generation of people. One such case is shown amongst the photographs of cases.

The gradual closure of wells, compulsory so in some cases where gross contamination was proved, together with the inauguration of an improved water supply to the town has resulted in the practical disappearance of typhoid from this district; but endemic goitre, whilst it has diminished in its prevalence and in the severity of its endemicity, has not disappeared as the tables of statistics show.

Statistics of Typhoid Fever in the Heanor Urban District Area since 1891

<u>Year</u>	<u>Population</u>	<u>No. of Cases</u>	<u>Case rate per 1000</u>
1891	9,779	0	0
1892	10,230	7	0.68
1893	10,440	32	3.06
1894	10,550	20	1.89
1895	10,800	26	2.68
1896	11,050	20	1.9
1897	11,250	54	4.8
1898	11,500	27	2.34
1899	15,860	28	1.76
1900	15,987	45	2.81
1901	16,249	29	1.78
1902	16,694	24	1.43
1903	16,955	24	1.41
1904	17,500	16	0.91
1905	17,880	11	0.61
1906	18,250	5	0.27
1907	18,623	15	0.80

Statistics of Typhoid Fever in the Heanor
Urban District Area since 1891(continued.)

<u>Year</u>	<u>Population</u>	<u>No.of Cases</u>	<u>Case rate per 1000</u>
1908	19,025	4	0.21
1909	19,451	7	0.35
1910	19,440	10	0.51
1911	19,941	5	0.25
1912	20,346	8	0.39
1913	20,634	8	0.38
1914	20,966	0	0.00
1915	20,918	3 (No:deaths)	0.14
1916	19,851	0	.00
1917	20,086	0	.00
1918	19,503	1	.05
1919	20,884	0	.00
1920	21,716	1	.04
1921	21,870	0	.00
1922	22,030	0	.00
1923	22,208	0	.00
1924	22,400	1	.04

From the consideration of these facts I was led to make some enquiries regarding the bacteriological purity of the present water supply. This water supply comes from the neighbourhood of Wirksworth, (some 12 miles north of Heanor), and also supplies the neighbouring town of Ilkeston. The combined population of these two places is, roughly, 55,000. At the present time the water is derived from two sources, viz.- The Meerbrook Sough and a bore hole. The bore hole is close by the water works and traverses the millstone grit and the carboniferous limestone shales, and has a yield of something like 30,000 gallons per hour. This yield so far has remained constant. The water is, when raw, of less hardness than the Sough water and bacteriologically sterile. Roughly, one third of the water required is obtained from this bore

hole and, at the moment of writing, another bore hole is in process of being sunk with as yet no result as far as the striking of water is concerned. (146 feet).

The Meerbrook Sough

The Meerbrook Sough, which is the chief source of supply*, is an underground tunnel some three miles in length which was cut in 1772. The first part of the Sough, that part in the neighbourhood of Wirksworth, was cut by convict labour. The second half, which has its outlet into the R. Derwent, by a Mr. Frank Hurts.

The Meerbrook Sough and its connections, the Cromford Sough, the London Company's Level, etc., were all driven for the purpose of draining the lead mines which, though now practically defunct, have been worked since very early times. From time to time evidence of lead mining during the Roman Occupation has been unearthed. Many quaint customs, similar to those regulating tin mining in Cornwall and Devon, still exist and are perfectly legal.

"By custom old, in Wirksworth wapentake,
If any of this nation find a rake
Or sign or leading to the same, may set
In any ground and there lead oar get.

They may make crosses, holes and set their
 stowes,
Sink shafts, build lodges, cottages or
 coes,
But churches, houses, gardens all are free
from the strange custom of the minery."

(Ed. Manlove 1653).

* This water is the supply for the towns of Elkes ton & Heanor - a joint water scheme. Elkes ton lies 4 miles south of Heanor. The combined population of both places is roughly 55,000 people.

The course of the Meerbrook Sough will be seen from a perusal of Maps 1 and 2. From a point, about $\frac{3}{4}$ mile north of Whatstandwell, the Sough empties itself into the R. Derwent. From its outfall it runs nearly due west through the millstone grit, then the carboniferous limestones shales and, lastly, through the mountain limestone itself. At Wigwellnook it dips south and runs underneath the town of Wirksworth, half encircling it, and ends abruptly after crossing the Derby-Wirksworth road. The Sough has numerous connections, the Bolehill Branch connecting the Sough with the London Company's Level, and by the floodgate junction, the true position of which is not known, to the Cromford Sough; by the Ravenwood Level a connection is made with the Cromford Level.

Map 3. shows a section of the Wirksworth Valley at its northern end and shows the true level of the Soughs and also the water levels.

The subsoil in this part of the valley is porous and gravelly (glacial drift) evidence of which may be seen when the cemetery is visited; and the limestone shales are also porous and fissured. The limestone itself, as is all mountain limestone, is a porous formation.

The Sough traverses the great clay band which has been faulted several hundred feet. It will be seen from an inspection of the Maps that there is no great barrier to the surface pollution reaching the Sough water, and that this pollution may take place

over a very wide area for at their levels these various Soughs drain a very large area of ground.

The Meerbrook Sough a Polluted Water

In 1902 this water was carefully analysed and declared to be free from sewage contamination and also free from lead. On a priori grounds lead as a soluble constituent of this water may be ruled out for its carbonate is insoluble. It is only moorland or upland surface waters containing peaty acids which may cause solution of lead. This Sough water, whilst raw, is a hard water but after softening is reduced to about 90 Clark, and it is this degree of hardness which obtains to the consumers. The water is thus a comparatively soft water. The bore hole water, which yields roughly one third of the water supply, is reduced after the same treatment to 4.50 Clark, so that by developing the bore holes a considerable saving will be incurred. Moreover, the bore hole water is a pure water, whilst the Sough water is polluted water. In 1910 the water was said to contain before treatment only 13 micro-Organisms per c.c. on gelatine media at 21oc after 48 hours and 4 organisms per c.c. on agar at 37oc after 48 hours. Presumptive tests showed that the organisms were B.Coli.* (1) in untreated water and after the treatment it contained none. This examination took place on 4th January 1910.

The water contains frequently much more Calcium - often 17-19 parts per 100,000

The contamination is liable to variation in

* (i) Derbyshire County Council M.O.H. Report 1910 Table ix

degree. being heaviest during the periods of heaviest rainfall. During storms it takes about 48 hours for the storm water to find its way into the Sough but in the ordinary course of affairs it takes some six months to alter the yield appreciably, which is 19,000,000 gallons per 24 hours. Thus, it takes roughly, a drought of six months duration for the flow to diminish and the yield is greater during the early spring.

In March 1924 I raised the question of the pollution of this water and, on examination, it was found to contain B.Coli in 1c.c.and enterococci in 10c.c. of raw water before treatment. After treatment B.Coli were present in 10c.c. and enterococci in 100c.c. Subsequent examinations have proved these organisms to be present.

This water has previously been declared a pure water but these examinations have proved that it is liable to heavy contamination. I am indebted to Mr. C. F. Peckham, the Assistant Bacteriologist to the Derbyshire County Council, for these examinations.

The village of Middleton, lying on the hillside N. of Wirksworth, is one of those numerous rural communities which has no sewage disposal scheme, and part of the sewage of this village is disposed of by allowing it to disappear down one of the numerous lead mine shafts, (marked X on Map One) which has not as yet become filled up. The late Dr. Barwise

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attempted to discover whether this Sewage was finding its way into the Meerbrook Sough, for it must be remembered that this village is well within the collecting ground of the Sough. The method used was placing a quantity of fluorescine dye down this particular shaft. Up to the moment this has not yet appeared in the Sough water and that is more than six months ago. Nevertheless, the fact that it has not appeared does not, I think, warrant one in stating that this sewage does not find its way into the Sough, for one cannot be sure that the amount of dye used was sufficient to cause any appreciable colouration of the Sough water or that if it did reach it, that at any given time it arrived there in any appreciable amount. There is also the possibility that by chemical interaction the dye may have been "neutralised" and thereby lost its original purpose and thus escape detection. From the close proximity of the shaft to one of the Soughs draining into the Meerbrook Sough and from a consideration of the dip of the strata, there is a strong probability that this may be one of the sources of pollution of this water. Mr. Smith, the Engineer to the Heanor & Ilkeston Water Board, assured me quite recently that he had examined water from the Soughs taken at various points and pollution from this source could not be detected. But there are other potential sources of pollution besides Middleton, viz.- Wirksworth, itself, and the farm dung

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heaps lying in the vicinity of the Sough. Some time ago, near the outlet of the Sough into the R. Derwent on the valley side lying on the millstone grit, there was a farm dung heap which was a source of pollution and this was removed after the land was acquired by the Board, and I am assured by Mr. Smith eventually the pollution was checked. But pollution exists at the present time and with a vengeance for the presence of B.Coli in 1 c.c. is an indication of a heavy contamination. Thus, we see that the mere presence of a dung heap in the vicinity of this underground river on the millstone grit, which is much less porous than any limestone, may cause pollution.

Until 1923, Wirksworth, itself, had no sewage disposal scheme of any nature; and at the present time has a considerable number of privy middens and pail closets. It is not unreasonable to suppose that many of the privy middens, and possibly also some of the pail closets, are leaky and sources of surface contamination and that this finds its way into the Sough. It is a fact, that until quite recently, the sewer which runs down the west side of Wirksworth (which was put down when the scheme was inaugurated) had never had any sewage in it at all; it was a virgin sewer.

The close proximity of the cemetery to the Sough will be seen from a perusal of the Maps; the

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subsoil here is gravelly and porous. From the point of view of a source of pollution of the Sough everything is in its favour. Now Wirksworth, lying at the head of a long valley (adjoining the Derwent Valley) and separated from it by a high plateau composed of the millstone grit, is a very goitrous locality and there appears little reason to doubt that faecal matter from this town does find access to Meerbrook Sough. There is evidence that the faeces of goitrous animals, details of which will be given later, can produce goitre as well as faecal filtrate, and it looks very much like as if the same experiment is being repeated in the case of Heanor and Ilkeston in regard to human beings.

It may well be that the pollution is not a constant one, but of an intermittent character, and this would explain the almost unanimous statement that this is a pure water. I am not aware that a very constant bacteriological examination of the water has been made. Pollution is most likely to occur during the heavy period of rainfall which, in this case, does not make itself felt until some six months later, in the spring or early summer, and it is during the months of April, May and June that other observers have noted that goitre has been known to arise frequently. I am not aware, however, that goitre shows any special tendency to make itself evident in Heanor about that time. It appears to be a constant factor, mostly so in girls and women

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subject to a slight variation only.

The pollution of the water supply has received independent confirmation from a totally unexpected quarter. The local gas company has for some considerable time experienced trouble with quantities of H_2S getting into the gas and after an exhaustive search for the cause without effect a skilled bacteriologist, recommended by the Gas Referees in London, traced the trouble to the water in the gas holders, which is from the town supply. The organisms present were B. Coli Communis, B. Proteus Vulgaris, and certain undifferentiated Streptococci. The only source of their ^{SE} organisms which is possible in the circumstances is the town water, and the trouble has not been continuous but intermittent. When water in a gas holder is highly contaminated with bacteria, reactions take place, one result of which is the evolution of H_2S which, if it exceeds a certain proportion becomes a danger and a nuisance, for when the gas is burnt, SO_2 is formed.

Iodisation of the Water Supply

(Sic.)
To Dr. James Goodfellow belongs the credit of being the first to use his power of persuading the Authorities to add small quantities of iodides to this water supply. This was commenced on December 6th 1924. At first K. I. was used and later Na. I. The daily output of the Crich Reservoir is about 1,600,000 gallons and to this quantity of water is added about 4 ozs of Na I, or 2lbs per week.

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By this means it is hoped to prevent the occurrence of endemic goitre in the population of Heanor and Ilkeston.

The Homeopathic enthusiasts, it appears, are not yet quite as dead as Queen Anne, for assuming the output of the Reservoir to be 1,600,000 gallons* daily and the iodid of sodium added daily to be 2lbs weekly, in one gallon of water there will be .02 m.g. of Na I, and assuming that the consumption of each individual is 2 pints per day, each and every day of the year, the amount of Na I introduced into the alimentary canal will be, roughly, ~~2.3~~^{7.3} milligrams per year of Na I. It is by no means certain that each individual absorbs this quantity of Na I. per year - assuming the average individual consumes 40 ozs of this water a day. Children do not drink so much as adults, and it is the children one aims at in prophylaxis most, for it is in the children that the disease has its commencement. Moreover, if that amount of iodide is imbibed, it does not follow that it is necessarily absorbed in toto through the intestinal mucosa, and even if it does it does not follow that it is all utilised by the thyroid gland, that it is absorbed and synthetised into thyroxin by that organ. Iodide, even in minute quantities, when absorbed is quickly excreted by the kidneys. True, it has been shown that when K. I. is administered the iodine of the thyroid gland

* This is the average daily consumption throughout the year.

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increases in quantity. (Cushny)(i).

The same author states that iodides may be absorbed from the skin and particularly the mucous membranes unchanged and that they appear in the secretions in five to ten minutes. It appears in the salivary glands, in the stomach as by hydriodic acid from which iodine may be formed, in the tears, in the sweat, milk, sebum and in the respiratory mucous membranes. He states (ii) that iodide is found in greater quantity in the blood than in the fixed tissues, the skin also being rich in iodide after administration - one would expect this if it is found in the sweat - also in the lungs, kidneys and lymph glands, and traces are found in the brain and fatty tissues. The greater part, however, of the iodides when administered are excreted by the kidneys, as iodides, and some undergoes decomposition in the body with the liberation of free iodine. The hair also contains an organic compound of iodine. When free iodine is liberated it combines with proteins. It appears, therefore, that a large quantity of iodide when administered in considerable doses is excreted and rapidly eliminated by the kidneys.

In regard to the water supply, the amount of iodide added is almost infinitesimal, per gallon daily, and the quantity of iodide an individual absorbs throughout the year is of a very small amount,

(i) Cushny, A.R. Pharmacology & Therapeutics 7th Ed:
p. 523.

(ii) Ibid. p.523-4.

certainly smaller than the needs of the average thyroid per year.

Dr. Goodfellow, in a manuscript communication to me, argued that iodide in goitre appeared to act more effectively in very small doses, the reason being that in extremely dilute solutions dissociation of the salt in the blood is more complete, and that rapid elimination of Na I., or K. I. does not take place as when large doses are given.

I have not observed in the eight months that this iodisation of the water supply has been carried out, that any appreciable effect upon goitrous subjects, recently acquired or of longer standing, has been attained. To me it appears that iodisation of water supplies in a wholesale manner is a wasteful method and it is by no means proved that these quantities are of practical value. More will be said in regard to this subject when the relation of iodine to goitre is discussed. To me it seems that one is just apt to get elimination of the iodide, whether it is present in small or large quantities, and what is needed by the thyroid will be absorbed, the rest eliminated. It by no means follows that because the iodine content of the food or water of a goitrous locality is low that, in that fact, we have an explanation of the cause of goitre. In such a community as Heanor, a very small part of the food consumed is produced in

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the locality, its origin is to a large extent foreign, that same food is supplied to other districts where goitre is absent or much less in evidence. Butter comes from Denmark or Ireland, the same with bacon, and to a great extent vegetables consumed are not indigenous to the district. The same applies to the meat and bread consumed.

A thyroid gland in a state of active hyperplasia is, to me, one which may very aptly be compared with a gumma, especially that form of parenchymatous goitre in which the hyperplasia takes the form of intervesicular cellular overgrowth. The microscopical pictures are, in many respects, very similar. Both are akin to one another and - "the specific effects of iodide in tertiary syphilis are exerted, not on the parasite but on the tissues in which it lives, and which have reacted to its presence by the formation of tumours; these lowly organised tumours dissolve under the action of iodides while the parasite remains unaffected; but it is now more readily accessible to the parasiticide drugs, mercury and arsenic";(i)

This may be one reason why iodide acts as a specific in goitre, whilst it is also possible that the increase of iodine in the thyroid gland after the administration of iodide in goitre may be due to the fact that the cells being degenerated are less resistant to the diffusion of salts. No one dreams of

(i) Cushny. Pharmacology & Therapeutics 7th Ed.
p.525.

of alleging that tertiary syphilis (gumma) is due to the lack of iodine, because iodides will cause resolution of such tumours. Whilst syphilis is fairly rife in this industrial district, I have failed to detect any marked specific taint amongst goitrous subjects, but a series of Wasserman reactions taken haphazard for various conditions revealed that 10% of the subjects had strong positive reactions. It is possible, though there is no actual proof of the fact, that goitre in this district may bear some relationship to syphilis. That is a matter to which I have seen no reference in the literature, viz.- what percentage of goitrous subjects show a positive Wasserman reaction. In a fair number of families, with several members of the family afflicted with goitre, I knew that one or other of the parents were syphilitic.

Organisms isolated from the Meerbrook Sough Water

The micro-organisms isolated from this water were B.Coli and Enterococci. In December 1924, the organisms were present both before and after treatment of the water and subsequent examinations have proved their presence both before and after treatment. The B.Coli isolated from the water were morphologically and culturally, and in their reactions typical. They did not produce indol.

E n t e r o c o c c u s

The enterococcus is an organism which has been found by Ross and Peckham (i), to be associated with a severe outbreak of dysentery at Chapel-en-le-Frith. They state that the organism was first described by Thiercelin, and later by Escherich, Tavel, Equet and Besson, as an encapsulated streptococcus, which may be considered either as a saprophytic organism, but which may become pathogenic, or as a pneumococcus, which has lost largely its parasitic properties and become very pleomorphic, as was suggested by D'Este Emery. French authors regard it as a very common cause of enteritis in infants, also of broncho-pneumonia and meningitis. Mr. Peckham informed me that he had never found the enterococcus in healthy stools, but that it commonly occurred in stools following typhoid fever.

Houston and McCloy (ii), state that it has been found in the blood and bladder of cases of a septic-aemic type, in "Trench Fever" and in cases where myalgia was a salient feature.

Muir and Ritchie (iii), state that it is a normal inhabitant of the intestine and that it has been found in the intestine of infants after birth. But against this fact we have the findings of Schmitz (iv), who in 1913 examined 3,500 specimens of faeces and found it

(i) Ross & Peckham - Lancet vol 1, 1919 p. 1362.

(ii) Quoted by Muir & Ritchie. Man: of Bact: 1919 p.206

(iii) *ibid* p.206.

(iv) Quoted by Ross & Peckham Lancet. 1919, p. 1362.

only fifteen times and never in the stools in health.

Besson (i), stated that the enterococcus grows best at 35° - 37° but may flourish easily at lower temperatures. It may closely resemble a pneumococcus or occur in streptococcal like chains. It retains its vitality and virulence in liquid media for a long time. It may be present in human faeces as a parasite. As regards its conditions of growth it is best grown under anaerobic conditions and is sometimes strictly anaerobic. The strict anaerobiosis can, however, be temporary and after passage through broth in vacuo the organism will grow aerobically. It is an organism which has been known to live for four years and is very resistant to adverse conditions. I allowed a culture tube to dry up and left it for a month and after that time succeeded in getting it going again by adding sterile bouillon. The organism is strongly gram positive. It grows well on agar or lactose litmus agar. The colonies are small, round, discrete, at first transparent becoming opaque later. It does not liquify gelatine and produces acid but no gas in lactose, maltose, mannite and glycerine. No indol is formed in peptone water. It may or may not coagulate milk.

T o x i n s

Besson (ii), stated that the enterococcus may kill rabbits by toxæmia. Following the injection of cultures into rabbits they become paraplegic and

(i) Besson, A. Bacteriology - Longmans 1913 pp.628-9.
(ii) ibid p.628-9.

cachectic and death takes place in 14-25 days. Large purulent lesions are found containing staphylococci as a secondary infection. If cultures are filtered and the filtrate injected the same result follows; and a like result obtains after boiling cultures for thirty minutes, or heating cultures at 110⁰⁰ for fifteen minutes. Besson also states that the addition of iodine has no effect on the cachexia producing properties of the toxin.

The enterococcus, then, is itself an organism resistant in a marked degree to adverse conditions. It can withstand lack of water, lack of food and high temperatures do not destroy its toxin easily. Even iodine does not inhibit the activity of the toxin. This is the organism which has been found in the water supply of Heanor and Ilkeston.

Bacteriological Examination of Faeces of Goitrous Persons

In a series of twenty-nine cases of endemic goitre taken at random, twenty-two were found to contain the enterococcus. Of the twenty-two positive cases four were cases of endemic goitre with toxic symptoms. (Adeno-parenchymatous goitre with toxic symptoms). Of the remaining cases in which it was not found five belonged to one family. The organisms were in all cases grown aerobically, but considering that Besson states that the enterococcus may grow under strict anaerobic conditions only, its absence in the five cases was not thereby excluded,

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for all the faeces were plated out on litmus agar under aerobic conditions. It is thus quite possible that the enterococcus might have been present in these cases. Seeing that the enterococcus was found present in so large a proportion of the faeces of goitrous subjects and that it has never been found by Schmitz in the stools in health, I believe one is justified in concluding that this organism, whilst not the actual cause of goitre in this locality, is an index of an unhealthy alimentary canal. The organism has not been found in the faeces of people in health in this district who are not suffering from goitre and who are drinking the same water. In the goitrous cases, the growth of enterococcus was very large compared to B. Coli, and the number of colonies was frequently 60% of the total.

The second point of interest is that goitre is very common in France and French observers (as I have stated above) have found the enterococcus to be a common cause of enteritis amongst infants. We have seen that in Derbyshire it was responsible for a severe outbreak of dysentery and that it commonly appears in the stools following typhoid fever. The dysentery may closely resemble typhoid itself and vaccines prepared from such cases have been successful in the treatment of the disease. If ^{the} enterococcus is introduced into the alimentary canal, as happened accidentally both to Mr. Peckham and myself on different occasions, symptoms of profound mental de-

pression and lassitude may follow - as it did in both of us. The trouble was neither more or less than that of alimentary toxæmia due to the enterococcus.

Thirdly, McCarrison (i), has stated that "the most common source of the thyroids' derangement is gastro-intestinal toxæmia", and again, " except in so far that all the epidemiological and experimental facts point to anaerobic organisms, as the casual agents of the disease (goitre) they do not permit of a more definite conclusion as to the identity of these organisms." (ii). The fact that the enterococcus is often strictly anaerobic is thus of special interest.

Geology of Derbyshire

The geology of Derbyshire is represented by three great periods, the carboniferous, the permian and the triassio. Of these three great formations the carboniferous occupies by far the greater portion of the county. In the north west the formations comprise a tract of the lower carboniferous rocks with millstone grit and, included in this area, are the picturesque Peak and Dale dsitriacts. The Peak district is formed partly of yoredale grits and shales, which appear in Mam Tor, (1,700 ft), whilst Kinder Scout, (2,088 ft) is formed of millstone grit. Contemporaneous volcanic rocks are associated in

(i) McCarrison. The Thyroid Gland, 1918 p.viii.
(Intro:)
(ii) ibid. p.100

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Derbyshire with the carboniferous limestone, chiefly in the region of Miller's Dale and Matlock, in the Via Gellia and also at Tissington. Scattered over the county, especially in the lower lying parts, are numerous evidences of glacial drift; a good example of glacial drift is seen at Crich and in the valleys, such as the Derwent and the Wirksworth Valley.

In the north eastern portion of the county are deposits of the upper group of the Permian, viz.- magnesian limestone, which consists of yellow, brown compact crystalline and earthy dolomites. It was from quarries near Bolsover that the stone was obtained with which to build the Houses of Parliament. The north eastern portion of the county is chiefly occupied by ^{the} coal measures and is an extension of the Yorkshire coalfield and reaches as far south as Stanton. The Leicestershire coalfield has an extension into the southern part of the county at Swadlincote and Hartshorn.

In the southern part of the county the rocks are composed of the Keuper and the Bunter sandstones, which consist of red and variegated sandstones often associated with gypsum, which is worked at Chellaston.

Relation of Goitre to Geology

In Derbyshire goitre occurs on all the formations which exist in the county and does not seem to bear any constant relationship to any particular formation, i.e. to surface geology. One must remember that a

locality may be on one geological formation and derive its water supply from another distant from it. Such an instance one sees in Heanor and Ilkeston. Both lie on the coal measures, but derive their water supply from a district situated on the carboniferous limestone and the millstone grit. The cities of Nottingham, Sheffield, Leicester and the County Borough of Derby all derive their water supply from the upper reaches of the Derwent, and Long Eaton, Ripley, Alfreton also take the same water supply for the major part.

The percentage of goitre amongst girls varies considerably in all these districts as the following table shows :-

Town	Water Supply	Geological Formation.	No. Examd.	% Goitrous
Leicester	Derwent Valley	Triassic	11,607	2.04%
Derby	-do-	-do-	2,767	3.6%
Sheffield	-do-	Coal Measures	-	4.4%
Long Eaton	-do-	Alluvium	249	17.0%
Ripley	-do-	Coal Measures	130	23.1%
Alfreton	-do-	-do-	155	3.2%
Nottingham	-do-	Triassic	-	-

In the case of Ripley, Alfreton and Long Eaton other water is also used, but the Derwent Valley water is the chief. Ripley takes 160,000 gallons daily. Long Eaton, 150,000 gallons daily and Alfreton, 220,000 gallons daily. Other districts which take the water supply are Bakewell Rural District Council, (300 gals.), Heage Urban District,

Council, (1,000 gals), and Shardlow Rural District, (9,000 gals.) daily. I do not know the statistics for the City of Nottingham which is supplied from this source. This table shows that geology (surface geology of a district) bears no relationship to the endemic in regard to these districts. The Triassic is the formation upon which Derby and Leicester are situated, where the percentage of goitre is low, and in two cases the percentage is low, on the coal measures (Sheffield and Alfreton), whilst Ripley has a high percentage (coal measures) and Long Eaton also is high (alluvium).

The statistics of goitre occurring in Derby, Leicester and Sheffield were kindly furnished me by the respective School Medical Officers for these places and refer to all girls examined - Elementary and Secondary School girls and to make matters more comparable I have included the Secondary School girls in Long Eaton as well, as it contains such an/one. If these were left out the percentage of goitre amongst girls in Long Eaton would be 3.6%. Whilst there appears to be a tendency for places supplied by this water to have a low incidence of goitre, there are exceptions but these exceptions occur in places with a dual supply, and it may be that this second factor is the one at fault. On the other hand it is probable that the other factors, such as social conditions, may explain the differences.

The Derwent Valley Water Board Reservoirs are situated on the millstone grit and the collecting ground is situated on the same formation.

Sir James Berry (i), has said - "The millstone grit formation is the source of water supply to so many towns in the north of England that the absence of goitre from it becomes a matter of importance." In the main this is so, as regards the cities of Sheffield, Leicester and Derby. I regret I cannot speak of Nottingham. Dr. Gillespie of Eastwood, just over the border in Nottinghamshire where the water supply is derived from the Derwent Valley Scheme, tells me that there is very little goitre in that neighbourhood. Eastwood lies on the coal measures, an extension of the Derbyshire coalfield to the east. Brinsley, which is close by, with a different water supply has a heavier incidence of goitre.

Eastwood is supplied with the Derwent Valley water

As regards the millstone grit and water supply, there is in Derbyshire one exception, that of Wirksworth. This place derives its water supply from springs in the millstone grit while the town itself lies on the carboniferous limestone and limestone shales. Wirksworth is a very goitrous locality and, as far as we have seen, social conditions markedly affect the endemic.

Now as regards the relation of goitre to the geology of a locality, Hirsch (ii), states that, "the

(i) Berry - Diseases of Thyroid Gland 1901 p.62
(ii) Handbook of Geogr. and Hist. Path: 1885 p.167.vol ii
New Syd:Soc:

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difficulty attending the solution of the problem lies essentially in the fact that there is a want of exhaustive and thorough information as to the conditions of the soil in the individual circumscribed localities which are the seats of goitre and cretinism; as well as the fact that, in forming our opinion, we should require to know not merely the upper layer of soil but also the character of the bottom which is often very different from the surface." and he further states, (i) "although this survey is far from an exhaustive one it serves to furnish evidence of several facts. The first of these, already pointed out by Boussingault, by the Sardinian Commission, by Lebert, Grange, Niepce and others, is that no geological formation precludes the occurrence of goitre and cretinism. The second is that the two diseases occur much more frequently, although not exclusively as Eshricht thinks, on the older formations (including the Trias) than on the newer. The third is that they occur only on those sedimentary formations, which are composed of the detritus of older rocks as for example, in the plains of the Rhine and of Lombardy and in the valleys of the Arve and Doria."

McCarrison (ii), says - "But whilst goitre does appear to be associated with limestone and dolomite

- (i) Handbook of Geogr & ^{Historical} Path: 1885.p.169.vol ii
New Syd:Soc:
- (ii) McCarrison - Etiology of Endemic Goitre 1913.
p.63

formations and marine deposits generally, this association is not a constant one. It must be admitted that not only are these formations often free from the disease, but also that goitre can and does prevail on almost every other formation from the most ancient to the most modern." As regards Derbyshire, the statistics of goitre show no particular relation to any geological formation, for the millstone grit, (e.g. Belper Urban), the limestone, (Wirksworth), the coal measures, (Heanor & Ilkeston), the trias, (Repton), all show high percentages of goitre and places on the same formations also show low percentages; one fact seems to arise - that the coal measures show a fairly constant relationship to a high incidence of goitre, (the eastern portion of the county), but again there are exceptions.

Clowne is situated on the magnesian limestone but has a low percentage of goitre among girls, (2.7%). Blackwell lies chiefly on the same formation and has a percentage of 7.7 amongst girls but derives its water supply from the Bunter sandstones in Nottinghamshire. One cannot, therefore, attribute the incidence of goitre in any particular locality to its geological formation, because there is such a variety in the incidence of goitre on the same formation. But one cannot dismiss the fact that there is a certain tendency for goitre to occur on certain formations and one must be guided chiefly by considering

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from what source that particular locality derives its water supply. Secondly, one must also remember ~~that~~ those geological systems which in other parts of the world have been found to be associated with goitre are those which occur in Derbyshire to a large extent. Their distribution is seen best in the geological map of the county.

Influence of Wet Soil

Goitre has been attributed to the wetness of the soil. Letsom, (i), regarded endemic goitre in Derbyshire as arising, or being helped, from the wetness of the soil in the county. The climate of Derbyshire has been libelled by many. Charles Cotton, the friend of Isaac Walton, said of Dovedale-

"In this so craggy, ill contrived a nook
Of this, our little world, the pretty brook
Alas ! is all the recompense I share,
For all th'intemperance of the air,
Perpetual winter, endless solitude
Or the society of men so rude
That it is ten times worse."

Appended are tables of the average rainfall in various districts of Derbyshire from 1904-1915.

(i) Quoted by Hirsch. loc.cit p.173

Handbook of Geographical and Historical Pathology.
Med. Soc. Lond. 1886. Vol II

Average Rainfall in the County of Derbyshire

(In inches)

	<u>Darley</u>	<u>Chesterfield</u> (<u>Linacre</u>)	<u>Castleton</u>	<u>Hope</u>
1904	28.54	27.75	31.33	36.16
1905	28.59	21.40	36.40	45.26
1906	31.66	25.92	<u>Chapel-en-le-Frith</u> 37.71	<u>Woodhead</u> 50.74
1907	34.19	25.56	35.61	43.88
1908	28.06	21.97	38.90	52.92
1909	31.97	25.52	49.91	34.22
1910	-	-	-	-
1911	27.01	20.67	-	-
1912	38.74	33.20	40.72	61.16
1913	32.31	27.06	32.98	41.87
1914	34.99	26.42	42.40	50.47
1915	35.84	26.09	36.85	50.16

	<u>Ashbourne</u>	<u>Derby</u>	<u>Belper</u>	<u>Wirksworth</u>
1904	28.11	19.91	24.50	27.89
1905	29.48	20.84	24.19	26.16
1906	36.48	28.39	29.55	35.82
1907	37.56	28.48	30.71	36.35
1908	34.19	26.51	27.42	31.61
1909	38.08	28.80	32.77	37.40
1910	-	-	-	-
1911	28.06	21.39	23.38	28.10
1912	44.96	36.67	40.40	47.87
1913	30.48	26.71	28.55	31.48
1914	39.09	29.26	32.40	34.04
1915	35.28	28.85	31.96	36.58

In Derbyshire goitre does not bear any relationship to rainfall. Wirksworth, one of the most goitrous localities, has not an excessive rainfall. Heanor is more goitrous than many localities in the north of Derbyshire where the rainfall is extremely heavy, whilst Heanor has a rainfall, approximately that of Derby where the percentage of goitre is low.

Theories of the Etiology of
Endemic Goitre

The number of theories which have at one time or another been held to be the cause of endemic goitre is legion. That eminent French writer on the subject,

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St. Lager, (i), mentions a great many, viz.- snow water, ice water, cold water, exhalations from glacier water, calcareous and magnesium waters, sulphurous waters, waters containing gypsum, silica, fluorine, barytes; waters containing too little iodine or bromine, waters not oxygenated, waters deprived of phosphates; the use of certain culinary salts; humid air and soil, stagnant air, air containing too much or too little oxygen, vicissitudes of temperature, cold air on the neck, vegetable and milk diet, ^{of} alcoholism, libertinage, onanism, consanguinity, bad nourishment, insanitary surroundings, poverty and lack of sunlight and air charged with electricity.

Effect of Certain Drinking Waters.

As regards drinking water being a cause, this belief is an extremely ancient one and has found numerous supporters down to the present day. St. Lager (ii). states that Hippocrates, Aristotle, Galen and Celsus recognised this fact.

The evidence that drinking water in certain cases is a cause of goitre is very strong. Because the belief is an ancient one should in no wise despise it, and the older writers had this advantage, that their observations of the inhabitants afflicted with this complaint were based ^{on} populations which were stationary to a much greater degree than obtains at the *present time.*

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- (i) St. Lager. *Études sur les Causes du Crétinisme et du Goître Endémique* - 1867. p.1 - 4
(ii) Loc. cit p.189.

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They were able to judge the result of the change of water supplies upon the endemic; to study the endemic under far better conditions than can be done now with the ever changing populations of rural districts migrating to the towns. McCarrison, to come to a modern author, had this advantage when he studied the distribution and cause of goitre in the Himalayas, for in the areas he studied most closely, the population was indigenous to the district. As regards my own district, the same obtains; I know from personal experience that the great bulk of the population is really indigenous to the district and that they and their forebears have resided in the district for decades past.

One ^{of} the main facts supporting the theory of drinking water as a cause of goitre is the existence of reputed goitre wells and the effect of change of water supplies upon the endemicity of goitre. The existence of these is vouched for by St. Lager.- "Plusieurs autres sources sont employées par les jeunes gens peu désireux de se couvrir de gloire sur les champs de bataille et de ceindre leurs fronts des lauriers qui attendent le guerrier vainqueur: telles en Maurienne les sources d'Argentine, de Pontamafrey, de Villard-Clément; dans le Briançonnais, la source de Saint Chaffrey." (1). He interrogated many independent people, clergymen, medical men, etc., as

(1) St. Lager, *Études sur les Causes du Crétinisme et du Goitre Endémique* 1867 - p.191.

regards the existence of this practice and all declared it to be a fact that goitre was produced by recruits imbibing certain drinking waters and thus gaining exemption from military service.

St. Lager (i), cites Hancke as stating that of 380 soldiers living in the fort at Silberberg in Silesia, only 70 did not develop goitre because they only drank boiled water or beer. McCarrison (ii), mentions Forster, the Ships' Surgeon to Captain Cook, stating that goitre suddenly appeared amongst the ship's crew after drinking melted snow water.

Baillarger's (iii), conclusion was that whilst it was not possible to be dogmatic on any etiological doctrine, nevertheless when all the facts were collated, goitre was due to a specific toxic agent in drinking water and perhaps also in edible plants. He states that the impurity of drinking waters was often commented upon in the reports of the various medical men to the French Goitre Commission (iv). "Dans les pays de montagnes, en particulier les eaux au moment des pluies deviennent troubles en se chargeant de particules terreuses et de matières organiques. L'impureté des eaux est signalée d'une manière spéciale comme l'une des causes de l'endémie du goitre et du crétinisme dans plusieurs des rapports adressés à votre Commission."

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- (i) St. Lager. *Études sur les Causes du Crétinisme et du Goître Endémique*. 1867. p. 193.
(ii) McCarrison. *Etiology of Endemic Goitre*-1913.p.
(iii) Baillarger. *Enquete sur le Goître et le Crétinisme*
Paris. 1873. pp. 369 - 370.
(iv) *Loc.cit.* p. 333.

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Changes of Water Supply Affect
the Endemic.

Changes of water supply have been frequently noted by many observers to affect the endemic. This has occurred in my own district, ^{Sw.} since the change of water supply in 1902, goitre has certainly diminished in the severity of its endemicity, and this has been observed by other medical men in the district who have been resident over long periods. Whilst the present water supply is liable to contamination, it is much better than the water supply obtained in former years.

"Le plus remarquable de ces exemples est celui du village de Bozel; où l'endémie régnait autrefois avec une intensité et dans lequel le goitre à presque disparu, depuis que la municipalité a fait venir dans ce village les eaux de Saint-Bon localité voisine tout a fait exempte d'endémie." The reverse occurred in the case of Bonnet (Canton de Vertaison), which when it changed its water supply goitre became more severely endemic. (i)

Biedl (ii), mentions that at Ruperswyl in Aargau a fresh water supply was brought from a goitre free soil and following this, in the space of twenty years, goitre and cretinism disappeared.

Kimball (iii), states that Shepherd in his report in 1918 on the occurrence of goitre in Canada, concluded that it was a water borne infectious disease directly comparable to typhoid fever.

(i) Baillarger. loc.cit. p.329.

(ii) Biedl. Internal Secretion - 1912 pp.81-82

(iii) Amer: Journ: Med: Science clxiii 1922 No 5 - p.634

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We have seen that in the Urban District of Heanor when the endemic was severe, typhoid was extremely common, but that since the improvement of the water supply typhoid has disappeared and endemic goitre has lessened in its severity but not disappeared, due to ^a definite cause. "In their manner of origin and spread, endemic goitre and typhoid fever closely resemble one another. The conditions which are favourable to the development and spread of the one are equally favourable to the other." (i)

McCarrison (ii), states that the Swiss medical men were unanimous in their opinion that endemic goitre has decreased considerably since better and more adequately protected water supplies had been introduced, a large number of the water supplies having been derived from unprotected surface streams.

At Pontcherra, (Isère) goitre and cretinism diminished since a new water supply derived from Breda was put into general use, (iii) and Beckmann stated that the same result accrued in the case of Steinseiffen in Schmeideberg, (iv).

In 1835 at Saxon in the Vallais, goitre was very common, but in that year a new water supply was obtained and since that date goitre has diminished very considerably. (v)

In the villages of Saint-Michel, Mornoz and

- (i) McCarrison. Practitioner. 1915 i. p.79
(ii) McCarrison. Etiology of Endemic Goitre 1913, p.137.
(iii) St. Lager. loc.cit p. 196.
(iv) St. Lager. loc.cit p. 191. quoting Beckmann.
(Hist:Geol: p.356)
(v) Bergeret. Compt: Rend: 1873 vol.77. No.13.p.15.

Aigle-Pierre, in the Jura near Salins, situated on one side of the ^{valley.} ~~low~~ goitre was prevalent, whilst on the other side goitre was very rare, the only difference being that there was a difference in the water supply, (i)

Robinson (ii), states that Dr. Johnson of Durham, saw goitre disappear from Durham Jail after a change had been made to a purer water supply. But whilst goitre may so very frequently be associated with a drinking water, it is not always the case for as Hirsch, (iii) remarks, Rosch in Wurtemberg, Rudlel in Middle Franconia, Schaussberger in Upper and Lower Austria, Meyr in Transylvania, Humboldt in New Granada, Bramley in Nepal, observed that in separate villages having the same water supplies, some were affected with goitre whilst in others it was absent. So much then for the facts regarding drinking waters themselves. The next thing to consider is what agent present in the water is the cause of goitre. One of the most commonly alleged is calcium and magnesium.

The Lime and Magnesium Theory

Klebs (iv), laid stress upon the presence of calcium sulphate in the water as the cause of goitre. There are many places in the world where goitre is

BULLET.
(i) ~~Bullet~~ de l'Acad: de Med: 1849.xv. p.193.
(ii) Robinson, W. Endemic Goitre 1885-p.2 (Thesis for M.D.Edin:) Churchill, London.
(iii) loc.cit p.188.
(iv) Klebs. ~~Arch~~ ^{Arch} ~~Für~~ ^{Für} Exper:Pathol: 1874 ii. p.85

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endemic and where lime is deficient. Hercus & Baker, (i) in New Zealand, found nothing to support the calcium and magnesium theory. They found in schools where rain water was the source of supply for drinking ^{that} the incidence of goitre was 80%, while at Greymouth with a river water supply the incidence was 58%. "Before the theory of calcium and magnesium salts being the etiological agents in goitre can be seriously upheld, it would be necessary to prove not only that in all endemic areas the water is hard but also, and more important, that wherever the water supply to a district is hard there ~~is~~ a high incidence of goitre ^{to} found. In the literature to which we have access no reference is made to this aspect of the question." (ii).

Hardwick Smith (iii), mentions that in the Christchurch district water was not impregnated with lime. Mitchell, (iv) observing endemic goitre in Nithsdale ^(Dunedin), states, (p.511) that the analysis of drinking water in the Upper Nithsdale did not reveal great excess of lime, and he knew many waters where lime was present in much greater amounts, yet localities drinking such water were free from goitre. In one of these cases it was 75% greater than the richest lime containing water in the Upper Nothsdale.

(i) Hercus, C.E. and Baker, E.S. N.Z. Med: Journ: 1923 pp. 79-89.

~~(ii) ibid.~~

(iii) Hardwick Smith, H. N.Z. Med. Jnl. 1921. pp. 20-32.

(iv) Mitchell, A. Brit: and Forgn: Med: Chiur: Rev: 1862 pp. 502-514.

Spurway, (i) found in West Hertfordshire and in Buckinghamshire, that in some goitrous villages nothing but rain water was drunk which was of bad quality and stored in cisterns.

Macnamara (ii), in India stated that many samples of water were examined where goitre was prevalent, and the facts ascertained revealed that an excessive quantity of lime and magnesia in the drinking water as a cause of goitre was disproved. Water was hard in Purneah, Tirhoot, Champarun and Sarun where goitre was endemic, and across the Ganges the water was equally hard, in Patna and Shahabad where goitre was absent.

Herberger, (iii) stated that the water in Rhein-zabern in the Palatinate, contained the merest trace of lime and magnesia, although goitre was endemic there and Black (iv), stated that goitre was endemic in Bolton, and lime was absent from the drinking water. In 1890 Berry (v), carried out a series of experiments on guinea pigs.

- (a) The first lot received a mixture of salts of lime, magnesia, potash and soda.
- (b) The 2nd lot received sulphate of lime only.
- (c) The 3rd lot received carbonate of iron.
- (d) The 4th lot acted as controls.

The results were entirely negative as far as goitre

(i) Spurway, J. Brit:Med:Journ: 1906 pp.1037-38
(ii) ~~Macnamara, F.N. Himalayan India. Its Climate & Diseases. London 1880 p.16.~~
(iii) Quoted by Hirsch. *ibid.* p.191.
(iv) Black. Trans: Prov: Med:Assn: 1837. v.7. p.125.
(v) Berry, J. Diseases of Thyroid Gland. 1900 p.68.
(II) *Macnamara. F.N. Climate and Medical Topography. in their Relation to the Disease Distribution of Himalayan India. etc. London 1880. p.16.*

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was concerned, and the experiments were carried out for nine months, neither sulphate or carbonate of lime, nor carbonate of magnesia or carbonate of iron had any effect in the production of goitre. The details of these experiments are published in the British Medical Journal, (1891 June 13th.)

Salts of Iron

St. Lager is so often quoted as the champion of the theory of water containing salts of iron being a cause of goitre, that it is as well to quote his own words. "Let us take care not to go too far, the sulphate of iron is for the present only an accused party until such time as culpability can be proved of it in a conclusive manner." (i)

Berry also found that carbonate of iron had no effect on the production of goitre. (*vide supra*).

Deficiency of Iodine in Relation to Goitre.

The first to discover the use of the element iodine in the treatment of goitre was Coindet of Geneva, in 1821, and the first to suggest the use of iodine as a prophylactic was Provost of Geneva in 1849, followed later by Chatin (ii). From a perusal of many papers by American Authors one is led to believe that they were the pioneers of the prophylaxis of endemic goitre with iodine.

(i) St. Lager. Études sur les Causes du Crétinisme, &c. 1867. p.454.

(ii) Roch, M. La Presse Medicale, Prophylaxie du Goitre par l'iode. pp.385-388. 1924. VOL. XXXII

Baillarger (i), records that prophylactic measures were carried out in three departments, in France, Bas-Rhin, Seine, Inferieuse and Haute Savoie with iodine preparations.

The theory of a deficiency of iodine being the cause of goitre is no new one and has of late years been revived, specially in America where it is the order of the day. But the etiology of goitre is by no means to be explained in so simple a way. If it were then the matter would be a very simple one.

The theory of deficient iodine in the food" said Quervain (ii), "as the cause of goitre seems very plausible at first sight. The comparative incidence of iodine in goitrous and non-goitrous countries has not been ascertained with sufficient accuracy to constitute definite evidence, notwithstanding the painstaking investigations of Chatin and others. The state of the thyroid varies in a striking manner from village to village, between one family and another, although the food conditions are identical so that this cannot be explained by the absence or presence of iodine."

Now various authors, notably McClendon and Hathaway (iii), and Fellenburg (iv), have attempted to show that endemic goitre arises as a result of

(i) Baillarger. Enquete sur le Goitre et le Cretinisme Paris 1873. p. 342 et seq.
(ii) Quervain. Goitre. 1924. pp.20.
(iii) McClendon & Hathaway. Journ:Amer: Med:Assn: vol. lxxxii. 1924 pp.1668-1672.
(iv) Quoted by Roch, M. La Presse Medicale. pp.385-88
1924, vol. lxxxii

iodine starvation. Fellenburg estimated the iodine content of foods in Le Chaux de Fonds and in Signau. I give the figures as quoted by Roch.*.

<u>Food examined</u>	<u>Iodine Content</u>	
	<u>Chaux de Fonds</u>	<u>Signau</u>
300 gr. de pain	4.9 r.	2.4 γ
500 gr. de pommes de terre	3.5	2.0
300 gr. de legumes divers	4.2	3.1
1500 gr. de lait	13.5	4.5
300 gr. de pommes	1.8	0.3
60 gr. de graisse	0.6	0.6
2000 gr. d'eau (boisson et cuisine)	2.8	0.1
10 gr. de sel	0.0	0.0
	<u>31.3</u>	<u>13.0</u>

Signau is a more goitrous locality than Le Chaux de Fonds. From these facts Fellenburg argues that Signau was more goitrous than Le Chaux de Fonds because the amount of iodine was less in given samples of food at Signau than at Le Chaux de Fonds. Fellenburg estimated that the inhabitants of Signau absorbed 18 r. of iodine each day less than those at Le Chaux de Fonds.

McClendon & Hathaway (i), in a paper on the Inverse Relation between Iodine in Food and Drink and Goitre (Simple and Exophthalmic) came to the same conclusion. In a very dogmatic way they assert that both simple and exophthalmic goitre have been proved

(i) Journ: Amer: Med: Assn: 1924. pp.1668-1672. vol.lxxxii.

*. La. Presse Medicale. 1924, xxxii pp. 385-388.

by them to be caused by iodine starvation. As regards the evidence on which they base their conclusions I append their table of analysis :-

Non-Goitrous Regions

<u>Food</u>	<u>*Iodine Content</u>	<u>Locality</u>
Wheat	4	Storrs. CONN:
Wheat	9.3	Edgecomb. ME:
Oats	23	Storrs. CONN:
Oats	175	Wiscosset. ME:
Corn	52	Wiscosset. ME:
Barley	73	Storrs. CONN:
Rye	3.5	Storrs. CONN:
Carrots	170	California Coast.
Salmon	45	Alaska.
Salmon	75	Oregon.
Salmon	115	Alaska.
Salmon	324	Alaska.
Goat's Milk	400	California Coast.

* Iodine content estimated in milligrams of iodine per metric ton of dry foodstuffs - (in non-goitrous and goitrous regions).

Goitrous Regions

<u>Cereals</u>	<u>Iodine Content</u>	<u>Locality.</u>
Oats	10	Minnesota
Wheat	1	"
"	6.6	"
Straight Flour	3.5	"
Bran	15.5	"
Shorts	9.6	"
Red Dog	3.7	"
<u>Pot Herbs</u>		
Spinach	19.5	Oregon
String Beans	29	"
Carrots	2.3	"
Soup Vegetables	13.5	"
<u>Fruits</u>		
Apples (peeled and cored).	3	"
Pears (-do)	15	"
Prunes	4.8	"
Bing Cherries	35	"
Peaches	11.1	"
Loganberries	160.0	"

(contd).

<u>Animal Foods</u>	<u>Iodine Content</u>	<u>Locality</u>
Skim Milk	12.0	Minnesota
Butter	140	"

From these tables of Fellenburg, and McClendon & Hathaway, we see that in neither case is iodine very appreciably deficient. In neither whether goitrous or non-goitrous is it absent. Indeed the iodine content of some foods from goitrous localities is considerable, comparatively speaking. There is evidence to show that goitre may occur in localities where iodine is available in considerable quantities in both food and water. Thus, St. Lager (i), mentions a well known goitre well in Beaulieu, (Oise) which contained large amounts of iodine. Cheltenham lies in a goitrous locality in England, yet iodides are found in several of its waters, (ii) Thus the Landsdowne Terrace Well contains 0.021 grains Na. l. per gallon, and the Pittville Well, 0.056 grains per gallon, and the Chadnor Villa Well, 0.037 grains per gallon. Woodhall Spa, in Lincolnshire, (iii) has a bromo-iodine water containing .5377 grains per gallon or 0.00768 grammes per litre. Nevertheless goitre is not absent from the neighbourhood of Woodhall Spa. "We have also the authority of New Zealand physicians for stating that goitre prevails in parts of the North

(i) Loc.cit. p. 240.

(ii) Spas of Britain. The Official Handbook of the British Spa Federation p.47.

(iii) Ibid. p.138.

Island where the only water used by the people of the district is that of the boiling springs." (i)

"Around the coast of the North Island, (New Zealand) may be found fairly numerous highly mineralised saline thermal waters, and it is suggestive that these coastal springs are peculiarly rich in iodine, chiefly in the form of sodium iodide but in some cases partly uncombines." (ii).

Niepce, (iii) in the plains of the Po, in Saone-Loire, in Val D'Aosta and in the valley of the Isere, found iodine in quantity, in the air, water and vegetation of these regions, all of which are goitrous localities.

Baillarger (iv), stated in his report to the French Goitre Commission "En resumé, l'absence d'iode dans l'air, le sol, et les eaux de certaines contrées ne saurait être regardée comme le cause de l'endémie du goître. Tout tend à prouver que cette endémie est due partout à un agent spécial, cause essentielle et toujours nécessaire de la maladie."

McCarrison (v), stated that goitre may arise as a result of deficiency of iodine and can be cured by small doses of iodine. But, he states, it commonly can arise in spite of a sufficiency of iodine, for when animals are kept in clean and dirty cages and

(i) McCarrison, R. Etiol. of Endemic Goitre-1913.p.102
(ii) The Spas of Britain. p.153.
(iii) Quoted by Hirsch. Handbook of Geo: & Hist: Path: New Syd: Soc: 1885. p.197.
(iv) Baillarger. Enquête sur le Goitre, &c. Paris. 1873. p.290.
(v) Brit: Med: Journ: 1922, 1, pp.636-7.

other conditions being equal, it arises only in the dirty cages and not only iodine but free chlorine in the water can also prevent the onset of goitre. Idiosyncrasy, both in animals and man, undoubtedly exists in the development of goitre in gastrointestinal infections. In 1913, McCarrison (i), found goitre was prevalent in an European school in India and was found to be associated with a very impure water supply. Above the age of 16 yrs, 65% of girls and 45% of girls were goitrous.

The water was purified first by iodine and later by chlorine and the laying on of a pure water supply led to its complete extinction.

The supply of iodine to the thyroid gland is dependent on the adequate absorption and the adequate assimilation of iodine. We have seen that iodine may be present in food and water to a considerable extent and yet goitre prevails. To say that goitre arises from a deficiency of iodine alone is equivalent to saying that malaria (and enlargement of the spleen which results from it), is due to a deficiency of quinine. If we see a case of chronic enlargement of the spleen (due to infection by the malaria parasite) and quinine causes the resolution of that enlarged spleen, no one would assert that the enlargement of the spleen was due to a lack of quinine.

(i) British Medical Journal - 1922, 1, pp.636-7.

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Yet it is precisely the same sort of thing which the iodine enthusiasts assert in regard to endemic goitre. Iodine is specific to the thyroid gland in the same way that quinine is specific to the spleen in malaria. We do not know what is the causal agent of endemic goitre, that is to say its exact nature. That it is an agent carried by drinking water, either polluted or liable to pollution, there is no doubt for I have seen goitre retrogress when the water has been boiled by the subject and nothing else was done.

If the thyroid has for one of its functions the combating of toxins, then its needs for iodine will be increased to form thyroxin. But the thyroid may become deranged on account of the inadequate assimilation of tryptophane. (i) and, as will be seen later, this lack of tryptophane can arise from intestinal putrefaction. In the opinion of Mellanby (ii), iodine deficiency was not common in this country and that the ordinary cause of goitre could not be alleged as due in its entirety to deficiency of iodine in the diet but due to some disturbance in the balance of the diet.

If the cause of goitre is due to deficiency of iodine in the diet and, one may add, in the soil, water or air then one would expect to find in localities where there is this alleged lack that all the

(i) McCarrison, R. Brit:Med:Journ: Some Problems of Thyroid Disease. 1923. June 13th. p.1065.

(ii) Brit:Med:Journ: 1922. i. p.832.

inhabitants of that district would be the victims of the disease. But goitre does not affect all the inhabitants in my locality and the same obtains in other districts of Derbyshire. There is indeed a marked idiosyncrasy, families living under identical conditions as to food, water, housing, sanitation and personal habits, vary in their tendency to contract the disease. Thus, one member of a family, or several, may be afflicted and others escape; different parts of the same locality vary in their incidence of goitre, other conditions being equal. These facts cannot support the contention that goitre arises from a lack of iodine where that amount is equal for all concerned, where that amount is equally ingested in the alimentary canal.

If a given amount of iodine is present in the food and it is all absorbed and assimilated by the thyroid gland and if, at the same time, there is a toxic condition present in the alimentary canal producing some disorder of metabolism, if there is present in the subject an alimentary toxæmia, then the needs of the thyroid are increased, (and also an adequate amount of thyroxin) and the thyroid hypertrophies to compensate for its increased demand. But it may also be regarded to enlarge as a result of a chronic inflammation of the gland itself due to a specific toxin for the cure of which iodine is specific. The argument will be developed more

fully in a later section but I desire at this point to emphasize that it is not the lack which is the essential cause. Give iodine in early goitre and the disease disappears. It does not follow that the cause is due to that lack. If an additional amount of iodine is added to that available in the ordinary way the thyroid is enabled to overcome the enemy, and the need for its increased action is thereby lessened. But in many cases of endemic goitre, (i) in many of the large fibrous or cystic goitre there is evidence that the thyroids are not functioning properly and symptoms of myxoedema are present. In these goitres plenty of colloid is found and this contains iodine. The whole picture of the goitre strongly suggests that of a chronic inflammation and in many of these cases there must be obstruction of the draining lymphatics through which the colloid finds its way into the body.

I have referred to Mellanby (ii),—in 1921 he performed some experiments on dogs. Puppies receiving cod liver oil as the only fat in the diet had small and normal thyroid glands, whilst those receiving butter as the only fat in the diet had large thyroid glands. The average weight of the thyroids of puppies receiving the cod liver oil was .586 grams, whilst those receiving butter was 2.77 grams.

(i) Schafer, A.S. The Endocrine Organs, 1924. p.41
(ii) Journ: of Physiol: 1921, iv. pp. 7-8. (E. & M. Mellanby).

Increasing the fat in the diet had a similar influence on the thyroids and their weight was on an average fourteen times as great as those fed with cod liver oil. When puppies were confined and received a large diet of fat (excepting cod liver oil), they tended to get a still greater hyperplasia; but when allowed freedom, or better still allowing freedom and reducing the fat intake, the thyroids were smaller and more normal. The conclusion draw from these experiments is stated to be that the reason the animals fed on cod liver oil show normal thyroids is due to its iodine content. But butter also contains iodine and before attributing the absence of goitre to the iodine content of cod liver oil one would require to know something regarding the iodine content of butter itself. Again we see the effect of unnatural conditions: confinement here appear to be necessary to cause the maximum results.

McCarrison,(i) performed some experiments of a similar nature with pigeons. He took -

- (a) 18 semi-wild pigeons which were confined in a large wire ~~netted~~ caged cage, 5' x 3' x 2', and which were fed on a mixture of grains consisting of white millett seeds - 12ozs, small dark millett seeds - 8ozs, split peas - 8ozs, and 3ozs of butter was mixed with the grain. They received this mixture daily. No sand or grit was given.
- (b) 18 semi-wild pigeons were confined in a similar manner and received in addition 6½ozs of freshly chopped onions. No sand or grit was given.

(i)British Medical Journal, 1922, i. pp.178-181.

- (c) 42 pigeons were similarly confined and fed on millett seeds only without addition of butter, onion or sand. These acted as controls.

his results were as follows :-

- (a) The average weight of the thyroids per kilogram of body weight was 82 milligrams in the control birds receiving mixed millett seeds only. In those which received mixed grains with butter and onions it was 129 m.g. and in those which received mixed grains with butter, only 183 m.g.
- (b) Goitre was present in 33 % of fifteen pigeons fed on butter and onions.
- (c) Goitre was present in 65% of seventeen pigeons which received butter without onions.

It is to be noted that in these experiments some of the controls also had goitres: considering that 42 pigeons were confined in a cage the same size as those in which the other experiments were confined at the same time, the overcrowding and consequent lack of exercise and output of energy was relatively small to the input and would act as an influence in the cause of these goitres. Commenting on the results of the experiments McCarrison says, " The cases that did not develop thyroid hyperplasia have a significance only in importance to those that did. They suggest that the excess of butter was not in itself the cause of goitre; but that it was made a potent or determining cause by the operation of some other factor or factors.

My previous work indicated the important part played by bacteria introduced into the alimentary canal in the causation of goitre. The restriction of such bacterial intervention would afford an explanation of the protective influences exercised by onions in restraining the thyroid hyperplasia; in view of the minute content of iodine in onions it seems unlikely that a sufficient explanation is to be found in an increased iodine intake consequent on the addition of onions."

McCarrison, (1) found that cod liver oil gave a complete protection against goitre and that free unsaturated fatty acid (Oleic) was a potent cause of goitre. "It would seem that in the presence of an excess of free oleic acid the iodine in the food is, in certain cases, either rendered unavailable for use by the thyroid gland or a larger amount of iodine is in these circumstances required by the thyroid gland; or that the absorption of oleic acid in excess creates increased demand for the thyroid secretion on the part of the tissues. In the presence of an excess of cod liver oil on the other hand it would appear that a supply of iodine sufficient to resist goitre producing influences of a high degree of intensity is provided by the oil." The cod liver oil contained .002% of iodine.

(1) British Medical Journal, 1922, i. pp.178-181.

Now all these experiments do not prove that goitre is due to lack of iodine. The pigeons which acted as controls developed goitre and they were particularly overcrowded. In the case of the butter experiment without onions, there is not record of its iodine content presence or absence and the amount contained, if any, and thus the goitres produced with butter alone seem to show that the goitre is not due to lack of iodine itself, as Mellanby remarked. Other factors, specially exercise, tended to produce a normal condition of the thyroids in puppies fed on a diet containing butter. McCarrison in a manuscript communication to me stated that excess of fats did not seem to have any effect unless the animals were confined and subjected to unhygienic surroundings. Such quantities of butter or oleic acid as these animals received in their diet constituted an abnormal amount of fat. But as will be seen the fat in itself did not seem to account for the occurrence of goitre, and it is not clear that the iodine content of the cod liver oil by itself could account for the absence of goitre. Some other factors were operating, viz.- confinement and unnatural surroundings. Thus whilst iodine was present it was not of a sufficient amount or it was inadequately absorbed. Butter also contains iodine in considerable amount, (see McClendon & Hathaway's Tables above), and we have seen that Mellanby found

that the butter fed puppies, when allowed exercise, did not develop goitre but they did when confined. It is likely that in these animals some disturbance of metabolism was produced or that the abnormal diet produced an abnormal intestinal flora with a consequent alimentary toxæmia.

Some chickens which I had for the purpose of fattening for table use, I divided into two pens. One lot received the ordinary food - a mixed corn consisting of, wheat, barley, maize, split peas, white millett and black millett seeds. The other lot received the same diet with 2ozs of butter a day for each bird, mixed well with the corn. Both lots were kept under the same conditions as regards freedom and drinking water. When the birds were killed, no change was seen in the thyroids of either lot. They were fed thus for three months.

I have remarked above that the food consumed by the people of Heanor is, to a large extent, not produced locally. The diet of the average person in the industrial district is by no means a poor one. Milk is not consumed in any great quantity and does not play a large role in the diet of children above the age of 5 years. The coal miners' families eat butter in preference to the cheap substitute, margarine, and fresh meat is largely consumed. The butter is not a local product. Agriculture is not a very flourishing industry here. The bread is made from

wheat which comes from abroad and the same is no doubt used for milling in other localities where goitre may be absent. Bacon is either American, Danish or Irish, for little is produced locally. In short, the great bulk of food consumed is an outside product and that same food is distributed to other places from the wholesalers and where goitre may or may not be endemic.

Goitre does not prevail in all parts of England, its occurrence is circumscribed to fairly well marked and definite areas, and even in these areas, great variations in prevalence arise.

I know farmers who go as far as Hawick and Kelso for their sheep; and butchers who go into Lincolnshire for sheep and cattle for slaughtering. The Lincolnshire district is scoured every week by dealers from Nottingham, Derby, Sheffield, Leicester and other industrial centres, and one may meet them in dozens any market day at such places as Boston and Sleaford. And these same beasts do find their way here.

Lincolnshire is not a goitrous locality, one meets with it occasionally in women, but its prevalence is a mere bagatelle in comparison with Derbyshire.

Very little of the meat consumed in Heanor is a local product even if it be English. Practically no wheat is grown in the Heanor district and very few vegetables, and the same applies to practically every other article of diet; and it is important to remember that other places receive their supplies

from the same source. Yet why does not goitre prevail in other places to a greater extent, and why the variations even in very small areas. It is absurd to get enthusiastic over analyses of iodine contents of food and drink, for in no case is it absent altogether; the essential cause of goitre cannot I submit be a deficiency of iodine in food for the great bulk of the food of the people of this country is imported. People realised that fact very forcibly during the War, and goitre occurs only in definite areas as an endemic.

Derbyshire is a county which does not lend itself to arable farming: the great bulk of it is dairying and cattle raising and by far the great majority of its produce goes to the industrial centres. Most of the milk goes to such places as Manchester, Sheffield or London.

Everything points, not towards a deficiency of iodine in the food or water, but towards some agent in the water supplies of different localities, and also to some social factors and personal factors. If iodine were deficient in the food, or in the soil in which that food was grown and in the water from which that water drains, then goitre ought to be more even in its distribution. But it occurs in this country in a very uneven manner. It has been stated (i), that goitre arises in Derbyshire because of its

(i) Iodine & Thyroid Sufficiency. Reprint from the Report of the County M.O.H. of Derbyshire: Sidney Barwise, 1924. p.1.

distance from the sea, that its contours are such that the valleys are protected from the winds carrying iodine in the air, and that the iodides once contained in the soil which, in far distant ages, was the bottom of the ocean, have long since been washed away. This is scarcely credible. Goitre may arise on the sea shore. It occurs on the Isle of Arran, and on the shores of the Barry Estuary in Glamorganshire and on the sea coast elsewhere in this country. (i). It also occurs in the Cotswold Hills district. Derbyshire is much more far removed from the sea than these places, and at Cheltenham iodides are constantly present in well waters there, and the same is found at Woodhall Spa in Lincolnshire. Dr. Goodfellow is very fond of citing the instance of Loch Katrine, from which Glasgow obtains its water supply, as containing appreciable quantities of iodide after storms as a result of sea spray containing iodide finding its way therein, and that this fact explains why goitre is practically absent in Glasgow (ii). But if this be so, why does goitre arise on the Isle of Arran, which is even more exposed than Loch Katrine. The city of Perth derives its water supply from the R. Tay, which is a tidal river; its sewage works are at the present time so placed that sewage at certain states of the tide is carried above the place where water is taken from the Tay for the inhabitants of

(i) McCarrison. Etiol: of Endemic Goitre. 1913 p.8-9
(ii) Iodine & Thyroid Sufficiency. etc. S.Barwise p.6.

Perth, and the place is one where goitre occurs in Scotland, a fact I myself observed in August of this year. London takes its water from the Thames, another tidal river which is grossly polluted, and goitre does occur in that city in spite of the careful watch kept on the purification of the water by storage and filtration. On many occasions when I have been in London I have observed numerous cases of well marked parenchymatous goitre occurring in women. When last I walked down Oxford Street I noted dozens of women with well marked enlarged thyroids. They could not all have been physiological swellings, nor could all of these subjects have been visitors like myself from goitrous localities. A fair smattering of these cases of goitre were colloid goitres and inclined to be cystic.

A good deal of doubt has been cast of recent years upon the deficiency theory of Beri-Beri, a disease which, in that it arises, or is favoured in its mode of spread by overcrowding and insanitary surroundings and in this respect resembles endemic goitre.

An outbreak of Beri-Beri occurred amongst the British troops at Basra in 1917, when neither the diet nor the cooking was at fault, and other troops receiving the same diet, ^{escaped.} (i). McCarrison (ii), observed that if pigeons brought into a pre-Beri-Beri condition

(i) Sprawson. Quoted by Manson-Bahr, Manson's Tropical Diseases, 1925. p.308.
(ii) Ibid. p.308.

were infected with *B. Suipestifer*, the infection determined an attack of neuritis and Manson (i) was convinced that Beri-Beri was infectious. Beri-Beri is a classical example of a disease commonly believed to be a deficiency disease. "In view of the possibility of further discovery, it is desirable somewhat to qualify this statement. It is just possible that the condition brought about by this deficiency merely predisposes to, or is necessary for, the operation of something else, perhaps an unknown germ which, in the absence of this deficiency would remain inoperative. Further, it may be that there are two or more diseases included under the name of Beri-Beri, each of them acknowledging a different specific cause. Indeed there are not a few facts suggestive of such possibility." (ii).

The same may be true of goitre in man, but that there are separate conditions with a different cause in man, no proof is forthcoming. True endemic goitre is most commonly connected with impure water supplies.

Hercus & Baker (iii), found that the administration of iodine to school children in New Zealand did not invariably prevent the occurrence of goitre. In arriving at their conclusion they "did not know and took pains not to know which children had been

(i) Ibid. p.308

(ii) Manson-Bahr, P.M. *Manson's Tropical Diseases* 1924, p.304.

(iii) *New Zealand Medical Journal*, 1923. pp.169-173.

taking treatment and which had not." Below is appended a table summarising their results in the Christchurch Schools.

<u>Normal (258)</u>	<u>No.</u>	<u>Treated</u>		<u>Untreated</u>	
		<u>Percent</u>	<u>No.</u>	<u>Percent</u>	
Unchanged	58	60.4	73	45	
Increased	38	39.6	89	55	
<u>Goitrous (789)</u>					
Unchanged	173	43.1	159	41	
Increased	86	21.4	160	43.5	
Decreased	142	35.4	60	15.4	

These results were obtained after treatment had been carried out for twelve months. The treatment given was a weekly dose for ten weeks in each term of 4 grains, 2 grains and 1 grains respectively in $\frac{1}{2}$ oz of water of Na. 1.

Standards 4, 5, & 6, and High School (11 years and upwards) received 120 grains per annum each.

Standards 1, 2 & 3, (8 - 11 years) received 60 grains per annum each.

Infant school children, (5 - 8 years) received 40 grains per annum each.

The types of goitre prevailing in New Zealand, according to Drennan (1), are the hyperplastic, diffused or localised colloid and so called adenomatous types, and in very few cases was the change uniform, some parts of the gland being hyperplastic and other parts colloid.

(1) New Zealand Medical Journal, 1924 pp.199-202.

Hercus (i), stated that there was, in New Zealand school children, a complete absence of myxoedema and of exophthalmic goitre.

Hardwick Smith (ii), mentions that the incidence of goitre in certain districts, such as Christchurch, is considerable and that the water is artesian and considered to be very pure and is not lime infected, "but it is drained down from the back plains of Canterbury where there is a liability of sewage "seepage" from the houses of infected settlers gradually permeating into the stratum which drains the water away."

I was looking over recently the reports of analyses of sewage effluents in the urban and rural districts of Derbyshire for the last three years, and in a large proportion the results were constantly of a bad character. The districts in the south of Derbyshire are very badly supplied with water and the villages obtain their water from surface wells which are liable to pollution from privy middens and farm dung hills. Moreover, the nature of the country makes it possible that sewage seepage takes place from the higher ground to the north, draining down from the infected strata in mid-Derbyshire.

Marine (iii), stated that the maximum storage of the human thyroid gland was 20 milligrammes of

(i) New Zealand Medical Journ: 1921. p.121
(ii) New Zealand Medical Journ: 1921. pp.20-32.
(iii) Public Health. Michigan, 1923. xi. pp.23 -24.

of iodine and such a store was sufficient to meet the need of the body for several months. He advocated the administration of 100-200 milligrams of iodine in any form twice a year. Kimball (i), in 1917 sent his first report to Klinger of Zurich, and 1918 prophylaxis of goitre with iodine was commenced in Switzerland. In America Kimball used sodium iodide, while Klinger used an organic iodide, a stable non-hygroscopic vegetable fatty acid compound with chocolate, each tablet containing 5 milligrams of iodine. Kimball stated that at St. Gallen in January 1919, 87.6% of the school children were goitrous after iodine prophylaxis.

In America they gave grs.1 of Na.¹ Sacchar Lactis, but later used the same preparation as the Swiss, each tablet containing 10 milligrams of iodine. One tablet is taken per week throughout the year. Kimball stated that no harm was observed to take place from these measures.

Marine & Kimball (ii), stated that 3i of Syr. Ferri. Iodid or Hydriodic Acid given over a period of two to three weeks or repeated twice yearly would seem to be sufficient: as a public health measure 2 grams of Na.¹ over a period of two weeks and repeated twice yearly. They state in America this dosage has prevented enlargement in 99% of cases but they are careful to state the district was a mildly goitrous

- (i) Western Reserve Univ: Bulletin. vol xxvi. July 1923. No. 7. pp. 121-3.
(ii) Arch: of In: Med: 1920. xxv. pp.661-672.

locality where this took place. In girls who had slightly enlarged glands and who took the prescribed treatment 57.7% decreased in size and of those not taking the iodine 13.9% decreased. In the case of those with moderate enlargements 79.7% decreased in size. The table below shows their results. -

	<u>Taking</u>	<u>Percent</u>	<u>Not Taking</u>	<u>Percent</u>
	<u>Totals</u>		<u>Totals</u>	
<u>Normal</u>				
Unchanged	906	99.8	910	72.4
Increased	2	0.2	347	27.6
<u>Slightly enlarged</u>				
Unchanged	477	41.9	698	72.8
Increased	3	0.3	127	13.3
Decreased	659	57.8	134	13.9
<u>Moderately enlarged</u>				
Unchanged	29	20.3	57	64.0
Increased	0	0.0	21	23.6
Decreased	114	79.7	11	12.4

Iodine, however, added to a water supply is not the only substance which will prevent the onset of goitre. Chlorine can act in the same way when added as free chlorine, (i), but whilst it may prevent enlargement of the thyroid gland, chlorine does not appear to be able to prevent hyperplasia.

The Role of Alimentary Toxaemia
in Goitre

According to Lorand (ii), the thyroid possesses antitoxic powers, because when it is extirpated infectious diseases are easily acquired. Thus myxoedemic subjects easily succumb to infections. We have

(i) McCarrison, R. Brit: Med: Journr: 1922, i, pp.636-637.
(ii) Lancet 1907. ii. pp.1318-1321.

seen that in a considerable percentage of series of unselected cases of true endemic goitre, the enterococcus was present in the faeces of the cases. The enterococcus is an abnormal inhabitant of the alimentary canal, and it is found in other conditions as for instance, following typhoid fever, and its presence may be regarded as an index of an unhealthy condition of the alimentary canal. To what agent then are we to attribute the development of goitre ? Mellanby (i), states that the indol derivatives are relatively innocuous compared with other substances and he said that for himself, in order to obtain a urine giving the indican reaction for demonstration to medical students, he took one from cancer of the liver. He suggested that we throw overboard the tryptophane derivatives and specially indoxyl sulphate.

A medical colleague in Nottingham assured me that for many years his urine had shown a strong indican reaction and yet he was and always had been perfect health.

Mellanby (ii), attributed alimentary toxæmia to certain amines produced by the splitting off of CO_2 from the proteolytic amino-acids by intestinal bacteria. He stated that the most important of these were parahydroxyphenyl - ethylamine (tyramine), iso-amylamine and B.Imidazolethylamine the amine of histidine/

(i) Proc: Roy: Soc: Med: 1913. Discussion on Alimentary Toxaemia. vol vi. part i. pp.250 et seq.
 (ii) Proc: Roy: Soc: Med: 1913, vol vi. part i. p.250
Discussion on alimentary Toxaemia.

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and he quoted Harvey as having produced marked arterio-
sclerosis and a renal condition resembling large white
kidney by feeding animals with tyramine and iso-amyla-
mine over long periods.

Mellanby urged that the key to the situation in
alimentary toxæmia lay, not in considering the bacteria
of the intestine nor the end product of bacterial
action but the mechanism which prevents the passage of
toxic substances across the intestinal mucous membrane
into the blood stream. That there is a defensive
mechanism is likely.

Hunter (1), stated that "the degree of putrefac-
tion depends on the amount of proteid in the food and
the abundance of B.Coli. Chronic constipation was,
therefore, a highly unnatural condition and always a
source of portal toxæmia. That it might exist in
certain individuals as an almost permanent condition,
without apparently causing ill-health, was solely due
to the power and protective action of the liver. It
was not any evidence of the comparative harmlessness
of constipation per se, but only an evidence that some
individuals possessed the caecum and colon of an ox,
with the liver of a pig capable of doing any amount of
detoxication."

Ledingham in the same discussion (p.141), criti-
cised the contention of the Metchnikoff School for
drawing attention to the anaerobes as the chief factors
in intestinal putrefaction, whilst attributing so much

(1) Proc: Roy: Soc: Med: 1913. vol vi. part 1. p.238.

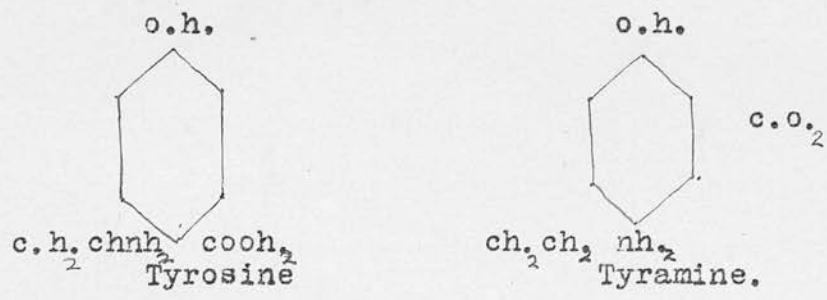
in alimentary toxæmia to indol produced by coliform organisms. He stated his difficulty in realising why indol should be regarded by Metchnikoff and his pupils as the chief toxic product of bacteria, for the ~~know~~ toxins of bacteria are of unknown chemical composition. He stated that Bertrand and Berthelot isolated from cases of alimentary toxæmia an organism which, when grown in special media, formed a product identical with B.-Imidazolethylamine which is a product of histidine and according to these authors the organism was B.Lactis Aerogenes, a coliform organism. They also asserted that the organism was never found in the faeces of healthy people. Ledingham also contended that there was no bacteriological basis for the view that activity of the lactic acid bacillus inhibits putrefaction in the intestine and the fact that intestinal putrefaction was inhibited by milk or its constituents (milk sugar) was known before the time of Metchnikoff. Such might be due to B.Coli acting on the sugar, but whilst there may be no bacteriological basis for the view, there is some evidence that in goitre the administration of fresh cultures in milk of the B.Bulgaricus has been successful. McCarrison (i), treated cases for period of 4 - 6 weeks in this manner. Of eight cases four were cured, two improved/and two showed no difference. All were

(i) Endemic Goitre 1913. p.149.

of some months duration and no change was made in the general mode of life.

Dixon (i), quotes Barger & Walpole as having shown that tyramine is formed in a sterile pancreatic digestion containing tyrosine when inoculated with faecal bacteria, and Dixon states that tyramine is not formed in a sterile pancreatic digestion containing tyrosine. Tyramine, he states, is a toxic substance which may be formed from tyrosine by decarboxylation.

cap 6



Tryptophane by a similar action of putrefactive organisms is changed into the poisonous indo-ethylamine and, a base also poisonous, is obtained from histidine by the same means. In all cases the amino-acids are harmless whilst the bases are poisonous. Indol and skatol are produced from amino-acids by putrefactive bacteria and of these amino-acids one is tryptophane. Dixon states that ~~the~~ two factors are essential - (1) Intestinal sepsis and (2) proteins containing the tryptophane group. The phenols and cresols he regarded as being innocuous and doubted whether they were of much significance. He mentions

(i) Proc: Roy: Soc: Med: 1913, vol vi. part i. p.132. Discussion on alimentary toxicemia.

one substance, sepsin, a violent poison produced from putrid yeast and blood but easily changed into a harmless substance, cadaverine.

McCarrison (i), mentions that the thyroid may become deranged from inadequate ingestion of tryptophane, besides iodine, and the remarks of Dixon make it clear how this can arise. Thus intestinal sepsis may play a large part in the etiology of goitre.

Said Frederick Langmead (ii), "Dogma is the child of ignorance - evidence is accumulating to show that among many functions of the thyroid gland one of the most importance is a protective action against circulating toxins. Complete removal of the thyroid leads not only to myxoedema, a condition which may be partly or completely cured by the administration of its internal secretion, but also, as is well known, brings with it considerable risk of fatal toxæmia. An important manifestation of this toxæmia is the symptom complex known as tetany. On very good grounds tetany is thought by many to be produced by toxins generated in the alimentary canal. I have described a series of cases where the same syndrome has accompanied dilation^{at} of the colon. When stagnation in the bowel was accompanied by grey pultaceous and offensive motions tetany followed and was only relieved by colonic lavation." and on page 321 Langmead states, "The last three cases of myxoedema which I have had under observation have all shown, together with severe oral sepsis and very offensive motions, anaemia of the pernicious

(i) Brit: Med: Journ: June 13th 1925 - p.1065.
(ii) Proc: Roy: Soc: Med: Discussion on Alimentary Toxaemia 1913, vol vi. part 1. p.319.

form which Dr, William Hunter has for so many years ascribed to lesions in the alimentary tract. If the thyroid undergoes enlargement to combat undue toxæmia it is reasonable to suppose that relieving it of part of its burden may cause a simple goitre to shrink; this, of course, cannot be expected if adenomata or cysts are present."

Langmead describes the treatment of cases with vaccines composed of organisms from the faeces of cases of goitre. In eight cases the results were encouraging. One case was completely cured; in all others it diminished. After the first injection the tumour became softer and after subsequent doses also. "Two of the patients have been able to do up their neck bands for the first time for several months after the first or second injection. A man who had taken to larger collars has now returned to those of his usual size. One girl who had definite stridor, even when lying in bed, has now no embarrassment of breathing except slightly after vigorous exertion. All are charitable enough to say they are better and free from symptoms which caused them to come for treatment, such as a feeling of suffocation, difficulty in swallowing and breathing." (p.322).

Arbuthnot Lane (1), discussing the effect of alimentary toxæmia upon the thyroid said - "Perhaps the organ which surprised me most by its behaviour

(1) Proc: Roy: Soc: Med: 1913 vol vi. part i.p.106/
Discussion on Alimentary Toxæmia.

was the thyroid, for though I had long recognised the dependence of breast conditions upon stasis I had obtained no certain evidence that the several changes the thyroid undergoes were produced by it also. I had short-circuited patients who were clearly exophthalmic or who had been so most distinctly at an antecedent period and were improving and had not been altogether surprised at the rapid and complete disappearance of their symptoms; as one knows they may occasionally subside or even disappear as it is called spontaneously.

" A patient was admitted under my care with marked stasis who had been driven to resort to operation by abdominal pain and vomiting and by the associated mental and physical misery and depreciation. For 8 years she had suffered from an enlarged thyroid which projected forwards in her neck and which interfered with respiration. It contained several large adenomata: as the anaesthetist hesitated to administer an anaesthetic for the resection of the large bowel because of the goitre, I urged her to consent to the removal of part of her thyroid in the first instance. This she fortunately refused to submit to saying she would have her bowel removed or go out of the hospital. Consequently this was done without any serious cause for anxiety, within a few days of the operation it was obvious that her thyroid was diminishing steadily in size and this diminution continued until she left the hospital when it was a little larger than

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normal. I understand that at the present time it is not larger than normal. " When this was related to Metchnikoff he exclaimed, "C'est un cas qui coute" and his rapid grasp of the importance of this result has been fully borne out by subsequent operations on similar cases, accompanied or not by exophthalmic symptoms. Kinnier Wilson (i), in a paper on "Progressive Lenticular Degeneration: A Familial Nervous Disease associated with Cirrhosis of the Liver", relates that besides the constant cirrhosis of the liver in the complaint, the thyroid gland shows also an increase of interstitial tissue, irregularity of vesicles, proliferation and activity of epithelium, and in many cases disappearance of colloid - those changes which one finds constantly in parenchymatous goitre. Wilson concluded that progressive lenticular degeneration was due to a toxæmia.

Rowell (ii), speaking of the result of chronic intestinal stasis upon goitre said, "In the case of a very athletic young lady of whom I have knowledge, who had a very large thyroid and some symptoms of chronic intestinal stasis, after a course of paraffin given freely three times a day for ten days, the thyroid had diminished to less than half its former size and the patient felt perfectly well. In Dr. Hale White's opening paper he adduces a case of exophthalmic goitre which disappeared during an

(i) Brain. vol xxxiv. 1912. p.431.

(ii) Proc: Roy: Soc: Med: 1913, vol vi. part 1.

Discussion on alimentary toxæmia. p.197.

attack of typhoid fever. The rest in bed, the milk diet and the diarrhoea during the illness obviously must have kept the patient without stasis for some weeks so that instead of providing an argument against the theory that exophthalmic goitre is associated with chronic intestinal sepsis, the case would seem to be in perfect accord with that belief."

Marine & Lenhart (i), described goitre arising in Brook Trout characterised by the growth of thyroid tumours which were visible externally, ventrally below the base of the tongue or dorsally in the floor of the mouth and phar anx between the first and third gill arches. Their observations were made at a fish hatchery on the mountains of Pennsylvania in 1909. The fish houses were in single file down the course of a stream, each containing four tanks and there were altogether about 36 tanks. Where the water supply was polluted, as it was in tanks Nos.19, 20 and 36, there the tumours were greatest and any difference apparent in the tanks was due to greater pollution of water. They concluded :-

- (a) That the so called carcinoma of the thyroid of Brook Trout was severe endemic goitre.
- (b) That overfeeding and overcrowding and a limited water supply were the three main factors in the production of filthy unhygienic tanks and ponds and these were associated with the development of thyroid hyperplasia.

(i) Journ: of Exp: Med: 1910. xii. pp.311-337 & 1911, xiii. pp.455-475

- (c) They were all able to prevent and cure the complaint by adjusting the amount of food and the number of fish to the water supply or by the addition of iodine to the water pouring through the ponds. (2c.c of Lugol's Solution to each tank twice daily for 22 days.)
- (d) That it was most marked in young fish and older fish were less susceptible to the disease and tended to spontaneous recovery under constant conditions.

McCarrison (i), observed that goats fed upon spore bearing organisms isolated from the faeces of a goitrous horse had smaller thyroids than normal animals thyroids, together with an increase in the animals weight, were such that the condition resembled one of commencing myxoedema. Vaccines prepared from this organism were successful in the treatment of goitrous cases.

Do variations in diet affect the causes of goitre ? McCarrison (ii), was unable to satisfy himself that the changes in the thyroid in goitre were due to excess of proteins, neither was he able to cause enlargements of thyroids in animals with excessive doses of certain amino-acids. With the exception that tryptophane gave rise to enlargement of the thyroid in tadpoles, the other amino-acids caused a reduction of the thyroid with a lowering of the number of vesicles. The ingestion of certain amines, this author stated, (tyramine & histidine) reduced the size of the thyroid gland in rats.

(i) Diseases of Thyroid Gland, 1918. pp.53 & 54.

(ii) Brit: Med: Journ: 1924, pp. 989-994. B. M. A.

Lectin on Goitre

Starch did not appear when given in excess to affect the thyroid but McCarrison noted that an excess of sugar in pigeons caused the vesicles to become distended with colloid. In the same paper he quoted the experience of Walton, "Twenty cases of goitre were treated with regular doses of Syr.Ferri.Iod. and twenty with intestinal antiseptics alone, about 50% of each group were cured. If the two treatments were combined a further 40% were greatly benefited."

The abundance of evidence produced by all these observers demonstrates that alimentary toxæmia plays a large part in the production of goitre and considering that tryptophane is so closely allied to thyroxin and that Dixon states that proteins containing ^{the}tryptophane group and intestinal sepsis ~~are~~ ^{are} essential for the production of indo-ethylamine, a poisonous substance in alimentary toxæmia, and we may consider that we may possibly have the cause for the production of goitre when it arises from, (a) a lack of tryptophane and hence of thyroxin, (b) that the production by intestinal bacteria of the poisonous indo-ethylamine places upon the thyroid an added burden for its detoxication.

Since Kendall (i), showed that the action of thyroxin is bound up to a large extent with certain amino-acids, the production of certain amines, by putrefactive organisms by the splitting off of CO₂ from proteolytic amino-acids; the intervention of

(i) Vide Supra. p.6.

these organisms creates an intestinal toxæmia, as well as depriving the organism of tryptophane. The deprivation of those amino-acids leads to a deprivation of iodo-amino acids, and hence of thyroxin. Vessie (i), in a paper on "A Biological Explanation of the Iodine Molecule" summarised the function of iodine as follows :-

- (1) Absorption of iodine - bearing food.
- (2) Formation of Iodo-Amino Acid.
- (3) Thyroxin.
- (4) Thyroxin as a carrier of O_2
- (5) Oxidation of the fatty acid molecule.
- (6) Formation of intermediate products.
- (7) Formation of CO_2 , the end product.
- (8) Stimulation of the Respiratory Centre by CO_2 .

Intestinal bacteria may intervene at stages one or two. They may possibly absorb some of the iodine present in the food supply and pass with it out of the body, or by splitting up the amino-acids which are formed by hydrolysis in the intestine from protein. Tryptophane, if thus split up with the formation of the amine indo-ethylamine, interferes with the third stage - the formation of thyroxin, or if thyroxin be formed in sufficient amount, there is an increased load placed upon the thyroid, as a consequence of the alimentary toxæmia, which causes it to increase in size. The increase is thus a ~~compulsory~~ ^{compensatory} increase. The fact that goitre may and does disappear of its own accord, may well be that intestinal putrefaction is not always a constant

(i) New York Med: Journ: 1923, cxvii. p.74

factor. The relief of alimentary toxæmia by cathartics, or liquid paraffin or by a rectification of diet, or by simple resolution of itself from varying conditions will relieve the thyroid of its greater need, and it shrinks in consequence. It is a fact that in my experience, a large number of goitrous people are habitually constipated, and Messerli (i), has treated successfully cases of goitre by laxatives alone.

Whatever may be the significance of indol, whatever may be its alleged role as a poisonous substance, there is no doubt as to its origin. "The destruction of albuminous bodies which is mostly involved in the wide and varied process of putrefaction can be undertaken by whole groups of different varieties of bacteria. The action of the latter on such substances is analogous to what takes place when albumins are subjected to ordinary gastric and intestinal digestion. In these circumstances, therefore, the production of albumoses, peptones, etc., similar to those of ordinary digestion, and can be recognised in putrefying solutions, though the process of destruction always goes farther, and still simpler substances, e.g. creatinin, indol and, it may be, crystalline bodies of an alkaloidal nature, are the ultimate results."

The fact that individuals and animals, whether in a state of nature or kept under experimental conditions, show an idiosyncrasy towards the development

(1) Le Goitre Endémique. Lausanne (Suisse) 1916 quoted by McCarrison The Thyroid Gland 1918, pp.246-8

of goitre, may be due to the fact that these subjects have a relative immunity.

In the experiments to be described, I found that B.Coli isolated from the water supply of Heanor were capable of producing fairly large goitres in rats, and these organisms were non-productive of indol, but nevertheless they were capable of producing goitre. One cannot therefore attribute that property to indol in this case. The doses of B.Coli which these rats received were massive. The bacillus coli may take on pathogenic properties, and may cause summer diarrhoea, infantile diarrhoea, and also be responsible for some food poisonings, (i). Its pathogenicity is also increased in certain diseased conditions of the intestine, specially typhoid fever (i). During an outbreak of diarrhoea last year, at a time when diarrhoea is not usually common, I had a good many stools examined, but in no case could any of the salmonella group of food poisoning bacteria be detected. No case could be traced to infected food, and one strongly suspected the water as a possible source.

Relationship between Endemic Goitre in Derbyshire and Infantile Mortality Rates in Urban and Rural Districts

The infantile mortality rate is the most sensitive index of the health of a community, many of the factors being social, personal and environmental.

(1) Muir & Ritchie. Man: of Bact: 1918. p.358

These are, I believe, factors which closely concern endemic goitre and the charts show that both in the urban and rural districts, where the infantile mortality rate increases, the percentage of goitre increases. To obtain a proper view of the infantile mortality rates, and hence of the factors producing them, it was necessary to take the average infantile mortality rates of a long term of years and I have taken the period from 1891-1921. I took this period for several reasons, one of them being that the latest returns of the number of inhabited dwellings available was the Registrar General's Census Report for the year 1921, and this was necessary for the purpose of calculating the percentage of privy middens and pail closets in the urban and rural areas; for the purpose of comparison I judged it would be better to make 1921 a starting point. Also to get the figures for the latest return of population in the different areas the Registrar General's figures had again to be taken from the last census report of 1921 and this was necessary to obtain the approximate number of people per acre.

Although I have taken the average infantile mortality rates from 1891-1921 - 1891 being the earliest year for which statistics were at my command, and the statistics of goitre refer to the year 1924, and the returns of infantile mortality rates are available up to 1923 and that, in many areas the infantile mortality rates have fallen - they have not

Infantile Mortality Rates per 1000 Births
1891-1921. of Urban and Rural Districts of Derby-
shire compared with the incidence of Goutre
in Girls. †.

<u>U r b a n</u> District	Infantile (i) <u>Mortality Rate</u>	Percent (ii) <u>Goutrous</u>
Alfreton	125	3.2
Alvaston & Boulton	102	-
Ashbourne	93	16.3
Bakewell	88	7.9
Baslow	95	60.0
Belper	131	25.0
Bolsover	141	2.2
Bonsall	70	9.1
Brampton & Walton	105	16.7
Chesterfield (Boro)	159	32.0
Clay Cross	152	3.4
Dronfield	135	33.5
Heage	107	29.6
Heanor	124	39.3*
Ilkeston	158	40.0
Long Eaton	116	17.2
Matlock	84	31.4
Matlock Bath	108	33.3
New Mills	127	8.8
North Darley	88	-
Ripley	113	23.1
South Darley	75	-
Swadlincote	122	4.4
Wirksworth	101	42.4
 <u>R u r a l</u>		
Ashbourne	77	3.8
Bakewell	90	7.2
Basford	123	55.5
Belper	99	33.5
Blackwell	139	7.7
Chapel-en-le-Frith	95	17.0
Chesterfield	132	10.8
Clowne	139	2.7
Glossop Dale	95	-
Hartshorne & Seale	114	9.5
Hayfield	101	42.8
Norton	84	11.8
Repton	99	14.7
Shardlow	101	12.1
Sudbury	70	5.3

* From examination of all children in Elementary Schools.

† Elementary and Secondary School children

(i) Calculated from reports of M.O.H. Derbyshire 1891-1921.
(ii) Report S.M.O., Derbyshire, 1924. Tables F, H. & G.
pp.32-33

Urban Districts

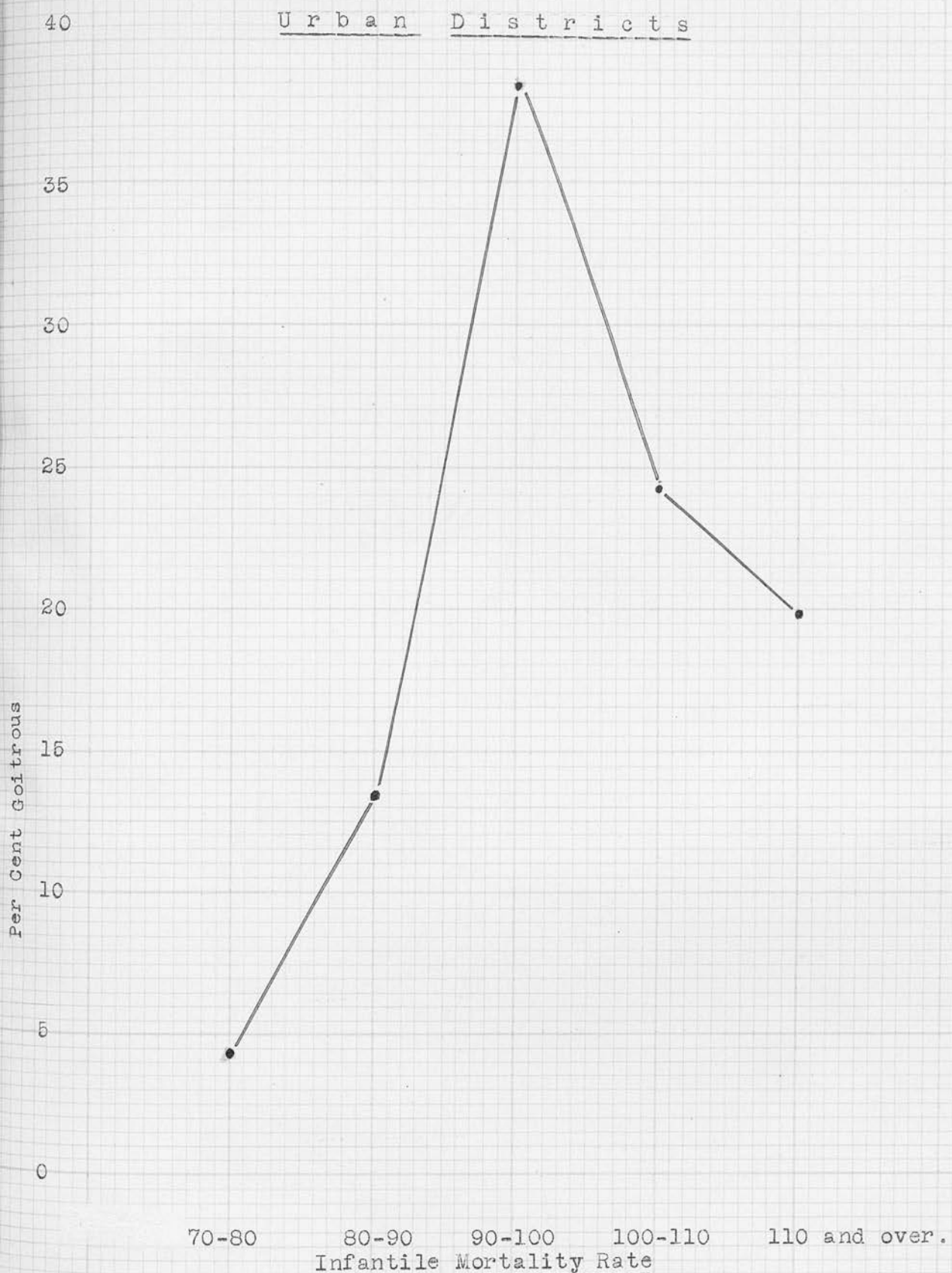
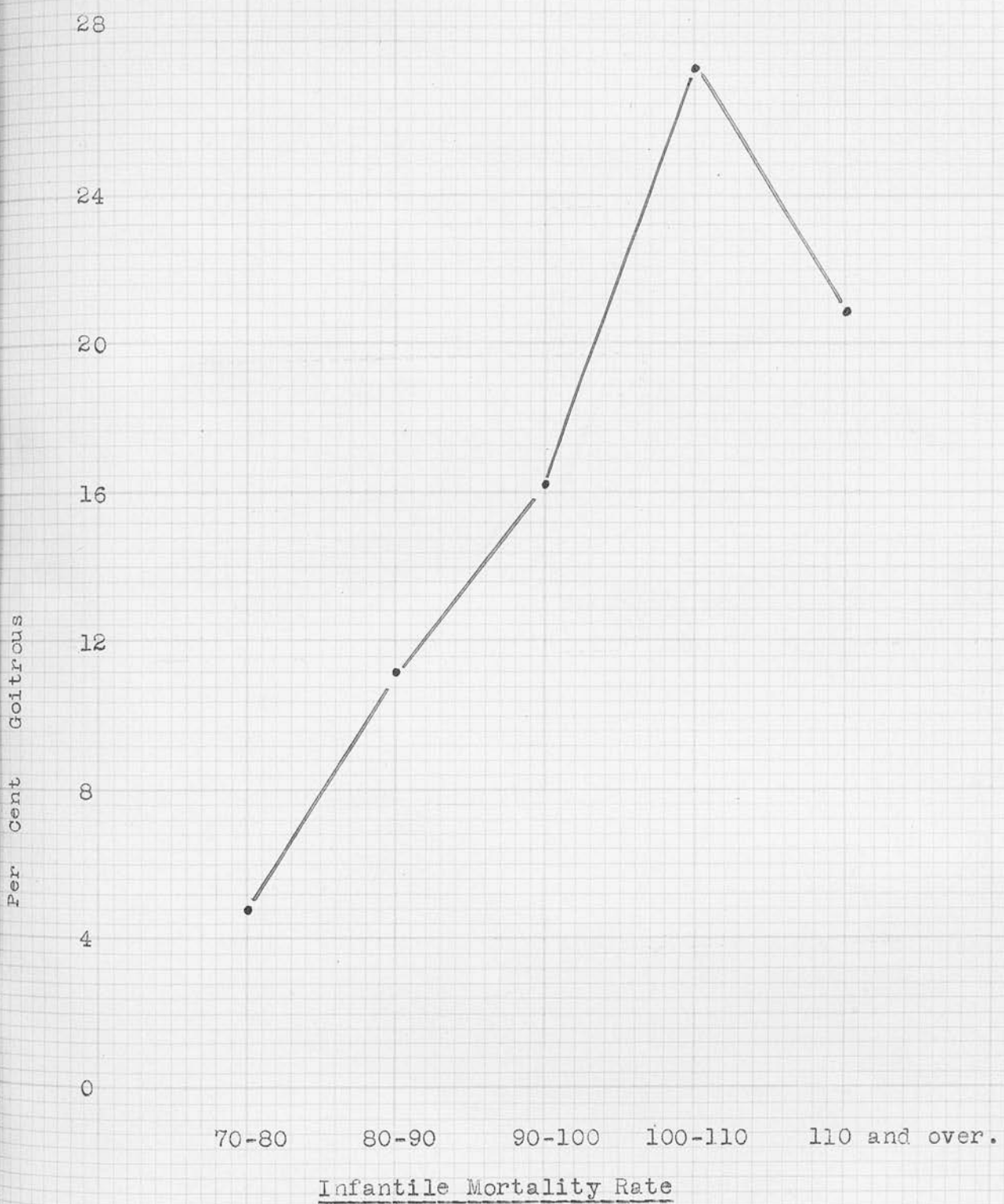


Chart showing the effect of high infantile mortality rates upon the incidence of goitre amongst Derbyshire School Girls in the Urban Districts.

Rural Districts



Infantile Mortality Rate
Chart showing the effect of high infantile mortality rates upon the incidence of goitre amongst Derbyshire School Girls in the Rural Districts.

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invariably done so , there is I think a true comparison. For one must remember that goitre in the county for many years has been decreasing. In its severity it has been decreasing in Heanor, and Dr. Fentem of Bakewell, notes that goitre in Bakewell area is less than in former years. Had the two years 1922 and 1924 been included in the averages, the net result would have been the same, namely, to show an increasing rise in the percentage of goitre where the infantile mortality rate increases.

On looking at the table it will be seen that there is a close association between infantile mortality rates and the high incidence of goitre in a large number of areas. It is not invariably so, and therefore the average percentages of goitre were taken occurring in the groups, as indicated in the charts. The charts show in both urban and rural areas that the higher the infantile mortality rate the greater is the incidence of goitre amongst girls: the conclusion to be drawn from these charts is inevitable and it is, I believe, a confirmation of the view that unhealthy surroundings are closely associated with endemic goitre. Speaking from my personal experience of endemic goitre as it occurs in my own locality, I had long been convinced that to a large extent its prevalence could be laid to the door of unhygienic surroundings, and that goitre in Derbyshire as a whole would show a like relation-

ship. We have all the writings of McCarrison showing that unhealthy in animals at least are very potent factors in the production of the disease and I have elsewhere quoted Dr. Watt when writing of the influence of bad social conditions favouring the development of the disease in Wirksworth.

Influence of the Prevalence of Privy Middens and Pail Closets in the Urban and Rural Areas of Derbyshire upon the Incidence of Goitre

If a large incidence of these objects has a relation to the infantile mortality rate, and a high infantile mortality rate is associated with a high incidence of goitre, then a high percentage of dwellings in urban and rural areas with privies and pail closets should bear some relationship to a high incidence of goitre. That this is so is seen from the charts showing the average in groups. Where the percentage of dwellings with these appliances is between 30-50 % the incidence of goitre is highest, both in the urban and rural areas and in both cases drops though not to a lower level than in the group, (0.30%) when that percentage is 60 or over.

It must be remembered that the prevalence of privy middens and pail closets is not the sole factor in the production of infantile mortality rate, and thus the relationship between the endemicity of goitre and the prevalence of pail closets and privy middens is not a constant factor.

Tables of Percentage of Separate Dwellings in
The Urban and Rural Districts of Derbyshire having
Privy Middens and Pail Closets with the Percent-
age of Goitre in Girls. †

<u>U r b a n</u>	<u>District</u>	<u>Percent Houses (i)</u> <u>Privies & Pails.</u>	<u>Percent</u> <u>Goitrous</u>
	Alfreton	68.2	3.2
	Alvaston & Boulton	21.0	-
	Ashbourne	1.91	16.3
	Bakewell	36.6	7.9
	Baslow	68.7	60.0
	Belper	26.7	22.1
	Bolsover	72.2	2.2
	Bonsall	96.6	9.1
	Brampton & Walton	99.6	16.7
	Chesterfield (Boro)	8.0	32.0
	Clay Cross	60.5	3.4
	Dronfield	52.6	33.3
	Heage	Not known *	29.6
	Heanor	70.6	36.6 ‡
	Ilkeston (Boro)	34.4	40.0
	Long Eaton	2.3	17.2
	Matlock	Not known *	31.4
	Matlock Bath	15.0	33.3
	New Mills	10.8	8.8
	North Darley	Not known *	-
	Ripley	67.8	23.1
	South Darley	100.0	-
	Swadlincote	45.2	4.4
	Wirksworth	44.1	42.4
 <u>R u r a l</u>			
	Ashbourne	88.8	3.8
	Bakewell	75.0	7.2
	Basford	Not known *	35.5
	Belper	50.0	33.5
	Blackwell	53.3	7.7
	Chapel-en-le-Frith	57.7	17.0
	Chesterfield	74.0	10.8
	Clowne	92.0	2.7
	Glossop Dale	87.0	-
	Hartshorn & Seals	11.5	9.5
	Hayfield	100.0	42.8
	Norton	48.4	11.8
	Repton	93.0	12.5
	Shardlow	57.6	12.1
	Sudbury	100.0	5.3

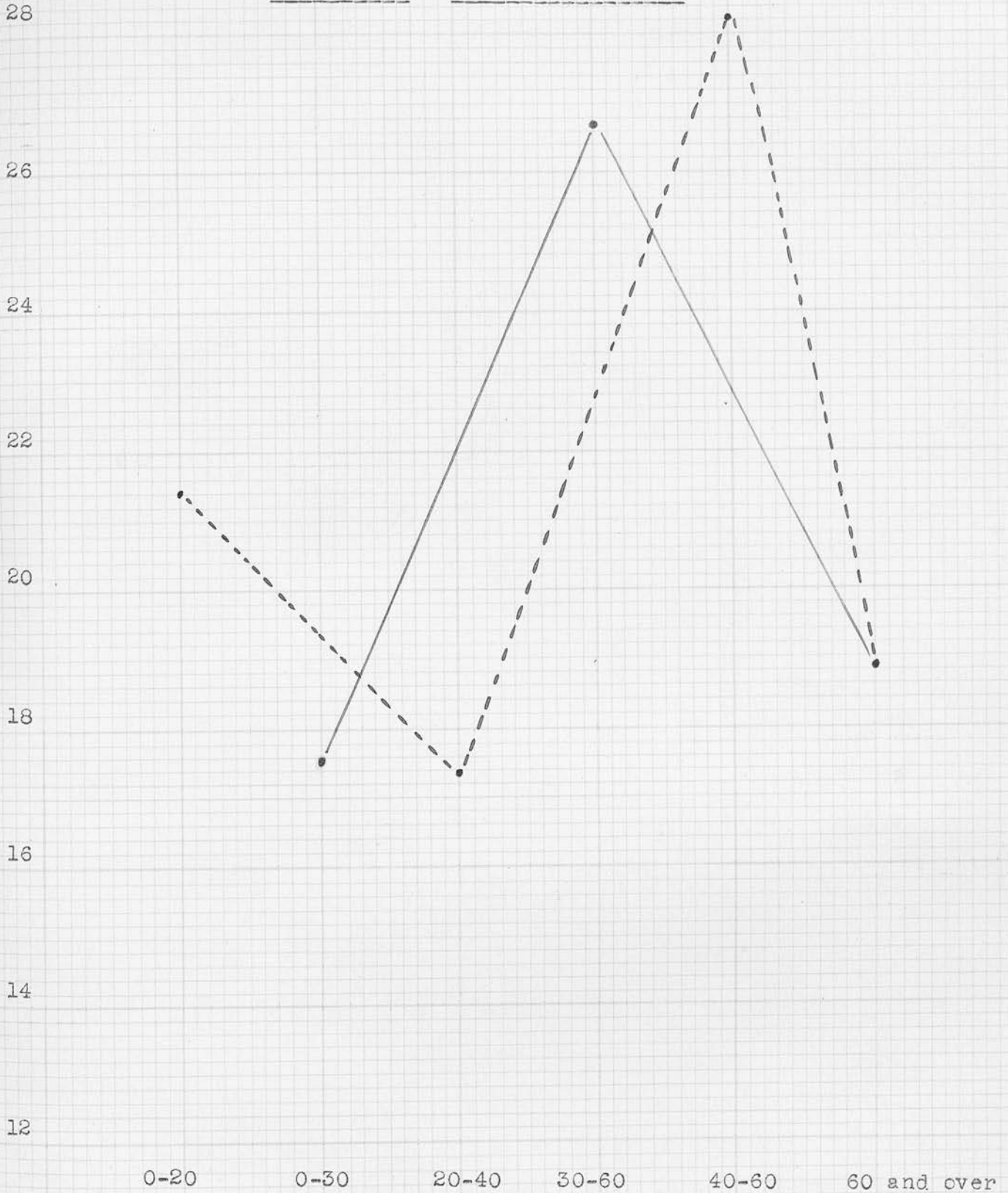
* Although the percentage of privies and pail closets are not known definitely the percentage is considerable in these areas.

† Elementary and Secondary School Children.

‡ Includes all school children examined.

(i) Calculated from M.O.H. Reports on Health of Derbyshire giving latest information re number of Privies, etc.

Urban Districts

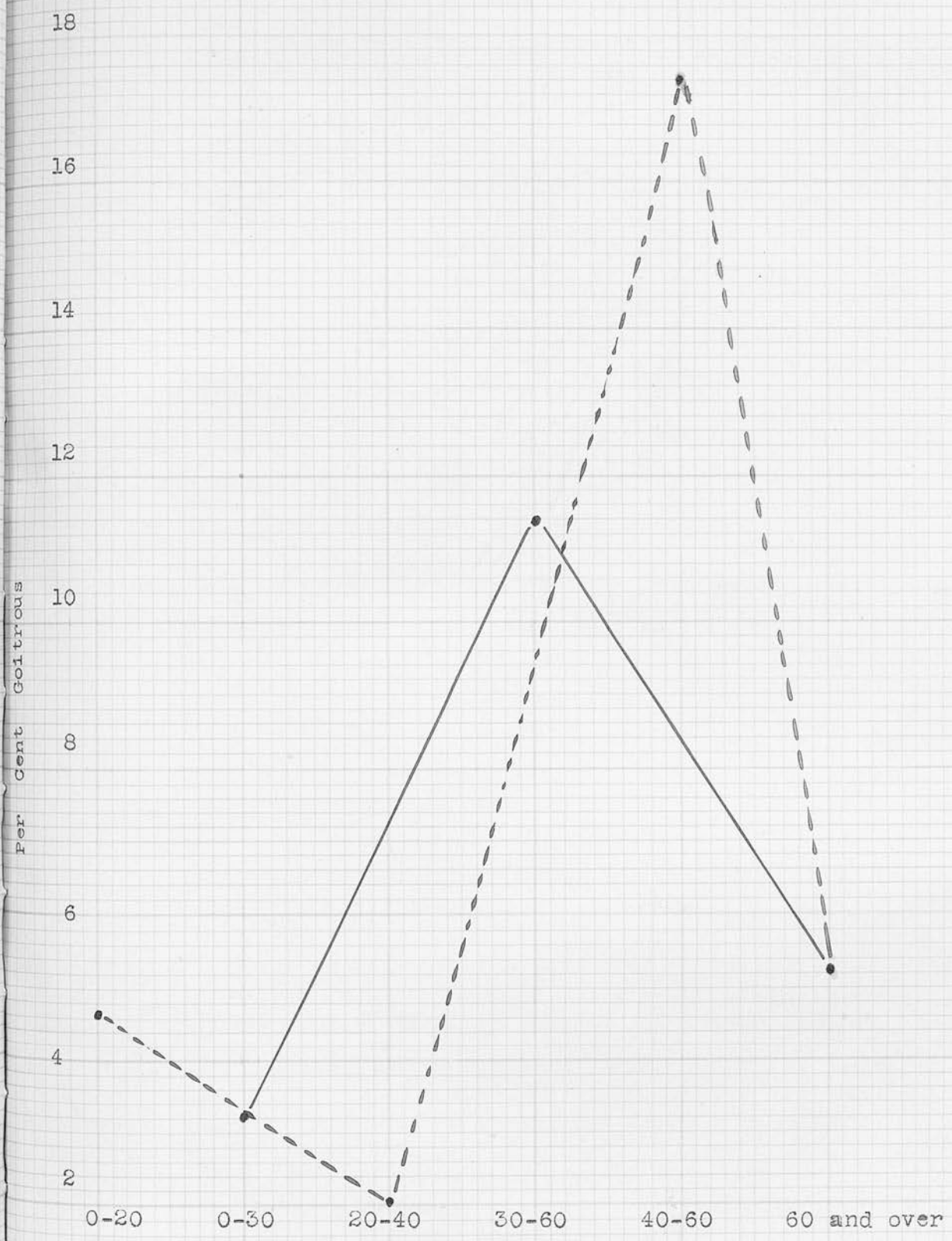


Per Cent Houses with Privies and Pails

Chart showing the effect of increase in percentage of houses with privy middens and pail closets upon the incidence of goitre in School Girls in the Urban Districts of Derbyshire.

Continued line Ages in groups 0-30 etc.
 Dotted line " " 0-20 etc.

Rural Districts



Per Cent Houses with Privies and Pail Closets

Chart showing effect of increase of percentage of houses with privy middens and pail closets upon incidence of goitre in School Children in rural districts of Derbyshire.

Continued line %ages in groups 0-30 etc.
Dotted line " " " " 0-20 etc.

The Influence of Increase of Population
Per Acre in Urban and Rural Areas upon the Incidence
of Goitre.

This is seen at its best in urban districts, for the analysis of the table shows that the increase in the percentage of goitre is progressive when there is increase of persons per acre. In the case of the rural districts the results are not so uniform. I think the reason for this is, that in calculating the number of people per acre in urban districts the area of the district bears a closer relation to the actual inhabited area than is the case with the rural districts, which are sparsely populated and the actual inhabited area in the case of the rural districts bears a much less relationship to the total area than obtains in the urban areas. Moreover, overcrowding of houses is not so prevalent in rural areas, there is more elbow room so to speak, there is not so much crowding together of houses or of crowding together in the houses. This reflects itself in the average of percentages of goitre in urban and rural areas. On the whole goitre does not seem so prevalent in rural areas as in urban areas.

Table of the Number of People Per Acre
In the Urban and Rural Districts of Derbyshire and
And the Percentage of Goitrous Girls.

<u>U r b a n</u>	<u>District.</u>	<u>No. of People per Acre (I)</u>	<u>Percent Goitrous (ii)</u>
	Alfreton	4.2	3.2
	Alvaston & Boulton	1.2	-
	Ashbourne	7.2	16.3
	Bakewell	.96	7.9

(i) Calculated from information given in M.O.H. Reports on Health of Derbyshire. for last Census Return.

(ii) Vide Supra.

U r b a n (contd)

<u>District</u>	<u>No. of People Per Acre.</u>	<u>Percent Goitrous</u>
Baslow & Bubnell	.14	60.0
Belper	3.7	25.0
Bolsover	2.3	2.2
Bonsall	.5	9.1
Brampton & Walton	2.3	16.7
Chesterfield	23.6	32.0
Clay Cross	6.2	3.4
Dronfield	4.2	33.3
Heage	Not known	29.6
Heanor	6.2	39.3
Ilkeston	13.0	40.0
Long Eaton	9.7	17.2
Matlock	4.0	31.4
Matlock Bath	5.0	33.3
New Mills	1.6	8.8
North Darley	.6	-
Ripley	4.7	23.1
South Darley	.3	-
Swadlincote	5.6	4.4
Wirksworth	1.1	42.4

R u r a l

Ashbourne	.14	3.8
Bakewell	.23	7.2
Basford	.42	55.5
Belper	.46	33.5
Blackwell	1.9	7.7
Chapel-en-le-Frith	.21	17.0
Chesterfield	1.1	10.8
Clowne	1.3	2.7
Glossop Dale	.21	-
Hartshorn & Seale	.75	9.5
Mayfield	.42	42.8
Norton	.54	11.8
Repton	.28	14.7
Shardlow	.75	12.1
Sudbury	.14	5.3

The analysis of the figures in the foregoing tables show that in the urban area goitre is more prevalent in those areas where the number of people per acre is largest and the increase is progressive as the number of people increases, thus :-

<u>U r b a n</u>	<u>No of People per acre</u>	<u>Percent Goitrous Girls</u>
	0-3	13.95
	4-6	18.61
	6 and over	22.45

R u r a l

<u>No. of People per acre</u>	<u>Percent Goitrous Girls</u>
0 - 0.3	13.95
0.3 - 0.6	18.6
0.6 - and over	3.5

Relation of Goitre to Infectious
Diseases and Infections

We have seen that goitre often bears a relationship to typhoid fever, that in Canada Shepherd concluded that goitre in that country, in its distribution, closely followed that disease, and that in Heanor the endemic goitre was severe when typhoid was also endemic. Has goitre any relation to other infectious diseases? Macnamara (i), states "Coates repeats the remark of an intelligent native gentleman who told him that he remembered the time when the whole of the locality where he lived was jungle but now, he said, "everybody cultivates, there is no jungle water to drink and goitres, fevers and spleens are much fewer than formerly."

Hume (ii), recorded thirty cases of marked enlargement of the thyroid gland *in malaria*. McKenzie (iii), was of the opinion that many points presented by goitre suggested that the cause might be one of the Protozoan Group and closely associated with malaria, but his observation did not confirm those of Granett of Montpellier, who stated that he

- (i) Macnamara, F.N. Climate & Med: Topography in their relation to the Disease Distribution of Himalayan India 1880 p.248
(ii) Quoted by Hercus, C.E. & Baker. U.S. N.Z. Med. Jnl. 1923 pp.79-89
(iii) McKenzie, D. Glasgow Med: Jnl. 1899.ii. pp.15-24

had found a parasite similar to that discovered by Laveran in malaria.

Nicholson (i), in a paper on the effect of Typhoid Inoculation on Endemic Goitre at the Lawrence Military Asylum, Sanawar, Punjab, concluded that typhoid inoculation, neither individually nor collectively, had any effect in any way on the course of endemic goitre. The vaccine used was that ordinarily used in the Army in India. Reductions were obtained but none such as would not have taken place in the ordinary course of affairs.

Macnamara (ii), states in comparing goitre to splenic conditions, "a point of likeness in the pathological history of the glands which has been asserted, and it is one which has a special interest in the present enquiry, is that diseases of either one or the other are associated with that peculiar condition of the blood to which leucocythaemia is given", and again the same author remarks on the relation of malaria to goitre, (p.45), that it was a common experience to meet with cases of enlarged spleen due to malaria associated with enlargement of the thyroid. and the fact that many animals such as goats, cows, dogs, etc., suffer from goitre afforded another consideration in favour of the opinion that the disease was malarious in origin.

Indian Med. Gazette, 1924, Vol 59, pp 289-292

(i) Nicholson, M.A. ~~Lancet. ii. pp.275-277.~~
(ii) Macnamara, F.N. Ibid p.43

Macnamara (i), found that goitre prevailed along the banks of marshy rivers of which the Secrana and the Dunnowtee are examples. In these districts he states that two-thirds of the inhabitants are goitrous and "while malarious diseases prevail throughout the district, they do so with the greatest violence in this area, (Cullen)."

Remarks on the Treatment of Goitre.

It will be seen that in many cases considerable reduction in the size of goitres may be obtained from the use of vaccines. One of the first results is frequently a softening of the goitre. The vaccines I used were prepared from the faeces of cases of goitre and also from the organisms isolated from the Heanor and Ilkeston water supply. The best results were obtained when a severe reaction occurred and it was this reaction to which many patients objected. It was only with difficulty that one could persuade them to submit to the procedure at all and some discontinued attendance and I was unable to obtain photographs of the final results. Many refused to be allowed to be photographed at all. But sufficient cases are illustrated to show both results and the type of goitre prevailing. I have been able to get results in cases of considerable duration - in others none where the duration has been much less.

(i) Ibid. p. 248

The vaccine treatment does not displace other methods of treatment, ^{and} of these the most certain is iodine therapy. When Tr.Iodi.Mitis was given in cases one started with m.v. or m.x. t.i.d. and working up to m.x.v. or m.x.x. t. i. d. in many cases, well diluted with water. Rarely have I seen any untoward result from such large doses. Thymol and salol were administered in cachets. When thymol was given, all fats and solvents of fats were rigidly excluded from the diet. My experience shows that both of these drugs are of value in the treatment of goitre.

It has been my experience that a large proportion of goitrous cases have been habitually constipated and, where this has been present, saline cathartics two or three times weekly have been recommended. All my cases have been extern cases and their diets and habits uncontrolled and not modified in any way, except where thymol has been given. It has been my practice to advise patients to drink boiled water only for obvious reasons. I doubt whether this has always been done, as it involves a little trouble. There is amongst the inhabitants a great apathy towards the disease and little regard for its serious consequences to health and comfort, and in too many cases one's efforts for the alleviation of their condition have been received with a discouraging indifference, even when the means employed have been of the simplest and easiest

from the view point of the patient. Indeed, goitre is regarded by many as a mark of distinction - as an acquisition for pride.

Besides thymol, salol, iodine, etc., others have used a variety of drugs with success in the treatment of goitre. Robinson (i), mentions that Corley of Dublin, treated cases of goitre successfully with quinine, 10 grains t.i.d. for six weeks, and the same author cites Woakes as having treated twenty cases of goitre with a .5% solution of fluoric acid, commencing with a dose of thirty drops and increasing up to two drachms if well tolerated. Of these twenty cases so treated, seventeen recovered and three were not benefited. The duration of treatment varied from one month to two years, in the majority of cases the duration being from three to nine months. The treatment of goitre with an ointment of biniodide of mercury has found much favour in India - The method as used by Major Holmes, I quote from Macnamara (ii), - Major Holmes treated several thousands of cases with an ointment of mercuric biniodide, 9 drachms of the biniodide to 3lbs of lard. "About an hour after sunrise apply the ointment to the goitre with a spatula made of wood or ivory; rub it well in for at least ten minutes. Let the patient then sit with his goitre held well up to the sun and let him remain so long as he can endure it.

(i) Endemic Goitre. 1885. p.53.
(ii) Climate & Medical Topography in their relation to the Disease Distribution of Himalayan India. London. 1880. pp.249-250.

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It is probable that about noon he will suffer severe pain from the blistering effect of the ointment. About 2 p.m. the ointment should be again applied with a very careful and tender hand and the patient should be despatched to his home with orders not on any account to touch the ointment with the hand but to allow it to be gradually absorbed, which absorption will be complete on the second day. This treatment is quite sufficient for an ordinary case. Should the case be a very bad one the patient is ordered to return next year for the removal of what remains of the tumour but, unless in goitre of the very largest size, this is seldom necessary."

During 1854 - 1855 upwards of 20,000 cases of goitre were treated in this manner in India.

Whilst there is no doubt of the efficiency of iodine in suitable doses and administered over a proper interval of time, in the treatment of cases of parenchymatous goitre the intestinal antiseptics such as thymol and salol, and the successful application of vaccines have their place and undoubtedly indicate that the etiology of goitre is not bound up solely with the question of the lack of iodine in food and drink.

Description of Cases Treated

Case 1. S.J.W. First observed on 7.7.22. Complained of enlargement of thyroid, palpitation and dyspnoea. Rheumatic fever in childhood. Periodic attacks of angina referred in pre-cordial region and

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Case 1 (Contd) - in neck. Thyroid - Enlargement noticed for considerable time prior to date of first observation. Tumour pulsatile; no murmur; some exophthalmos and tremor. No loss of weight. She was given thyroidectin for some considerable time with no benefit. Digitalis and belladonna gave temporary relief. On 7.5.24 the faeces was examined and found to contain the enterococcus in abundance.

<u>Date</u>	<u>Neck Measurements</u>		<u>Treatment</u>
12.5.24.	A. $14\frac{3}{4}$ "	B. 14"	Kerol m.iii.b.i.d.
19.5.24.	"	"	" "
26.5.24.	"	"	Enterococci 100,000,000
2.6.24.	A. 14"	B. $13\frac{1}{2}$ "	-do- 150,000,000
9.6.24.	A. $13\frac{3}{4}$ "	B. 13"	B. Coli. 300,000,000
16.6.24.	"	"	-do- 500,000,000
24.6.24.	"	"	-do- 800,000,000
7.7.24.	A. $13\frac{1}{2}$ "	"	-do- -do-
15.7.24.	"	"	-do- -do-
1.8.24.	A. $13\frac{1}{4}$ "	"	K. l. grs.vii. t.i.d.
20.8.24.	"	"	(B. Coli 1200,000,000
			(K. l. grs.vii. t.i.d.
27.8.24.	"	"	K. l. grs x. t.i.d.
			(B. Coli. - 2000,000,000

She was also given salol, grs.x. bis in die from 9th June 1924 for a month K. l. was given for the anginal pains which were greatly relieved by it. No reduction in the thyroid took place under K. l. and the Wasserman reaction was negative. Her heart was very bad and she suffered from both aortic and mitral regurgitation. I have seen her recently, (7.7.25). There is no return of goitre; the pulse rate is 80, tremor has gone and she is back at work. Angina is her present trouble which she keeps under control with amyl nitris. This case was not a case of exophthalmic goitre, but a case of parenchymatous goitre with toxic symptoms and treatment centred on removing her alimentary toxæmia alone brought about the resolution of her goitre and the toxic symptoms.

Case 2. E.N.P. aet 42. An Iron Moulder by trade. Large parenchymatous goitre of both lobes, greatest on right side. Swelling uniform but some fibrosis present and small adenomata. Duration 15 years, with greater increase in recent years. Wife, one brother and two sisters are goitrous. Mother also had goitre.

<u>Date</u>	<u>Neck Measurements</u>		<u>Treatment</u>
20.5.24	A. 16"	B. $15\frac{1}{4}$ "	Thymol grs.x. b.i.d.
27.5.24	A. $15\frac{1}{2}$ "	B. "	-do- -do-
3.6.24	A. 15"	B. $14\frac{3}{4}$ "	-do- -do-
9.6.24.	"	B. $14\frac{1}{2}$ "	-do- -do-

Case 2. (Contd)

Date	Neck Measurements		Treatment
17.6.24.	A.15"	B.14 $\frac{1}{2}$ "	Thymol grs.x. b.i.d.
24.6.24.	A.14 $\frac{3}{4}$ "	B. "	-do- -do-
9.7.24.	A. "	B. "	-do- -do-
12.8.24.	A.14 $\frac{1}{2}$ "	B.14 $\frac{1}{4}$ "	-do- -do-
16.9.24.	A.14 $\frac{1}{2}$ "	B.14 $\frac{1}{4}$ "	-do- -do-
1.10.24.	A. "	B. "	-do- -do-

After this date he was given salol, grs.x. bis in die and ungu. hydrarg Iodid. Rub. to rub on the neck night and morning, until 25th November 1924, when the neck measurements were A. 14" B. 13 $\frac{3}{4}$ ".

Case 3. William C. aet 34. Coal Miner. Duration not known, some years. Pressure symptoms severe on exertion with husky voice.

Date	Neck Measurements	Treatment
3.3.25	17"	Ext:Thyroid grs.v.t.i.d.
11.3.25.	"	-do- -do-
17.3.25.	"	Ext:Thyroid sicc: grs.ii. t.i.d.
31.3.25.	"	-do- Thymol.grs.x. b.i.d.
10.4.25.	16 $\frac{3}{4}$ "	-do- -do-
21.4.25	"	-do- -do-
5.5.25.	16 $\frac{1}{2}$ "	-do- -do-
26.5.25	16 $\frac{1}{4}$ "	-do- -do-
18.6.25.	16"	-do- -do-
29.6.25.	16"	Tr:Iodi:m.vii. t.i.d.
20.7.25.	16"	-do- m.x. t.i.d.

The second photograph was taken in 29th June 1925. He is greatly relieved of his dyspnoea, can wear collars one inch smaller than formerly, and these fit looser than the larger collars did. He has now left this district and resides in Nottingham. The goitre has not disappeared but it is visibly improved.

Case 4. Mrs. W. aet 47. Always been a very thin person. Poor social conditions. Two daughters both have goitres. First seen on 6.8.24. weight 8st.4lbs. Goitre has been present for three years and has been small but increased the last three months. Exophthalmos is present and also tremor. (the blurrings of the photograph is due to tremor). Pulse rapid. The goitre, it will be seen, is chiefly on the right side but the lobe is involved as well. As in Case 1, this is a case not of true exophthalmic goitre but one of parenchymatous goitre associated with toxic symptoms. The nodule left is an adenoma. There was present in this case a very bad old standing pyorrhoea which I had cleaned up.

Case 4. (Contd)

Date	Neck Measurements	Treatment
6.8.24.	13 $\frac{1}{4}$ "	B.Coli. 100,000,000
12.8.24.	"	-do- 150,000,000
21.8.24.	13"	-do- 400,000,000
28.8.24.	12 $\frac{3}{4}$ "	-do- 600,000,000
5.9.24.	"	-do- 800,000,000

The photographs illustrate well the change in the goitre. Her general condition improved. The pulse rate came down to within normal limits and she was able to resume her housework.

Case 5. M.W. aet 21. Parenchymatous goitre: duration three years and steadily progressing.

Date	Neck Measurements.	Treatment
29.5.24.	A. 14 $\frac{3}{4}$ " B. 13 $\frac{3}{4}$ "	B.Coli. 150,000,000
6.6.24.	A. " B. "	-do- 300,000,000
12.6.24.	A. " B. "	-do- 600,000,000
20.6.24.	A. 14 $\frac{1}{2}$ " B. "	-do- 1000,000,000
25.6.24.	A. " B. "	Tr.Iodi. m.x. t.i.d.
9.7.24.	A. " B. "	-do- -do-
17.7.24.	A. 14 $\frac{1}{4}$ " B. 13 $\frac{1}{4}$ "	-do- -do-
7.8.24.	A. 14 $\frac{1}{4}$ " B. 13 $\frac{1}{4}$ "	Ext.Thyr: grs.v. b.i.d.
18.8.24.	A. " B. "	-do- -do-
26.8.24.	A. " B. "	-do- -do-
25.9.24.	A. " B. "	-do- -do-
2.10.24.	A. " B. "	Na.l. grs.x. t.i.d.
14.10.24.	A. " B. "	-do- -do-
28.10.24.	A. " B. 13 $\frac{1}{8}$ "	-do- grs.xx. t.i.d.
12.11.24.	A. 14" B. "	-do- -do-
9.12.24.	A. 13 $\frac{1}{2}$ " B. 12 $\frac{3}{4}$ "	-do- -do-
1.1.25.	A. " B. "	-do- -do-

She was habitually constipated and for this, during the duration of the treatment she took bi-weekly doses of saline cathartics. At the end of treatment she developed some symptoms of hyperthyroidism and lost weight, and the photographs show this as well as the changed appearance. The hyperthyroidism was probably that form known as Basedow-Iodism, which comes on when adenoparenchymatous goitres are given large doses of iodine. The effect of vaccine alone at the commencement was noticeable and, as events showed, this case was stubborn to other methods as well.

Case 6. Hannah P. aet 18. Hosiery Hand. Both lobes and isthmus enlarged. Duration not known.

Date	Neck Measurements	Treatment
29.8.24.	A. 15 $\frac{1}{4}$ " B. 15"	Salol grs.x. t.i.d.
12.9.24.	A. " B. 14 $\frac{3}{4}$ "	-do- -do-
22.9.24.	A. 14 $\frac{3}{4}$ " B. 14 $\frac{5}{8}$ "	-do- -do-
10.10.24.	A. " B. 14 $\frac{1}{4}$ "	Thymol.grs.x. b.i.d.
17.10.24.	A. 14 $\frac{3}{8}$ " B. 14"	-do- -do-

Case 6. (Contd)

<u>Date</u>	<u>Neck Measurements</u>		<u>Treatment</u>
24.10.24.	A. 14"	B. 13 $\frac{1}{2}$ "	Thymol. grs.x.b.i.d.
14.11.24.	A. "	B. "	-do- -do-
21.11.24.	A. "	B. "	Syr.Fr.Iod. t.d.s.
2.12.24.	A. 14 $\frac{3}{4}$ "	B. 14 $\frac{1}{4}$ "	Tr.Iodi.m.v. t.i.d.
9.12.24.	A. "	B. "	-do- -do-
24.12.24.	A. "	B. "	Tr.Iodi.m.x. K.I. gr.v. t.i.d.
13.1.25.	A. "	B. "	Ext:Thyr: grs.v.b.i.d.
22.1.25.	A. 14 $\frac{1}{2}$ "	B. 13 $\frac{3}{4}$ "	-do- -do-
3.2.25.	A. 14 $\frac{1}{4}$ "	B. "	-do- -do-
25.2.25.	A. 14 $\frac{3}{8}$ "	B. 14"	Sod.Sal:grs.x.t.i.d.
11.3.25.	A. 14 $\frac{5}{8}$ "	B. 13 $\frac{1}{2}$ "	-do- -do-
30.3.25.	A. 14 $\frac{3}{8}$ "	B. 13 $\frac{1}{4}$ "	-do- -do-

Here exacerbations took place during the course of treatment, on 21st November 1924 after she had been taking Syr.Fr.Iodid. An increase in size took place. It could not be accounted for by menstruation and measurements were taken over the same places each time. As in other cases marks were made on the neck, back and front, with a silver nitrate pencil. Another increase took place on 25th February 1925 while she was under thyroid extract and this subsequently disappeared with sod.salicylate.

Case 7. Ethel P. Sister of Case 6. aet 15.
Hosiery Hand. Duration not know.

<u>Date</u>	<u>Neck Measurements</u>		<u>Treatment</u>
28.8.24	A. 14"	B. 13 $\frac{1}{4}$ "	Salol grs. x. 5.i.d.
17.9.24	A. 13 $\frac{3}{4}$ "	B. 12 $\frac{7}{8}$ "	-do- -do-
24.9.24	A. "	B. 12 $\frac{5}{8}$ "	-do- -do-
7.10.24	A. "	B. "	Thymol grs.x. b.i.d.
14.11.24	A. 13 $\frac{1}{2}$ "	B. 12 $\frac{1}{2}$ "	-do- -do-
5.12.24	A. 13 $\frac{1}{4}$ "	B. 12 $\frac{3}{8}$ "	-do- -do-
23.12.24	A. 13 $\frac{1}{2}$ "	B. "	-do- -do-
31.12.24	A. 13 $\frac{1}{4}$ "	B. "	-do- -do-
9.1.25	A. "	B. 12 $\frac{1}{4}$ "	Thyr.Ext.grs v. b.i.d.
16.1.25	A. "	B. "	-do- -do-
23.1.25	A. "	B. "	-do- -do-
3.2.25	A. 13"	B. 12 $\frac{1}{4}$ "	-do- -do-
17.4.25	A. "	B. "	-do- -do-

This case is illustrated.

Case 8. Mille B. aet 15. Poor social conditions. One sister also goitrous. Duration five years, gradually becoming worse.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
16.6.24	A. 14 ⁵ / ₈ "	B.Coli.150,000,000
22.6.24	A. "	-do- -do-
7.7.24	A. 14"	-do- 300,000,000
14.7.24	A. " B.13 ³ / ₈ "	-do- 600,000,000
21.7.24	A. " B.13"	-do- 200,000,000
28.7.24	A. " B. "	Tr.Iodi.m.x. t.i.d.
11.8.24	A. " B. "	Salol.grs.x. b.i.d.
18.8.24	A. 13 ³ / ₄ "B."	-do- -do-
26.8.24	A.13 ¹ / ₂ "B.12 ³ / ₄ "	-do- -do-
12.9.24	A. " B. "	B.Coli.400,000,000
19.9.24	A.13 ³ / ₈ "B. "	B.Coli.800,000,000
26.9.24	A.13 ³ / ₈ "B.12 ³ / ₄ "	(Salol.grs.x. b.i.d.) B.Coli.1000,000,000
6.10.24	A. " B. "	(Salol.grs.x. b.i.d.) Tr.Iodi.m.v. t.i.d.
13.10.24	A. " B. "	-do- -do-
27.10.24	A. " B. "	-do- -do-
3.11.24	A. " B. "	-do- m.x. t.i.d.
29.11.24	A.13" B.12 ¹ / ₂ "	-do- -do-
20.1.25	A.13" B.12 ¹ / ₂ "	-do- -do-
3.2.25	A. " B. "	-do- -do-

(for a month)

Case 9. Mary A. set 16. Hosiery Hand. Small uniform parenchymatous goitre. Poor social conditions. Enterococci in faeces.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
13.5.24	A. 14" B. 13 ¹ / ₂ "	Enterococci 250,000,000
19.5.24	A. 13 ¹ / ₂ " B. 13"	Kerol. m.iii. b.i.d.
26.5.24	A. " B. "	Enterococci 500,000,000
2.6.24	A. " B. "	(Kerol.rep.) Kerol.m.ii. b.i.d.
9.6.24	A. 13" B. 12 ⁵ / ₈ "	(Enterococci 500,000,000) -do- -do-
16.6.24	A. 12 ³ / ₄ " B. "	(Salol. grs.xv.b.i.d.) -do- -do-
22.6.24	A. " B. "	-do- -do-
30.6.24	A. " B. "	-do- -do-
7.7.24	A. " B. "	Tr.Iodi.m.xv. t.i.d.
21.7.24	A. " B. "	-do- -do-

Case 10. Isabella W. aet 17. Duration not known. Steadily increasing in size. Enterococci in faeces. Constipation.

Case 10. (Contd)

Date	Neck Measurements		Treatment
30.4.24	A.15 $\frac{1}{4}$ "	B.14"	Enterococci 12,500,000
7.5.24	A. "	B. "	-do- 50,000,000
12.5.24	A. "	B. "	-do- 250,000,000
16.5.24	A. "	B. "	-do- 375,000,000
19.5.24	A.15"	B.14"	-do- 500,000,000
26.5.24	A.14 $\frac{3}{4}$ "	B.14"	-do- -do-
2.6.24	A.14 $\frac{1}{2}$ "	B. "	-do- -do-
10.6.24	A. "	B.13 $\frac{1}{2}$ "	-do- -do-
16.6.24	A. "	B. "	Tr.Iodi.m.x. t.i.d.
7.7.24	A. "	B.13 $\frac{1}{4}$ "	-do-m.xv. t.i.d.
21.7.24	A. "	B. "	-do- -do-
12.8.24	A. "	B.13 $\frac{1}{4}$ "	-do- -do-
12.9.24	A.13 $\frac{3}{4}$ "	B.13 $\frac{1}{4}$ "	-do- -do-

Case 11. Ernest P. aet 19. Small uniform parenchymatous goitre; right lobe chiefly. Duration said to be 5 years. Complained of some dyspnoea. Faeces contained the enterococcus. One sister has a goitre and an infant born in the house had a congenital goitre.

Date	Neck Measurements	Treatment
30.4.24	15 $\frac{1}{2}$ "	Enterococci 12,500,000
7.5.24	"	-do- 50,000,000
12.5.24	"	-do- 250,000,000
16.5.24	"	-do- 375,000,000
22.5.24	"	-do- 168,000,000
28.5.24	15"	-do- 400,000,000
4.6.24	14 $\frac{3}{4}$ "	Salol.grs.x. b.i.d.

Salol. continued for a month. No further reduction took place.

Case 12. Sidney A. aet 13. Soft parenchymatous goitre. Duration two years, increasing in size. The photographs are taken before and after vaccine treatment.

Date	Neck Measurements		Treatment
22.5.24	A.14"	B. 13 $\frac{1}{2}$ "	B.Coli.100,000,000
26.5.24	A.13 $\frac{1}{2}$ "	B. 13 $\frac{1}{4}$ "	-do- -do-
29.5.24	A.13 $\frac{1}{4}$ "	B. 13"	-do-250,000,000
5.6.24	A.13"	B. 12 $\frac{3}{4}$ "	-do-400,000,000
12.6.24	A.12 $\frac{1}{2}$ "	B. 12"	-do-1000,000,000
19.6.24	A.12 $\frac{1}{2}$ "	B. 12"	-do- -do-
23.6.24	A.12 $\frac{1}{2}$ "	B. 12"	-do-1600,000,000

After the 23rd June 1924, he was given Tr.Iodi.m.x. t.i.d. but on account of gastric irritation this had to be discarded after two days. The only case with gastric irritation with iodine I have met with. Ung.Iodi.Denigrescens was substituted and some im-

Case 12. (Contd)

provement took place with persistent use.

Case 13. Mary T. aet 58. Huge irregular goitre. Isthmus cystic. Both lobes also adenomatous. Swelling is hard but movable, the right lobe has enlarged recently. States that it is usually larger in summer than in winter. Duration twenty years. The recent enlargement of the right lobe she attributed to a recent attack of influenza.

Date	Neck Measurements.	Treatment
15.5.24	19 $\frac{1}{2}$ "	Thymol. grs.x. b.i.d.
22.5.24	19"	-do- -do-
29.5.24	18 $\frac{1}{2}$ "	-do- -do-
3.6.24	18 $\frac{1}{2}$ "	-do- -do-
12.6.24	18 $\frac{1}{4}$ "	-do- grs.x. b.i.d. and Tr.Iodi. grs.m.x.t.d.s.
19.6.24	18"	-do- -do- -do-

She continued with Thymol and Tr.Iodi. as above, until the 7th July 1924, when the neck measurement was 17 $\frac{3}{4}$ ", but had to discontinue the iodine on account of the development of symptoms of "Basedow-Iodism" with a very rapid pulse. This lasted some considerable time. The reduction took place in practically the right lobe alone, i.e. the growth of recent origin. The use of iodine in cases where there is adenomatous degeneration is not to be recommended.

Case 14 Jane M. aet 35. Smalley. Duration not known. This case showed some improvement under Salol. grs.x. b.i.d. alone, but died from tetanus following an operation before treatment had been completed.

Case 15 Margaret P. aet 16. Both lobes and isthmus affected. Dyspnoea severe. Stertorous breathing. Duration two years.

Date	Neck Measurements	Treatment
26.5.24	A. 16" B. 15 $\frac{7}{8}$ "	B.Coli.100000000 (Salol. grs.x.b.i.d.)
2.6.24	A. 15" B. 14 $\frac{3}{4}$ "	B.Coli.300000000 (Salol.grs.x.b.i.d.)
10.6.24	A. 14 $\frac{1}{2}$ " B. 14 $\frac{1}{4}$ "	B.Coli.500000000 (Salol.grs.x.b.i.d.)
17.6.24	A. " B. "	B.Coli.800000000 (Salol.grs.x.b.i.d.)
22.6.24	A. " B. "	As before. Tr.Iodi.m.x. t.d.s.

She then ceased attending until the 13th August 1924, By that time her condition had greatly improved,

especially the dyspnoea.

<u>Date</u>	<u>Neck Measurements</u>		<u>Treatment</u>
13.8.24	A. 14 $\frac{1}{4}$ "	B. 13 $\frac{3}{4}$ "	B. Coli. 1000,000,000
22.8.24	A. "	B. "	-do- -do-
4.9.24	A. "	B. 13 $\frac{1}{4}$ "	-do- 500,000,000
6.10.24	A. "	B. "	-do- 2000,000,000

Salol.grs.x.b.i.d. was combined with the vaccine and Ung:Iodi:Denigrescens externally also. She was improved so much as to be free from respiratory distress and discontinued treatment on her own accord. I saw her recently and the condition has recurred. A fact that I have observed on more than one occasion.

Case 16. Dorothy P. aet 17. Uniform swelling of both lobes and isthmus. Duration not known. Enterococci in faeces. This case and the five following all belong to the same family. All were goitrous and all harboured the enterococcus in their faeces.

<u>Date</u>	<u>Neck Measurements</u>		<u>Treatment</u>
8.5.24	A. 16"		Enterococci. 50,000,000
13.5.24	A. "		-do- 250,000,000
20.5.24	A. 15 $\frac{1}{2}$ "		-do- -do-
27.5.24	A. 15"		-do- 350,000,000
3.6.24	A. "		Tr.Iodi. m.vii. t.i.d.
10.6.24	A. 14 $\frac{3}{4}$ "		-do- m.xv. t.i.d.
17.6.24	A. "		-do- -do-
24.6.24	A. "		-do- m.xx. t.i.d.
9.7.24	A. 14 $\frac{1}{2}$ "		-do- -do- -do-
15.7.24	A. 14 $\frac{1}{4}$ "		-do- -do- -do-
22.7.24	A. "		-do- -do- -do-
5.8.24	A. "		-do- -do- -do-

Case 17. Irene P. aet 15. Uniform parenchymatous goitre. Duration not known. Faeces contained enterococci.

<u>Date</u>	<u>Neck Measurements</u>		<u>Treatment</u>
9.5.24	A. 15 $\frac{1}{4}$ "	B. 14 $\frac{1}{2}$ "	Enterococci. 50,000,000
14.5.24	A. "	B. "	-do- 200,000,000
21.5.24	A. 15"	B. "	-do- -do-
28.5.24	A. "	B. "	-do- 350,000,000
4.6.24	A. 14 $\frac{3}{4}$ "	B. 14"	Salol.grs.x. b.i.d.
11.6.24	A. 14 $\frac{1}{4}$ "	B. 13 $\frac{3}{4}$ "	-do- -do- -do-
19.6.24	A. "	B. 13 $\frac{1}{2}$ "	-do- -do- -do-
26.6.24	A. "	B. "	-do- -do- -do-
9.7.24	A. 14"	B. 13 $\frac{1}{4}$ "	K.I. grs.x. t.i.d.
16.7.24	A. "	B. 13"	-do- -do- -do-
23.7.24	A. "	B. "	-do- -do- -do-
7.8.24	A. "	B. 12 $\frac{3}{4}$ "	-do- -do- -do-

Case 18. Louisa P. aet 14. Goitre parenchymatous and uniform. Whole gland affected. Enterococci in faeces.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
9.5.24	A. 14"	Enterococci.50,000,000
24.5.24	A. 13 $\frac{3}{4}$ " B.13"	B.Coli. 150,000,000
1.6.24	A. " B. "	-do- 300,000,000
9.6.24	A. 13 $\frac{1}{4}$ " B.12 $\frac{3}{4}$ "	-do- 500,000,000
16.6.24	A. " B. "	-do- 600,000,000
22.6.24	A. " B.12 $\frac{1}{2}$ "	-do- 1000,000,000
29.6.24	A. " B. "	Tr.Iodi.m.v. t.d.s.
13.7.24	A. " B. "	-do- m.x. t.d.s.
27.7.24	A. 13" B.12 $\frac{1}{4}$ "	-do- -do- -do-

Case 19. Frank P. aet 13. Well marked uniform goitre.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
8.5.24	A.14 $\frac{1}{2}$ " B. 14 $\frac{1}{4}$ "	Enterococci.50,000,000
13.5.24	A. " B. "	-do- 100,000,000
20.5.24	A. 13 $\frac{3}{4}$ "B.13 $\frac{1}{4}$ "	-do- 200,000,000
27.5.24	A. 13 $\frac{1}{2}$ "B.13"	-do- 300,000,000
3.6.24	A. 13 $\frac{1}{4}$ "B.12 $\frac{3}{4}$ "	-do- 500,000,000
10.6.24	A. 12 $\frac{3}{4}$ "B.12"	-do- -do-
17.6.24	A. " B. "	Tr.Iodi.m.x. t.i.d.
1.7.24	A. " B. "	-do- -do- -do-
29.7.24	A. 12 $\frac{1}{2}$ "B.11 $\frac{3}{4}$ "	-do- -do- -do-
8.8.24	A. " B. "	-do- -do- -do-
22.8.24	A. " B. "	Salol. grs.x. b.i.d.
10.10.24	A. 12 $\frac{1}{4}$ "B.11 $\frac{1}{2}$ "	-do- -do- -do-

Case 20. Harold P. aet 11. Uniform parenchymatous goitre. Enterococci in faeces.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
8.5.24	A.13 $\frac{1}{2}$ " B. 13"	Enterococci 50,000,000
13.5.24	A. " B. "	-do- 100,000,000
20.5.24	A.12 $\frac{1}{4}$ " B. 12 $\frac{3}{4}$ "	-do- 200,000,000
27.5.24	A.12" B. "	-do- 300,000,000
3.6.24	A. " B. "	-do- -do-
16.6.24	A.12" B. "	-do- -do-

Case 21. Annie P. aet 9. Faeces contained enterococci. Goitre parenchymatous.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
8.5.24	11 $\frac{1}{2}$ "	Enterococci 50,000,000
13.5.24	11"	-do- 100,000,000
20.5.24	"	-do- 200,000,000
27.5.24	10 $\frac{1}{2}$ "	-do- 300,000,000
3.6.24	"	-do- -do-
16.6.24	"	-do- -do-

Case 22. Blanche M. aet 19. Uniform parenchymatous goitre. Duration not known. She received Salol grs.x. b.i.d. and Kerol m.iii. b.i.d. increased later to m.vi. b.i.d. for five weeks. The neck measurements were - A.13", B.12½" and at the end of the treatment they were - A.12½", B. 12¼". The mother of this girl is the victim of myxoedema. One sister and a brother also suffer from goitre and one sister is an imbecile. - A microcephalic idiot.

Case 23. Sybil P., Shipley. aet 20. Parenchymatous goitre. Mother and one sister also affected. Enterococci in faeces of this girl and also sister and mother. Water supply from Shipley - separate from that of Heanor. Treatment was discontinued before completion, refusing further treatment.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
30.4.24	A.14¼" B.13½"	Enterococci 12,500,000
7.5.24	A. " B. "	-do- 50,000,000
12.5.24	A. " B. "	-do- 250,000,000
19.5.24	A. " B. "	-do- 500,000,000
26.5.24	A.13½" B.13½"	-do- -do-
2.6.24	A. " B. "	-do- -do-

Case 24. Maud P. aet 13. Sister of Case 23. Parenchymatous goitre chiefly of right lobe. This case also refused further treatment after the 2nd June 1924. Enterococci present in faeces.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
30.4.24	A.13½"	Enterococci 12500000
7.5.24	A. "	-do- 50000000
12.5.24	A. "	-do- 250000000
19.5.24	A. "	-do- -do-
26.5.24	A.13"	-do- 500000000
2.6.24	A.12¾"	-do- -do-

Case 25. Doris C. aet 15. Large parenchymatous goitre with some fibrous degeneration. Duration not known but much worse recently. Enterococci present in faeces in abundance.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
8.5.24	A.16" B.15⅞"	Enterococci 50,000,000
13.5.24	A. " B. "	-do- 250,000,000
20.5.24	A.15¼" B.14½"	-do- -do-
27.5.24	A.14⅞" B.14"	Thymol.grs.x. b.i.d.
3.6.24	A.14½" B. "	-do- -do- -do-
10.6.24	A. " B. "	Salol. grs.x. b.i.d.
24.6.24	A. " B.13½"	Tr.Iodi. m.x. t.i.d.

Case 25 (Contd.)

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
1.7.24	A. 14 $\frac{1}{2}$ " B. 13 $\frac{1}{2}$ "	Tr. Iodi. m.x. t.i.d.
7.7.24	A. " B. "	-do- -do- -do-
18.7.24	A. " B. "	Thymol grs. x. b.i.d.
19.8.24	A. " B. "	-do- -do- -do-
26.8.24	A. " B. 13 $\frac{1}{4}$ "	-do- -do- -do-
16.9.24	A. 14" B. "	-do- -do- -do-

Case 26. Ada H. aet 17. Parenchymatous goitre. Duration one month.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
9.7.24	A. 15" B. 14 $\frac{1}{4}$ "	B. Coli 150,000,000
16.7.24	A. 14 $\frac{3}{4}$ " B. 13 $\frac{3}{4}$ "	-do- 400,000,000
23.7.24	A. 14 $\frac{1}{4}$ " B. 13 $\frac{1}{4}$ "	-do- 800,000,000
30.7.24	A. 14 $\frac{1}{2}$ " B. 13 $\frac{1}{2}$ "	-do- 1000,000,000
6.8.24	A. 14" B. 13 $\frac{1}{8}$ "	-do- 2000,000,000
13.8.24	A. " B. "	Salol grs. x. t.i.d.
27.8.24	A. " B. 13"	-do- -do- -do-

Case 27. Lizzie B. aet 25. Parenchymatous goitre - Goitre varies in size, getting larger specially in summer and often when patient has a cold.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
16.6.24	A. 15 $\frac{3}{4}$ "	B. Coli 150,000,000
22.6.24	A. "	-do- 300,000,000
7.7.24	A. 15 $\frac{1}{2}$ "	-do- 600,000,000
14.7.24	A. 15 $\frac{1}{4}$ "	-do- 1200,000,000
21.7.24	A. 14 $\frac{3}{4}$ "	-do- 2000,000,000
28.7.24	A. 14 $\frac{3}{4}$ "	Tr. Iodi. m.x. t.i.d.
29.8.24	A. 14 $\frac{3}{4}$ "	-do- -do- -do-

Patient discontinued on her own accord.

Case 28. Bertha P. aet 40. Duration two years, gradually increasing in size.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
22.5.24	A. 14 $\frac{1}{2}$ " B. 13 $\frac{3}{4}$ "	B. Coli 300,000,000
29.5.24	A. " B. "	-do- 450,000,000
5.6.24	A. 14 $\frac{1}{4}$ " B. "	-do- 600,000,000
12.6.24	A. 14" B. 13 $\frac{3}{4}$ "	-do- 800,000,000
20.6.24	A. " B. "	-do- 1200,000,000
25.6.24	A. " B. "	Tr. Iodi. m.x. t.d.s.
12.8.24	A. " B. "	-do- -do- -do-
26.8.24	A. " B. 13"	-do- -do- -do-
21.10.24	A. " B. "	-do- -do- -do-
28.10.24	A. 13 $\frac{1}{2}$ " B. 13"	Ung: Hydrarg: Iodid. Robra.

Case 29 Archer P. aet 29. Coal Miner. Had a "full" neck for a long time but says that it has become worse this last year or so. Some pressure symptoms are present. He did not carry on when he got relief but was good enough to confess that he had more room in his shirt collar than formerly and was relieved of his dyspnoea.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
9.2.25	A.15 $\frac{1}{2}$ "	B.Coli 150,000,000
16.2.25	A.15 $\frac{1}{2}$ "	-do- 250,000,000 ^x
27.2.25	A.14 $\frac{3}{4}$ "	-do- 150,000,000
4.3.25	A. "	-do- 250,000,000
12.3.25	A. "	-do- -do-

x Very severe reaction occurred on this occasion. Subsequently he was given Salol grs. xx. and Sodium Salicylate grs.xx. t.d.s. during the rest of the period.

Case 30. James J. G. aet 50. Coal Miner. Duration twelve months. Social conditions poor. Wife subject of Myxoedema (aet 50). Two sons. aetat 16 and 18 with goitre and one daughter aetat 13, also goitrous. Wife's sister has a very bad goitre. His brother, who lives in Nottingham, has a goitre also. The patient and his family have lived in Heanor for twenty years. This case was treated with Thyroid Extract, which was pushed until symptoms of thyroidism occurred, later with Tr.Iodi. internally and K. I. in large doses for a long period, and later with B.Coli Vaccine, Salol and Sodium Salicylate. No effect was observed in four months.

Case 31 Mrs. W. aet 34. Diffuse parenchymatous goitre of long standing. Gland is nodular and apparently fibrous. Under Thymol grs. x. b.i.d. and Extract Thyroid gr. v. t.i.d., the neck measurement went down from A.13 $\frac{1}{4}$ " B. 12 $\frac{1}{2}$ " to A.12 $\frac{3}{4}$ " B. 12" in two months. There is still a fair amount left but this is persistent in spite of iodine administered internally for a further period of a month.

Case 32. Clarice L. P. aet 15. Hosiery Hand. Parenchymatous goitre involving the whole gland. Mother goitrous. Social conditions very poor. House chronically dirty. One sister goitrous. Duration of goitre said to be fine years.

Case 32. (Contd)

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
21.5.24	A.14 $\frac{1}{2}$ " B.14"	Thymol grs. x. b.i.d.
28.5.24	A.14" B.13 $\frac{1}{2}$ "	-do- -do- -do-
4.6.24	A.13 $\frac{3}{4}$ " B.13"	-do- -do- -do-
18.6.24	A. " B.12 $\frac{3}{4}$ "	Salol grs. x. b.i.d.
24.6.24	A.13" B. "	-do- -do- -do-
7.7.24	A.12 $\frac{3}{4}$ " B.12"	-do- -do- -do-
15.7.24	A. " B. "	Tr.Iodi. m.x. t.i.d.
21.7.24	A.12 $\frac{1}{2}$ " B. "	-do- -do- -do-
5.8.24	A.12 $\frac{3}{4}$ " B. "	-do- -do- -do-

I saw the girl's mother a short time back when she informed me that the goitre had again resumed its old proportions. Where cases are subjected to the same influences which procured the disease in the first instance, after treatment the condition is likely in many cases to recur - in spite of the iodide in the water supply, if they remain in this locality and do not boil their drinking water.

The following cases were treated with iodine alone:-

Case 33. Doris B. aet 14. Hosiery Hand. Uniform parenchymatous goitre. Duration not known.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
26.5.24	A. 13 $\frac{1}{2}$ "	Tr.Iodi. m.x. t.d.s.
2.6.24	A. 13"	-do- -do- -do-
22.6.24	A. 12 $\frac{3}{4}$ "	-do- -do- -do-

Case 34. Mrs. Alice M. aet 29. Said to have been present since childhood. This woman belonged to a very goitrous family and lived under very bad social surroundings.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
20.5.24	A. 15 $\frac{1}{4}$ "	Tr.Iodi. m.v. t.i.d.
27.5.24	A. "	-do- m.x. -do-
4.6.24	A. "	-do- m.x.v. -do-
16.6.24	A. 14 $\frac{1}{2}$ "	-do- -do- -do-

The goitre here was greatly diminished.

Case 35. Lucy O. aet 12 $\frac{1}{2}$. Diffuse parenchymatous goitre involving the whole gland. Also the subject of tubercular submental glands. Duration of goitre six months. Enterococci in faeces.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
20.5.24	A.12 $\frac{3}{4}$ " B. 12 $\frac{1}{2}$ "	Tr.Iodi. m.x. t.i.d.
2.6.24	A.12" B. 12"	-do- -do- -do-

Case 35 (Contd)

She had for some time previously been directed to massage into the neck, Ung. Iodi. Denigrescens each night.

Case 36. Hilda B. aet 15. Duration one year. Laundry Hand. Very poor social conditions. No others with goitre. The goitre was of the parenchymatous variety. This case improved under Tr.Iodi. grs. m.x. t.i.d. in three months.

Case 37. Maud G. aet 14. Duration one year, gradually increasing parenchymatous goitre. The administrations of Tr.Iodi. m.x. t.i.d., from 17.11.24 to 27.1.25 increased to m.xv. t.i.d., for the last fortnight with K.I. grs.v. added, resulted in no reduction being observed whatever during that period.

Case 38 Mark D. aet 22. Diffuse parenchymatous goitre recurring after operation four years ago. Family very goitrous. It will be observed from the photograph that he also has adenoids. Altogether he was a very unhealthy weedy object, dull mentally and mildly myxoedemic.

<u>Date</u>	<u>Neck Measurements</u>	<u>Treatment</u>
10.12.24	A.15 $\frac{1}{2}$ " B.14 $\frac{3}{4}$ "	Syr. Fr.Iodi $\bar{3}$ i.Pot.Iodid. grs. vii. t.i.d.
19.12.24	A.14 $\frac{7}{8}$ " B.14 $\frac{1}{4}$ "	-do- -do- -do- -do-
29.12.24	A.14 $\frac{3}{4}$ " B. "	-do- -do- -do- -do-
6.1.25	A. " B. "	-do- -do- -do- -do-
22.1.25	A.14 $\frac{1}{2}$ " B.14 $\frac{1}{8}$ "	-do- -do- -do- -do-

DONE

Pathology of Goitre and the Changes
In the Thyroid in Acute Hyperplasias (Bacterial
Infections and Toxaemias.)

In many cases changes have been observed to take place in thyroid glands of human beings dying from a great variety of conditions, as well as animals artificially infected. All these changes are identical with those of the early changes to be seen in the thyroids of cases of endemic goitre. Whether the toxaemia be acute or chronic these changes are the same, varying in degree only.

They are first, congestion. The gland is very dark in colour, macroscopically and on section the vessels are seen to be full and dilated. There is also a good deal of intervesicular congestion, and if this is severe minute haemorrhages may be observed to occur into the vesicles. Coincidentally with this congestion one notices changes in the colloid itself - It becomes more granular, staining poorly, vacuolated and receding from the wall of the vesicle until complete absorption has taken place. At the same time changes are to be found in the cells lining the vesicles; they become either cuboidal in shape or highly columnar filling the vesicles completely. The nuclei of the cells stain more deeply than in sections of normal thyroids and become eccentric in position, whilst the protoplasm of the cells themselves show certain changes such as granulation and is often completely disintegrated and the cells desquamated into the

vesicle so as to completely fill in. Whilst this cellular hyperplasia is proceeding there may be or may not be a connective tissue cell hyperplasia. In certain cases this increase of fibroblasts may be the predominant feature or it may be overshadowed by the vesicular hyperplasia. When this increase of fibroblasts with cellular hyperplasia is well advanced the picture is then what one finds in myxoedema, the fibrous tissue being predominant.

There is also seen in many cases budding of epithium in the vesicles - the precursors of new vesicles.

My observations show that the size of glands of rats do not show great changes in size in acute toxasemias, when microscopically they present a picture of hyperplasia, - what difference in size is apparent is probably due to the intense congestion.

Farrant (i) has described hyperplasias occurring in the thyroids of man and animals in various conditions, viz.- infections by B. Aerogenes Capsulatus, B. Anthracis, B. Coli Communis, B. Diphtheria, B. Disenteriae, B. Gaertner, B. Mallei, B. Tetanus, B. Tuberculosis, Meningococcus, Malaria, Measles, Bronchopneumonia, Whooping Cough, Chronic Nephritis, Cirrhosis of the liver, Rheumatic and Scarlet Fever and Pernicious Anaemia. He found (p.51) that no changes occurred with infections with the B. Typhosus, from 4-9 weeks infection but Bayon (ii), has showed that

(i) Proc: Roy: Soc: Med: 1914. vol vii. part iii. p. 50-7. ^{Part Sect.}
(ii) McCarrison, R. Etiol. of End: Goitre 1913 p. 135 and 57-68.

thyroid hyperplasia can be induced by typhoid toxin, also by poisoning with phosphorus and his conclusion was that, "Any cause which is capable of altering the function of the thyroid so as to damage the secretory epithelium can lead up to the production of colloid, diffuse or nodular goitre."

What does the reaction of the thyroid mean in these acute toxæmias ? It is, I think, a reaction on account of an excessive metabolism. If the stimulus is maintained for a sufficient duration, and the destruction of thyroid tissue not too great, an increase then takes place in the thyroid gland from the formation of an increased number of vesicles.

The changes which are seen in the sections are, in a large number of cases, those of inflammatory reaction where goitre is not present, the changes may be apparent and in such cases the thyroid may be said to be in the "pre-clinical" stage of goitre.

"Le goitre est un effet, au début une prolifération cellulaire qui ne diffère en rien que l'on constate dans les reins, dans les capsules surrénales, etc. Après l'ablation de l'autre organe symétrique, c'est à dire dans les cas d'hypertrophie compensatrice, Il est rare que le goître reste à ce stade, et que l'on ne constate pas d'autres troubles q'une hypertrophie compensatrice; en générale il sert des phénomènes d'^{ir}ritation dont les uns sont peut-être attribuables à des infections microbiennes, les autres à des auto-

intoxications, parties des cellules privees de leur iode normal et reagissant sur la glands." (i).

Besides these hyperplastic changes, we often see in goitre distension of the vesicles, with colloid - the so called colloid goitre, and another change of frequent occurrence is the advent of adenomata. Both of these conditions are the result of hyperplasia. Marine & Lenhart (ii), declared that all goitres with enlarged colloid vesicles are the result of previous periods of hyperplasia, alternating with the periods of more or less complete return to the colloid state; and we get illustrations of this in the enlargements of the thyroid gland, of menstruation, of repeated pregnancies, or in any gland which has undergone hyperplasia and involution more than once, and thus we get ^a step like enlargements of such glands as each menstrual period comes on or as each pregnancy develops, so the enlargement does not return to its original size after each succeeding event.

In the true parenchymatous variety of hyperplasia the enlargement is not very great - the larger varieties are seen in the colloid or cystic stages. When the hyperplasia has gone on for a time, other changes take place in the gland. The connective tissue cell reaction (fibroblasts) give rise to a great increase of fibrous tissue which often gives rise to a very complete replacement of the normal tissues. The size of such thyroids may, and frequently is, smaller than normal, and if it is sufficient in amount, the animal

(i) Louis D'or. Gaz:des Hosp; 1903 pp.501-505.
(ii) Arch: Int: Med: Chicago 1911- vol.vii.pp.506-535

is myxoedemic. It is the occurrence of this fibrosis which constitutes the reason why many cases of parenchymatous goitre resist the most drastic medical treatment of the most varied kind, or pushed up to the limit of tolerance. In an old standing case one may succeed considerably because the fibrosis varies in degree. Since the colloid escapes into the lymphatics - it may frequently be seen to be in the lymphatics - the advent of this fibrosis will explain the occurrence of colloid goitres. The secretion is dammed up in the vesicles on account of impairment of its passage through the lymphatics. Cysts apparently develop in the same manner increasing in size through many vesicular walls breaking down and forming one large cavity.

Farrant (i), in a paper on Thyroid Action and Reaction concluded that the hyperplasia caused by the injection of diphtheria toxin was due to the attempt of the thyroid to form antitoxin, for by feeding them for a period before the injections with thyroid substance enabled the animals to live longer than controls. Moreover, the blood serum of a thyroid fed rabbit was antitoxic to diphtheria toxin; and antitoxin fed rabbits developed the same symptoms similar to those of thyroid feeding, whereas thyroidectomised rabbits were more tolerant to feeding with antitoxin.

Experimentally Produced Goitres.

Many workers have been able to produce goitre in animals - in India, - in Switzerland, - in France, -

(i) Proc:Roy: Soc: Med: 1913, vol.vi. part iii.pp21-48
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in America and recently in Holland.

Repin(i), fed white ^{rats.} ~~rabbits~~ with goitrogenous water from September 1910 to June 1911. "On leur a donné à boire chaque jour de l'eau franchement puisée à une source goitrigène. Simultanément des rats restée à Paris recevaient de l'eau d'une autre source de la Maurienne importée directement tous les deux jours et notoirement goitrigène aussi." (p.226).

He succeeded in producing goitres of large dimensions in this way. He states that water boiled did not prevent goitre to a complete degree but the agent was destroyed by subjecting it to a temperature of 120°C. His conclusion was that it was the radio-activity of the several waters which was the offending agent, a conclusion which has not been supported by others. There are many radio-active waters elsewhere where goitre is absent or only slightly evident. In Derbyshire the thermal waters of Buxton are radio-active but goitre is not prevalent there.

McCarrison was successful in producing goitre in rats experimentally, by feeding them for periods of several months upon aerobic cultures from the faeces of goitrous persons and, also to a greater extent upon anaerobic cultures from the faeces of goitrous persons, also upon feeding rats upon the filtrate from faecal emulsions of goitrous persons. (ii)

He was also able to produce the disease experimentally in man (iii), including himself in 1906 in

(i) Comptes Rendus et Mem: Soc: Med: De. Biol: 1911. pp. 225-227.

(ii) Disease of Thyroid Gland, 1918. pp. 254-255.

(iii) Etiol: of Endemic Goitre, 1913. pp. 86-94.

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Gilgit; and also in 1911 in Kashrote within a few weeks by drinking small quantities of the water in question containing a considerable quantity of the sediment and those who developed goitre were cured by taking thymol. The experiments in 1906 lasted fifty-two days and the goitres were largest on the thirtieth day. The swellings first appeared on the 13th-15th day.

In the early part of 1925, I carried out a series of experiments upon white rats with deposits from certain water supplies which serve the towns of Heanor, Ilkeston, Chesterfield, Derby, Nottingham, Sheffield and Leicester. Roughly the combined populations of these and other places is 1,250,000 and all derive their water supplies from collecting grounds situated in Derbyshire. The Derwent Valley Water Board supplies the cities of Nottingham, Sheffield, Leicester and the County Borough of Derby, Alferton and part of Ripley, Long Eaton and Heage. The Reservoir is situated at the head of the Derwent Valley in the extreme north of Derbyshire. The gathering ground is situated in the Peak district where the population is practically nil except for a few isolated farmsteads and is situated on the millstone grit and the water is upland surface water. The Chesterfield Borough Reservoirs are situated at Linacre and the water draining into the reservoirs is also an upland surface or moorland water. I have described the Heanor and Ilkeston water supply in detail in an earlier section.

Not only may human habitations pollute water

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supplies, but farm dung heaps, etc., may do so as well. An instance of this occurred in 1904. Dr. Barwise (i), states that Dr. Peck, the M.O.H. for Chesterfield Borough said "that water was liable to pollution by cattle and an inspection of the gathering grounds of the brooks showed that the sewage of a farm entered one of them, but this was promptly cut off." (i). Thus pollution from such sources as these is not entirely ruled out in such a wild region as that in which the Derwent Valley Reservoir is situated. Nevertheless the fact remains that those places which take their supplies from this source, either wholly or in the main, show on the whole a lower percentage of goitre than other regions, such as Heanor and Ilkeston, or Chesterfield Borough. Derby, Sheffield and Leicester show small percentages of goitre amongst school children compared with, say Chesterfield Borough, and the water is of much the same character except that the gathering ground of the Linacre Reservoirs is situated in a more populous (agricultural) region and is, for this reason, in all probability more liable to pollution by cattle and from farms.

The experiments of McCarrison suggest that faecal organisms are the cause of goitre. In regard to this part of the subject, Durham (ii), suggested that there might possibly be an interaction between the pollution and mineral constituents of the soil and

(i) Report on the Health of Derbyshire, 1905. p.29.

(ii) Journ: of Hygiene. 1920-1, vol.xix. pp.399.

water. By means of bacterial action insoluble substances in the soil may be rendered soluble. Fresh soil to which carbohydrate, (sugar or starch) was added by the aid of its own bacteria showed from three to five times more soluble potash, silica and phosphoric acid than untreated soil. (Gardener's Chronicle 1919, p.91) and Durham (i), suggested that the bacterial pollution of water may affect the dissolved mineral constituents of the water coming from a given soil; and thus explain why goitre should apparently prefer some districts more than others.

One reason why goitre appears to favour limestone districts, (where the water is, that is to say derived from those districts) maybe that such rocks are amongst the most porous, and their powers of filtration poor in comparison to such as the gritstones.

Experimental Work

The object of these experiments was to determine the effect on the thyroid glands of white rats; of the deposits from various water supplies in Derbyshire supplying known goitrous localities, and in the case of the Heanor and Ilkeston water of organisms isolated from the water supply by feeding. The deposit from the Heanor and Ilkeston water was obtained by filtering large quantities of water through Pasteur Chamberland Filters and scraping off the deposit on the candles daily. This deposit was then mixed with the drinking water of the rats and also small cubes of bread were inoculated with the deposit - this was

(i) Journ: of Hygiene 1920-1. vol xix.pp.399.

was done daily. In the case of the Derwent Valley Water Board water, sludge was used from the roughing filters at Bamford. The deposit in the case of the Chesterfield Borough, (Linacre), water was obtained from the filter beds. I am indebted to the various water engineers for the constant supply of these deposits.

The rats were confined in metal cages, measuring 18" x 12" x 13", with removable zinc wire netted bottoms fixed one inch from the bottoms of the cages. Underneath the wire netted bottoms were sliding trays for catching droppings, etc. The food and water receptacles were fixed on the wire doors above the level of the wire netted bottoms in order to lessen the liability of faecal contamination of food and ^{water.} ~~matter~~. The cages were frequently scrubbed with hot water and lysol, (one percent) and kept as hygienic as possible. The water was changed daily. When a foreign sludge was used the sludge was mixed with distilled water; the rats were fed on bread and mixed corn, consisting of wheat, maize, barley, peas, white millet and black millet. The following series of experiments were carried out :-

- (1) Rats fed on residue from Heanor and Ilkeston water before treatment.
- (2) Rats fed on residue from Heanor and Ilkeston water after treatment (i.e. after filtration at water works).
- (3) Rats fed on residue from Heanor and Ilkeston water after treatment and after iodisation at water works.

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- (4) Rats fed on residue from Chesterfield (Linacre) water.
 - (5) Rats fed on residue from Derwent Valley Water Board water, (the chief source of Derby, Sheffield, Nottingham and Leicester).
 - (6) Rats fed on B.Coli isolated from the Heanor and Ilkeston water.
 - (7) Rats fed on Enterococci isolated from the Heanor and Ilkeston water.
 - (8) Rats kept as controls.
 - (9) Rats fed on Oleic Acid.
 - (10) Rats as in No.9, but kept under very unhygienic conditions.
 - (11) Rats injected with Diphtheria Toxin.
 - (12) Rats injected with Dysentery Toxin, (Shiga).
 - (13) Rats fed on Phosphorus.
 - (14) Rats injected with ^{Typhoid.} ~~Thyroid~~ Cultures.
 - (15) Rats injected with Cholera Cultures.
 - (16) Rats injected with B.Coli.Vaccine.
 - (17) Rats injected with Bovine Tuberculin.
 - (18) Rats injected with Coley's Toxin.

Results of Experiments

It must be noted that animals, like human beings, show an idiosyncrasy towards the development of goitre. Female animals show a greater tendency towards the disease than males. Before carrying out the experiments I have taken from each batch several animals and killed them, examining specimens microscopically as well in order to ascertain their condition. All rats which have been confined in cages show some evidence of previous hyperplasia - though in the majority it

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is slight. In series (2) the rats were of two varieties, mole coloured and white, but both were bred from the same species. They were alike as regards age and sex and the average weight was 130 grams. They were confined in wooden cages of the same size and under the same conditions as regards diet as they had been accustomed since birth, both they and their ancestors. I killed several specimens of both varieties on receiving them and the thyroids were normal in all respects. One lot was given the Heanor and Ilkeston water after filtration through a Berkfield filter; another lot, the tap water with the residue from the candle of the filter scraped off daily and their cages were kept as clean as possible and their water free from other contaminations; whilst a third lot received distilled water only and were allowed to live under the same conditions as the others, but their cages were allowed to become dirty. No controls were kept during the course of the experiments; I contented myself with keeping the animals under conditions identical as regards diet, size of cages, number of rats per cage (six), etc., to which they had been accustomed for some time past and killed a number of specimens of each lot prior to the commencement of the experiments. All these specimens were normal.

Of the experimental rats, (see photographs) differences were seen between the mole coloured rats and the white rats. Two rats died during the course

of the experiment and were partially eaten before being discovered. Of the rats receiving filtered water, three showed massive enlargements and two were moderately enlarged. Of the rats receiving distilled water alone, three showed massive enlargements, one moderately so and two were normal. Three of the rats (white) receiving the tap water with the candle residue showed some enlargement and the remaining two thyroids were not enlarged. Although no controls were kept during the course of these experiments the animals were kept under conditions to which they had lived all their lives and three rats of each kind, killed prior to the commencement of the experiments, showed normal thyroids.

I think, therefore, that conclusions of a certain character may be drawn from these experiments.

- (1) There is an idiosyncrasy in animals to the development of goitre and, as far as this particular batch of animals was concerned, the difference is most appreciable amongst the white rats; but the mole coloured rats also show an idiosyncrasy in both batches.
- (2) Filtering water through a Berkfield filter gives no protection to the onset of goitre and that the agent is in the water.
- (3) Unhygienic conditions of living are capable of giving rise to goitre.
- (4) That faecal contamination of the water is particularly productive of goitre (the rats receiving distilled water were allowed to contaminate their water with faecal matter).

In another series (1), where all the rats were of the same age and variety and controls were kept during the course of experiment the results were as follows :-

- (1) Heanor and Ilkeston water. Rats fed on deposit from water after filtering through a Berkfield Filter, after the water had been treated at the waterworks at Whatstandwell but before iodisation. Two showed moderate enlargements and ~~the~~ one was normal.
- (2) The same, but after treatment at the waterworks and after iodisation, i.e. deposit on the filter candle after filtering water from a house tap. Two showed moderate enlargements of the thyroid and one was normal.
- (3) The same, but deposit was taken from a filter after filtering the raw untreated water. One showed a fairly large hypertrophy, the other two were normal in size.
- (4) Organisms from Heanor and Ilkeston water - Enterococcus. Rats fed on cultures (broth) of enterococcus, isolated from the Heanor and Ilkeston water for three months. Two have enlarged thyroids of both lobes. The remainder were showing commencing hypertrophy of one lobe.

B.Coli. Rats fed on cultures of B.Coli. (peptone water) isolated from Heanor and Ilkeston water. All three showed enlarged thyroids. One massive. Duration as before.

- (5) Rats fed on sludge from the filters of the Chesterfield Borough water. Two showed hypertrophy of thyroid and one was normal.
- (6) Rats fed on sludge from filters of Derwent Valley water. One died during the course of the experiment. Of the two remaining one had a fair sized goitre.

All rats of this series were kept in the metal cages as described above. Controls kept during the course of the experiment were at the end normal. None were goitrous.

(7) Rats fed on Oleic Acid. Each rat received daily 3 c.c. of Oleic Acid mixed intimately with the food. One series of rats was kept under extremely hygienic conditions. The other series being allowed to become very dirty. Of those kept/clean, one had both lobes of the thyroid enlarged, and two had one-sided hypertrophies. Of those kept under dirty surroundings all showed enlarge-ments/of thyroid. The controls were normal in size. Duration of experiment was three months. These rats were also kept in the metal cages.

These experiments show :-

- (1) That iodisation of the water supply in its present condition is not sufficient to prevent the onset of goitre. Iodisation of the water supply has been in force now for nine months and I have not observed, as yet, any difference in the incidence of goitre in this district.
- (2) That the causal agent, as far as the water is concerned, may be traced to the faecal organisms which it contains and that the B.Coli. isolated from the water are capable of producing goitre as well as entero-cocci.
- (3) The Heanor and Ilkeston Water is goitriginous both before and after filtration at the water works.
- (4) The deposit from the raw water of the Derwent Valley and the Chesterfield Borough are also capable of producing goitre.
- (5) That Oleic Acid (unsaturated fatty acid) in abnormal amounts, by creating a disturbance of fat balance in the diet, may produce goitre but it is most

evident in the presence of unhealthy conditions of life.

Experiments with Toxins

C h o l e r a

A twenty four hour old agar tube culture was washed in 2 c.c. of normal saline and a bacillary emulsion made. This was killed with Chloroform Vapour - $\frac{1}{2}$ c.c. was injected into one rat and 1 c.c. into one rat. Rats were killed five days later. The thyroids were normal in size but were very congested in appearance. The rat receiving 1 c.c. of the B. E. was sectioned.

T y p h o i d

A twenty four hour old agar culture tube was washed with 2 c.c. of normal saline and killed with Chloroform Vapour. Two rats each received 1 c.c. of this emulsion hypodermically and were killed five days later. The thyroids were normal in size but were intensely congested. One specimen was sectioned.

T u b e r c u l i n

Two rats were each given hypodermically $\frac{1}{2}$ c.c. of Bovine Tuberculin (P.T.O.), and were killed after five days. Sections were made of these thyroids.

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C o l l e y ' s T o x i n

(Toxins of streptococcus Erisipelatus and B.Prodigiosus). Four rats were injected hypodermically with $\frac{1}{4}, \frac{1}{4}, \frac{1}{4}$, and 1 minim of this Toxin respectively. The rat receiving 1 minim died in four days. The other rats were resistant and at the end of five days apparently well. They were given repeat doses for a month and at the end of that time killed. The thyroids were not enlarged but were markedly congested in appearance.

B a c i l l u s C o l i

One rat was injected hypodermically with 500 millions of a B. Coli Vaccine prepared from organisms isolated from Heanor water and the faeces of goitrous persons, and was killed in five days. A second rat was given in the same manner 1,000 millions of the same vaccine. Death took place in two days. The thyroids of both rats were normal in size but deeply congested. Sections of these were made.

T u b e r l i n (BOVINE P.T.O.)

Two rats injected with $\frac{1}{2}$ c.c. each of Bovine Tuberculin (P.T.O.) The rats were killed with chloroform after 5 days. The thyroids were intensely congested and were sectioned.

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Phosphorus

Rats were given 1 gram of Rodine Rat Paste on bread. Death occurred in three days. The thyroids showed externally the same appearance macroscopically, and sections were made of these.

Diphtheria Toxin

Four rats were given $\frac{1}{4}$ c.c. $\frac{1}{4}$ c.c. $\frac{1}{2}$ c.c. $\frac{1}{2}$ c.c. of toxin respectively. The M.L.D. for rats was not known but for guinea pigs it was $\frac{1}{100}$ c.c. They were killed after five days. The thyroids were normal in size but deeply congested.

Dysentery Toxin (SHIGA)

Four rats were given $\frac{1}{4}$ c.c. of this toxin respectively hypodermically. All died in five days. The M.L.D. for rats was $\frac{1}{3}$ th c.c. The thyroids presented the same appearance macroscopically as in the above instances.

Control Rats

Unselected samples of rats were killed from the batch which formed this series of experiments and showed normal thyroids, macroscopically and microscopically. Control rats kept under identical conditions as the experimental animals during the experiments were found normal in all respects.

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I am much indebted to Prof. J. C. D. Ledingham and Dr. MacConkey of the Lister Institutes in London and Elstree/ respectively for kindly supplying me with Toxins.

S u m m a r y

CLINICAL CONCLUSIONS

(1) Endemic Goitre is a disease which affects both sexes, but is more prevalent in females.

(2) It arises during any period of life, but chiefly during -

- (a) Foetal Life.
- (b) Puberty.
- (c) Pregnancy and Lactation

It rarely arises after 45 years of age.

(3) Its behaviour as an endemic closely resembles that of typhoid fever, both in its mode of origin and method of spread. There is a definite idiosyncrasy to the development of the disease.

(4) The disease shows a decided tendency to affect certain families.

(5) Bad hygiene - social and personal, favours the occurrence of the disease.

(6) The treatment of cases of endemic goitre may be successfully carried out with vaccines, prepared from organisms isolated from, (a) faeces of goitrous

persons, (b) the water supply in the case of Heanor and Ilkeston, provided that the cases have not developed fibrosis to any great degree. Intestinal anti-septics, such as thymol and salol, are also of value in cases. Their use is of both practical and academic interest, and from an etiological point of view ^{is} are of great interest.

(7) The occurrence of goitre in definite localised areas, the variations of its endemicity over long periods of years, the occurrence of epidemics of goitre all point towards its being caused by a living agent. Other facts supporting this are - the disappearance of goitre in persons leaving the localities or by the use of boiled water only.

(8) In the Heanor District the endemicity of goitre has diminished since the present water supply was laid on, and although polluted, is of a greater purity than was the case formerly. Cretinism, though present, is not a common complaint.

Primary and Secondary Causes

PRIMARY CAUSE

(1) The primary cause may be said to reside in the water supply. As regards Heanor and Ilkeston this is the faecal pollution. Both B.Coli and Enterococci isolated from this water proved capable of causing goitre.

SECONDARY CAUSES

- (1) Intestinal Toxaemia. This may be due to exogenous influences, (drinking polluted water), or endogenous influences, (intestinal stasis).
- (2) Pollution of soil from numerous privy middens, etc., overcrowding and bad sanitation generally.
- (3) Menstruation, Pregnancy, Lactation, excess of fat in diet. In these metabolism is at a higher level and calls for increased oxidation of the products of metabolism - and thus an increased burden is cast upon the thyroid.

Pathological Conclusions.

(1) The microscopic appearances of goitre in humans and in experimental animals strongly resembles those of an inflammatory reaction to a toxin.

The steps are a congestion - hyperplasia of vesicular epithelium and of connective tissue, - disappearance of colloid, - and last stage of all nearly complete fibrosis, or, with either colloid goitre or cysts. Adenoma^{ta} are very prone to develop during the disease.

(2) The parathyroids in endemic goitre and in experimental goitre do not appear to be affected.

(3) The hyperplasias of bacterial infections and of toxaemias produced experimentally resemble those of endemic goitre.

(4) Endemic goitre cannot be said to arise from deficiency of iodine in food and drink. per se. The deficiency of iodine if it arises does so, not primarily, but secondarily as a result of toxæmia in the alimentary tract, or other chronic infections.

The hypertrophy of the thyroid is thus of a compensatory nature - due not to a deficiency of iodine in the diet but a reaction arising from an increased need for thyroxin for the purpose of oxidising the products of metabolism, in which are included the toxins of bacteria.

On the Etiology of Endemic
Cochic.

with Special Reference to
The Urban District of Huanor in
The County of Derby.
by