The Cawthron Institute
NELSON, NEW ZEALAND.

CAWTHRON LECTURE
SEPT. 5TH, 1929.

Goitre in the Light of Recent Research
—by—
C. E. HERCUS, M.D., D.S.O.,
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I am deeply sensible of the honour of being invited to give the Cawthron Lecture for 1929. Nelson conjures up to the mind of the average New Zealand citizen three things, sunshine, fruit, and the Cawthron Institute. In the brief ten years of its life the Institute has made some remarkable contributions to agriculture, more particularly as regards the fruit industry, and has become a centre in the scientific life of the Dominion. It is impossible to envisage a more fitting memorial to your far-sighted founder, Thomas Cawthron.

Some three years ago, Dr. S. A. Gibbs in his Presidential Address at the Annual Conference of the British Medical Association in Nelson, stressed the urgent need for the establishment in this country of a similar Institute for the study of the health problems of man. With this striking example before him of the value of the application of scientific methods to the problems of agriculture, it was fitting and natural that a Nelson citizen should give this lead. I regret to say that the scheme has not yet captured the imagination of a Thomas Cawthron. Institutes of Medical Research have been established by private benefactors in Canada, South Africa and Australia, and New Zealand must supply this missing link in the Imperial chain. It is true that the Department of Health, as far as its funds have permitted, has contributed to medical research in New Zealand, that the late Mr. Travis, of Christchurch, left a sum of money for the study of Tuberculosis and Cancer in Canterbury, and that the recently established New Zealand Branch of the British Empire Cancer Campaign has secured a research worker for Cancer Research for three years; but valuable as these efforts are, they in no way affect the fundamental need, which is a Medical Research Institute in close affiliation with the National School of Medicine, established by private endowment, and independent of any semblance of political control. I can imagine no more worthy object for private benefaction.
With the advent of a New Zealand Institute of Medical Research, there would come, I believe, a closer linking-up between the students of plant, animal and human pathology, to their mutual advantage. Although the anatomy and physiology of plants and animals are so dissimilar, there are great masses of knowledge, of vital and common interest to all, which tend to be overlooked. Many examples could be given, that which first occurs to the mind of a bacteriologist relating to the action of such living agents as bacteria, fungi, protozoa and viruses, which produce disease in both plants and animals. There is much common ground in the study of such environmental factors as temperature, humidity, nutrition, immunity and epidemiology. The study of the filterable viruses in plants has helped materially in the study of similar viruses affecting man. The study of pollens has thrown much light on the causation of hay fever and hay asthma, and on their successful treatment. In virtue of the isolation and compactness of our community I believe we could give to the world a unique example of the advantages of close co-operation and free interchange of thought and method.

The subject of my lecture illustrates the value of such co-operation in a limited field of investigation. Goitre might appear to be of interest only to the medical profession, and yet it provides a common meeting-ground for chemists, physicists, geologists, biologists, veterinary workers, social economists and farmers, not forgetting the workers in the most important laboratories in the land—the homes of the people. Women and children are critically interested in goitre. The work which I propose to outline this evening could not have been done without the closest co-operation between the Departments of Preventive Medicine, Pathology, Chemistry, Geology and Home Science of the University of Otago, and the Government Departments of Health and Education.

Goitre is the term applied to all enlargements of the Thyroid Gland. The Thyroid Gland has been of interest to mankind since the dawn of history. The Atharvaveda, an ancient Hindu collection of incantations dating back some 2000 years before Christ, contains extensive forms of exorcism for goitre. I doubt if there is another gland in the body around which a more voluminous literature has accumulated.

**THE THYROID GLAND.**

The Thyroid Gland is a ductless gland situated in the front portion of the neck of all vertebrate animals. In man it consists of two lobes, each in size and shape not unlike a Brazil nut, which lie one on either side of the
FIG. I.
SECTION OF NORMAL RESTING THYROID.
X 100 diameters.

(a) Follicles filled with "colloid," which contain the active secretion of the gland.
(b) A single layer of colloid-secreting cells lining the wall of the follicle.
(c) The fibro-elastic stroma or framework of the gland.
upper part of the windpipe under cover of the muscles and soft tissues of the front of the neck. The two lobes are united by a narrow band lying across the front of the windpipe, so that the latter is embraced by the gland in more than a half circle. The blood-supply of the gland is very extensive, more extensive indeed than in the brain or kidney, which is indicative of the highly important functions over which the thyroid presides. The gland shows considerable variations in size according to such factors as age, sex, altitude, and season of the year. It reaches its maximum development at puberty, and slowly decreases in size after the age of thirty.

While these facts have been well established for many years, the minute structure of the gland has recently been in dispute. The traditional teaching has been that the gland consists of a mass of follicles or thin-walled chambers supported by a connective framework and surrounded by a capsule of connective tissue. The appearance of a section of the normal resting gland is shown in Figure 1. It will be seen that the follicles are more or less separate compartments, oval or budded in shape. The follicles are lined by a single layer of gland cells which elaborate the specific secretory product of the gland and pass it into the colloid, which is a sticky, yellowish fluid occupying the interior of the follicle. Williamson and Pearce (1926), using special staining methods, described coiled cylindrical columns of flattened cells lying within a fibro-elastic capsule forming a lymph channel, and a network of fine black lines in the substance of the cells lining the follicles of the gland. On this histological basis they suggest that there are two distinct secretory processes to be recognised in the normal thyroid gland. One is a relatively passive process resulting in the storage of colloid; the other is an active process resulting in the formation of a distinct product which is not colloid. Wilson (1929) in a valuable contribution to the subject, shows that these tubules of secreting epithelium described by Williamson and Pearce are in reality solid thickenings of the intercellular cement substance, and surround the cells in a vast interlacing network.

Physiology.

The functions of the gland are numerous and of primary importance to the health of the body. Substantial progress in understanding the constitution and action of the active principle manufactured in the gland cells has been made in the last thirty years, but there are still many gaps in our knowledge. The cells of the normal gland discharge their secretion into the interior of a vesicle, whence it passes into the blood stream. There is no evidence that even during prolonged increased functional
activity the normal gland cells’ secretion passes directly into the blood capillaries; but in exophthalmic goitre, function being abnormal, the droplets of secretion are discharged directly into the capillaries. Congenital absence of the thyroid prevents growth and intellectual development, thus producing a remarkable condition of cretinism. This condition constitutes a grave economic problem in regions where goitre has been prevalent for many generations. In the Alpine districts of Switzerland, France, Italy, India and South America cretinism and deaf mutism abound. In New Zealand the disease has appeared, and 24 deaths occurred from this cause between 1916 and 1925, but it does not yet, and never should, constitute a serious problem. The loss or diminution of the secretion of the gland in adult life, either from operation or from degenerative changes, produces the curious condition of Myxoedema, in which the body fires burn slowly and the patient becomes sleepy and stupid, and altered in various characteristic ways. The function of the gland is essentially the same in the lower animals. Conditions due to defective thyroid secretion in animals have the same geographical distribution as cretinism and goitre in man, and are of considerable economic significance in badly goitrous districts. Kalkus (1920) records a loss of 83% of lambs from goitrous hairlessness and weakness in the United States of America in the States of Montana, Minnesota and Washington. In Montana 90% of the losses occur in the drainage system of the Yellowstone River. The affected district, it is significant to note, is frequently a narrow valley half a mile wide, and land on either side is unaffected. Death rates of a similar magnitude have been recorded in several goitrous districts in the South Island of New Zealand. Myxoedema in the domestic fowl has only recently been recognised. Laudauer (1929) describes chickens which cease to grow at six weeks and acquire peculiar characteristics. They become deaf, develop a dry skin, ragged feathers, large head, swollen tongue, and swellings round the eyes. The sex glands and the secondary sexual characters are entirely undeveloped, and the thyroid gland is twice its normal size. Goitre is not uncommon in trout reared in captivity in Christchurch, Dunedin and Clinton. Figure 5 shows an affected trout.

If there is an excess of thyroid secretion in the body, from whatever cause, there results an acceleration of all the body functions. This condition is of considerable importance in New Zealand, 2083 people being admitted to our public hospitals for treatment for Exophthalmic Goitre—a form of goitre in which the secreting function of the gland is excessive—between 1916 and 1928, and during the same period it caused the deaths of 568 persons. Though
less common, the same condition occurs in the lower animals. Fox terriers, horses and rats are to my personal knowledge affected. Between these extremes of thyroid action there are many gradations. In clinical medicine the activity of the thyroid is measured in terms of the basal metabolic rate, by which is meant the minimum heat production when at rest. This is estimated by an analysis of the end products of metabolism, or processes of combustion in the body, more especially the amount of oxygen used and of carbon dioxide produced. With extreme functional deficiency of the gland this rate is about 40% below normal; in severe cases of exophthalmic goitre it may rise to 50-60% above normal. The regulation of the basal metabolic rate is apparently one of the main functions of the thyroid.

The function of the thyroid has also been studied from another angle, for it is possible by the use of extracts of the gland to study its effect on the normal tissues of animals and plants. In man, in addition to its use in connection with thyroid anomalies, thyroid extract is used in the treatment of obesity, the loss of weight being due to the burning up of the deposited fat owing to increased metabolic activity. Emerson (1905) observed that the amphibian *Typhlomolge rathbuni* which remains permanently in the larval stage, has no thyroid gland. Babok (1911) showed that the axolotl larva of the Mexican Salamander (*Ambystoma tigrinum*), which normally retains the larval form, can be induced to undergo transformation into the adult form by thyroid administration. Gudernatsch (1912) showed that thyroid feeding to amphibians stops the growth and greatly accelerates change to the land form. Hoskins and Hoskins (1918) found that removal of the thyroid from tadpoles prevents metamorphosis, and the tadpoles grow to an abnormal size. It is evident, therefore, that metamorphosis in amphibians depends upon thyroid secretion.

If cocks are given thyroid gland extract their plumage becomes henlike. Removal of the thyroid in the adult hen leads to the development of new feathers whose structure is of the male type.

Reid Hunt (1905) has shown that thyroid extract fed to mice enables them to acquire a markedly increased resistance to acetonitrile, a poison the effects of which are diminished in proportion to the oxidising activity of the tissues, and this has proved a delicate and useful test for the activity of thyroid extracts. Budington (1925) has shown that thyroid extract has a stimulating effect on the protoplasm of plants. The undifferentiated cells just
proximal to the root cap of Narcissi roots showed acceleration of growth when grown in nutritive media containing thyroid extract.

**Chemistry of the Thyroid Gland.**

While physiologists, biologists, and medical men have been accumulating this body of evidence as to the functions of the thyroid gland, chemists have been studying the chemical structure of the active principle of the gland. With Baumann's discovery in 1896 that iodine was present in relatively high concentrations in the normal thyroid gland, a revival of interest in the significance of iodine in the physiology and pathology of the thyroid gland arose. The principal landmarks in the recent biochemical study of the thyroid gland have been (1) Kendall's isolation from thyroid glands of a crystalline organic iodine compound which he named thyroxin, (2) the demonstration by Harington that thyroxin has the empirical formula C\(_{15}\)H\(_{11}\)O\(_3\)N\(_4\), (3) Harington and Barger's brilliant synthesis of thyroxin identical in chemical and physiological properties with the compound isolated from the thyroid. The synthesis confirms the constitutional formula

\[
\text{HO} \quad \overset{\text{O}}{\text{O}} \quad \text{CH}_3 - \text{CH(NH}_2\text{)} - \text{CO}_2\text{H}
\]

previously suggested by Harington as the result of degredational studies, (4) the resolution by Harington (1928) of the synthetic thyroxin into dextro and laevo modifications, the d form having about three times the physiological activity of the l variety, (5) the adducing of evidence by Harington and Randall that the whole of the acid soluble iodine in the thyroid exists as diiido tyrosine, whereas the acid insoluble iodine is probably all present as thyroxin.

Harington and McCartney have shown (1929) that an isomeric substance of the same composition as thyroxin and having the same diido phenolic groups, but with the benzene rings joined through carbon instead of through oxygen, shows no trace of physiological action. Such effects of chemical structure upon physiological activity are of course well known, e.g., Cacodylic acid is non poisonous though containing 70% of arsenic; again the removal of a molecule of water from Morphine, a hypnotic, produces apomorphine, a violent emetic.

From the above evidence it will be seen that the thyroid gland provides a substance or substances which are essential for growth, for the maintenance of a normal basal
FIG. II.
THYROID SECTION—EXOPHTHALMIC GOITRE.

x 150 diameters.

(a) Disappearance of Colloid: secreting cells multiplied, giving an appearance of a solid mass of cells.
(b) Ingrowth of mass of secreting cells into a follicle.
FIG. III.
PRIMARY GRAVES' DISEASE OR EXOPHTHALMIC GOITRE SHOWING
IODINE REACTION.

(a) Follicles becoming filled again with Colloid, but small and irregular
and showing empty white vacuoles.
(b) Secreting cells still greatly increased in number.
(c) Enlargement of blood vessels.
FIG. IV.
THYROID SECTION—SIMPLE OR COLLOID GOITRE.
× 75 diameters.

(a) Follicles distended with colloid. Interfollicular walls broken down in places.

(b) Degenerated layer of secreting cells.

(c) Greatly increased fibrous tissue.
metabolic rate, and for the metabolic processes of the body. One of these substances is an iodized amine known as thyroxin.

The thyroid has also important though ill-understood relationships with other glands of internal secretion. Swale Vincent (1922) summarises a confusing literature by stating that there is clear evidence that subthyroidism causes increased growth and activity of the pituitary gland, a ductless gland situated inside the base of the skull which powerfully influences the disposition of fat in the body, the skeletal structure, and the secondary sex characters. There is a definite relationship between the development and growth of the reproductive organs and the thyroid. There is some evidence that it stimulates to increased activity the suprarenal glands whose function has to do with the control of blood pressure, and regulation of the amount of sugar in the blood. The field is, however, a difficult one, and current theories regarding the importance of inter-relationships in the functions of the various glands of internal secretion have far out-stripped our certain knowledge of the facts.

**The Pathology of Goitre.**

Space will not permit of more than the briefest mention to this important subject, which is fully discussed by Drennan (1927). Pathological changes in the thyroid occur in response to abnormal demands on the gland on account of defective supplies of raw material, or because of lack of balance in the constituents of the food. Diets containing a high proportion of unsaturated fats, such as butter fats, may induce goitre in dogs. The initial disturbance is but an exaggeration of the normal responses of the healthy gland. There is increased glandular activity which is compensatory in nature, and with the increase in the weight and activity of the gland is associated a reduction in the percentage concentration of iodine. In experimental infections and toxæmias in animals the iodine content of the thyroid may be reduced by as much as 50%. This increased glandular activity may persist and produce the symptoms of exophthalmic goitre, the typical microscopic structure of which is shown in Figs. 2 and 3. The more common response is for the gland to revert to the resting state with certain anatomical changes. The follicles retain their normal shape, but through passive dilatation, coalescence, or budding, they may increase in size three to five times. Some of the follicles rupture and fuse with one another and form a common cavity. Associated with this great increase in size of the follicles there is a slight diminution in the relative and absolute size of the lymph spaces. In Fig. 4, which shows a typical simple
FIG. VI.
UREWERA MAORI WITH TYPICAL GOITRE.
goitre, the colloid appears denser, is of a lower iodine concentration, and is increased in quantity. Sooner or later, secondary changes occur in these follicles, and the gland may later in life give rise to trouble. Such glands give much occupation to the operating surgeon. Both effects—the increased function of the secreting cells, and the passive accumulation of colloid distending the follicular chambers—are commonly present in the one gland, some areas showing glandular activity while other areas show resting colloid areas.

**Goitre in New Zealand.**

I propose to confine my observations to the distribution, cause and prevention of the so-called simple, colloid goitre.

It is commonly stated in medical writings that goitre does not occur in proximity to the sea. If this generalisation were true New Zealand should have no goitre problem, for nowhere in this country can one be more than one hundred miles from the sea, and the four principal centres of population all lie within a radius of eight miles from it. Unfortunately goitre is extremely prevalent in New Zealand, as all visitors to the country observe. That it is not a new problem, peculiar to the advent of the European population, is evident from Maori tradition. Elsdon Best (1924) mentions that the disease “tenga” was known to the Maori in pre-European days, and he states that in 1875 goitre was very noticeable in women of the Tuhoe tribe in the forest-clad and mountainous Urewera district. In a personal communication Mr. Best informs me that he did not observe the disease in the coastal tribes of Taranaki, Hawke's Bay and Wellington, although to-day the Maori children in the goitrous portions of the latter two provinces show an incidence of goitre equal to that of the European children. In 1925 I examined some 300 Maoris of both sexes and all ages in the Urewera country and found 18% with well-marked goitre. Maoris of the same tribe living in the Whakatane-Rangitikei district were found to be less affected, due apparently to the liberal use in their dietary of marine products. Figure 6 shows a Maori woman of this district with a large goitre.

The first reference to a goitre problem among the European population was made by Hacon (1888). Hacon was appointed to the Christchurch Mental Hospital in 1880, some 30 years after the establishment of the Canterbury settlement, and he was at once impressed by the frequent occurrence of goitre in Christchurch. Colquhoun (1910) establishes the fact that goitre is prevalent in many districts in New Zealand. In the replies which he received
to a questionnaire sent to all doctors, Dr. Walter Thomas, of Christchurch, states that on coming to Christchurch from Victoria in 1882 he was much struck by the frequency of goitre. The condition was evidently present in Nelson, for a Nelson doctor, in his reply to Dr. Colquhoun, states: "We have a very still atmosphere in Nelson, especially during the winter, and I have been inclined to attribute its comparative prevalence to that factor."

The first statistical figures of value were obtained during the examination of recruits in the late war, when over 1500 men out of 130,000 examined were rejected for active service on account of goitre. While this evidence gives no measure of the prevalence of goitre it establishes the fact that over 1% of the men had goitres of a size sufficient to warrant rejection from active service, at a time when recruits were badly wanted.

In 1920, with the assistance of Dr. Eleanor Baker, of Christchurch, I carried out observations on the size of the thyroid glands of 15,000 school children in Canterbury and Westland. Thirty-two per cent, were found to have markedly enlarged glands, and in a further 29% the glands were enlarged beyond the usual normal limits. An unexpected fact was that 30% of the children at the age of five years had clearly defined goitres, the sex incidence at this age being equal. An investigation at St. Helen's Maternity Hospital in Christchurch over a period of twelve months showed that 60% of the mothers had goitre, and 8% of the babies were born with goitre. A study of the factors leading to goitrous condition at birth would be of extreme interest. The observations on school children showed that as puberty approached, the glands in both sexes showed an increase in size, particularly marked in the case of the girls. After puberty the incidence fell definitely in both sexes, more markedly in the case of the males. It has been stated that these enlargements are physiological, and that after this period of maximum activity is past the glands return to normal. Unfortunately neither of these assumptions can be maintained. The physiology of the children of North Auckland and Taranaki does not differ from the physiology of those of Canterbury and Westland; yet these marked enlargements do not occur in the former districts. An examination of the boys and girls of the secondary schools in Christchurch and Timaru, whose ages range from 12 to 18 years, revealed a high prevalence of goitre more marked in the athletic members of all the schools. The patients at the Mental Hospital in Christchurch were examined, and 58% of the women and 52% of the men had goitres, large and well-defined. In 20% of them the goitres showed marked, bulging deformity.
The employees of a large factory in Christchurch numbering 121 women and 44 men were examined, and 68% of the women and 34% of the men had goitres of considerable size.

Extensive goitre surveys of school children throughout New Zealand have now been carried out, and the goitrous areas have been clearly defined. The incidence is indicated in the attached maps. The arresting facts are the widespread prevalence of goitre and the remarkable district variations. These have been discussed in detail in previous publications.

From these facts it is evident that endemic goitre presents a very real and pressing problem in this country. It is happily true that in the majority of cases the enlargement of the gland amounts to no more than a disfigurement, the gland and the body adapting themselves harmoniously to the new conditions. In an appreciable number of cases, even in children, there are minor disturbances of health arising from the goitre. As age advances the individual with a goitre is exposed to certain special risks. The gland may continue to enlarge and produce symptoms of pressure on adjacent structures. Degeneration changes may occur in the gland, producing atrophy and varying degrees of deficient thyroid secretion amounting in some cases to myxoedema. Many of the simple goitres become toxic and produce symptoms referable to the heart and the nervous system. The spectre of cretinism is ever before us, though I do not believe it will ever be permitted to be the problem in New Zealand that it is in Switzerland. It is well to remember the French dictum that "Endemic goitre is the stepping-stone to cretinism."

CAUSATION.

Despite centuries of observation and speculation there still exists a sharp division of opinion as to the fundamental cause of goitre. At the recent International Coitre Conference at Berne protagonists were found for many theories. Colonel McCarrison, of the Indian Medical Service, who has devoted over a quarter of a century of work to this subject, even goes so far as to assert that there are at least three different types of simple goitre having distinctive causes. He still maintains that the classical type of goitre of the Himalayas is due to a positive toxic agent derived from the digestive tract. Leon Berard, representing a section of French opinion, maintains that there is a multiplicity of causes, the sum of which disturbs iodine metabolism in the body and produces goitre. He considers that drinking water plays the chief role as the carrier of these unknown factors. The century old theory
of a deficiency of iodine in the food-supply of affected areas received considerable support, notably from Switzerland, America, Norway and New Zealand. This simple theory of causation was first suggested by Prevost in 1849 as a result of his successful treatment of goitre with iodine. Chatin in 1850, as a result of his pioneer studies on the distribution of iodine in nature, independently formulated the same hypothesis. The savants of the day did not consider the theory worthy of serious consideration, so minute were the quantities of iodine involved. For over seventy years the iodine deficiency theory languished. The germ theory of disease, then in its lusty infancy, was receiving increasing attention as the cause of disease. Vitamines, the mineral constituents of the food, and factors of reciprocal balance between food-stuffs, were not as yet considered of importance in diet.

Meanwhile, the significant facts concerning iodine already referred to, viz., the presence of iodine in the thyroid gland in relatively high concentration, the inverse relationship between the amount of iodine in the gland and its functional state, the low iodine content in goitrous glands, and the isolation of thyroxin all contributed to a reconsideration of the simple hypothesis of Prevost and Chatin.

The field evidence in New Zealand early led to a systematic investigation of the iodine-deficiency theory. The reasons which caused the discarding of the current views in favour of this theory have been fully discussed in previous publications (Hercus, Benson and Carter, 1925). If iodine deficiency is the basic cause of endemic goitre in New Zealand, it should be possible to demonstrate an inverse relationship between the incidence of goitre in different localities and the amount of iodine in the soils. It should be possible also to demonstrate that a direct connection is maintained between the iodine content of the various soils and of the vegetable and animal produce grown upon them. The chemical investigations were commenced by Carter in 1922, and were at first confined to determining the iodine present in the form of soluble iodides and iodates in the soils. The refined methods designed for the detection of the minute amounts of iodine present in soil and in biological products which have been elaborated by V. Fellenberg (1923) and by McClendon (1924) had not yet been published. In 1924 Roberts, working with minor modifications of V. Fellenberg's method, determined the iodine content of a wide range of plant and animal foods from goitrous and non-goitrous districts. Full details of the methods and the results have been published. (Hercus and Roberts, 1927.)
Over 500 representative samples of soil were analysed, and though in a preliminary survey of this kind the sampling of different districts could not be regarded as adequate, the analyses showed a wide variation in iodine content ranging from 0 to 700 parts in ten million. Soils derived from the basic igneous rocks contained the most iodine, while sedimentary rocks, especially if sandy or gravelly, contained least. The soils which contained less than one and a-half parts of iodine per million were those derived from mica-schists, greywacke, well leached Tertiary marine sediments and river alluvium. Sandy soils free from humus were iodine-free, while fertile brown or red loams were found to contain the greatest amount.

When these data were correlated with the goitre incidence among school children a very striking inverse relationship appeared, considering the large number of disturbing factors, and this was too consistent to be fortuitous. There were a few important anomalies, such as in North Auckland, Cape Colville Peninsula and Gisborne, where the soil-iodine and the goitre incidence were both low, and in the Waikato and Piako Plains where the soil-iodine was relatively high and the goitre incidence likewise high. More intensive study on similar lines has since been carried out by the Departments of Health and of Scientific and Industrial Research, using Fellenberg’s method for the soil analyses, in which I believe the inverse ratio is again established. The anomalous findings in the Cape Colville Peninsula are receiving further attention.

Analyses of a number of samples of water showed a variation of from 0 to 16 microgrammes per litre. No connection between the iodine-content of the water and the occurrence of goitre could be established.

The following table has been compiled from three years’ studies on the iodine-content of biological products from goitrous and non-goitrous districts.

<table>
<thead>
<tr>
<th>District</th>
<th>Goitre incidence in school children</th>
<th>Soil Iodine in $10^7$ (mean of 9 analyses)</th>
<th>Water Iodine in $10^9$ (mean of 12 analyses)</th>
<th>Foodstuffs Iodine in $10^9$ (mean of 6 analyses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samoa</td>
<td>Nil</td>
<td>285</td>
<td>1.5</td>
<td>394 (mean of 12) 11 (mean of 6)</td>
</tr>
<tr>
<td>Otago</td>
<td>19%</td>
<td>64</td>
<td>2.4</td>
<td>58 (mean of 12) 8 (mean of 9)</td>
</tr>
<tr>
<td>Canterbury</td>
<td>64%</td>
<td>25 (mean of 9)</td>
<td>1.1</td>
<td>41 (mean of 12) 6 (mean of 9)</td>
</tr>
</tbody>
</table>
IODINE IN FOODSTUFFS.

In the course of the work interesting seasonal variations in the iodine content of vegetables were demonstrated. There is a minimum content for grass in September, October and November. It has long been known that there is a seasonal variation in the iodine content of the thyroids of ruminants, and recent work by Dewborn (1929) working in Adelaide under the Animal Products Research Foundation, shows that during these same months the thyroid glands of Victorian sheep show 25% less iodine than the average. From these results it might be expected that a seasonal variation in the size of goitres might be detectable. The unequal distribution of iodine throughout the different parts of various plants has also been noticed. The leaves of turnips were found to contain eight times as much iodine as the roots. Both in fruit and in root vegetables we find that the skin has a higher iodine content than the flesh. Wheat germ was found to contain 40 microgrammes, whereas the white flour contained only 3 microgrammes per kilogramme. Seaweeds were used for the treatment of goitre in the time of Hippocrates (460-361 B.C.), and the element iodine was first discovered by Courtois in 1912 during a chemical examination of the ash of seaweed. Kelp was indeed for many years the principal source of commercial iodine. That different species of seaweed contain very different percentages of iodine has been known for many years, and Cameron (1914) found variations in the iodine content of seaweeds from 0.001 to 0.7 per cent., the species richest in iodine growing below the tidal zone. In the Otago University laboratories a number of iodine determinations on seaweeds have been carried out, particular attention being paid to the Gigartinas, which constitute the principal edible seaweeds; their iodine content has been found to vary between .01 and .03 per cent. The investigation has included the iodine content of diatoms obtained from the sea, from an estuary and from a fresh-water stream. Their iodine contents in microgrammes per kilogramme (dry weight) were found to be 424,800 in the sea diatoms, 96,300 in the brackish water, and 2,679 in the fresh water. The reflection of the iodine of the environment is thus well exemplified. As the iodine content of the sea-water was found to be 18 microgrammes per litre, the astonishing power which the phytoplankton of the sea possesses of concentrating iodine is clearly shown. Fresh water diatoms have also the same power, as the iodine content of the water in which they were growing was only 2 microgrammes per litre. Watercress grown in the same stream gave an iodine content (dry weight) of 1453 microgrammes per kilogramme.
These results may be summarised by stating that marine products are richest in iodine, next in order comes food derived from fresh water, and then come eggs, whole-meal cereal products, leafy vegetables and milk. The iodine content of fruit, root vegetables and refined cereal products is low.

Analytical data on the iodine content of a wide range of animal material, including thyroids, blood, flesh, excretory products, etc., of many animals, goitrous and non-goitrous have been obtained. As in plant life, the iodine content of animal tissues reflects that of the food by which they have been sustained. Thyroid glands of sea-fish were found to contain 0.293 milligrammes per gramme, while the thyroid of a land locked salmon was .139 milligrammes per gramme. The iodine content of the thyroids of rats on low iodine diet was found to be as low as .03 milligrammes per gramme, compared with 0.5 milligrammes per gramme for the thyroid of a rat on a normal diet. Undried oysters were found to contain in microgrammes per kilogramme 880, whitebait 96, tidal water trout 50, fresh water trout 24.

The iodine content of the common Teleosts, which constitute the great majority of the sea fish in daily table use, is being investigated.

There is ample evidence from these researches that the iodine content of animal food products varies with the iodine content of the vegetable products of the district, which, in turn, is dependent upon the iodine available in the soil.

Through the kindness of Dr. Helen Easterfield, the first holder of the Lady King Scholarship, it was possible to compare the iodine content of human milk of mothers in Auckland with those of Dunedin. The Auckland specimens contained more than twice the amount of iodine found in those from Dunedin.

**Summary of Causes.**

When the important and varied functions of the thyroid gland are considered, it is evident that many different demands may induce thyroid enlargement. Many of these demands, such as those occurring at puberty, and in the female during menstruation and in pregnancy, are physiological. Some are of pathological origin, as seen in the enlargement of the gland during certain infections. Such enlargements of the thyroid occur despite the presence of adequate iodine in the food. It is not contended that iodine deficiency is the only cause of goitre in New Zealand, and that these accessory factors cannot produce goitre in isolated cases. The weight of evidence in this country clear-
ly indicates that deficiency of iodine in soil and food supply is the basic cause of the widespread endemic type of goitre occurring in well-marked areas. This somewhat negative conception of the cause of the disease will raise little surprise in the minds of those who are familiar with the valuable work done by members of this Institute on the presence of Xanthin calculi in the kidneys of sheep in the Moutere Hills, where there is a lack of phosphates and lime in the soil, or with the evidence produced by Aston of the relationship of bush sickness to iron deficiency. The importance of apparently trifling deviation from normal in the constitution of various inorganic constituents of food is being increasingly recognised, particularly in connection with New Zealand pastures where mineral deficiency on a large scale has been shown to occur. It cannot be assumed that the inorganic constituents of food are necessarily supplied adequately in an ordinary diet. The history of Osteophagia—that is, eating of bones—among the animals of South Africa supplies what in our opinion is an interesting parallel to goitre in New Zealand. In a valuable review, Green (1925) shows that Osteophagia is due to phosphorus deficiency and to nothing else, and that it can be cured by supplying the deficiency. Animals subjected to lack of phosphates in diet develop a remarkable craving for bones, the only accidentally available source of phosphorus. Animals in our goitrous areas develop a similar craving for soil containing salt and iodine in high concentration (9000 microgrammes per kilogramme). That the instinct is not for the salt alone is shown by exposing salt licks alongside of the soil licks, when the animals prefer the latter. In South Otago it is found that sheep wherever they can gain access to the sea coast show a remarkable craving for seaweed.

**PREVENTIVE MEASURES.**

The problem of prevention is rendered more difficult on account of the painless nature, the insidious onset, and the widespread prevalence of the disease.

If goitre in New Zealand is due fundamentally to iodine deficiency, as the evidence from the field and laboratory studies indicates, it should be possible to prevent the disease by supplying the need. The value of iodine in the prevention of goitre has been abundantly proved on a commercial scale in the prevention of goitre in trout, sheep and pigs. There is sufficient evidence, however, that in man iodine is a double-edged weapon in goitrous districts. Many people with simple goitre have had occasion to regret overdosage with iodine. It is essential that iodine should be supplied in carefully controlled dosage, or better, as a constituent of a natural food. In the course of the
investigations it was found that the mean iodine intake per person on a liberal well-balanced diet in goitre-free Taranaki was 40 microgrammes per day, whereas in Christchurch it was 25 microgrammes, a difference of 15 microgrammes. It is interesting to find that Fellenberg, in a similar study in Switzerland, found differences of intake of 18 microgrammes. The upper limit at which the daily iodine-intake becomes dangerous to individuals with large goitres is estimated by Hotz (1922) to be 700 microgrammes. The preventive problem therefore resolves itself into supplying daily not less than 15 microgrammes of iodine and not more than 700 microgrammes. One ounce of potassium iodide divided amongst the present population of New Zealand daily would supply, roughly, enough iodine for the normal requirements of the thyroid gland. The simplest and most obvious plan would be to follow the example of Japan, where goitre is unknown and where marine products, and particularly edible seaweeds, are in daily use in every household. The freedom from goitre of the coastal tribes of Maoris in pre-European days was doubtless due to their fondness for marine products. Although we live in islands with a coast-line of some 5000 miles the extent to which marine products enter into our food supply is for various reasons very small. Seaweeds do not take any place in the national dietary and, though various cooking experiments carried out in Dunedin on the Gigartinas indicate that a palatable and iodine-rich food can be prepared from them, it is unlikely that their use can become an important factor in the prevention of goitre. Fish and particularly oysters, which are rich in iodine, are too expensive for popular use, though one oyster a day would be a sufficient preventive. The depletion of the fisheries of Hauraki Gulf and Tasman Bay indicates also that our supplies are not inexhaustible, and shows very clearly the need for the control of our fisheries, and for far more research on the distribution of fish in New Zealand waters. One average serving of tinned salmon would supply 50 microgrammes of iodine, and constitutes an excellent source of iodine for country districts. Dried fish is being advocated as a prophylactic in Norway.

If we are unable to supply the deficiency from foodstuffs naturally rich in iodine, the restoration of the iodine to the depleted soil by means of iodine-rich manures would appear to be the logical method of attack.

This aspect of the problem has received a considerable amount of attention. The iodine content of all the artificial manures in common use in New Zealand has been determined, and an endeavour has been made to estimate to what extent iodine-rich manures can increase the iodine-content
of plants. It is evident that there are many factors which are capable of affecting these experiments. The nature of the soil, particularly as regards its absorptive powers and its reaction, are of fundamental importance. The results of the use of iodide of potassium and various iodine-rich manures have been already published (Hercus and Roberts, 1927). The addition of 1 gram of potassium iodide per square yard increased the iodine content of lettuces fourfold and of turnip-roots fivefold. Chilean nitrate, 10 grams to the square yard, increased the iodine in the leafy tops of immature turnips from 28 to 40 microgrammes per kilogramme (fresh weight). Further work on dried seaweed with an iodine content of 48,000 microgrammes per kilogramme in the proportion of 1 cwt. per acre did not increase the iodine content of grass or silver beet. Four months elapsed between the manuring and the collection of the samples, which may have been insufficient for the liberation of the organic iodine. Fish manure containing 1200 microgrammes per kilogramme was also found to give negative results.

Further experiments on the influence of various commercial manures on the iodine content of grass have been carried out at Lincoln Agricultural College, thanks to the kindness of the Director, Mr. R. E. Alexander. No definite relationship has been established from these investigations, which may be due to the fact that the soil conditions render the iodine unavailable. These experiments require more detailed study, as do the various factors which control the increase and decrease in the iodine content of the soil.

It is of interest to reflect on the possibility of iodine in sufficient concentration being as essential to the healthy growth of plants as to that of animals. In soils deficient in iodine it may be that maximum yields of crops are not obtained. When it is realised that grass is the raw material for 94% of our total exports, and that much of it is grown in districts where soil iodine is deficient, the possible significance of the problem is indicated. The Department of Scientific and Industrial Research is at present carrying out further investigation on the subject.

Orr, Kelly and Stuart (1928) found that the addition of iodine to the extent of 0.0001 grammes per litre to culture solution in which peas were grown increased the weight of the plants by 5 to 10%. Stoklasa (1926) finds that plants differ in their reaction to iodine according to species. He has devoted much attention to the effect of iodine on sugar beet and finds results of economic importance. The total sugar yield was found to be increased by about one-third. In soils with an iodine-content below
the optimum, manuring with Chilean nitrate gives better results with sugar beet than an equivalent amount of nitrogen in other fertilizers, which Stoklasa attributes to the iodine factor. Further work on these lines is indicated, particularly with regard to pastures. Stoklasa has found that iodine has a favourable effect on the formation of root nodules in the Leguminosae, the growth of the nitrogen-fixing micro-organisms in these nodules being markedly accelerated.

The final method of prophylaxis to consider is the addition of a prescribed quantity of iodine to some article of diet in universal use. Common salt, to which a trace of iodide of potassium has been added, would appear to be the most suitable means of restoring the deficient element. The method is in extensive use in Europe and America, and to a certain extent in New Zealand. After five years' experience, Austria reports most favourably on the results. Since 1924, when the New Zealand branch of the British Medical Association urged the Government to introduce iodised salt into endemic areas, this method has been available in New Zealand. The amount of iodine in the salt is .0004% or one part of potassium iodide in 250,000 parts, which is calculated to supplement the intake of the average individual by some 38 microgrammes. To accomplish this it is essential that the iodised salt be used for both cooking and table purposes.

It is too soon to make any definite statement as to the results of preventive measures, though in certain controlled observations in Dunedin the evidence of the value of the method, both in prevention and in treatment, are undoubted. It is disappointing to find that in spite of the propaganda by the Department of Health and the medical profession, the importation of iodised salt is less than one-sixth of the actual domestic requirements of the people. If the importations of iodised salt into the North and South Islands for 1928 are considered separately, it is seen that the North Island with two-thirds of the total population imported 3154 cwt., the South Island 6874 cwt. As each person requires approximately five lb. of salt per year it will be seen that the North Island is importing only sufficient salt for approximately 8% of the population as against 30% for the South Island. There is ample scope for more extensive educational propaganda in this campaign to restore to our national dietary an inorganic food-stuff of the greatest importance.
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GOITRE INCIDENCE.

- OVER 40%.
- UNDER 5%.
- SOIL SAMPLES.