

## ENDEMIC GOITRE IN THE SOUTH-WEST PACIFIC

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THE term "endemic" is applied to a disease which is more or less constantly present in a locality. It was Hippocrates who first made the distinction between endemic and epidemic diseases. In "Air Waters and Places" he observes that the endemic diseases of different places differ and he set himself the task of studying the factors of local endemicity.

Goitre occurs endemically in many parts of the world, and it has been termed "the endemic disease par excellence." Etymologically, the term endemic goitre should include in New Zealand at least toxic goitres, but usage has determined that the term "endemic goitre" should be limited to the so-called "simple" enlargements of the thyroid gland; the simplicity, however, is more apparent than real. All too commonly this simple enlargement leads on to impairment of health.

### *Distribution of Simple Goitre in the South-west Pacific Area.*

Outside of New Zealand and the Singatoka Valley of Fiji I know of no area of endemicity in the South-west Pacific. Occasional sporadic cases of simple goitre have been reported from Samoa and the Cook Islands, but the incidence is so low as to merit the term goitre-free being applied to these islands. The Singatoka is the second largest river of Viti Levu. It has a course of a hundred miles and runs into the sea on the south coast. It is an extremely fertile valley and many villages containing both Fijians and Indians are dotted along its banks. Simple goitre is endemic in both races except in the Fijian villages near the mouth of the river, where much sea-food is eaten. The Indians in the valley are using exactly the same dietary as Indians living in other river valleys in Fiji in which goitre is not endemic. This information was obtained by Drs. Dovi, Satyanand and Sahu Khan, Fijian graduates of the Otago Medical School, who carried out these studies during their fifth year of undergraduate work.

The distribution of simple goitre in New Zealand is too well known to warrant detailed description. Speaking generally, our immature, recently deposited soils predispose to the development of goitre, and all parts of New Zealand can be said to be goitrous. There is no evidence to suggest that the endemic areas have altered since the earlier surveys on school children were carried out, though the incidence has decreased substantially since iodine prophylaxis has exerted its effect. There have been no recent reports of fluctuations in incidence such as were reported by Mecredy in the Taranaki district in 1933. The localisation of the endemic areas appears therefore to be relatively stable. The incidence of simple enlargements of the thyroid in the people of New Zealand remains unduly high and contrasts sharply with the position in the Island Dependencies and in the mandated territory of Western Samoa.

### *Environmental Factors Determining the Geographical Distribution.*

Since Prévost in 1830 put forward the theory that goitre was due to a lack of iodine in the environment there has been continued dispute as to the rôle which iodine-lack may play in the causation of endemic goitre. It is salutary to find in a recent number of the *Journal of Clinical Endocrinology*, an American chemist, Greenwald, answering his own question, "Is endemic goitre due to a lack of iodine?" in the negative and concluding that "Endemic goitre is not due to a lack of iodine."

It would not be profitable at this time for me to attempt to follow in detail the evidence which leads him to this conclusion. There are many fallacies in his logic, but he has done a service in drawing attention to weak links in the chain of evidence which supports Marine's original contention that "the immediate cause of thyroid enlargement is a relative or absolute deficiency of iodine." Let us briefly review the supporting evidence on which the iodine-deficiency theory stands, always remembering the fallacy of denying the operation of one cause of a phenomenon because another cause is found to operate. There are four lines of evidence which point to the conclusion that iodine deficiency plays a pre-eminent part in the causation of goitre. The first is physiological, iodine is an essential component of the active principle of the thyroid—65 per cent. of the thyroxin molecule is iodine. Baumann's isolation of iodine from the thyroid gland in 1895 and Kendall's discovery that the iodine was linked with an amino-acid (tyrosine) and that this substance had a high degree of physiological activity, provide the final proof of the essential rôle that iodine plays in the

activity of the thyroid. Iodine deficiency therefore must produce some disturbance if the deficiency is sufficiently severe.

The second line of evidence may be termed anatomical. Marine, in 1909, showed that the iodine-content of thyroid glands varied inversely with the degree of hyperplasia; that as soon as the iodine-content fell below a certain critical level, hyperplasia became detectable histologically. He also demonstrated experimentally the effects of the administration and the withdrawal of iodine on the histological structure of the thyroids of dogs. In other words a low iodine intake experimentally leads to thyroid hyperplasia.

The prophylactic value of iodine in the prevention of goitre, shown first in 1910 by Marine and Lenhart in the case of brook trout and later by Marine in the prevention of human goitre in Ohio, and since widely instituted in many goitrous districts, may be regarded as support for the etiological importance of iodine in goitre. Even the opponents concede the prophylactic value of iodine, but they make the reservation that iodine prevents the disease not by remedying a deficiency of iodine in the diet, but by drug action.

The final evidence comes from field and laboratory investigations. If iodine plays the decisive rôle in the causation of goitre which is claimed for it, it should be possible to demonstrate a negative correlation between the iodine level of the environment and the occurrence of simple goitre. It is here that the weakest links in the chain can be found, and it is here that Greenwald makes his most effective attack. There are inherent weaknesses present both in the accurate determination of minute quantities of iodine in biological material and in the appraisalment of the extent of the endemic. The assessment of the extent of thyroid enlargement is based solely on the opinion of the observer and as in other nutritional studies, great variations in assessment occur not only with different observers but with the same observer at different times. Since the early work on the estimation of iodine in organic material, more accurate methods have been devised, but the iodine intake in endemic and non-endemic areas has not yet been determined by these improved methods.

Chatin in 1850 was the first to claim that there was a negative correlation between the iodine intake and the incidence of goitre. His claim was disregarded. Von Fellenberg in 1923 and 1924, using improved methods of iodine analysis, produced better evidence for this negative correlation. Our work here in New Zealand and Samoa supported these findings. Owing to the difficulties of accurate determination of the iodine-content of foodstuffs we found that a more practical method was to measure the iodine excretion in a 24-hour specimen of urine. Representing as it does a large fraction of the iodine actually absorbed from the food, it provides a means of estimating the level of iodine available to the thyroid.

The results of our studies on iodine excretion in the urine showed that for New Zealand the average daily urinary iodine excretion was 65 micrograms. For Australia, Abaiang (Gilbert Islands) and Samoa the combined average was 165 micrograms. The lowest value obtained in a goitre-free area was in Abaiang, where the average was 114 micrograms.

This evidence supports the iodine-deficiency theory and suggests that to prevent goitre developing the iodine intake should be at a level which will produce a urinary excretion of about 110 micrograms per day.

A multitude of known and unknown factors play upon the thyroid gland. New knowledge has revealed the importance of the *relative* deficiency in iodine. New compounds have been found which possess antithyroid properties. The thiourea group of drugs interfere with the synthesis of thyroxine and lead to marked hyperplasia of the gland. Age and sex-genetic factors all play a rôle in the causation of goitre. The recognition of these facts does not affect the positive finding that iodine lack is an immediate cause of goitre.

#### DISCUSSION.

Mr. Fleischl inquired concerning Government action to ensure iodisation of salt. Dr. Dempster pointed out that a recent survey by the Health Department of the usage in the community of iodised salt, showed that in various districts up to 90 per cent. of the salt used was iodised, though in other areas it was much less.

Mr. Ferguson asked if there was any difference in the value of "natural" iodine products as opposed to inorganic chemical compounds like sodium or potassium iodides, when given therapeutically. Sir Charles in reply stated that

sodium and potassium iodides were very soluble and were known to be entirely absorbed, whereas the amount of iodine actually absorbed from the so-called natural sources could not be so accurately estimated.

In reply to a question by Dr. Hubert Smith on the value of salt obtained from sea water, Sir Charles stated that the amount of natural iodides therein was extremely small, but the iodine concentration power of various plankton was very great, and thus the amount of iodine available from evaporating sea water would essentially depend upon the amount of contaminating plankton in the salt obtained therefrom.

## PROTEIN AND AMINO ACID THERAPY IN MEDICAL AND SURGICAL CONDITIONS—A REVIEW

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WE may summarise the purposes of protein in the body as follows:—

For growth.

For repair, including that in current daily metabolic degradations and that in diseased processes.

For the formation of enzymes for digestion, muscular movement, secretion and excretion.

For the production of antibodies such as gamma globulin.

For the manufacture of hormones.

For enabling the liver to form plasma proteins, important in maintaining the water balance and the circulatory pressure.

For detoxifying certain poisons.

For forming the blood-pigment haemoglobin.

For chromosomes, and therefore for breeding and heredity.

It has been well expressed by Fox (1947) that proteins are not only the building material but also the workmen that do the building and the repairing.

Recent advances in the knowledge of the biochemistry of the proteins have established the fact that our body proteins are far from being static. We have previously imagined them to be stabilised in the structure of the muscle or the gland or other body tissue, or circulating as blood plasma in a closed system. Our only additional concept in the past has been that there is a certain amount of "wear and tear," terms of which we did not know the real meaning. We have known, too, that body protein is utilised for fuel when, during starvation, the stores of carbohydrate and fat have been exhausted. We have also said, with a hazy idea of its meaning, that protein is used for repair of the tissues.

But no one had any idea of the extent of the losses of body protein that were required for repair until, of recent years, measurements were made of the nitrogen excretion following burns or fractures or operations or of the volume of fluid and of protein lost from the blood when such an irritant as lewisite had been dropped on the skin and caused it to blister.

The use of plasma has been an effective form of protein therapy in burns, both thermal and chemical, and in a variety of acute medical and surgical conditions. This form of therapy is now familiar to all of us.

What is less familiar is the more gradual and less perceptible loss of protein that occurs with any form of injury, whether from the agency of bacterial toxins, or of an invading carcinoma, or of a mere break in the continuity of the tissue caused by a fracture or by the surgeon's scalpel. To understand the phenomenon of daily wear and tear of protein in the body, or of repair in injured tissues, we must get back to the modern concept of body protein as being in a constant state of change. This perpetual state of activity on the part of our body proteins has been revealed by Schoenheimer (1942), who used the method of marking or tagging with the isotope of nitrogen ( $N^{15}$ ), preparing synthetic amino-acids with it to