WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTÉ

REGIONAL OFFICE FOR THE WESTERN PACIFIC
BUREAU RÉGIONAL DU PACIFIQUE OCCIDENTAL

REGIONAL COMMITTEE

Seventeenth Session
Manila
21-27 September 1966

WPR/RC17/9
1 July 1966

ORIGINAL: ENGLISH

Provisional agenda item 16

THE EPIDEMIOLOGY OF ENDEMIC GOITRE IN THE WESTERN PACIFIC REGION*

1 PREVALENCE AND GEOGRAPHICAL DISTRIBUTION OF ENDEMIC GOITRE

1.1 General

Goitre occurs with varying intensity in almost every country; few countries appear to be entirely free from it. It usually occurs quite independently of climate, season or weather. Moreover, in its incidence goitre makes no distinction of race, nationality, colour, creed or class.

Without doubt the most notorious goitre centres of the world are located in high mountain regions, but goitre is also known to occur with considerable intensity in comparatively low-lying areas and even at sea level.

Students of iodine geochemistry have a ready explanation for these diverse phenomena. They say that the types of terrain in which goitre is for the most part found, be they at high altitude or low, are just those which have been subjected either to flooding or to intense glaciation and from which most of the soil iodine has been washed out and carried through the rivers to the sea. During the last Ice Age, earlier soils were swept away and new soil-making materials were generated by the grinding-up of virgin crystalline rock containing, at the most, one-tenth the average iodine content of mature agricultural soils.

The number of goitrous people in the world is not known; but if the statistics available for some countries may be taken as a guide, the total is probably not far short of 200 million. Although the geographical distribution of goitre has not apparently altered in the last hundred years, the intensity of the disease has substantially declined in certain countries. The endemics in Switzerland, the United States of America and New Zealand, for example, have been largely eliminated within the past

/thirty-five ...

*Largely extracted from Endemic Goitre, Geneva (World Health Organization: Monograph Series No. 44, 1960).

thirty-five years through the prophylactic use of iodized salt. Nevertheless, there are countries where the prevalence of goitre is exceedingly high and a matter of serious public concern, and many others where the people live so near the critical level of iodine intake that whenever the slender resources of the thyroid gland are abnormally taxed, as, for example, during the nutritional privations of war, epidemic outbreaks of goitre result.

In the Western Pacific Region the following countries and territories have been listed as the ones where the occurrence of endemic goitre has been recorded: Australia, Cambodia, China (Taiwan), Cook Islands, Fiji, Japan, Laos, Malaysia, New Guinea, New Zealand, Philippines, Republic of Korea, Republic of Viet-Nam, Samoa and Tonga.

1.2 Australia

Australia and New Zealand are among the countries in which the frequency distribution of goitre may be correlated with the areas and extent of quaternary glaciation where soils have not been sufficiently saturated with postglacial air-borne oceanic iodine. Examination of 75 000 children in New South Wales revealed considerable areas of goitrous country in the Great Dividing Range. In 1947 the city of Canberra was found to be in a goitrous area. Gippsland at the south-eastern end of Victoria is the home of goitre in this State. In Bairnsdale, one of the chief towns of Gippsland, rates of 20% to 33% in boys and of 32% to 47% in girls, were recorded, the maximum rate in boys being in the 9-11 years' age-group, whilst in girls maximum intensity occurred between 12 and 14 years of age. The only endemic goitre area in the state of South Australia lies in the Adelaide Hills.

Practically the whole of Tasmania is goitrous. In 1949 Clements examined 8000 schoolchildren and found visible goitres in approximately 6% of boys and 20% of girls in the age-group 12-14 years. Iodine therapy did not control goitres in some areas. Clements and Wishart later suspected a goitrogenic substance in cow's milk which interfered with the synthesis of thyroxine and so the subjects drinking that milk were not amenable to the standard iodine preventive measures. The goitrogenic substance was consumed by cows feeding on pastures containing a certain variety of Brassica; the children were being given increased quantities of milk under a free milk scheme. Later, a goitrogenic iso-thiocyanate was isolated from these plants and the milk of the cows eating them (Bachelard and Trikojus, 1960).

1.3 China (Taiwan)

Goitre is exceedingly common in Taiwan, the overall prevalence based on 318 116 individuals examined in 1940 being 8.5%. An affected area in the northern part of Taiwan had a rate of 26.4% in 1941. A Japanese worker considered that mere deficiency was not entirely responsible for the high prevalence and that geochemical and climatic factors which raise the demand for iodine must also be taken into account.

/1.4 Japan ...

1.4 Japan

There is general agreement that simple goitre is not a problem of any magnitude in the main islands of Japan. However, the country is not by any means free from simple goitre. Rates of 11.1% and 22.4% have been recorded for the Gunma and Shizuoka Prefectures. A rate of 50% was found among 2434 girls and young women, of ages 13 to 26 years, in Gifu Prefecture in central Japan. Goitre foci are known also in Hokkaido. Shikoku island contains a markedly endemic area in Ehime Prefecture to the west. On Kyushu, a similar area is found in Wakamatsu. Heavy losses of newborn lambs and kids in Nagano during recent years are attributed to iodine deficiency.

1.5 Malaysia

Visible thyroid glands are common in most undeveloped mountainous inland areas of Malaya, the overall rate being about 40%. In the northern third of Malaya, the areas chiefly affected are the hills and valleys of Kedah and Upper Perak. By comparison, the rate among communities near the sea is only between 1% and 2%.

Goitre is endemic over a large area of Sabah. In Sarawak, the disease is common in certain inland areas, sometimes to a serious extent, whereas other inland areas not far distant are completely non-goitrous. This immunity applied particularly to the upper Baram river district in the interior of the 4th and 5th Divisions of Sarawak where the people are goitre-free because they use an iodine-rich salt derived from local salt springs.

1.6 New Zealand

Goitre is endemic in both the North and South Islands and affects Maoris and Europeans alike. Before the introduction of iodized salt on a voluntary basis in 1924, Otago and Southland showed an average goitre rate of 26% rising to 30% and 40% in the Taieri and Clutha valleys west and south-west of Dunedin. The North Island Provincial Districts of Wellington, Taranaki and Hawke's Bay had an average goitre rate of 21% while in a west coastal county the rate reached 46%.

Broadly speaking it was found that in New Zealand iodine is lowest and goitre highest on all clayless sandy soils and gravels from which iodine is easily leached out by weathering.

1.7 Papua and New Guinea

In 1936 Clements found that the distribution of goitre throughout New Guinea was patchy and highly localized. In 1959 McCullagh confirmed the wide distribution of goitre throughout the Territory. He estimated that at least one third of the 300 000 people who lived in the goitre areas actually developed the disease. A substantial degree of control was successfully achieved by intramuscular injections of iodized oil.

/This method ...

This method was preferred because little salt is available to or consumed by the villagers in remote areas. It seems quite effective on a long-term basis (Buttfield et al., 1965).

1.8 Philippines

According to Miller, the Filipinos show the highest goitre frequency of any people residing in the Orient. Goitre is found in nearly all the provinces, the chief goitre region being the province of Nueva Ecija in central Luzon where the twin municipalities of Penaranda and Papaya are notorious as the home of goitre in the Philippines.

1.9 Republic of Korea

Apparently the only part of Korea where goitre is endemic is the Kangai neighbourhood in the northern hilly section of the country. A nutritional survey of Korean military forces conducted in 1956 disclosed virtually no evidence of goitre. Palpable thyroid enlargement was observed in only 0.8% of individuals examined.

1.10 South Pacific Islands

Absolute proof that goitre can be endemic in an extreme maritime environment is found in the South Pacific. Proximity to the sea does not necessarily protect all the peoples inhabiting these islands. The disease occurs in Fiji and cases have been reported from Tonga, Samoa and the Cook Islands.

2 ETIOLOGY OF ENDEMIC GOITRE

Goitre is produced by a mechanism in which the anterior lobe of the pituitary is concerned as well as the thyroid gland, which is acted on by pituitary thyrotropic or thyroid-stimulating hormone (TSH). Since the secretion of TSH is regulated by thyroxine and its analogues, thyroid-pituitary interaction dominates the pathogenesis of goitre. Decrease in thyroid hormone secretion brings about increased secretion of TSH which, in normal subjects, re-establishes the production of the thyroid hormones and their release into the circulation in normal amounts. In turn the thyroid hormones inhibit the production of TSH. Such a self-regulating mechanism ensures a physiological balance in the secretory activity of the thyroid only if the latter responds adequately to TSH, which seems to activate simultaneously all stages of the biosynthesis and secretion of the thyroid hormones. A permanent falling off of thyroid activity results in hypertrophy and hyperplasia of the gland, which, initially at least, are compensatory processes. In experimental goitre no further changes take place. In the endemic disease, however, these reactions are succeeded by regression of the hyperplastic gland (exhaustion atrophy), a phenomenon characterized by the appearance of vesicles full of colloid, with the epithelium in the resting stage. It follows that the etiological study of endemic goitre

/should take ...

should take into account disorders in the pituitary secretion of TSH and in the biosynthesis and secretion of the thyroid hormones, as well as the response of the gland to prolonged disturbances of endocrine functions.

The opinion that endemic goitre is due to, or closely linked with, iodine deficiency is very widely held. Regions where air, water, soil, and consequently foodstuffs are poor in iodine are almost always the site of endemic goitre, and only under rather special conditions does it occur outside regions where the diet is deficient in iodides. Nevertheless, it does not follow that endemic goitre is caused solely by iodine deficiency. The addition of iodides in a quantity not exceeding normal requirements to the foods of persons living in an endemic region is frequently not enough to prevent goitre formation, and this shows the multiplicity of the etiological factors involved. Although it is difficult to state the exact iodine needs of human adults, it is certain that they increase during pregnancy and lactation. Moreover, milk is poor in iodine. The thyroid becomes enlarged in pregnant women and the foetus, as well as in nursing mothers and the new-born baby, if the maternal diet does not include an adequate amount of iodine. This hypertrophy rapidly regresses on the administration of iodides, and is not seen at all if iodine is given prophylactically. However, the action of certain goitrogenic thiourea derivatives in food is not inhibited by the ingestion of iodides, so that under conditions where goitre is associated with the consumption of foods rich in such substances, it cannot be prevented with certainty by the administration of iodized salt.

The observations showing most clearly that the goitrogens in the diet are a definite etiological factor in human goitre are undoubtedly those of Clements and Clements and Wishart. These authors showed that in certain parts of Australia and Tasmania, children drinking milk from cows fed on marrowstem kale developed goitres which cannot be prevented by the administration of 10 mg of potassium iodide weekly. The presence of a very active goitrogen (an iso-thiocyanate) was demonstrated by Bachelard and Trikojus (1960) in the milk of these cows and in the marrowstem kale (a Brassica species) they eat when thyroid hypertrophy was induced experimentally by adding either this milk or the kale to the diet of calves and rats. The uptake of radioiodine by the thyroid gland decreased greatly after consumption of milk from cows fed on this type of kale. Leaves of sweet potatoes, consumed in large quantities in certain parts of New Guinea were also suspected of goitrogenic action by Gajdusek (1962).

In conclusion, it might be stated that the etiology of endemic goitre involves many factors, whose nature and mode of action have not been completely defined. It is certain that iodine deficiency in the diet plays an important part in most cases but it cannot be taken as certain that it is the primary cause of goitre, despite the obvious preventive effect of iodized salt. Dietary, or possibly, bacterial, goitrogens exercise a more direct action on the thyroid, inhibiting iodine metabolism in the gland. Other dietary factors may complicate the picture, but the role of these factors appears to be a subordinate one. In addition, genetic factors may intervene, particularly in regions where

/endemic goitre ...

endemic goitre has persisted for generations. These genetic factors may cause, inter alia, a decrease in thyroid functional capacity or faulty renal tubular re-absorption of iodide. There is also a partial correlation between cretinism, deaf-mutism and other neurological abnormalities in some goitrous regions (Gajdusek, 1962; McCullagh, 1963).

Endemic goitre necessarily involves alteration in thyroid iodine metabolism and a group of processes tending to compensate for this. But various factors, including the consumption of goitrogenic products, may also directly or indirectly impair thyroid functions. The origin of endemic goitre remains complex.

3 PROPHYLAXIS OF ENDEMIC GOITRE

3.1 Principle of Prevention

It has often been stated that successful prevention of any disease depends upon a thorough understanding of its etiology and epidemiology. It is now recognized that goitrogenic factors in food may be responsible for iodine-refractory endemic goitre and that excessive intake of calcium salts can be goitrogenic. But none of these advances has shaken the fundamental principle of the mass prophylaxis of endemic goitre, which is to increase the intake of iodine, within limits of safety, to ensure that it not only makes good the deficient intake but also, where possible, overcomes the effects of any goitrogenic factors present.

It is needless to emphasize that any large-scale programme of goitre prevention should be preceded by a study of the etiology of the disease and an assessment of the degree of iodine deficiency in that area. There may be situations where the intake of iodine per se is adequate, but where goitre is still prevalent because of other factors, for example, excessive hardness of drinking-water. In such cases it may be possible to reduce the incidence of goitre by changing the water-supply from hard to soft water without increasing the intake of iodine.

3.2 Medium for Supplementary Iodine

It is generally accepted that the most practical method of providing supplementary iodine is iodization of salt. Other methods have been tried from time to time, such as the iodization of water-supplies, the iodization of bread, and the periodical administration of iodide tablets and sweets for the protection of vulnerable groups of the population, but these methods for one reason or another have not proved to be satisfactory.

3.3 Level of Iodization of Salt

In deciding upon the level of iodization of salt to be adopted in any area, the following factors must be taken into consideration: the normal requirements of iodine, the intensity of the environmental iodine deficiency, the presence of goitrogenic factors, if any, and the daily per caput consumption of salt.

/The WHO Study ...

The WHO Study Group on Endemic Goitre recommended in 1952 that on the assumption that the daily consumption of salt is about 10 g and the salt is dry and pure, it would be advisable to iodize the salt with potassium iodide at a concentration of 1 part of iodide in 100 000 parts of salt. The Study Group also stated that where the daily consumption of salt has been shown to be significantly different from the above figure of 10 g, suitable adjustments should be made in the concentration of the iodine compound added. According to these recommendations, an individual is expected to receive about 76 ug of iodine daily from salt alone.

Concerning suggestions for other levels of iodization, Marine, the pioneer of iodine prophylaxis, made the following statement in 1954: "Since the dangers of Jod-Basedow are serious in endemic goitre regions with a high incidence of advanced adenomatous goitre, it would seem advisable to use (as Switzerland has) a conservative iodide supplement (1: 100 000) rather than greater concentrations." It should be emphasized, however, that suitable adjustments of these levels should be made according to local conditions. Indeed, it is believed that in the present state of knowledge it may be advisable to use different levels of iodization in different countries, and even within the same country, to assess their relative efficacy in controlling goitre.

3.4 Iodine Compound for Iodization of Salt

In selecting the level of iodization of salt a factor of great importance is the purity of the salt. In large parts of the world where goitre is endemic the salt habitually used for domestic consumption is unrefined and has a relatively high moisture content. Until very recently, the iodine compound used for fortification was either sodium or potassium iodide, more commonly the latter because it is less hygroscopic. It is now known that the impurities and moisture in unrefined salts facilitate the breakdown of iodides, with resultant loss of iodine. When using iodides for the fortification of unrefined salt, therefore, consideration must be given to the amount of iodine that is likely to be lost during storage and suitable adjustments must be made in the level of iodization. It has been shown that potassium iodate is the compound of choice for iodizing such salts, since it is far more stable than the iodide and has a wide margin of safety. It is important to remember, however, that potassium iodate contains only 59.3% of iodine whereas potassium iodide contains 76.45%. Thus a salt containing 1 part of potassium iodide in 100 000 parts is equivalent in its iodine content to one containing 1 part of potassium iodate in 78 000 parts of salt.

4 PILOT PROJECTS IN GOITRE CONTROL

An outstandingly well controlled study on the prevention of endemic goitre in the Himalayas is reported by Sooch and Ramalingaswami (1965). The prevalence of goitre was effectively reduced by either potassium iodide (1 part in 50 000 parts of salt) or potassium iodate (1 part in 40 000 parts of salt). With a salt consumption of 15 g daily, this

/added an ...

added an estimated 229 ug and 223 ug of iodine respectively to the daily diet. Potassium iodate showed some slight superiority. There were no toxic reactions.

In the Western Pacific Region, the main goitre control projects are in China (Taiwan) (using iodized salt), Australia (iodine fortification of bread in Canberra) and New Guinea (iodized oil injections). Good control of goitre has been observed in all these areas but documentation is incomplete.

REFERENCES

Bachelard, H.S. and Trikojus, V.M. (1960) Nature (Lond.), 185, 80.

Buttfield, I.H., Black, M.L., Mason, E.K., Hoffmann, M.J. and Hetzel, B.S. (1965) Lancet, ii, 767.

Clements, F.W. (1936) Med. J. Aust., i, 451.

Clements, F.W. and Wishart, J.W. (1956) Metabolism, 5, 623.

Gajdusek, D.C. (1962) Pediatrics, 29, 345 (357).

McCullagh, S.F. (1963) Med. J. Aust., i, 505 and 769

Marine, D. (1924) Medicine (Baltimore), 3, 453.

Miller, H.W. (1929) Chin. Med. J., 43, 226

Miller, H.W. (1933) Chin. Med. J., 47, 953.

Sooch, S.S. and Ramalingaswami, V. (1965) Bull. Wld Hlth Org., 32, 299

Trotter, W.R. (1960) Brit. Med. Bull., 16, 92.