
ENDEMIC GOITER

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Reprinted from NUTRITION REVIEWS
Vol. 15, No. 6, June, 1957
Printed in U.S.A.

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The prevalence of endemic goiter has decreased so markedly in the United States in recent years that it now receives relatively little attention. In Michigan, for example, 38.6 per cent of school children showed goiter in 1924 and only 1.4 per cent in 1951 (B. E. Brush and J. K. Altland, *J. Clin. Endocrinol. Metab.* **12**, 1380 (1952)). In Ohio the incidence of goiter has recently been found to have declined from 32.3 per cent in 1925 to 4.0 per cent in 1954 (G. J. Hamwi, A. W. Van Fossen, R. E. Whetstone, and I. Williams, *Am. J. Pub. Health* **45**, 1344 (1955)).

Although the widespread use of iodized salt is believed to have had a major influence in the decline of goiter in the United States, other factors were also involved. A food marketing system has developed which introduces food from areas with adequate iodine into those in which it is deficient. There have also been trends toward an increased consumption of sea food and other changes in dietary habits which might be expected to reduce the likelihood of iodine deficiency.

While endemic goiter is no longer a major problem in the United States, it is still a widespread public health menace in many other parts of the world. It is characteristic that the true prevalence of goiter is rarely suspected until specific surveys are done, and thus not all goitrous areas have been identified. This has been the recent experience of a number of Latin American countries which did not recognize their serious goiter problem until surveys were done. In the Central American area, the incidence of goiter in the rural school children of El Salvador was found to be 29 per cent (A. Cabezas, T. Pineda, and N. S. Scrimshaw, *Am. J. Pub. Health* **43**, 265 (1953)), in the school children of Honduras, 29 per cent (E. A. Borjas and Scrimshaw, *Ibid.* **44**, 1411

(1954)), in adults in one province in Panama, 47 per cent (J. M. Reverte, *Arch. Med. Panameños* **3**, 121 (1954)), in school children in Costa Rica, 17 per cent (C. Pérez, A. Salazar-Baldioceda, O. B. Tandon, and Scrimshaw, *Am. J. Pub. Health* **46**, 1283 (1956)), in children and adults in Guatemala, 38 per cent (J. A. Muñoz, Pérez, and Scrimshaw, *Am. J. Trop. Med. Hyg.* **4**, 963 (1955)) and most recently in the population of Nicaragua, 28 per cent (A. Arce Paiz and Pérez, *Boletín Sanitario de Nicaragua*, p. 53, July 1956).

In South America the incidence in the school children of Colombia has been reported to be 53 per cent (J. Góngora y López, N. Young, and A. Iregui Borda, *Revista de Higiene (Colombia)* **24**, 291 (1950)). In Peru, S. T. Salazar ("Bocio Endémico en el Perú", *Lima, Peru* (1952)) finds an incidence of 36 per cent in men and 64 per cent in women. Endemic goiter is also known to be a public health problem in areas of Argentina, Brazil, Bolivia, Chile, Ecuador, Mexico, Paraguay and Venezuela (N. S. Scrimshaw, *Bol. Of. San. Pan.* **34**, 277 (1954)).

Authoritative information on the public health consequences of goiter is much more difficult to obtain than incidence figures. The reports cited above from Panama and Peru mention that cases of cretinism were observed. In most of these countries the incidence of deaf-mutism and feeble-mindedness is reported to be relatively high, but no causal relationship to endemic goiter has been definitely proved. Direct evidence of the adverse consequences of endemic goiter has come from Australia, where F. W. Clements (*Med. J. Australia*, p. 894, Dec. 4, 1954) has observed an increased incidence of thyrotoxicosis in goitrous areas and a drop in thyrotoxicosis paralleling a drop in endemic goiter. Since J. E. Sokal (*J. Am. Med.*

Assn. **154**, 1321 (1954)) has shown that thyroid cancer arises more frequently in toxic than in nontoxic goiter, the sequence of at least some of the cases of endemic goiter would seem to be the development of thyrotoxicosis and subsequently of cancer.

There is abundant evidence that adding very small quantities of iodine to salt is effective in eliminating goiter as a public health problem. The classic studies in Switzerland are generally considered to have established this point (H. Eggenberger, *Tr. Third International Goitre Conference* (1938)). Iodized salt has played an important role in reducing goiter in Michigan and Ohio. In the Ohio study, children not receiving iodized salt had nearly twice the incidence of enlarged thyroid glands (6.06 per cent) as children whose history showed regular usage of the iodized product. In an earlier survey in Michigan, O. P. Kimball (*Ohio State Med. J.* **35**, 705 (1939)) found that the over-all incidence of goiter in children had dropped from 38.6 per cent in 1924 to 8.2 per cent, while in those using iodized salt regularly it was only 2.9 per cent.

Any doubts as to the effectiveness of salt iodization should be removed by the results obtained in the department of Caldas, Colombia (J. Góngora y López and F. Mejía, Caicedo, *Med. y Cirugia (Colombia)* **16**, 357 (1952)), where the use of salt iodized at a level of 1 part of iodine in 20,000 parts of salt caused the incidence of goiter in school children to drop from 83 per cent to 34 per cent in two years. H. H. Stacpoole (*Bull. World Health Organization* **9**, 283 (1953)) showed that there was a drop in goiter incidence in a district in Mexico when candies containing 10 mg. of potassium iodide were given weekly to school children.

In field trials carried out by INCAP (N. S. Scrimshaw, A. Cabezas, F. Castillo, and J. Méndez, *Lancet* **I**, 166 (1953)) a tablet was given weekly to simulate the approximately 5 mg. of iodine ingested when salt is iodized at the level of 1 part in 10,000. Control groups given a placebo showed no

change in incidence. These studies, carried out in 661 children in El Salvador and 159 in Guatemala, showed both potassium iodide and potassium iodate to be effective in lowering markedly the incidence of goiter in school children. The average incidence of goiter, which varied initially from 30 to 55 per cent, decreased 42 per cent in fifteen weeks in El Salvador and 65 per cent in twenty-five weeks in Guatemala.

These observations are particularly significant since they suggest that potassium iodate, which is more stable than potassium iodide, would be a suitable vehicle for adding iodine to salt in underdeveloped areas. Formerly the iodization of salt with potassium iodide required that the salt be dry and free of impurities and that after the addition of stabilizing chemicals, it be packed in moisture-proof containers. While this procedure has proved suitable for the marketing of salt in highly developed countries, it is impractical for the areas in which most of the salt used is both crude and moist. The stability of potassium iodate in a crude moist table salt has been confirmed by G. Arroyave, O. Pineda, and N. S. Scrimshaw (*Bull. World Health Organization* **14**, 183 (1956)). Potassium iodate can be mixed directly with crude salt without any special storage precautions, thus making the iodization of salt practical in tropical and other underdeveloped areas which are likely to have adverse conditions for salt conservation and marketing.

Recently the (United States) Food and Drug Administration has authorized not only potassium iodate but also calcium, sodium and magnesium iodate for use in mineral mixtures and feeds for animals. Such use has not yet been approved in the United States for human consumption, but this step is expected to follow shortly since work of M. M. Murray (*Bull. World Health Organization* **9**, 211 (1953)) in England and in the National Institutes of Health (J. M. Hundley, *personal communication* (1955)) indicates a margin of safety for iodate similar to that for iodide. In the meantime, on the basis of

the recommendations of the WHO Study Group on Endemic Goiter (*Bull. World Health Organization* 9, 293 (1953)), the Third Conference on Nutrition Problems in Latin America, jointly sponsored by FAO and WHO (*FAO Nutrition Meetings Report Series No. 8, Rome (1954)*) and the Fourth Meeting of the Joint FAO/WHO Expert Committee on Nutrition (*FAO Nutrition Meetings Report Series No. 9, Rome (1955)*), Guatemala has begun the iodization of salt with potassium iodate and a number of countries are planning to initiate salt iodization with this compound in the near future. In the long run calcium iodate may become the compound of choice since it is even more stable, gives promise of being cheaper and is equally effective.

Each of the international conferences to discuss the subject has considered the safety of prophylaxis with iodized salt as beyond question. The WHO Study Group on Endemic Goiter (*loc. cit.*) pointed out that "In no country in which iodine prophylaxis has been used on a community scale, has this measure had any adverse effects on the health of the population." The Third Conference on Nutrition Problems in Latin America (*loc. cit.*) further noted that "... all reports of unfavorable effects which have been investigated have proved to be false or explainable on the basis of coincidence." The Joint FAO/WHO Expert Committee on Nutrition (*loc. cit.*) agreed "that there was no reason to expect any undesirable effects from the introduction of salt iodized at any of the levels referred to..."

Each of the three international meetings mentioned has also accepted the following statement on the etiology of endemic goiter: "The immediate cause of simple goiter is failure of the thyroid gland to obtain a supply of iodine sufficient to maintain its normal structure and function. This failure is usually brought about by an absolute environmental deficiency of iodine; it may also be caused by factors which interfere with the availability of dietary iodine or which

impose an abnormal demand on the thyroid gland." Upon occasion historical records which make little or no mention of goiter have been cited as evidence that endemic goiter was absent in a given place at some previous time. These references have been used in turn to "prove" that endemic goiter behaves like an infectious disease by appearing suddenly in areas in which it was not formerly present. The evidence cited to support this belief does not, however, stand up under critical and informed evaluation.

On the other hand, there is no doubt that goitrogenic factors exist which can increase the need for dietary iodine. As has been reviewed in detail by M. A. Greer (*Physiol. Rev.* 30, 513 (1950)), plants of the family *Brassicaceae* often contain a factor which increases the physiologic demand for iodine. F. W. Clements (*Med. J. Australia*, p. 369, Sept. 3, 1955) has recently cited evidence to show that milk from cattle fed on one of the *Brassicaceae* (thousand-headed kale) has contributed to the incidence of endemic goiter in school children in Tasmania. There is also evidence that persons consuming "hard" water are more likely to develop goiter (M. M. Murray, J. A. Ryle, B. W. Simpson, and D. C. Wilson, *Med. Res. Council (London) Memorandum No. 18 (1948)*).

H. Haubold (*Verhandl. deutsch. Ges. inn. Med.* 57, 112 (1951)) has demonstrated that vitamin A deficiency may be associated with an increase in goiter. However, in recent INCAP studies in Guatemala, vitamin A was given daily to school children among whom the prevalence of goiter was approximately 40 per cent and whose diets were relatively deficient in vitamin A activity. The administration of 5000 i.u. of vitamin A in oil for twenty-three weeks and of 15,000 for ten weeks failed to produce any detectable decrease in the prevalence of goiter.

Without attempting a complete review of the world incidence of endemic goiter such as is now being prepared by the World Health Organization, it can be concluded from the evidence cited that endemic goiter

is still an important nutritional and public health problem in many areas of the world, including most of the countries of the Western hemisphere. The cosmetic and surgical consequences of endemic goiter are obvious, and the relationship of goiter to cretinism, thyrotoxicosis and thyroid carcinoma has been demonstrated. A correlation between the frequency of endemic goiter and the incidence of deaf-mutism and feeble-mindedness has been repeatedly mentioned, but satisfactory evidence for such a conclusion is still lacking.

When the incidence of endemic goiter in an area exceeds 10 per cent, salt should be iodized. The level and method of iodization has been discussed in detail by the Third Conference on Nutrition Problems in Latin America (*loc. cit.*). Present evidence suggests

that, in this hemisphere at least, a level of not less than 1 part of iodine in 20,000 of salt nor more than 1 part in 10,000 should be employed. Through the use of potassium or calcium iodate, crude moist salt can be iodized without special handling and packaging. The number of countries in which iodized salt is required by law can be expected to increase sharply in the near future.

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