

HISTORY OF THE PREVENTION OF ENDEMIC GOITRE

O. P. KIMBALL, M.D.

Doctors' Clinic, 12337 Cedar Road, Cleveland, Ohio, USA

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SYNOPSIS

The importance to the community of the prevention of endemic goitre—a food-deficiency disease which causes feeble-mindedness, deaf-mutism, and general physical and mental degeneration from one generation to the next—and the simplicity of prevention, have only gradually been realized in the course of the past hundred years. In the early 19th century, potassium iodide was used in goitre prevention, but the experiment was abandoned about the year 1858. The first controlled experiment was made in 1916-20, when a course of sodium iodide followed by 5,000 schoolgirls in Akron, Ohio, USA, proved 100% efficacious against the development of the disease. An investigation of the 20th-century development of endemic goitre in West Virginia, USA, carried out in 1922, established a direct connexion between the abandonment of the use of locally available natural iodized salt and the development of a high incidence of endemic goitre in an area hitherto goitre-free. In 1924, an attempt to eliminate endemic goitre by replacing plain salt by iodized salt was made in the State of Michigan, USA. The experiment was at first resisted by the goitre surgeons; opposition was finally dispelled when a survey, carried out in the State four years later, proved that not one case of toxic goitre due to the consumption of iodized salt had occurred in three counties chosen as the test area. As a result of analyses made at a follow-up survey in 1936, it was recommended that all iodized salt be standardized at 0.01% of iodine. Since iodized salt is more expensive to produce than plain salt, support of the medical profession alone is not enough. Co-operation on the part of both governments and business is essential if iodized salt is to become available throughout the world at as low a price as plain salt. Recent experience in Argentina, where the introduction of iodized salt was accompanied by a prohibitive increase in selling price, illustrates this necessity.

Goitre prevention as practised today is based entirely on the teachings of David Marine. As early as 1915, he was teaching that “endemic goitre is the easiest known disease to prevent”. This statement was based upon ten years of experimental study of the physiology and chemistry of the

thyroid gland. The results of this important study have been recorded and re-emphasized many times and will not be restated here.

The original experiment for the prevention of goitre in man—planned late in 1916—was made in the schools of Akron, Ohio, USA. The experiment was carried out over four years (1916-20) and approximately 5,000 girls agreed to undergo the preventive treatment, which was 3 grains of sodium iodide taken daily in their drinking-water for a period of ten days in the spring and in the autumn. An equal number who preferred not to undergo treatment became the controls. These girls were all from 11 to 18 years old—the age at which the incidence of goitre is high. Of the girls undergoing this prophylaxis who had normal thyroids at the original examination, not a single one developed goitre. Of those who had goitre at the beginning, two-thirds were diagnosed normal on later examination. Of the controls who originally had thyroid enlargement, none showed a tendency to return to normal, except those who were being treated by their family physicians. Of the controls who had been classified as normal at the original examination, half developed thyroid enlargement. Thus, by 1920 the truth of Marine's statement had been demonstrated.

This clinical experiment was quickly taken up in other countries, and Switzerland started to carry out similar prophylactic measures in several cantons. In 1922, the State Department of Health of West Virginia invited me to make a study of endemic goitre in the schools of Huntington and Charleston. A slightly higher incidence of goitre was found here than in Akron, Ohio: approximately 60% of the girls in high-school had a definite visible thyroid enlargement. It was a well-known fact that endemic goitre had been practically unknown in West Virginia before the year 1900. Soon after that date, goitre became prevalent and a rapid increase was noted by many physicians and by the State Department of Health. From investigation, it was found that the only change in food during this period had been a change about the year 1900 in the type of salt consumed. Before this, all the salt used in the State of West Virginia had come from local wells in the Kanawha River Valley. Soon after 1900, refined and free-flowing salt was introduced from Michigan and Ohio, and the local product, which was a coarse, brownish salt and not free-flowing, could not compete with it. By changing their salt supply, the people unknowingly cut off their main source of food iodine, and within less than a quarter of a century endemic goitre was as prevalent in West Virginia as in the most goitrous areas of the USA. It had been noted by the teachers at the State Agricultural College that none of the domestic animals showed a tendency towards goitre. We also learned that there was still one salt well in that neighbourhood producing salt for agricultural purposes. A sample of this crude salt was found to contain approximately 0.01% of iodine. It was this experience which led to the development of the general use of iodized salt as the preventive against endemic goitre.

Dr. J. Grange of Geneva, Switzerland, and a few of his associates, used the same percentage of potassium iodide (1 mg to 10 g of salt) in the treatment of goitre in their patients as in its prophylaxis.¹ This use of iodized salt in the treatment of goitre was practised by physicians from 1842 to 1858, when such treatment was severely criticized by Dr. Rilliet.⁶ The use of iodized salt was given up in about the year 1858, and iodized salt was not used again on a large scale until reintroduced in the State of Michigan, USA.

The prevention of endemic goitre by the general use of iodized salt was begun in Michigan in May 1924. The programme was started by obtaining the co-operation of the salt producers, the wholesale grocers, and the State Department of Health, all working together. The producers and the wholesale grocers each bore one half of the added expense so that the iodized salt would not cost the consumer one cent more. The Department of Health gave all the instructions and advice so that there was no advertisement or comment by the salt producers. There was no law or mandate forcing anybody to do anything, only a spirit of co-operation directed towards one purpose—the prevention of endemic goitre.

The first difficulty in originating this programme was due to the United States Department of Agriculture, Bureau of Chemistry, which at first insisted that each carton of salt should be labelled with the skull and cross-bones, because iodine is a poison. But finally this idea was abandoned, and within the first year approximately 94% of the homes were using iodized salt continuously.

The next prejudice to be overcome was that of the goitre surgeons of the USA, who were greatly exercised lest the use of iodized salt should cause an epidemic of exophthalmic goitre. While there never had been any scientific data to justify their concern, yet the fear of such a result was there and kept growing until 1928. At this time the Michigan State Department of Health arranged with three county medical societies to set up a goitre clinic in their county. These counties were three of the original four in which all the schoolchildren had been examined for goitre in 1924. The State and County Departments of Health and each doctor advised all adults who had goitre to come to these clinics for study. During this survey, 1,299 adults with long-standing goitre were examined for toxic effects from the use of iodized salt. Not a single case of toxic goitre which, by any stretch of the imagination, could have been diagnosed as toxicity from the use of iodized salt was found. The majority of the toxic cases were under treatment from a physician and in most instances had never used iodized salt, having been specifically advised against it by their physicians. An account of this survey was published in the *Journal of the American Medical Association* in August 1928, under the title "The efficiency and safety of the prevention of goitre".³ Possibly the effects of this publication, or the obvious fact that goitre was rapidly disappearing

from medical practice, added considerable encouragement to the spread of this prophylactic measure.

In 1936, a follow-up survey of the four original counties in Michigan was begun to determine both the percentage of goitre and the extent of the use of iodized salt throughout the State. These four counties had been selected in the first instance because they were equidistant, on a diagonal line, from Lake Superior to the north and from Lake Erie to the south. The percentage of goitre in the schools of these four counties was taken as the basis of calculation for goitre incidence throughout the State. Thus, in 1924 the incidence of goitre in Michigan was 38.6%. In 1936, it was 8.2%. During the same period, a follow-up survey was made throughout the parochial schools of Cleveland, Ohio, where—because of active propaganda against its use—only half the homes were using iodized salt. In 1924, the incidence of goitre in the same schools of Cleveland had been 30%. In 1936, among the 5,000 children from homes who had never used iodized salt, the incidence of goitre was 30.7%. Among the 5,000 who had used iodized salt continuously in the home, only 7% had an enlarged thyroid.

During this same period, the percentage of goitre surgery decreased gradually. McClure^{4, 5} found that, in 1929, 3.2% of all operations in nine large hospitals in Michigan were for goitre, while by 1950 the figure was less than 1%. From 1936 to 1948 the only progress attempted by the Endemic Goiter Committee of the American Public Health Association was to persuade as many States as possible to initiate campaigns of education for the prevention of goitre by the use of iodized salt. During the follow-up study of goitre and the use of iodized salt carried out in Michigan in 1935-6, many analyses were made to determine the actual amount of iodine in the various brands of iodized salt. In 1924, the amount specified by the Michigan State Department of Health was 0.02% of potassium iodide. It was known that this amount, 1 : 5,000, was at least twice the physiological need for goitre prevention, but it was not known with certainty whether or not iodized salt would hold its iodine accurately. In addition, it was decided that an extra amount would have a greater curative effect so that, in consequence, the value of this measure would be more obvious to all.

The survey of 1935-6 showed that the average amount of iodine in the several brands of iodized salt was 0.01%, yet this amount had been sufficient to prevent, and in a high percentage of cases to cure, the simple hyperplasias. Persons using one of the two brands which always showed an iodine content of 0.02% showed no injurious effects. After this experience it was recommended that all iodized salt be standardized at 0.01% of iodine. The fact that this is a higher percentage than that used in England or Switzerland is thoroughly appreciated. Dr. George M. Curtis, a member of the Endemic Goiter Committee of the American Public Health

Association, has always agreed with the findings of Th. von Fellenberg² that the daily iodine requirements of normal, healthy, young adults is 0.2 mg. This is one-fifth of the amount of the average daily intake from iodized salt in the USA, where the iodine content is 0.01%, or 1 mg of iodine to 10 g (the average daily intake) of salt. Nevertheless, I have seen an occasional case of a boy or girl, at a time of rapid growth at the age of puberty, develop a goitre while using iodized salt regularly. Dr. H. J. Wespi of Herisau, Appenzell, Switzerland, who visited me in Cleveland, Ohio, in 1949, told me that while the incidence of goitre and cretinism has been greatly reduced since the use of iodized salt in that country, an occasional cretin is still seen. No case has been recorded in the USA of a cretin born of a mother using iodized salt. Dr. Wespi and I tried to estimate the cost to any community of care for a cretin; we found it out of all proportion to the extra cost of providing sufficient iodine to prevent cretinism and other defects.

By 1948, the Endemic Goiter Committee felt that it was time that the disease was properly classified, namely, as a food-deficiency disease, and that an attempt should be made to carry on prophylaxis by the continuous use of iodized salt without its being labelled conspicuously as iodized salt. To this end, an endeavour was made to introduce the use of this improved salt throughout the USA by federal legislation. This legislation failed to pass, but similar legislation did pass in Canada and Colombia.

My most interesting study of endemic goitre was made in 1950 when WHO asked me to review this problem in Mexico, Central America, and some of the South-American countries, and to report to the second Conference on Nutrition Problems in Latin America, held in Rio de Janeiro, Brazil, in June 1950. In these countries I found great variations in the incidence of endemic goitre. The white urban population is comparatively free from goitre, while out in the mountainous areas only a few miles from cities, goitre—with all its degenerative conditions—is very common. In an Indian village only 25 miles (40 km) from Mexico City, 65% of the total number of inhabitants had unmistakable goitre. Cretins were common and deaf-mutes were more frequent than we had ever expected to find. The same condition obtained in Guatemala and all the other Central-American States, and in Colombia, Ecuador, and Peru.

Mexico was the first of the American countries to introduce legislation concerning the use of iodized salt for the prevention of endemic goitre. A federal law was passed in 1941 and iodized salt was produced two years later. In Mexico, the price of salt is government-controlled, and at a level which does not allow for the expense of iodized salt. The Department of Public Health pays the extra cost, but the salt may be used only in areas where the incidence of goitre is 35% or more.

Colombia provides another example of a natural iodized salt completely preventing endemic goitre for centuries with never a report of

harmful effect. In the Department of Caldas, on the west slope of the Andes, all food salt came from one mineral spring until 1915. It had long been reported that there was no goitre in this Department, while there was a high incidence of goitre in all adjacent areas. A survey of every school was made by the Department of Health in 1915 : not a single case of goitre was found among the schoolchildren, and not a cretin was seen. It was at this time, however, that the present owner of the salt mines on the eastern slope of the Andes started to produce a better grade of salt and to ship it to all parts of the country at a selling price below that of the coarse, crude salt available in Caldas. The salt in Caldas, which was from a mineral spring, was produced by solar evaporation and was crudely prepared ; the quantity was just enough to supply the Department, none of it being shipped out of Caldas. Like the residents of West Virginia, the people of Caldas could now buy a finer, whiter salt for less money than their coarse, crude salt ; shortly thereafter, the production of salt from this original salt spring rapidly declined.

In 1945, the health authorities of Colombia became aware of the growing incidence of goitre in the Department of Caldas and made a further survey. At this time, just 30 years after the previous survey, it was reported that 85% of the children in the schools had goitre, and that every parochial district had a small home to take care of the cretins. I obtained a sample of crude salt from the original salt spring and by careful analysis found that its iodine content was sufficient. This is another example of salt consumption affecting goitre incidence : when a natural iodized salt was used for centuries, goitre problems did not exist ; but once this source of food iodine was lost, within a period of 30 years severe endemic goitre had developed.

In 1951, it was decided to repeat the examination throughout the four counties in the State of Michigan which had been originally examined. The purpose of this follow-up study was educative—the conclusions drawn from it were to be applied in other States. The results were even more striking than had been anticipated. In all, more than 50,000 schoolchildren were examined. The incidence of goitre was 1.4% where it had been 38.6% in 1924, and not one substantiated case of harmful effects resulting from the use of iodized salt had been recorded in 25 years.

Goitre has too long been thought of as a lump in the neck instead of as an endemic disease causing degeneration from one generation to the next, breeding feeble-mindedness and deaf-mutism, and giving rise to a general lack of development, both physical and mental. According to the anthropologists of Peru, the men of the Incas tribe about a thousand years ago were 6-7 feet (1.8-2.1 m) tall. Today, the tallest of these tribes are only average size while the majority appear small and underdeveloped. There is evidence of congenital deficiencies from one generation to the next, and while the people suffer from many food deficiencies, it is possible that endemic goitre has played the chief role in this type of degeneration through the centuries. In Guatemala, in a village of 300 Indians, 12 or

14 deaf-mutes who also showed other signs of congenital hypothyroidism were observed. Among these mountain people there were no cretins, but this is because life is too rigorous and they die young. Every possible step of this degenerative disease can be demonstrated in any one of hundreds of villages on the sides of the mountains of Central and South America, while comparatively little endemic goitre is to be found among the whites in the cities.

Such conditions can all be eliminated; years of experience have proved that the most efficient method of elimination is the use of iodized salt. All people use salt in approximately the same amount, which makes this the best and most rational means of accurately supplying food iodine. It will be necessary either to iodize crude salt or to induce the underdeveloped countries to produce a good grade of iodized salt and then to put it in the moisture-proof bags which are now available. The latter method would be more accurate and less expensive for the inhabitants of underdeveloped areas than selling the crude salt by the handful as is being done today.

The support of government and business must be enlisted if any attempt to prevent endemic goitre is to succeed. One need only review the work in Argentina in 1952 to emphasize the importance of this co-operation. In the Province of Mendoza, goitre is endemic and the incidence is moderately high. For several years a goitre study committee has worked very diligently to introduce iodized salt as a prophylaxis for endemic goitre. In 1952, following a legislative order, iodized salt was introduced, but the cost was double that of the previous plain salt. This unfair increase in price has created a formidable obstacle to this health measure. Dr. Jorge Labat, Minister of Health of Mendoza, in a recent discussion of this problem, stated that it would be very difficult for the Ministry of Health to instruct the people in the value of this health measure in face of the suspicion created by the abnormal increase in the price of salt. This example shows clearly that it is of vital significance that both government and business understand the importance of this "food-deficiency disease", appreciate the principles of prevention, and act in a co-operative manner; without this support, the mere teaching of the scientists will not prevail.

RÉSUMÉ

En 1915, David Marine déclarait, à la suite des études faites au cours des dix années antérieures sur la physiologie de la thyroïde, que le goitre endémique était la maladie la plus facile à guérir. Le traitement du goitre par l'iode avait été entrepris en 1842 par des médecins suisses, puis abandonné à la suite des critiques qui lui avaient été opposées. Le problème fut repris aux Etats-Unis d'Amérique; les premiers essais de prophylaxie furent effectués avec grand succès de 1916 à 1920 sur des écolières, dans l'Etat d'Ohio. En 1922, un essai analogue fut organisé dans l'Etat de la Virginie Occidentale où 60% des écolières présentaient une hypertrophie de la thyroïde. Ce phénomène était inconnu dans

cet Etat avant 1900, date à laquelle du sel raffiné avait remplacé le sel brut, brun et grossier, d'origine locale. La source d'iode alimentaire avait ainsi été supprimée et, en moins de 25 ans, cet Etat était devenu l'un des plus fortement atteints par l'endémie thyroïdienne goitreuse. Aucune trace d'hypertrophie n'était observée, par contre, chez les animaux, qui continuaient à recevoir du sel brut naturel. L'usage général du sel iodé pour la prévention du goitre fut introduit en Suisse en 1922 et dans l'Etat de Michigan en 1924; au cours de la même année déjà 90% de la population de cet Etat consommait du sel iodé. Aucun cas de goitre exophtalmique, attribuable à cette consommation, ne fut observé. Une enquête de contrôle effectuée en 1935-36 dans l'Etat de Michigan montra qu'une teneur du sel en iode de 0,01% en moyenne avait suffi à empêcher, et dans certains cas à guérir, les hypertrophies simples de la thyroïde. A la suite de ces observations, on recommanda l'iodisation à raison de 1 mg par 10 g de sel (consommation quotidienne moyenne). Cette dose est beaucoup plus élevée que celle qu'ont adoptée la Suisse et la Grande-Bretagne.

En 1948, la Endemic Goiter Commission des Etats-Unis reconnut le goitre endémique comme maladie de carence et estima que la prophylaxie par le sel iodé devait être encouragée. Une tentative faite pour introduire la consommation du sel iodé sur le plan fédéral, par voie législative, échoua. De telles mesures furent adoptées par contre au Canada et en Colombie.

Le Mexique a été le premier pays du continent américain qui ait introduit — en 1941 — des dispositions législatives en vue de l'utilisation du sel iodé dans la prévention du goitre. L'Etat a pris à sa charge les frais d'iodisation, mais le sel iodé ne peut être utilisé que dans les régions où la fréquence du goitre est de 35% au moins. La Colombie fournit l'exemple d'un pays où l'utilisation de sel brut, naturellement iodé, a empêché toute apparition du goitre pendant des siècles. Dès 1915, dans le Département de Caldas, sur le versant occidental des Andes, le sel fut raffiné et vendu sous cette forme à un prix inférieur à celui du sel brut. Il s'ensuivit qu'en 1945, 85% des enfants des écoles présentaient des goitres et que les cas de crétinisme, autrefois nuls, étaient devenus nombreux. Il est possible que le goitre endémique ait été la principale des causes de dégénérescence, chez les descendants des Incas, qui ont souffert depuis des siècles de maladies de carence. Au Guatemala, l'hypothyroïdisme congénital est évident, dans maint village. Ce processus dégénératif, visible à divers stades dans les montagnes de l'Amérique centrale et de l'Amérique du Sud, est quasi inconnu dans les populations de race blanche des villes. Les dégénérescences d'origine thyroïdienne pourraient être supprimées par l'utilisation de sel iodé. Il s'agirait ou bien d'iodiser le sel brut ou bien de produire, dans les pays insuffisamment développés, un sel brut, iodé, de bonne qualité, conservé dans les emballages protégeant de l'humidité dont on dispose maintenant. De plus, une collaboration doit s'établir entre le gouvernement et les fabricants, afin que d'une part l'utilisation du sel iodé soit introduite par voie législative, et que, d'autre part, le prix du produit ne soit pas un obstacle à sa consommation.

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