Evolution of Modern Medicine

This section, which has as its primary purpose a review of the contributions of medical investigators and observers of the past to the present-day concepts of disease, is under the special editorship of Dr. Arthur Bloomfield, 2598 Sacramento St., San Francisco 18.

His editorial in the August, 1937, issue of the A.M.A. Archives of Internal Medicine, gives further detail of what it is hoped to accomplish in these articles. Contributions or comments for this section may be sent directly to Dr. Bloomfield, or to the Chief Editor for transmission to him.

Prevention of Endemic Goiter in Man

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This paper is historical in character, with interpretations and corrections, bringing the work of many scientists of this and other countries for the past 50 years into one complete whole, into an understandable bit of medical history. Endemic goiter is one of the oldest diseases known, and, in addition to the methods of treatment by the Ancient Greeks, there have been during the past 3 centuries repeated contributions to the growing knowledge of endemic goiter.

The prevention of endemic goiter in man, as it is known today throughout the world, is based entirely on the findings and teaching of David Marine. His investigations were started in 1905 at Western Reserve University. The first report on the study of the Relation of Iodine to the Structure of the Thyroid Gland was published in 1906 by Marine and Williams. The next publication in 1909 was by Marine and Lenhart on the Relation of Iodine to the Structure of Human Thyroids.

It was demonstrated that the relationship of histological changes to iodine content found in human thyroids was the same for all domestic animals studied—dogs, sheep, and cattle. It was shown that so long as the iodine content remained at or above 1 mg. of iodine per gram of dried thyroid, the cellular changes (hypertrophy and hyperplasia) did not occur; and as soon as
the iodine content fell below 1 mg. per gram of dried thyroid, the cellular changes did take place. From this it was concluded that a deficiency of iodine, relative or absolute, is the basic cause of the histological changes or goiter formation.

An iodine deficiency as the cause of goiter was suspected by Roussingault in 1824, and again by Prof. Chatin in 1851, but it was first demonstrated in Marine and his associates from 1905-1910. In each of Marine’s papers, credit for discoveries by earlier scientists is given and reference to the work is carefully filed. Therefore, few references to the previous studies will be given here, since they are a part of Marine’s early publications.

Iodine had unknowingly been used in the treatment of goiter long before iodine was discovered by Corti in 1811. The favorite treatment for goiter by the Greeks was the ashes of burned sea sponges, which unknown to them, was rich with iodine. In 1820, the Swiss physician Cooliet showed that iodine in one gram (60 mg.) doses would cure some cases of goiter. Also, he pointed goiterous throats with tincture of iodine and claimed equally good results. In 1895, Baumann showed that iodine is a normal constituent of the thyroid.

In September, 1910, Marine was teaching that “Endemic goiter is the easiest known disease to prevent.” He explained that the cellular changes, hyperplasia and hypothyroidism, are the first steps in goiter formation, and that they are due to a deficiency of iodine in the gland. As long as the iodine content is kept at or above 1 mg. of iodine per gram of dried thyroid, these cellular changes will not take place.

The physiology of the thyroid was demonstrated in our study of cases in the goiter clinic of the dispensary at Lakeside Hospital. The thyroid gland was described and explained to the girls and teachers. They were told that where the thyroid is normal, the lateral lobes, which lie against the trachea about 1 inch below the larynx, are too small to be palpated. Each lobe is like a lime bean close to the side of the trachea, and a thin band containing some thyroid follicles passes over the trachea connecting the lower poles of the two lateral lobes. This band is called the isthmus or median lobe, and occasionally it enlarges quite prominently with a small goiter. Frequently we demonstrated a small goiter by

Kendall
TABLE I.—GOITER SURVEY IN APRIL, 1917

| Total number of thyroid examined | 6,262 |
| Total number of thyroid normal | 6,190 | or 98.0% |
| Total number marked abnormal    | 72  | or 1.1% |

Tipping the child's head back, and we could see the outline of the slightly enlarged lateral lobes. It was called a small goiter until the lateral lobes became large enough to meet in front and cause the neck to appear thick and disfigured. All such goiters were called moderate enlargements. There were only a few designated as large goiters. Thus, the classificiations were (a) normal gland, (b) slight enlargement, (c) moderate enlargements, and (d) marked enlargement.

Frequently we had the opportunity to demonstrate and to explain the meaning of a persistent thyroglossal stalk, or a distinctly nodular adenomatous goiter. All such occassions were used to emphasize the importance of the prevention of goiter during pregnancy for both mother and child.

The first goiter survey was made in April, 1917. There were 3,572 girls examined, and the condition of the thyroid was charted as follows:

Prophylactic treatment consisted of sodium iodide in their drinking water. Large bottles were prepared so that one teaspoonful contained 2 grains (0.12 gm.) of sodium iodide. Treatment was given by a teacher or nurse, by putting one teaspoonful of iodide solution in a partially filled paper cup of water, and the girl drank it right there in front of the teacher. The first year, the older girls in the 8th grade, were given 4 grains (0.25 gm.) of sodium iodide and younger girls received 2 grains (0.12 gm.). After the first series of prophylactic iodine in May, 1917, all girls were given 2 grains (0.12 gm.) daily for 10 days, or a period of 2 weeks twice a year, in May and December.

All were advised to take prophylactic iodine, but no one was urged to participate. All were examined each year; therefore, those who preferred not to participate became the controls.

Reexamination of all those examined in April, 1917, and the new fifth graders and all who entered the school in Fall of 1917, was made in November, 1917. Prophylaxis was continued each December and May.

The third examination was made in November, 1918, and the fourth complete study was made October, 1919. This fourth survey, together with the data and charts of the 3 previous surveys, became the fourth published report.

These observations on the prevention of simple goiter in man on a large scale, over a period of 30 months, showed that endemlc goiter can be prevented very simply and without any untoward effects.

Soon after the completion of the study in Akron, and publication of the fourth paper, the Health Commissioner of the State of West Virginia invited me to make a goiter survey in that state and advise on a method of prevention. In West Virginia, we found a most unusual and important situation which was eventually to teach us the rational method of administering food-iodine.

Early in the Fall of 1920, arrangements were made for a goiter survey in the high schools of Charleston and Huntington. To our great surprise, we found the incidence of endemic goiter here as high as that in upper Michigan or the Lake Superior region. Sixty per cent of the girls in high school had a definite goiter.

Some of the older physicians informed us that there had been no goiter in the state before the turn of the century; but soon thereafter goiter began to appear at an ever-increasing rate. In fact, there had been formed among the doctors, goiter study groups, in an effort to learn how best to treat these goiters and to learn why the change from a nongoitrous to a goitrous district, beginning around 1900. That was indeed a real problem, but with the assistance of the Health Commissioner, I soon learned that: (1) The shackles of abandoned mills along the Kanawha River had been producing so (2) that we advised the salt; (3) the salt were the only a few years of process of using from the producer. The pro was well still in a large salt lake, which had salt in the soda well still in a large salt lake. Here we ob serve crude salt f analysis was Health Lab Y Young, M.D. that the crude crystalline salt of (4) the analysis was why the salt was no longer made.

Endemic goiter became a problem among adult men and women. In 1898, t the degree of give one of crude salt,

The process continued until the 400 F, the process.

The man insisted that

Kindall
producing salt wells 20 years previously; (2) there were along the road large signs advising the use of a "refined white table salt"; (3) the billboards advising a refined salt were the advertisements of the salt companies of Ohio and Michigan, where the process of refining salt started in 1898; (4) from the producers we learned that it took only a few years until the refined salt was substituted for the so-called dirty brown salt, and the local wells had closed down.

The professors in the Agricultural Division of the State University informed us that none of the domestic animals had endemic goiter. Further, they told us that there was one local salt well still producing salt for agricultural purposes and that the domestic animals were given this coarse salt, which had been the source of all food-salt in the state for generations. The salt well is still in operation is run by the Dickens Company at Malden, W. Va., and here we obtained a good sample of the crude salt for iodine determination. The analysis was made in the Michigan State Health Laboratory, by the Director, C. C. Young, M.D. Dr. Young reported to me that the crude salt contained approximately 20 mg. of iodine per kilogram of salt. From this analysis, we learned the secret as to why the state of West Virginia, where endemic goiter was unknown before 1900, became within 22 years a severe endemic goiter district where the incidence of goiter among adolescent girls was as high as in any well-known goiter district in the United States.

In 1898, the University of Michigan gave the acon of Science to a young man for devising a method for recrystallizing crude salt. This process consists of heating the coarse salt to 600 F in an inverted retort; at this temperature a partial vacuum is created, and the large crude salt crystals recrystallize into fine crystals, producing the so-called refined salt. Since iodine volatilizes at 400 F, every trace of iodine is lost in the process of refining.

The managers of the large salt companies insisted that they did not remove any iodine from the coarse salt in the process of refining. The argument went on for several years until around 1920, when the manager of one of the large salt wells in Michigan invited Dr. Young, Director of Laboratories, and Dr. C. C. Slemons, Health Commissioner, to visit their plant and see how the process of refining was made. They accepted the invitation, and the manager made every effort to demonstrate each step of the process. They were getting near the end of the demonstration and near the top of the huge inverted retort walking along a cat-walk behind the manager. They came to a large valve in the pipes where a small jet of steam was escaping. The manager walked through this jet of steam without noticing any physical evidence of escaping iodine. His visitors were wearing white starched collars, and as they passed through the jet of steam, their collars turned blue. Thus was settled the question of removing iodine in the process of recrystallization of crude salt.12

In the Spring of 1938, with the cooperation of Dr. John Porterfield, Assistant to the U.S. Surgeon General, we were able to analyze the crude salt from most of the large salt companies. The iodine content was determined before it was refined and compared to the iodine content of the refined (noniodized) salt of the same companies. All of the companies were most generous in furnishing a supply of fresh unrefined salt for analysis, and the plain refined salt of each brand was picked up in the grocery store. The analyses were made in the United States Department of Food & Drugs, more specifically, in the chemistry laboratory, Division of Food, Bureau of Biological and Physical Sciences, under the supervision of Frank A. Vorhes, Jr. The iodine content was expressed in p.p.m. (parts per million.) Stated briefly, the samples of crude salt from the various sections of the country, except West Virginia, were very similar in iodine content. Careful analysis showed a range of 0.6 p.p.m. to 1.0 p.p.m. or from 0.6 μg. to 1 μg. of iodine per gram of salt. The sample of crude
salt from the Dickenson Company, Maldon, W. Va., showed 12.3 p.p.m. or 12.5 mg. per gram of salt. An adult using the average amount of salt would get 125 mg. of iodine daily from this salt, but only 6 mg. to 10 mg. from the other leading salt wells throughout the country. There was not a trace of iodine in any of the samples of refined, non-iodized salt procured in the stores.

The first extensive goiter survey in Michigan was made by Dr. C. C. Shanons and myself through the schools of Grand Rapids. Here, both boys and girls from the first to the twelfth grades were included. In all, 26,215 pupils were examined, and the incidence of goiter was 30%. In the spring of 1923, prophylaxis through all of the public schools of Grand Rapids was started, and here prevention consisted of each child taking a chocolate tablet containing 10 mg. of iodine once a week throughout the year.

In January, 1924, the Michigan State Department of Health decided to carry out a definite program of iodine determination of the water supply and at the same time make a goiter survey through several counties. Following these studies, they planned to carry out some method of prophylaxis, with resurveys to determine the efficiency of the preventive measure. In order to represent average conditions in the state, 4 counties were selected; namely, Houghton on Lake Superior, Wexford and Midland in the interior, and Macomb on Lake St. Clair, all on a line diagonally across the state from northwest to southeast.

Iodine determinations of every main source of drinking water in the county were made, with the average of these determinations representing the iodine content of the county.

The goiter survey of each county showed quite clearly that the incidence of goiter is inversely proportioned to the food-iodine (Fig. 1).

In 1928, a resurvey for goiter among the school children was made to learn the efficiency of prophylaxis with iodized salt (Fig. 2).

Following the goiter surveys in 1924, there was a state-wide campaign by the Department of Health to emphasize the fundamental causes of endemic goiter and the principles of its prevention. Also during the Spring of 1924, the State Medical Society appointed a special committee to work with the Health Department in carrying out this work. These 2 groups, representing the medical profession, and myself continued the study of endemic goiter through the country in 1928 and 1929, and the incidence of goiter in the children examined was 21.8%.

In 1928, school children examined 50,134, incidence of goiter 9.5%.

Fig. 1.—Goiter survey of school population: iodine in water estimated in parts per billion.

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Epidemic Goiter Prevention

The Goiter Study Group that directed the special study from 1924 forward.

For the first 4 years, the iodized salt contained one part of KI to 5,000 parts of salt. After the resurvey in 1926, this amount of iodine was cut in half, so that since 1936 the iodine content has been 1 part of KI to 10,000 parts of salt. This standardization has long been recognized as 100 mg. of KI to a kilogram of salt.

The resurvey in 1928 included with the goiter survey a goiter clinic through the original counties. The clinic for adults was arranged by the County Medical Society. The purpose of this special clinic was to study every case of long-standing goiter to learn if any had been made toxic by the use of iodized salt.

The result of this survey was given before the American Medical Association meeting on June 14, 1928, entitled: The Efficiency and Safety of the Prevention of Goiter. Sufficient to say here that the incidence of goiter had decreased from 38.6% in 1924 to 9.9% in 1928. In the clinics, 1,229 cases of large, long-standing adenomatous goiters were studied. These were divided in 2 classes: (1) those using iodized salt regularly, and (2) those who never used iodized salt. Of those using iodized salt (Class 1), 27, or 4.1%, either were or had been toxic since using iodized salt. In Class 2 (those who never used iodized salt) 233, or 53.5%, either were or had been toxic since 1924. It appeared that iodized salt had prevented toxicity in many.

Artificial iodized salt as a prophylaxis for endemic goiter was first used in this country in 1924, yet it was used both as treatment and prevention in Switzerland as early as 1840. Iodine as 1 mg. KI to 10 gm. of salt was used by Dr. J. Grange of Geneva and a few of his associates from 1840 to 1858, when such treatment was severely criticized by Dr. Killiet.

Iodized salt was introduced throughout Michigan by the State Department of Health during May, 1924. The technique used in introducing this new health measure was responsible for its immediate and permanent success. From the experience in West Virginia, it appeared that food-salt was the most accurate and the easiest way to furnish iodine to everyone. Table salt is used by all, and with the least variation in amount used when accessible to everyone as it is in this country. The Health Authorities agreed with this suggestion, and to that end we approached 2 well-known salt producers in Michigan, the Morton and the Mulkey Companies. They understood our problem and agreed to produce an iodized salt if the wholesale grocers would bear half of the extra cost of its production, so that the salt would sell for the same as non-iodized salt. To this suggestion the wholesale grocer agreed and it was further agreed that neither the grocer nor the producer would in any way try to promote the sale of iodized salt: the Health Department would explain the purpose of extra food-iodine and urge everyone to use iodized salt. And to this end, before iodized salt was on the market, every newspaper carried articles by the State Health Department and every school had placards in language the children could understand, explaining what a goiter is and how to prevent it. In every way the Department of Health advised the use of iodized salt.

In 1936, a follow-up survey of the 4 original counties in Michigan was made to determine both the incidence of goiter and the extent of the use of iodized salt throughout the state. In 1924 the incidence of goiter in these 4 counties, or throughout Michigan, was 38.6%. In 1936 it was 8.2%.

During the same period (1924 to 1936) a follow-up survey was made through the

<table>
<thead>
<tr>
<th>Table 2.—Goiter Survey, Michigan, 1936</th>
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<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Used iodized salt regularly</td>
</tr>
<tr>
<td>Never used iodized salt</td>
</tr>
<tr>
<td>Used iodized salt</td>
</tr>
<tr>
<td>Never used iodized salt</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total</th>
<th>Goiter</th>
<th>% Goiter</th>
</tr>
</thead>
<tbody>
<tr>
<td>-------</td>
<td>--------</td>
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</tbody>
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parochial schools in Cleveland, Ohio (Fig. 3), where, because of an active propaganda against its use, only half of the homes were using iodized salt. In 1924, the incidence of goiter in the same schools was 30%. In 1936, among the 2,500 children from homes who had never used iodized salt, the incidence of goiter was 30.7%. Among the 2,700 who had used iodized salt continuously in the home, only 7% had an enlarged thyroid.

In Cleveland, we were not permitted to make a goiter survey through the public school because of the open opposition by a goiter surgeon. However, we did make a complete survey through the parochial schools, since they were under the City Health Department, and a resurvey in 1936. These results are shown in Table 3.

These findings are also expressed in Figure 4—in comparison with the findings in Michigan.

For important details on the controversy of this health measure in Cleveland, you are referred to the publication Prevention of Goiter in Michigan and Ohio by Kimball (J.A.M.A. 108:860, 1937).

The Goiter Study Committee which was formed in 1924 is still functioning. It is composed of 2 men from the State Medical Association, 2 from the State Health Department, and 1 from the State University. This committee, together with my direction, made the resurvey in 1928, 1936, and again in 1951.

Following the report of the 1936 resurvey through Michigan, the American Public Health Association became interested, and eventually formed the Goiter Study Group as a subcommittee of the A.P.H.A. Also, during the 1930's, there were many studies to determine the iodine content of food and drink of whole areas and its relation to the incidence of endemic goiter. The most detailed and extensive report on this point was by Prof. J. F. McClendon of the University of Minnesota. Professor McClendon's book

**Table 3.—Division of Health, Cleveland: Goiter Survey, January, 1936**

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Normal No. 1</th>
<th>Small No. 2</th>
<th>Med. No. 3</th>
<th>Cong. Ad.</th>
<th>Hyperplastic</th>
<th>% Goiter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using iodized salt</td>
<td>2,003</td>
<td>1,966</td>
<td>149</td>
<td>1</td>
<td>35</td>
<td>14</td>
<td>7.7</td>
</tr>
<tr>
<td>Not using iodized salt</td>
<td>2,029</td>
<td>1,782</td>
<td>257</td>
<td>20</td>
<td>49</td>
<td>268</td>
<td>30.7</td>
</tr>
<tr>
<td>Indefinite use</td>
<td>701</td>
<td>624</td>
<td>126</td>
<td>1</td>
<td>15</td>
<td>22</td>
<td>18.0</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td>5,033</td>
<td>4,370</td>
<td>1,002</td>
<td>22</td>
<td>99</td>
<td>244</td>
<td>18.0</td>
</tr>
</tbody>
</table>

Iodine and the incidence of Goiter seemed only with the geographical distribution of iodine, its place in milk, its relation to the incidence of g at volume, published in 1939 by the Minnesota Press, gives a study of this food deficiency disease.

Boussingault, as early as 1824, the salt in northern Colombia, South America, was responsible for endemic goiter. He suggested to the government of Colombia that iodized salt be used to prevent the disease. Prevost stated in 1849 that goiter is the result of a lack of iodine in the diet, with Chatin (1830 to 1858) in the water, soil, food, and air of the area surrounding its place and stated that goiter is due to iodine. His statement, as well as a careful analysis, was not accepted by many scientists and was eventually discarded. Grange of Switzerland had used iodized salt for both prevention from 1842 to 1858, of Geneva, objected to this treatment. A decade later, this was taken up by Dr. Kocher, with his enthusiastic teaching again the treatment of goiter the progress in this direction years; until after the demonstration in 1858, that endemic goiter could be prevented with iodine.

Probably the most basic research was that originated by M. Curtis, Professor of the University of Minnesota. In the diurnal Research of the University and his associates studied The creation of Iodine Feeding upon extent of Goat’s milk. They found that the iodine content of milk is increased by increased iodine. The iodine content of milk receiving extra iodine varies in area. The average iodine content milk in several goat’s regi as 2.8% of all milk in goats.
ENDEMIC GOITER PREVENTION

Iodine and the Incidence of Goiter is concerned only with the geographical distribution of iodine, its place in nutrition, and its relation to the incidence of goiter; this volume, published in 1939 by the University of Minnesota Press, gives a step-by-step study of this food deficiency disease.

Boussingault, as early as 1824, stated that the salt in northern Columbia, South America, was responsible for endemic goiter. In 1831, he suggested to the government of Columbia that iodized salt be sold by the government to prevent endemic goiter. Prevost stated in 1849 that goiter was the result of a lack of iodine in the water. Following this, Chatin (1850 to 1853) analyzed the water, soil, food, and air of several countries surrounding his area in France, and stated that goiter is due to a lack of iodine. His statement, as well as his chemical analysis, was not accepted by other scientists and was eventually discredited. Dr. Grange of Switzerland and his associates used iodized salt for both treatment and prevention from 1842 to 1858, when Kiliert of Geneva objected to this type of treatment. A decade later, this same opposition was taken up by Dr. Kocher of Berne, and his enthusiastic teaching against the use of iodine in the treatment of goiter stopped the progress in this direction for many years; until after the demonstration in this country that endemic goiter could be safely prevented with iodine.

Probably the most basic and useful research was that originated by Dr. George M. Curtis, Professor of Surgery at Ohio State University. In the division of Surgical Research of the University, Dr. Curtis and his associates studied The Effect of Increased Iodine Feeding upon Iodine Content of Cow’s Milk. They demonstrated that the iodine content of milk can be readily increased by increased iodine feeding. The iodine content of milk from cows not receiving extra iodine varies according to the area. The average iodine content of cows’ milk in several goiterous regions is reported as 2.5µg. %, while in goiter-free areas it is greater, say 6.0µg. %, as in South Carolina. In a controlled experiment in the area of Columbus, Ohio, they found an average throughout the year of 2.5µg. %.

The milk from iodized cows contained 7 to 10 times as much iodine as that from the controlled cows. An average milk iodine of 80µg. % was obtained from iodized cows throughout a midyear period of 5 months.

In 1950, there was published in Finland a monograph of Iodine in the Finnish Diet and Its Relation to Goiter Incidence by Panu Vilkki. He found that in Finland milk is the most important source of food-iodine. Milk in the areas where goiter is prevalent contains approximately 40% less iodine than milk consumed in areas where the incidence of goiter is low.

Calculated on the basis of nutrition studies, the mean iodine supply per person per day is about 50µg. in the area where goiter is prevalent and about 70µg. in the area with a low incidence of goiter. The mean iodine supply in Finland is considerably below the 100µg. per person per day recommended by the World Health Organization.

Vilkki points out the number of attempts that have been made to increase the intake of food-iodine by legislation. The first attempt to get iodized salt throughout the country was in 1936. Again in 1940, the Committee on Public Nutrition advised the prophylaxis of endemic goiter by the addition of KI to food salt in the relation of 1:200,000—or 5 mg. of KI to a kilogram of salt. Again in 1947, and in 1950 the same legislation was refused; but in 1949 iodized salt was placed on the grocery shelves beside the noniodized salt, and at the end of 5 years a study was made to learn the results of this technique of letting the public choose or refuse iodized salt.

In 1954, an investigation by the State Medical Board and the State Nutritional Committee showed that the use of iodized salt had been unimportant, being less than 10% of the total. And further, iodized stock food had been used irregularly for several decades, yet the milk iodine
was very low. The scientists of Finland still hope for legislation making iodized salt mandatory throughout the country.

In 1940 some of the members of the original Goiter Commission of Michigan, and others who were especially interested in endemic goiter, became the "Goiter Study Group" of the American Public Health Association. This committee consisted of:

Haven Emerson, M.D., Prof. of Public Health, Columbia University
Brock Brush, M.D., Surgeon, Henry Ford Hospital
Harry Towsley, M.D., Prof. of Pediatrics, University of Michigan
George M. Curtis, M.D., Prof. of Surgery, Ohio State University
W. H. Schrrill Jr., M.D., Director of Medical Research, U.S. Public Health Service
Hazel Stiebeling, Ph.D., Chief Nutritionist, U.S. Department of Agriculture
E. M. Nelson, Ph.D., Chief Chemist, U.S. Department of Food and Drug Administration
Charles G. King, M.D., Ph.D., Director, Nutrition Foundation, Inc.
Russell Wilder, M.D., Emeritus Professor, Mayo Foundation
David Marine, M.D., Consultant to the group
O. P. Kinball, M.D., Chairman to the group

During the period of 1940 to 1946, no research or change in the distribution of food-iodine was attempted. The occasional meetings during this time only emphasized the importance of federal legislation to have all food-salt iodized. During the legislative term, 1947, such a bill was submitted by Representative Frances P. Bolton. However, it never came up for a vote until July, 1948, and that was at a time when Congress was ready to adjourn. The committee which was holding the iodized salt bill, without notice to the author of the bill, took it up for consideration. Representative Bulwinkle of North Carolina suggested that since his state had no endemic goiter, it did not need any iodized salt. Then further, he moved that this bill be referred to the states, so that those states where goiter is endemic could decide for or against iodized salt. Naturally, this was an easy way out, and that was the end to our dream of federal legislation for uniform iodized salt throughout the country. It is hoped that Congressman Bulwinkle eventually read the little bulletin from the U.S. Public Health Service about the area of endemic goiter with cretinism in the western part of North Carolina, which was published a few weeks previous to his erroneous statements in Congress.

In the Spring of 1950, it was arranged that I, as consultant on endemic goiter to the World Health Organization, would make a survey of goiter and its needs in Mexico, Guatemala, Colombia, Ecuador, Peru, and areas of Brazil and report the findings at the World Health Organization meeting at Rio de Janeiro on June 15. The same fundamental condition was true of Mexico and all Central and South American states. In the capital cities or large cities, you see very little goiter, but a few miles into the country among the native Indians and poorer people the incidence of goiter, including large deforming tumors, goiters, and deaf-mutes was very high. In each of these countries, we studied villages within 10 miles of the big city where the incidence of goiter would be 60%-70% of children and adults; and cretins and deaf-mutes each averaged 3%-4% of total population. There was in each country an institution of nutrition. Each country had a Health Commissioner who understood endemic goiter and its prevention, yet nothing was being done.

In 1941, Dr. Herbert Stackpole, Health Commissioner of Mexico City, visited me in Cleveland, and we talked goiter and iodized salt for several days. In 1942, Mexico passed an iodized salt bill, but it read as follows: "Every one must use iodized salt," but there wasn't any iodized salt in the country. By 1950, through the persuasion of Dr. Stackpole, the Health Department was furnishing iodized salt in villages where the incidence of goiter was 35% or more.

In Guatemala City, you seldom saw a goiter among the Spanish or white race, while among the Indian or original Guatemalan race, goiter was very common. In the villages a few miles from Guatemala City the incidence of endemic goiter would average from 50% to 70% of population, and 3% to 4% were congenital deaf-mutes. The same in 1950 was by the "Institute of Nutrition." The Nevin Scrimshaw, and 2 unit, the institute explained to the purpose of the study and the visit. In 1951 and 1952, in the assistance of the Institute and the World Health Organization, the salt producers lea produce iodized salt and collected the distribution of iodized salt in Guatemala. However, the refiners, then the addition of iodine and blenders, cost and energy. Rest室福s during years by the same institute show that less than 10% of used in Guatemala is iodized, to the city because distribution of "Institute of Nutrition" and that nothing less than legislation only iodized salt be sold, endemic goiter and its sequelae.

The situation in Equador is comparable to that in Gufive World Health Organization only iodized salt be sold in the yet their government has not been to carry out this public health program.

The State of Colombia has endemic goiter problem, one that has for over a century, and proposed prevention in 1830, but prevention has been made. P. severe endemic goiter prove the advice of the World Health Organization, all of the food-salt in ti been iodized since 1952, and of goiter has decreased markedly.

One of the interesting finds of the 1951 reexamination of counties in Michigan which lie in 1924, 1928, 1936, at We were anxious to have them expressed in 2 groups: (1) ti
DELICATE GUTTER PREVENTION

Average from 50% to 70% of the total population, and 3% to 4% would be cretin or congenital deaf-mutes. The survey made here in 1950 was by the "Pan American Institute of Nutrition," the Director, Dr. Nevin Scrimshaw, and 2 native residents of the institute explained to the natives the purpose of the study and the value of prevention. In 1951 and 1952, with the financial assistance of the Pan American Institute and the World Health Organization, the salt producers learned how to produce iodized salt and actually started the distribution of iodized salt throughout Guatemala. However, the refining of coarse salt, then the addition of iodine, with stabilizer and drying agents, costs both money and energy. Resurveys during the past few years by the same institute of nutrition show that less than 10% of the food salt used in Guatemala is iodized, and this goes to the city because distribution is easier. The "Institute of Nutrition" understands now that nothing less than legislation requiring only iodized salt be sold, will prevent endemic goiter and its sequelae throughout the country.

The situation in Ecuador and Peru was comparable to that in Guatemala. The World Health Organization advised that only iodized salt be sold in these 2 countries, yet their government has made no effort to carry out this public health measure.

The State of Colombia has an important goiter problem, one that has been known for over a century, and Boussingault suggested prevention in 1830, but no attempt at prevention has been made. Paraguay had a severe endemic goiter problem, but taking the advice of the World Health Organization, all of the food-salt in the country has been iodized since 1952, and the incidence of goiter has decreased markedly.

One of the interesting findings is in the result of the 1951 reexamination of the 4 counties in Michigan which had been studied in 1924, 1928, 1936, and now 1951. We were anxious to have the results expressed in 2 groups: (1) those using iodized salt for several years, and (2) those not using iodized salt. I made up the report card (Fig. 5), and the school was given the card one week before the examination, and each teacher was requested to make every effort to get the facts on the use of iodized salt before she filled in the information on the goiter card.

This survey showed the total number of children examined as 53,503. Of this number, 51,717 had used iodized salt regularly, and 2086 had never used iodized salt. In 1924 the incidence of goiter in these same counties was 38.6%. In 1951, it was 2.36% (Table 4).

These same data were used by J. K. Altland, M.D., and Brock E. Bush, M.D., in a paper, Goiter Prevention in Michigan, published in the Journal of the Michigan State Medical Society, August, 1952. However, they did not take into account the 2086 children who had never used iodized salt, and consequently there is a slight difference in their published report and Table 4.

Among the 2086 who had never used iodized salt, the incidence of goiter was practically the same as among the 51,717 who had used iodized salt regularly for years. At first this was hard to understand, but, at the next meeting of the Goiter Study Group, I asked Dr. George Curtis for assistance on this point. He recounted for me the work of himself and associates on Increasing the Iodine Content of Milk by Feeding the Dairy Cows Iodized Salt, and...
Ground Food Enriched with Iodine and Other Trace Elements.

Soon after the origin and use of iodized salt for human consumption, iodized block salt was prepared for cattle. In 1929, Orr and Leitch demonstrated the effectiveness of milk containing increased iodine as a goiter prophylactic in man. By 1939, Curtis and Meyer had demonstrated that dairy cows fed iodized salt and the average amount of feed enriched with trace elements produced milk containing 80 μg % of iodine. This was the average of 2 dairy herds over a period of 5 months during mid-year. Thus a child drinking 8 oz. of milk per day would get 192 μg of iodine daily, which is sufficient to prevent goiter in otherwise normal healthy children.

Since an increase of food-iodine was being urged throughout Michigan by the State Health Department and the State Medical Association, it is natural to expect that the use of iodized block salt for dairy herds would be increased manyfold. Professor Hart of the Department of Agriculture, University of Wisconsin, had for years been teaching the importance of iodized block salt and feed containing trace elements including iodine for dairy herds. This teaching also helped to highlight the importance of iodized block salt and enriched feed for dairy herds throughout Michigan. After considerable study, it was thought that those who avoided iodized salt got sufficient iodine from milk.

In 1934, Hanford, Supplee, and Wilson reported a study showing the amount of iodine in milk from different areas of this country. In South Carolina the milk contained 6.9 μg % of iodine, while in Wisconsin there was only 3.2 μg %. In New York only 2.7 μg %. South Carolina is a goiterous state, while Wisconsin and New York are goiterous areas. Because of the increased iodine content of all vegetables grown in South Carolina, it is known as the Iodine State. The increased iodine content of milk in South Carolina is only an index to the iodine content of all foods grown there and indirectly tells of the presence or absence of endemic goiter.

In 1956, Panu Vilki reported a similar study throughout Finland. He stated that you can fairly well estimate the incidence of endemic goiter in any community by the amount of iodine in the milk.

Block salt containing iodine and other trace elements was introduced about 1928. The enriched feeds for dairy herds have been growing in popularity since the mid-thirties, and together these 2 important supplements of dairy feeding practically insure sufficient food-iodine to prevent goiter in children.

During the 1940’s a fear of using iodized salt in cooking or the preservation of food seemed to be spreading. It was not uncommon to read in the daily papers a recipe for preserving some food such as pickles.

Table 4. — Thyroid and Salt Survey of Four Michigan Counties, 1931

<table>
<thead>
<tr>
<th>County</th>
<th>No. Enriched</th>
<th>No. Unenriched</th>
<th>% of Food-Salt Sold</th>
<th>% of Food-Salt Sold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genesee</td>
<td>6,700</td>
<td>6,726</td>
<td>1,500</td>
<td>134</td>
</tr>
<tr>
<td>Wexford</td>
<td>3,450</td>
<td>3,400</td>
<td>12</td>
<td>111</td>
</tr>
<tr>
<td>Midland</td>
<td>2,750</td>
<td>2,607</td>
<td>17</td>
<td>133</td>
</tr>
<tr>
<td>Muskegon</td>
<td>31,200</td>
<td>22,652</td>
<td>163</td>
<td>1,497</td>
</tr>
<tr>
<td>Total</td>
<td>43,850</td>
<td>41,317</td>
<td>1,934</td>
<td>2,096</td>
</tr>
</tbody>
</table>

Percent of Goiter: 2.54% 2.36% 2.23%
with the admonition: "Don't use iodized salt." To correct these errors, a special study was made at Ohio State University in 1954. This was a contribution of the Department of Horticulture and the Institute of Nutrition and Food Technology under the direction of Prof. H. D. Brown. The American Canners Association held their annual meeting in this department in the late summer of 1954, and their experts were the judges of this experimental study. All kinds of foods that are usually processed with salt were prepared. Result: the judges could detect no difference in any food processed with iodized salt from that in which noniodized salt was used. The tomato juice was processed with varying amounts of KI. The experts could detect no difference when 25 times the usual amount of KI was used. Thus, another erroneous theory was corrected.

The Alps mountain area, and especially Switzerland, is the best-known endemic goiter district. The doctors of Switzerland have studied and written about goiter, cretinism, and deaf-mutism, and the possible relation of this degenerative disease to an iodine deficiency for more than a century. As stated above, iodized salt was used as a cure and prophylaxis by Dr. Grange around 1850. Again in 1918, Dr. O. Baylard introduced iodized salt into 3 mountainous communities of Canton Wallis. In February, 1922, iodinated salt was authorized for the first time for wholesale and public offering for the prophylaxis of goiter in the Canton of Appenzell A.-Rh. This salt acquired the name "Full Salt," and its consumption has increased steadily. This recognition of the prophylaxis of goiter by the use of iodized salt was due entirely to the initiative and persistence of H. Egggenberger of the Canton Appenzell A.-Rh. Later, the restudies were made by Dr. H. J. Wespi of Aarau.

The goal set by H. Egggenberger for full-salt prophylaxis was that 90% of the total salt used should contain 10 mg. of potassium iodide per kilogram of salt. This goal has been reached in the cantons of St. Gallen and Appenzell A.-Rh. The remaining cantons use the cure plus full-dose of 5 mg. KI/kg selected in 1923.

At the last report that I have (1959) 19 of the 25 Cantons have reached the 90% level. That is, 90% of all food-salt is iodized but contains only 5 mg. KI/kg. In the Canton Thurgau and Glarus it is between 80% and 90%. In the 4 Cantons of Bern, Solothurn, Baselland, and Nenonburg, the consumption of full-salt is below 80%. Wespi states that in one. still sees an occasional congenital goiter in families where "full-salt" of 5 mg KI/kg is used. And further, tests with radioactive iodine seem to indicate that the dosage of 5 mg. KI/kg is too low since Swiss thyroids still react as iodine deficiency glands. Efforts to increase the dosage from 5 to 10 mg. KI/kg are being continued.

A most scientific but little-known experiment was made by Wespi and his associates from 1946 to 1954. They were able to have the iodine dosage in salt augmented from the usual 5 to 20 mg. KI/kg in a small part of the Swiss Canton Thurgau. The results were controlled by Matonovitch of the University of Zagreb, and Rodriguez and Wespi of the Canton of Aarau.

In 1946 they had been able to feel and measure all thyroids. In 1953 they found that a considerable number of thyroids were so small that they were not able to feel or measure them. For that reason, they introduced a new category in the statistics: thyroids neither to feel nor to measure—0 and 0-I. They had established a basic scientific fact, up to then unknown in Swiss medical literature: the normal thyroid in children is too small to be palpated or measured.

In 1954, this experiment was stopped for political reasons, yet the scientific data were all good. When we were attempting to get federal legislation for iodized salt in the United States, the Commissioner of Health of Canada asked me for a copy of the proposed

| Ord. Supplie, and Wilson showing the amount of iodine in different areas of the U.S. only 3.2% and in one area 2.7% South Carolina, while Wisconsin and New York are goiterous areas. Increased iodine content of milk in South Carolina is with indirect tests or absence of endemic goiter reported by Finland. He stated that they eliminate the incidence in any community by the eating of milk.

Vilkki, Finland, and other areas introduced about 1928, for dairy herds have popularity since the mid-19th century these 2 important supplies feeding practically insure iodine to prevent goiter in 10-9's a fear of using iodized salt the preservation of food. It was not uncommon to have food such as pickles...
legislation. I gave him a concise, simplified form of the proposed legislation we were attempting, and he gave it to the Canadian Parliament where it was immediately made the law of the land. Since April, 1948, only salt that contains iodine 120-100 mg. KI/kg may be sold for food. There is no mention of iodized salt in the new health legislation, there is only a concrete definition of food-salt, with the authority to enforce this health measure, as is applied to any pure food law. A personal letter, March, 1960, from C. A. Morrell, Director, National Health and Welfare, states that the iodized salt regulation has continued in force since 1948. There have been no recent surveys to establish accurately the incidence of goiter. They know from medical records that there has been no authenticated case of ill effects from the use of iodized salt.

Following the meeting of World Health Organization, June, 1950, that organization urged the countries where goiter is endemic to use iodized salt. It gave assistance to obtain the machinery to iodize salt and engineering know-how to get the process working. The little country of Paraguay has continued the use of iodized salt, and the reduction of endemic goiter has been phenomenal according to the Director of Pan American Institute of Nutrition, Kevin Scrimshaw, M.D. Other countries started the program of iodized salt, but for one reason or another soon gave it up. Argentina has an endemic goiter district in the western part of the country extending into the Andes. An iodized salt was produced and put on the market by an independent salt producer, but at such an increase in price that it was never accepted by the people, and the program soon disappeared.

Equador and Peru showed little interest in the advice of the World Health Organization regarding the prevention of goiter. Ironically, Equador had just completed a fine new stone building called "The Institute of Nutrition." This new institute was a gift to Equador by "Pan Americana."

It failed its first great opportunity to improve the nutrition of the country by not endorsing iodized salt. During the study in Quito, May, 1950, I visited the National Director of Health, Education, and Nutrition. His office was in a beautiful building with high pillars and many marble steps on each side. While climbing these steps, I was accosted repeatedly by little cretin beggars asking for money to buy food. I gave generously by their standards, and by the time I got to the top of the steps, they were literally coming from every direction. I was in their country by invitation to study the problem of endemic goiter, and I explained to the Commissioner that these children were an integral part of the goiter problem. I explained that his government could prevent goiter for much less than they were paying to care for these walls and cretin beggars. To my surprise, he answered "Yes, doctor, but we pay nothing to care for these—they take care of themselves or else." Therein lies the answer to the prevention of goiter in Equador.

It is important to relate here that Colombia furnishes another outstanding example where one state that has never known endemic goiter becomes a severe endemic goiter area by changing its source of food-salt. The State of Caldas is in the Cauca River Valley between the middle and western ranges of the Andes. It was general knowledge, even mentioned by Boussingault in 1824, that Caldas had no endemic goiter for 200 years. In 1915 the National Department of Health investigated, and not one goitrous child could be found in Caldas. Soon after this date (1915) a fine white salt in cloth bags was sent into Caldas by the national producers from the Zipaquira mine on the eastern slope of the eastern range of the Andes. It is interesting to recall that Boussingault had the Zipaquira salt and the Cauca River salt analyzed for iodine in Paris, and the analysis showed that the Zipaquira salt contained no iodine, while the Cauca River salt contained iodine. And further, I have in my desk a sample of the

the Cauca River salt, and so I had it analyzed for iodine: reported 14.5g. per gram, as reported the iodine content a gram of salt.

Previous to 1915 all of the Caldas was a coarse salt, sold and from one large mineral spring happened here the West Virginia; the local succeeded because everyone preferred white salt, and the people in their main source of food-salt.

In 1947 the Director of Nutrition of Colombia visited land to discuss his survey of in Caldas in 1945. The incidence among the school children was 85% in many of the districts: parochial center they had a for cretins and cretin index 30 years Caldas had changed endemic goiter to the worst in all of Colombia.

The price of salt is limited erum in Mexico and some Central American countries where salt is not a lux under any circumstances, and erum limits the selling price of salt. The local agencies which controls the Price adjustment sufficient to cost of iodination, yet not exorbitant to be allowed, and it was safest and least expensive w out this important health measure.

In December, 1952, I attended the World Health Organization meeting to further the discussion and the topic of endemic goiter in Europe. East. The representative for the Dr. Joseph Matovinovic, who the prevention of goiter for I was given detailed instructi

Kimball
first great opportunity to improve the nutrition of the country by utilizing salt. During the study in 1930, I visited the National Health, Education, and Nutrition was in a beautiful building and many marble steps. While climbing these steps, I repeatedly by little crenin beg for money to buy food. I gave them their standards, and by the top of the steps, they coming from every direction.

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To relate here that Colombia another outstanding example state that has never known becomes a severe endemic changing its source of food. In the Cuca between the middle and west of the Andes. It was general mentioned by Bonning that Caldas had no endemic goiter in 1915 the National Departament investigated, and not one could be found in Caldas. At date (1915) a fine white salt was sent into Caldas by producers from the Zipaquira eastern slope of the eastern Andes. It is interesting to re-

A salt analyzed for and the analysis showed that salt contained no iodine, while other salt contained iodine. And in my desk a sample of the

ENDEMIC GOITER PREVENTION

the Cuca River salt, and on 2 occasions I had it analyzed for iodine, one analysis reported 14 mg. per gram, and the other reported the iodine content as 13.6 mg. per gram of salt.

Previous to 1915 all of the salt used in Caldas was a coarse salt, solar evaporated, and from one large mineral spring. The same thing happened here that happened in West Virginia; the local salt production ceased because everyone preferred the fine white salt, and the people of Caldas lost their main source of food-iodine.

In 1947 the Director of Health and Nutrition of Colombia visited me in Cleveland to discuss his survey of endemic goiter in Caldas in 1945. The incidence of goiter among the school children was as high as 87% in many of the districts, and in every parish center they had a separate home for cretins and cretin imbeciles. In just 30 years Caldas had changed from no endemic goiter to the worst goiter district in all of Colombia.

The price of salt is limited by the government in Mexico and some of the South and Central American countries. The production of salt is not a lucrative business and, under circumstances, and when the government limits the selling price, there is very little room for extra expense such as iodination. It would seem therefore that the responsibility for carrying out this health measure is with the government agency which controls the selling price. Price adjustment sufficient to pay the extra cost of iodination, yet not allow the excessive profit as was tried in Argentina, could be allowed, and it would still be the safest and least expensive way of carrying out this important health measure.

In December, 1952, I attended the meeting in London of the World Health Organization which met to further the prevention of endemic goiter in Europe and the Near East. The representative from Yugoslavia, Dr. Joseph Matovinovic, was interested in the prevention of goiter for his country. He was given detailed instructions on how to add iodine and stabilize a good grade of fine salt. The most important part was to get his government to order that only iodized food salt could be sold in his country. This government backing was obtained, and an edict was issued that beginning January 1, 1954, all food-salt must contain iodine. The amount of iodine was specified as not less than 10 mg. of iodine per kilogram of salt. This method of prophylaxis was continued, but I know of no research to show the good results which certainly have taken place by now.

During the last decade, it has become obvious that the important factor for complete and permanent success in the prevention of endemic goiter is the strong support by the government. As DavidMarine has repeatedly stated, “Endemic goiter will be prevented only when society decides to do it.” In preventive medicine it may be difficult to know the will of society and even more difficult to get it translated into action by the government. It can be done, however, as demonstrated in Canada. In the United States, the Federal Government refused to take a stand for the universal use of iodized salt. However, the education on this subject fostered by the state governments and the medical profession throughout the country, together with the good business methods of the large salt producers in making an excellent grade of iodized salt available to everyone throughout the country with no increase in price over plain refined salt, have produced excellent results. All of these forces together have accomplished, temporarily at least, what the government refused to consider as a permanent health measure.

Should the Goiter Study Group of the United States have, now or in the near future, the opportunity to guide Federal legislation to have all food-salt contain iodine, we would now specify that the amount of iodine be 20 mg. KI/kg, instead of the present 50-100 mg. KI/kg. We do not feel that the physiological need for iodine has increased, but rather that some

Kimbell
excellent detailed studies in this country and others have demonstrated that the actual need was never quite as high as we first thought. Curtis of the Ohio State University demonstrated and taught that the average daily need of iodine for active healthy young people, men and women, is 200μg. Von Fellenberg of Switzerland placed the requirement at one-fourth as much, or 50μg, daily. It was on this recommendation that the iodized salt used in 1922 by Eggenberger contained 5 mg. KI/kg., but this has been shown to be too little.

As pointed out in the discussion of food-iodine in Michigan, we must take into consideration the increase in food-iodine from milk. Also, we should remember the complete safety of an iodized salt where 100 mg. KI/kg. is used.

We now feel that the universal use of a food-salt containing 20 mg. KI/kg would be ideal.

Mexico is just now ready to rewrite its so-called iodized-salt law which was passed 20 years ago but has been entirely useless. It now reads “Everyone must use iodized salt,” yet there is no iodized salt in the country. It should read “It is illegal to sell food-salt that does not contain iodine.” The amount of iodine should be fixed by the Department of Health, which I hope will be adequate to prevent all endemic goiter with all of its ugly sequela throughout the entire country.

In a recent letter, Dr. Scrinshaw, Director of Pan-American Institute of Nutrition in Guatemala, states that Guatemala is expected to pass a law in the near future making it “illegal to sell food-salt that doesn’t contain iodine.” Such a law, with penalties and the will to enforce them, will prevent endemic goiter in Guatemala, and in any country where society so wills it.

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REFERENCES


12. This experience was told to me in detail by Dr. Young and Dr. Stemness. It was never published, by agreement with the manager of the plant.


15. Mathews; Curtis, and Meyer: The Effect of Increased Iodine Feeding upon the Iodine Content of Cow’s Milk, Dept. of Research Surgery, the Ohio State University, Columbus, Ohio, Vol. X, No. 3 (Sept.) 1939.


The mechanism whereby digested and absorbed has been much controversy during the last 10 years has been reviewed. Briefly, there have been two views of thought. One school postulated that fat was completely hydrolyzed, and free fatty acid of the small intestine caused that by the small-intestinal mucosa to be resynthesized into fatty acid, while the other that hydrolysis was minimal of the fat was transported unaltered into the small subject has been investigated during the last 10 years, not surprising that the true

Submitted for publication by the Department of Medicine, Roy L. London, W.C.I., England (Dr. I. Medical School, Gastroenterologic Diseases General Hospital, Boston).