

# THYROID SURGERY AS AFFECTED BY THE GENERALIZED USE OF IODIZED SALT IN AN ENDEMIC GOITRE REGION—PREVENTIVE SURGERY

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THE chemical composition of the earth's surface as well as its physical contour has gradually changed through the ages and it is still being changed by erosion and by the washing out of the soluble compounds from the land and their transference to the sea. The soil is also exhausted by agriculture unless that agriculture is scientifically done. Some civilizations that have attained great heights have probably fallen because their soil became exhausted by their crops and the inhabitants had no suspicion of the possible reason or the means of its prevention. Early plant and animal life on the earth probably grew under chemical temperature and radiant energy conditions very different from those of today and the changing chemical make-up of the soil and water probably had profound effects on our evolution. Certainly it is not only the anatomy of animals and plants that has changed.

As the halogen group of elements occur in rather soluble compounds it is natural that ocean water is rich in these compounds and that great areas of land have gradually been depleted of them. Today scientists are reclaiming bromine from sea water on the North Carolina coast in large quantities. As the agricultural scientist is attempting to replace in the fields depleted chemicals it is of interest to read this year of the successful attempts of a Swiss physician<sup>1</sup> in replacing iodine in the soil of his garden thereby raising vegetables richer in iodine content which in turn have proven of value in the prevention of endemic goitre.

Although ancient peoples made pilgrimages to the seashore for seaweed and though burnt sponge<sup>2</sup> was used in the treatment of goitre in the thirteenth century it was not until 1812 that Courtois discovered the element iodine and not until 1895 that Baumann<sup>3</sup> discovered the normal presence of iodine in the thyroid gland. Sporadic attempts had been made both in France in 1860<sup>4</sup> and in Switzerland to treat endemic goitre with iodized salt. Breuer, Kocher,<sup>5</sup> Halsted and others came to the belief that iodine might do more harm than good and attempts to follow through with its use received a setback. Iodine hyperthyroidism (Jodt Basedow) was described by Breuer in 1900.<sup>6</sup>

The work of Marine and his associates awakened a new interest in iodine and goitre. In 1907 Marine reported that iodine is necessary for the normal functioning of the thyroid and that in colloid goitre the amount of iodine present was reduced. He found that if the store of iodine in the thyroid fell below .1 of 1 per cent. the thyroid gland would enlarge. He and his

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associates found out that the iodine store could be increased by the addition of small quantities of iodine by any one of several methods. This arrested the hypertrophy of the gland and the thyroid cells returned to their resting form. In 1928<sup>7</sup> Marine reports: "As a result of the numerous studies of the relation of iodine to the thyroid gland our present views regarding the cause of goitre assume that it is a compensatory hypertrophy of the thyroid depending on a relative or absolute deficiency of iodine. This deficiency of iodine may be due to: (1) Factors which bring about an abnormally low intake of iodine; (2) factors which interfere with the absorption or utilization of an otherwise adequate intake; (3) factors which increase the needs of the body for the iodine containing hormone." The chief factor under number one is the lack of iodine in the food and water supply. Factors under number two are not so well known though there have been recent papers on this subject. Under number three—it is common knowledge that the thyroid is prone to enlarge at puberty, at menstruation, during pregnancies and sometimes in cases of malnutrition and with infections.

Our own experience in Detroit in an endemic goitre region in treating adolescent children with enlarged thyroids with sodium iodide tablets before 1924 showed that the thyroid which enlarged at menstruation did not enlarge after the regular use of iodine. The same satisfactory effect was present in the use of sodium iodide in controlling the enlargement of the thyroid during pregnancy.

That certain articles of food may cause rabbits to develop goitre has been shown by Chesney and Webster<sup>8, 11</sup> when they fed animals on a diet rich in cabbage. When these animals, however, are given additional iodine, the goitre will not develop. McCarrison<sup>12</sup> has for years advocated the infectious theory of goitre and cites an instance of the clearing up of an endemic goitre area in India by substituting a pure water supply for the polluted water supply. An explanation of this may possibly depend again on iodine supply. There is an instance of the opposite effect as cited by Marine and Kimball<sup>13</sup> when a pure water supply from the Cascade Mountains was given to Portland, Oregon, Seattle and Tacoma, Washington. This new water supply was deficient in iodine. Crotti<sup>14</sup> is the leading exponent of the infectious theory in this country.

Iodized salt was first introduced to the public in Michigan in 1925 as a prophylactic measure against endemic goitre. There were, of course, prophets who predicted a dire outcome and there was some foundation for their belief based on the earlier teachings of Breuer, Kocher, Halsted and others, but there was no foundation in actual experience in Michigan.

Michigan lies in one of the two greatest although mild endemic goitre areas of the United States.<sup>15</sup> Surveys of the incidence of endemic goitre have been made in different sections of Michigan by Olin,<sup>16</sup> and Kimball and Slemmons. Serious consideration of the goitre problem in Michigan was the result of the findings of the draft boards during the World War: "Goitre was so prevalent that in some groups as high as 30 per cent. of the persons were

incapacitated for army service, owing to disqualifying toxic goitres in 583 registrants."<sup>17</sup> There were many interesting findings in these surveys—a few miles separation was often marked by a tremendous difference in the incidence of goitre. At Mount Clemens, Michigan, 26 per cent. of the children had enlarged thyroids while at Romeo, Michigan, twelve miles distant 75 per cent. of the children had enlarged thyroids. The water supply at Mount Clemens contained twenty-five parts of iodine per billion while at Romeo the water supply contained not a trace of iodine in fifty litres.

*Michigan Experience.*—Ten years will soon have passed since the introduction of this salt with iodine and we can check on the results of its use. Through coöperation of the Michigan State Medical Society, the State Board of Health, Dr. O. P. Kimball, and the salt manufacturers iodized salt was introduced in 1924 through the grocery stores without any legislative law. Wide publicity of this effort was obtained at that time through letters from the State Board of Health to school children, parents, and organizations. In the clinic of the Henry Ford Hospital we had for a number of years previous to this been treating non-toxic diffuse goitre (simple colloid) in children with sodium iodide tablets with such uniformly good results and no bad results that we believed in the probable efficacy of iodized salt distributed in this manner if it were universally accepted.

Iodized salt in Michigan contains .01 per cent. of sodium iodide. The committee from the Pediatric section of the State Society recommended that the use of this salt should preclude the use of any other form of iodine and to be effective that it should be used for cooking as well as for table use. The salt producers estimated that each inhabitant of Michigan on the average consumed between five and six pounds of salt a year, whereas other estimates placed the consumption at eight pounds per year per individual. The committee accepted the eight pounds per year as a safe average. This would give the average consumer about one milligram of sodium iodide per day.

The iodine content of the thyroid gland, which gland contains over three fourths of the iodine in the body, varies in different geographical areas from 2.4 to 23.7 milligrams with an average of eight milligrams. Orr and Leitch<sup>4</sup> claim the minimum iodine requirement of the body to be about forty-five gammas for an adult and 150 gammas for a child per day. A gamma is 0.000001 Gm. A grain is 0.064 Gm. or 64,000 gammas. As two or three milligrams of sodium iodide per week will prevent goitre and ten milligrams has been proved to do no harm, the average percentage derived from the Michigan iodized salt lies well within safe limits.

*Extent of Use of Iodized Salt in Michigan.*—A letter from the largest salt distributor in Michigan (September 1, 1931) states that "in 1924 we shipped 45,079 cases of plain table salt to the State of Michigan. In 1930, 58,643 cases of iodized salt and 7,057 cases of plain table salt." Letters from the other large distributing salt companies showed the same ratio of about eight of iodized to one of plain salt. A letter received from a large salt

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company shows the following figures for three years of their sales in Michigan.

	Iodized Per Cent.	Plain Free Running Per Cent.
1930.....	84.8	15.2
1931.....	87.4	12.5
1932.....	94.8	5.2

For a few years after the publicity in this matter our patients knew if they were using or were not using iodized salt. Today without the publicity the patient does not know, as a rule, whether he is or is not using iodized salt. Perhaps the lack of publicity too will result in a decreasing use of this

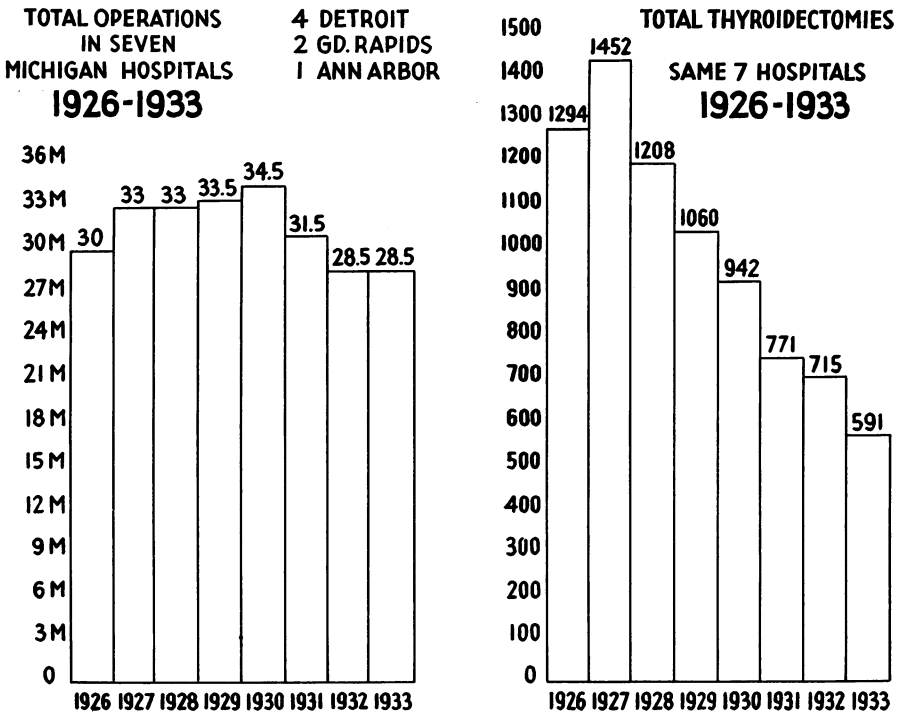


FIG. 1.

salt. Recently a large chain store reported that they are selling only five iodized salt to one plain package.

In 1927 in our clinic there was a gradually increasing number of goitre patients coming to operation in spite of or perhaps because of the introduction of iodized salt. The large majority of the cases were of toxic nodular goitre and we reported our results at that time.<sup>18</sup> The rising curve of operations and the goitre death rate curve in Detroit suggested that the iodine might be harmful and that the experience in Switzerland and France of giving up the use of iodine was correct. However, the iodized salt sales

were under such headway that no effort of discouraging its use was thought of.

During the next few years the number of goitre operations in our clinic fell off so rapidly in spite of an increasing total number of all operations that I was led to ask the seven largest hospitals in Southern Michigan for their statistics. These included University Hospital, Ann Arbor; Harper, Grace, Henry Ford and Receiving Hospitals, Detroit; Blodgett Memorial and Butterworth Hospitals, Grand Rapids. Their figures were freely given to us and curves plotted of each of these and then a composite curve made. (See Fig. 1.)

This curve shows exactly the same results that we were having in our own clinic. In the seven hospitals there were only 591 goitre operations in

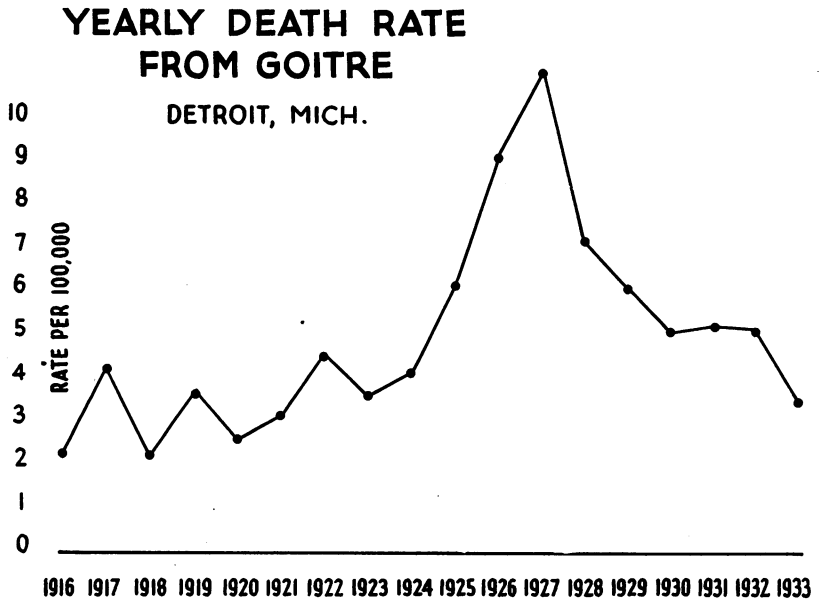


FIG. 2.

1933 as compared to 1,452 such operations in 1927 while the total number of all operations during the depression years dropped—a 60 per cent. drop in goitre surgery compared to 17 per cent. drop in all surgical operations.

The yearly death rate from goitre supplied to us through the courtesy of the Detroit Board of Health suggests too that there was some harmful effect the first few years after the introduction of iodized salt. (Fig. 2.)

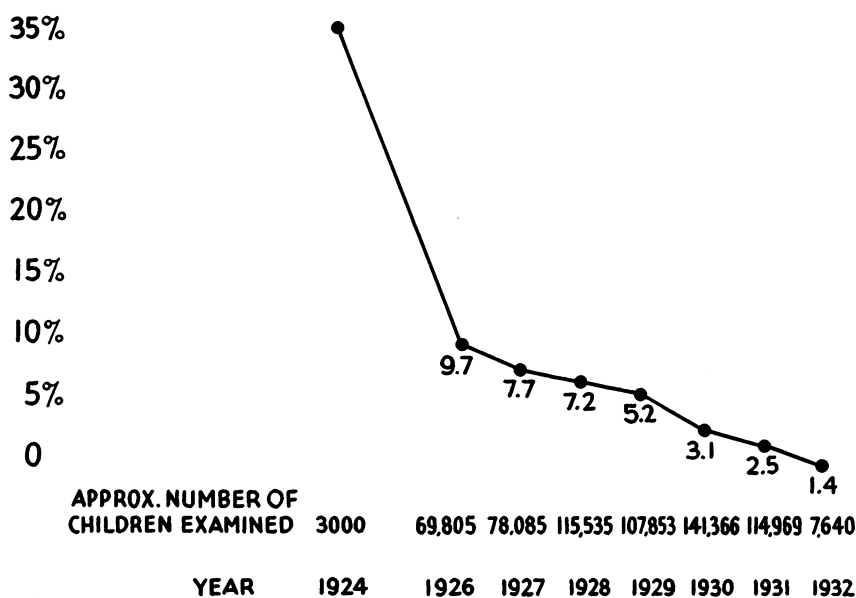
It should be noticed that the death rate is lower than before the introduction of iodized salt for the greatly increased (doubled) population of Detroit in the eighteen years shown.

The most striking figure (Fig. 3) we present here is that showing the incidence of goitre or enlarged thyroid glands in the children in Detroit schools.

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In 1924<sup>19</sup> 35 per cent. of all the Detroit school children showed enlargement of the thyroid. In 1932 only about 1 per cent. had any enlargement of the thyroid. McClendon<sup>20, 21</sup> from the draft board statistics has shown that the incidence of exophthalmic goitres throughout the United States is proportional in every locality to the incidence of endemic goitre. The above two statements have been borne out by our findings as reported here. In this region since the introduction of iodized salt coincident with the great dropping off in the number of enlarged thyroids there has been a dropping off in the number of thyroid operations for hyperplasia and adenomata of the thyroid.

### INCIDENCE OF GOITRE IN DETROIT SCHOOLS \*



\* DR. O. P. KIMBALL

FIG. 3.

DISCUSSION.—As shown in our charts the first year after the introduction of iodized salt in Michigan the rising curve suggests a possible harmful effect and if the iodized salt had been stopped at that time we probably would not have seen the later striking drop in the curve. Kocher in 1904<sup>5</sup> had warned against the indiscriminate use of iodine because of symptoms of hyperthyroidism in adenomatous or nodular type of goitre. Kocher<sup>22</sup> in 1910 and 1911 in papers on Jodt Basedow told of the untoward effects of iodine in exophthalmic goitre. The very name fixed in the minds of his followers the possible dangers of iodine in the treatment of goitre.

From Cleveland in 1926 Hartsock<sup>23</sup> reported that many individuals with goitre are precipitated into a state of hyperthyroidism by the use of iodized

salt but he writes to me in August, 1933: "At the present time we doubt very much if we see any cases that are of this nature, *i.e.*, iodine hyperthyroidism."<sup>24</sup>

Cowie, of Ann Arbor, has been especially interested as one of the responsible committee in investigating several cases of hyperthyroidism supposed to have been induced by the use of iodized salt. He reports: "We have run down several reports of ill effects from the use of iodized salt, but in each instance we have found that the reports were fallacious."

Arnold Jackson<sup>25</sup> reported fifty cases of iodine hyperthyroidism. He also reports:<sup>26</sup> "Simple adenoma is one form of endemic goitre which closely follows colloid goitre in regional distribution. The incidence of adenoma of the thyroid is decreased by the prophylactic treatment of colloid goitre. Apparently adenomas frequently start in neglected colloid goitres as a form of compensatory development. Adenomas rarely cause constitutional symptoms before the patient is twenty years of age unless provoked by iodine medication."

In studying our records we failed to find any goitre patients who had developed iodine hyperthyroidism or Jodt Basedow of Breuer following the use of iodine prescribed by their physicians or the use of iodized salt. Some of our patients with toxic diffuse goitres as well as with toxic nodular goitres became iodine fast or iodine resistant. The improvement stopped and they again became more toxic. The iodine administration was stopped after it failed to hold the improvement as shown by the basal metabolism tests. We then became interested in looking up a group of patients who really received large doses of iodine over a long period of time.\*

Can iodine hyperthyroidism be produced in an individual with a normal thyroid with enormous doses of iodine? We believe that this does not occur. We quote reports from two large divisions of syphilis where patients receive huge doses of iodine. Dr. Earl Moore, of the Division of Syphilis of the Department of Medicine at the Johns Hopkins Hospital, reports to me that they have records of over 10,000 patients treated with large doses of iodides with no record of a case developing iodine hyperthyroidism. Dr. Frank Menagh, of the Henry Ford Hospital, reports to me that among 6,000 cases of syphilis treated with large doses of iodides there was only one patient that presented symptoms suggestive of iodine hyperthyroidism and this was very questionable. These patients in our syphilis clinic were, of course, living in an endemic goitre region, so many had mild simple goitre.

Marine and Kimball<sup>13</sup> reported: "The administration of any salt of iodine in any manner completely protects the remaining thyroid against compensatory hyperplasia."

#### CONCLUSIONS

(1) Iodized salt as used in Michigan did at first apparently increase the number of thyroid operations.

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\* Authorities pretty well agree that the iodine is readily used by the body whether taken in the form of Lugols, KI, Na.I., hydriodic acid or syrup of ferrous iodide.<sup>27</sup>

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(2) The increase was in the nodular goitre or adenoma group, and we believe the iodized salt may have activated a group of quiescent adenomata producing toxic goitre symptoms.

(3) The increase reached its peak in the second year after the introduction of iodized salt.

(4) An increase in the death rate from goitre as shown by the Board of Health statistics reached its peak in the second year after the introduction of iodized salt.

(5) There was no increase in hyperthyroidism excepting in the nodular goitre or adenomata group.

(6) The number of operations for toxic diffuse and toxic nodular goitre has rapidly and steadily decreased after the apex of the second year increase had been reached.

(7) The incidence of endemic goitre or enlarged thyroid has been reduced almost to nil since iodized salt has been so widely used.

(8) We now see no cases which show the slightest ill effects from the use of iodized salt.

(9) Toxic nodular goitre and toxic diffuse goitre are less apt to occur when there has been no previous enlargement of the thyroid (endemic goitre), at least this would seem a safe conclusion based on our experience.

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