THYROID STUDIES I. THE DISTRIBUTION OF GOITRE AMONG INDIANS; ITS BEARING UPON THE ETIOLOGY

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"Goitre" is here used in its broad sense to indicate all thyroid enlargements. Even a meagre review of the literature will show the complexity of this condition by the numerous theories offered. The outstanding factors concerning the etiology which seem to have the most accurate scientific support are iodine deficiency [Marine and co-workers (1)] and the accumulation of toxic products [McCarrison (2) and others (3, 4, 5, 25)].

Marine and his co-workers have shown the great affinity of the thyroid for iodine (1). Many investigators have shown the constant presence of iodine in thyroid tissue. Iodine as such has been used with favorable results for treating goitre since the early part of the nineteenth century (1). In 1917, Marine, Kimball, Lenhart and Rogoff demonstrated the beneficial effect of iodine as a prophylactic in cases of thyroid instabilities. Since then this work has been repeated in Switzerland and also in this country (9). The results point strongly toward a relationship between thyroid disturbances and the iodine obtainable. An uneven distribution of iodine throughout the country suggests that goitre districts are probable iodine deficiency districts. The early works of Forbes and Beegle (6) on iodine distribution throughout the United States needs supplemental information because of later improved methods for iodine determination. McClendon (7, 8) has undertaken a recent study of iodine distribution by an improved technique. In this preliminary report he shows a striking parallelism between iodine distribution and goitre districts. These results are indicated in Figure II. The statistics for goitre incidence used by McClendon are those

compiled by the War Department and are the only ones available for the country at large.

Many investigators have shown the effect of various toxic materials upon the thyroid gland. McCarrison found that fecal contamination could produce thyroid changes (2). Burget produced changes in the histological appearance of the gland by unhygienic surroundings (3). Sows which are fed a high protein diet, thus increasing intestinal putrefaction, gave birth to goitrous pigs (11). Therefore not only the iodine assimilation but toxic materials as well have been shown to affect this gland.

It appeared to us that an approach toward the selection of fundamental factors involved might be made by a detailed study of the incidence and distribution of the disease. Such a study would indicate the location of goitrous regions. The factors peculiar to these regions could then be studied. Many limited survey studies have been made and goitre districts of this country as well as the world at large have been mapped out, yet it seems that no satisfactory explanation has been given which will apply equally to all of these districts. A complete survey of the incidence of goitre in this country would be invaluable. Such an undertaking is beset with numerous difficulties. We believe that a contribution might be made by undertaking a goitre survey of one class of people, inclusive enough to be indicative of the whole country yet small enough to make possible a careful survey. A class should be chosen which is made up of un-nomadic inhabitants of the localities being investigated. This class must be one that would not show any racial immunity to the disease.

The native North American Indians seem to meet all requirements very well. This race is numerous enough to give indicative figures of the localities being investigated. Moreover, the Indian population is not too massive for an accurate survey, especially since the tribes are cared for on reservations under supervision. A study of Indian life shows the un-nomadic characteristics of the race. This is probably more pronounced with the Indian than with any other class of American people (12). Consequently these people have not come under the influencing factors of outside regions. Since the Indians have

goitre and the incidence is very high in some districts, racial immunity does not exist.

Our information concerning the incidence of goitre among the Indians was kindly furnished by Doctor R. E. L. Newberne, Chief Medical Supervisor of the Indian Commission. A questionnaire was sent throughout the Indian population during the Fall and Winter of 1922-1923. The data were gathered by the respective Indian physicians, compiled by the Indian Commissioner's office and forwarded to us. The results obtained from this survey are shown in Figure I, the incidence of goitre being arranged according to States.

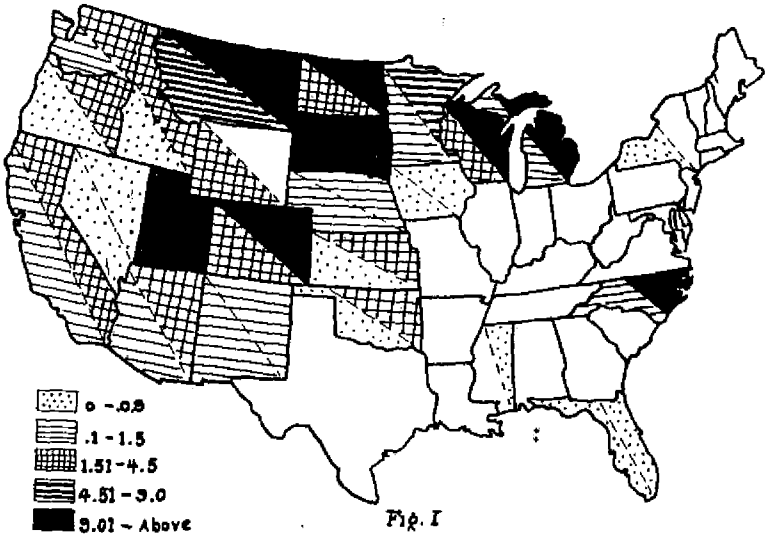

Figure I. Indian surveys. Goitre incidence by states. Lower and left hand half indicates incidence of goitre as shown by the survey of 1908 (Hrdlicka). The upper and right hand half indicates the incidence as shown by the survey of 1923. States left blank indicate states from which no statistics were obtainable.

A complete goitre survey among the Indians was compiled in 1908 by Hrdlicka (13), who was working, at that time, in conjunction with the Indian Commission. These data are shown in Table I; they give the proportions per thousand of population for the various tribes. We have rearranged these figures to show the incidence of goitre according to States.

A study of the results of these Indian surveys shows goitre to be present among this race. It also bears out the generally reported observation that goitre in the United States is regional

TABLE I

Goitre among Indians. Proportions per thousand of population.

Tribe	State	Per 1000	Tribe	State	Per 1000
Blackfeet and Sioux	S.Dak.	61.4	Shoshoni and Arapaho	Wyo.	3.6
Ute	Utah	35.4	Mission Indians	Calif.	3.1
Oneida	Wis.	26.7	Apache (White Mt.)	Ariz.	2.9
Cheyenne	Mont.	25.6	Sioux (branch)	S.Dak.	2.9
Sioux	S.Dak.	14.3	Sioux (branch)	S.Dak.	2.9
Menominee	Wis.	10.9	Sioux (branch)	N.Dak.	2.8
Indians (Genoa School)	Nebr.	10.0	Hopi	Ariz.	2.1
Sioux (branch)	S.Dak.	7.8	Oneida	Wis.	1.9
Chippewa	Mich.	6.7	Cheyenne	Okla.	1.8
Crows	Mont.	6.6	Coeur d'Alenes	Wash.	1.7
Indians (Ft. Berthold)	N.Dak.	6.6	Piegan	Mont.	1.5
Southern Ute	Colo.	5.6	Pawnee	Okla.	1.6
Rio Grande Pueblos	N.Mex.	5.3	Yuma	Calif.	1.5
Sioux (branch)	S.Dak.	4.3	Cherokee	N.Car.	1.4
Sioux (branch)	Mont.	4.2	Apache	S.Colo.	1.3
Navajo	Ariz.	4.1	Sioux (branch)	S.Dak.	1.2
			Sioux (branch)	S.Dak.	1.1

From Bull. 34 Bur. Am. Ethnology. Physiological and Medical Observations among Indians. Hrdlicka.

in distribution. These regions are considered to be in the Pacific Northwest, the North Central States, Great Lake District and in the Appalachian Highlands. Thus, excepting the Pacific Northwest, the incidence among Indians is roughly parallel with the incidence among the population as a whole. It will also be further seen that goitre has been increasing among the Indians. This increase seems to be quite general although more pronounced in the goitre regions. The number of cases reported in 1908 was 376 for an Indian population of 125,000, giving an incidence of three per thousand. In 1923, this increased to 3092 cases for a population of 189,200, giving an incidence of 16.3 per thousand.

In the light of Marine's work to which reference has been made it would seem most logical to turn to a possible iodine deficiency as the etiological basis for this affliction. While definite experimental data are incomplete to show this factor to be responsible for goitre development, the prevention work with iodine is highly suggestive. If this deficiency is the cause, districts with a scarcity or absence of iodine must be present and these districts must coincide with the goitre districts. McClendon's work points in this direction but, as the author states, it is far from complete (7, 8).

Because of the lack, then, of complete information concerning iodine distribution, attention may be turned to these conditions that may influence its deposition. Iodine is found in small quantities on the earth's crust widely distributed, but by far in greatest amounts in the sea. It is the most sparingly deposited of the halogen salts (14). Analysis of sea-water shows iodine to always be present, the amount usually being stated as 100 mg. per litre. Iodine is found in nature almost exclusively as sodium iodide, the most soluble of natural salts. This salt is about five times as soluble as sodium chloride. This difference of solubility can easily account for the abundance of sodium chloride and the scarcity of sodium iodide.

When salts are deposited the most insoluble will be the first to reach saturation and consequently deposition (16). On the contrary, the most soluble will be the last deposited. Thus the most soluble salt will continuously be kept in solution if more water is added to the evaporating body of liquid and also it will be the soluble salt which will run off if the supernatant fluid escapes. Therefore, as Hayhurst has indicated (14), iodine is scarce upon the earth's crust because: (1) "it has been carried off by supernatant fluid during the process of the drying-up of saline waters; (2) the dissolving-out process that occurs as a result of the percolation of the rains and subterranean waters carries out the soluble salts (iodine); (3) the pent-up deposits and brines have been perfused so long by fresh waters as to carry away their more soluble constituents."

Geographic districts that would be favorable to iodine deficiency should therefore be those regions which show at least some of the following meteorological and geological characteristics. First, they must have been thoroughly washed by fresh water perfusion. This may have been caused by the washing from the melting of old glaciers, the percolation of abundant rainfall or the perfusion by subterranean waters. Secondly, the slope of the country must be such that the water will rapidly flow off, thus removing the soluble constituents from the region. Thirdly, these regions farthest removed from the sea would have the least opportunity for replenishing the iodine lost.

The goitre districts of this country are situated in such regions. The Pacific Northwest, although of relatively recent

geologic origin, has been, nevertheless, subjected to many washings. The flow from the old glaciers passed over this country. Again we find great fresh water perfusion as the result of heavy yearly precipitation. Notwithstanding that this country is along the sea coast, its slope is such as to favor rapid movement of both surface and subterranean waters. No other sea coast of the United States has the slope or the precipitation this coast shows. Therefore iodine loss might be expected to be greater than any iodine deposition from sea air. Consequently iodine deficiency can be expected.

The Rocky Mountain States are in a rugged country. Although their rainfall is but moderate, the slope offers rapid drainage. As has been indicated by Hayhurst (14), the mountains are the first to lose their supply of iodine. The glacier water also washed these soils. Therefore this district should also show an iodine deficiency.

The Great Lakes territory was influenced more by the glacier period than any of the vicinities previously mentioned. The precipitation of this district is moderate and the slope gentle. Consequently it would seem that past periods have had more bearing upon the depletion than present conditions. However, the continual fresh water perfusion that is now taking place makes the depletion more complete. On the other hand, the Appalachian Highlands are apparently affected more by percolating rains and fresh water perfusion. It may be pointed out that the area in western North Carolina shows the heaviest rainfall of the East. This district is also mountainous, which insures rapid drainage. Thus, if our hypothesis is correct, other iodine deficiency areas should be located in these regions.

The South appears to be comparatively free from goitre. This part of the country has a gentle slope. The waters which arise in the North, particularly the North Rocky Mountain, North Central and Great Lakes States, flow down over the gentle slope of the South. During the course of this flow the more soluble substances of the soil will be carried off from the North, only to be deposited in those regions where evaporation makes the concentration sufficient. As evaporation is continually taking place and as the Southern States have the gentle slope which retards the movement of the flow, iodide salts could be

deposited in these regions. Moreover, as the slope at the sea coast is much less abrupt in both the East and South, iodine deposited from the sea air should not be washed out as rapidly as in the Northwest. The Southwestern States are the most arid of the United States. Although this district is somewhat mountainous, the geographic formation is more of a high plateau. As a result of these conditions the percolation due to rainfall and the fresh water perfusion is lacking. The Southern States were not affected by the glacier period and consequently the South should be a land rich in iodine.

Previously it was stated that the results from the Indian survey (1923) indicated a parallelism of the incidence of goitre among the Indians and the country at large. Exceptions, however, will be noted as occurring in the Pacific Northwest. In this area goitre was practically absent from the Indians in 1908 and at the present time is much less frequent than among the white race. Three explanations may be offered for this variation. The primary cause, apparently, is found in the Indian diet. The American Indian, like most aborigines, uses those articles of food most easily obtained (12). Among the chief substances of diet of the Northwest Indians is salmon, and to a lesser degree other sea foods. Salmon composes a very large part of the diet not only during the fishing season, but it is eaten in the dried form a greater part of the year. Fishing is universal among these Indians and even the inland tribes obtain this sea food. Jordan (20) has shown that salmon run to the headwaters of the Northwest streams to a distance of 2500 miles. It has been shown [Cameron (21)] that "all sea species of animals contain iodine." The iodine obtained from the diet of salmon by the Indians should, on the basis of Marine's results, serve to prevent the development of goitre. Attention may also be called to the fact that the Indian of the North depended also in a large part on game for food. Unlike the white people, the Indians utilized the whole animal, which would include thyroid gland in the diet. The average amount of iodine found in thyroid tissues varies from 0.050 to 0.777 mg. per gm. of fresh tissues (1), depending upon the activity of the gland. Even so small an animal as the rabbit would furnish about 0.155 mg. of iodine. As it has been shown that 100 to 200 mg. of iodine twice

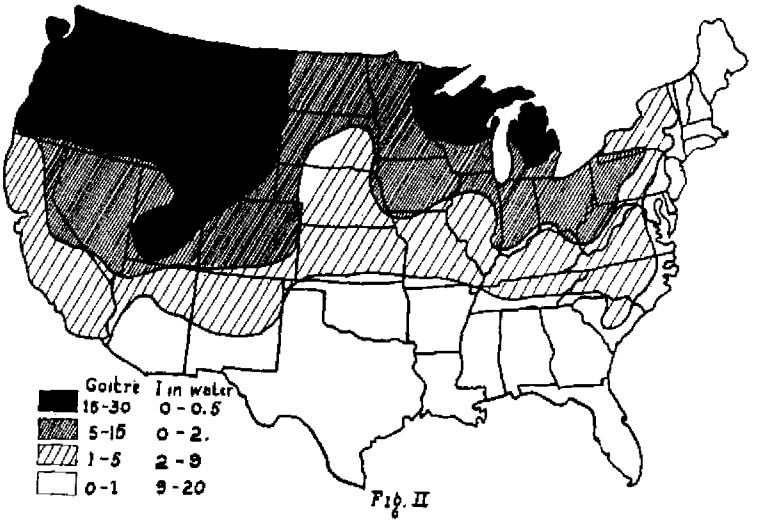

Figure II. Shows the incidence of goitre per thousand as determined in "Defects Found in Drafted Men, War Department, 1920," and the amount of iodine in the water. The curves have been rounded off. (McClendon, 7.)

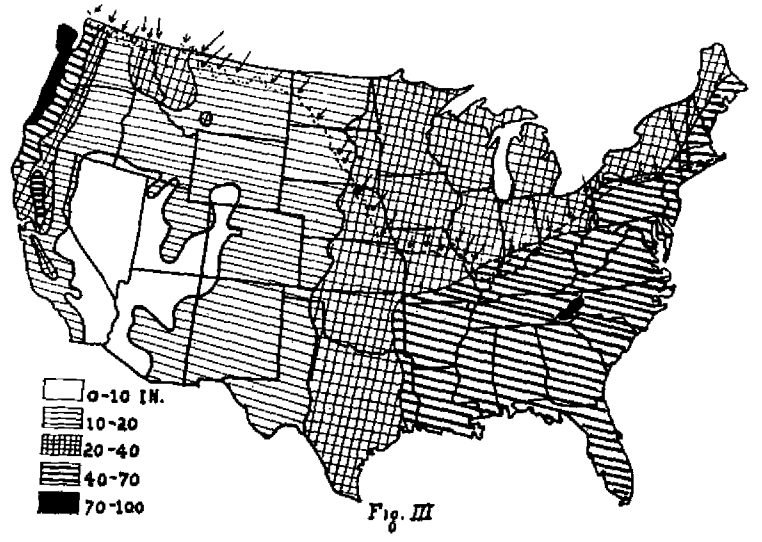

Figure III. The shaded areas show the annual precipitation of the United States (U. S. Department of Agriculture, Weather Bureau, Bull. Q, Climatology of the United States, by A. J. Henry). The dotted line indicates the old glacier line from which waters flowed over the northern part of the United States. (Geology by Chamberlain and Salisbury.)

a year is sufficient to prevent simple goitre in man (1), this source of supply would offer a significant amount. Third, it may be suggested that the modern method of agriculture tends to rob the land of iodine without any means of replenishing the supply. This is brought about by the constant use of the soil, the plants taking up the available iodine. The greater ease of fresh water perfusion in cultivated land is also a factor. Studies made in Germany (22) show an increased amount of goitre during the war, which is in part explained as due to the discontinuation of nitrates, containing also iodides, shipped in from Chile and the substitution of guano for fertilization.

This survey shows a decided increase in incidence of goitre among the Indians. It would seem that the tendency of the Indian to adopt the habits of civilized life can not account for it. If this were the case, the whites of non-goitrous regions should show a higher incidence. The diet, however, deserves consideration. In the Northwest, for instance, the salmon is taking a smaller and smaller place in the diet of the aborigines. This scarcity of salmon for the Indians has already been the cause of much complaint and court action (23). The purified foods, including white salt, are becoming the larger part of the diet. Thus the Indian of this district is being placed under the same living conditions as the whites. He also is starting to show the same high incidence of goitre as found among the white people of this district. In other parts of the country the sea food factor is eliminated. However, the question of diet is not eliminated. The Indian of today has not the quantity of wild game which was previously consumed. The salt supply of these natives was often crude salt which in many localities contains iodides. It would seem, then, that the purified diet may be a factor concerning the increased incidence of goitre in other districts.

Two districts other than the Northwest show decided increases of goitre that deserve special note. Oklahoma shows an increase from .02 per thousand to 1.6 per thousand. This State has been the great gathering point for many Eastern tribes. Although a careful study of the conditions could not be made, it seems probable that a change in environmental factors would explain this increase. North Carolina has an incidence which

has increased about 8000 times during the interval between surveys. These conditions, likewise, could not be carefully studied. The entire results from the second survey were obtained from the Cherokee school situated at Ashford, North Carolina. This city is also in the heart of the East's greatest precipitation area as well as being in a mountainous country. Therefore the factors are present in this locality which would favor iodine depletion.

Utah, although partly in the arid region, shows a high incidence of goitre in both surveys. This State's average is accounted for by the high incidence found among the tribes located in the northeastern part of the State. This location has a moderate rainfall and also is more mountainous district than the rest of the State. The tribes of southern Utah show practically no gaitre.

While most of our evidence points to iodine deficiency, the second class of etiological agents, i. e., toxic products, seems to play its part. Investigations have indicated that changes occur in the thyroid tissue following the administration of fecal substances (26). Such data would suggest an increased demand made upon the thyroid during intoxications by such substances. Farrant (25) has shown that many intoxicating diseases cause an increased activity of the thyroid gland as demonstrated by hyperplasia of this gland. He has even classified diseases by the manner in which they affect the thyroid substance. Among the afflictions which cause this change in the gland is tuberculosis. The increasing prevalence of this latter disease among the Indians has long been shown (24). It is suggested that the body needs more iodine during such a strain upon the organism and leads to the assumption of an iodine balance in this gland. As McCarrison (19) has pointed out, an iodine sufficiency may become a deficiency if some extra load is thrown upon the gland.

SUMMARY

1. Goitre is present among the Indians and the incidence of distribution is, for the most part, parallel to the distribution among the white population.

2. The greatest exception is noticed in the Pacific Northwest, where the natural Indian diet contains more iodine (salmon) than does the white man's diet.

3. Goitre is increasing among the Indians and this increase seems to be explainable by two factors, iodine deficiency and toxic influences upon the organism.

4. Simple goitre seems to be the result of iodine deficiency, produced by a low amount of iodine or an increased thyroid demand.

5. These results seem to offer further support of the work by Marine and co-workers (1) and McClendon (7).

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