ONE THOUSAND ONE HUNDRED FORTY-SIX GOITERS IN ONE THOUSAND SEVEN HUNDRED EIGHTY-THREE PERSONS

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INTRODUCTION

Obscurity and darkness in the field of medicine excite the profession to research. This applies directly to the goiter question, where much has yet to be learned in order to unearth a causative factor which may act directly or indirectly, but, where possible, a careful study of a large series of persons will add, at least, a stepping stone to the necessary knowledge. In this country, before the last draft of men for our army, no thorough tabulation of thyroid enlargements in relation to large numbers examined, and to so many sections of the United States, could have been accomplished with any degree of accuracy. Previously, these data were collected from irrelevant groups, except in a few instances (O. P. Kimball and D. Marine¹), but we must centralize our information about a thorough classification of many individuals in definite districts, and eventually, compare cause or causes from different areas. Bircher² and others in central and southern European countries have given us their results from such collections.³

Therefore, the opportunity appealed to me in the comparative tabulation in the draft which I reported in March, 1919.⁴ Since that time, on account of the great many statements made and which are not based on any records as to the relative proportion of goiters at the various ages, in the sexes, in periods of life, etc., I examined 1,783 unselected persons, in 1918 and 1919 living in our community, which lies distinctly in the Great Lakes goiter belt, in their relations to enlargements of the thyroid.

I have chosen the district in Torch Lake and Schoolcraft Townships of Houghton County, Michigan. Here there happen to be three distinct water supplies; first, spring water from the Gregory Springs;

1. Kimball, O. P., and Marine, D.: Prevention of Simple Goiter, *Arch. Int. Med.* **22**:41 (July) 1918.

2. Bircher: Etiology of Goiter, *Practical Med. Ser., Surgery* **2**:275, 1918.

3. Goyanes: Endemic Goiter and Cretinism in Spain, *Endocrinology* **4**:491 (July-Sept.) 1920.

4. Levin, Simon: Discussion of Goiter in Five Hundred and Eighty-Three Registrants, *J. Mich. M. S.* **18**:98 (March) 1919.

TABLE 1.—THE RECORD OF EXAMINATION OF 1,783 PERSONS FOR GOITER IN
TORCH LAKE AND SCHOOLCRAFT TOWNSHIPS, HOUGHTON
COUNTY, MICH., IN 1918-1919

Age	Males	Females	Single	Married	Born Here	Born Elsewhere	Total Goiters
1	19	33	52	..	50	2	8
2	23	22	45	..	44	1	12
3	19	25	44	..	40	4	17
4	16	12	28	..	23	5	13
5	26	16	42	..	36	6	19
6	15	17	32	..	30	2	23
7	14	15	29	..	26	3	18
8	21	38	59	..	52	7	42
9	18	24	42	..	33	9	33
10	20	30	50	..	45	5	44
11	18	18	36	..	29	7	29
12	20	37	57	..	52	5	51
13	15	26	41	..	33	8	37
14	24	27	51	..	46	5	43
15	14	21	35	..	30	5	26
16	14	34	48	..	43	5	41
17	24	22	46	..	41	5	39
18	22	24	43	3	42	4	43
19	11	28	37	2	36	3	37
20	16	19	29	6	29	6	28
21	16	12	24	4	25	3	24
22	6	18	19	5	23	1	19
23	10	25	19	16	28	7	28
24	16	23	23	16	32	7	27
25	13	11	7	17	17	7	15
26	13	17	17	13	25	5	23
27	13	14	8	19	17	10	17
28	11	13	8	16	20	4	17
29	10	9	2	17	15	4	12
30	12	21	6	27	21	12	23
31	10	15	7	18	16	9	18
32	12	11	6	17	14	9	14
33	4	14	3	15	9	9	12
34	11	22	1	32	20	13	22
35	7	12	3	16	15	4	12
36	17	12	3	26	21	8	18
37	5	15	0	20	12	8	16
38	10	15	1	24	14	11	15
39	7	14	1	20	11	10	13
40	13	19	3	29	22	10	17
41	11	6	2	15	9	8	10
42	10	14	2	22	8	16	16
43	10	8	2	16	10	8	13
44	15	13	3	25	18	10	14
45	13	12	3	22	15	10	16
46	4	8	0	12	4	8	11
47	7	8	2	13	4	11	9
48	10	12	1	21	3	19	11
49	12	9	1	20	5	16	9
50	4	8	0	12	2	10	6
51	5	6	0	11	0	11	8
52	3	7	0	10	2	8	5
53	5	6	0	10	4	7	6
54	4	2	2	4	0	6	3
55	2	5	0	7	0	7	3
56	7	6	0	13	1	12	6
57	7	2	1	8	0	9	4
58	5	7	0	12	2	10	6
59	1	1	0	2	2	0	2
60	10	6	1	15	0	14	5
61	44	33	2+	66+	2+	31+	19

second, Lake Superior water, and third, well water, which is spring water. The people are Americans, the larger percentage of French Canadian extraction, above the average in intelligence and in living conditions. The unhygienic conditions usually found in the poorer districts are absent. Each home has plenty of sunlight and ventilation and a lot or two for gardening. I am personally and professionally acquainted with nearly every person examined. Therefore, my knowledge of them would be of greater value than a simple school examination of many strange groups, whether adults or children. I have compiled the results as shown in the charts, making them as complete and self explanatory as possible. The charts demonstrate very clearly the numbers and percentages in the various ages and sexes from new-born to 61 years plus, in their social and residential relationship, and various types of goiter found in these individuals. There were 790 males and 993 females; 242 full family records; 714 married and 1,029 single; 1,243 were born here and 538 were born elsewhere. Three hundred and forty-one of the latter lived here fifteen years or more.

The definitions used in these examinations were those usually in use.

Group 1.—Simple goiter is one giving no symptoms, except an homogeneous enlargement of both lobes and isthmus that may be small, moderate or large. Six hundred and eighty-two goiters were found to be in this group.

Group 2.—Adenoma, whether fetal or adult, is an enlarged thyroid with a circumscribed mass, or masses, occupying any portion or portions of the gland, being single or multiple. These tumors were classified as small, moderate and large. The cystomas could not always be differentiated macroscopically from adenomas, as our living surgical pathologic specimens demonstrate. Therefore, I classified that group as adenomas and cystomas. Four hundred and twenty goiters belong to this group.

Group 3.—Colloid goiter is an enlarged thyroid gland, firm, symptomless, except from pressure, all the gland involved. The gland feels firmer, doughier and of a different consistency than simple, having no circumscribed masses. Forty-four goiters belonged to this group.

Exophthalmic goiter was also noted, but the proportion was comparatively small. It is rather surprising that among so many goiterous individuals we see so few cases of true exophthalmic goiter, whereas, it is very common to see hyperthyroidism, especially during puberty and the menopause. I find that adenomas becoming active make up the larger proportion of the latter class. In my operative work, the partial thyroidectomies for hyperplastic adenoma for hyperthyroidism

also comprised a large proportion, which only signified that the danger from this phase predominates in the goiter situation in our section, pressure and cosmetic phases comprising a lesser proportion.

The record of infection in each individual was not complete, although many observations would justify my saying something further in this regard. Cretins are very rare in our community, and cases of hypothyroidism are not common. The two cretins here are members of goitrous families in which the maternal parent had a goiter. The families with definite morons are not common, but during the draft examination I found a few families with several morons in each family whose maternal parent or both parents had developed enlargements of the thyroid. I must grant that the numbers and percentages of goiters startle one on examination of the charts, but my observations can be verified by any capable observer who attends an evening or afternoon entertainment in summer.

TABLE 2.—TOTAL NUMBER OF PERSONS AND DIFFERENT TYPES OF GOITERS

	Total Persons	Total Goiters	Group 1 Simple Goiters	Group 2 Adenomas and Cystomas	Group 3 Colloid Goiters
Males.....	790	355	230	119	6
Females.....	993	791	452	301	38
Totals.....	1,783	1,146	682	420	44

TABLE 3.—PERCENTAGE OF DIFFERENT TYPES OF GOITERS TO THE TOTAL NUMBER OF PERSONS AND SEXES EXAMINED

	Total Persons	Total Goiters, per Cent.	Group 1, per Cent.	Group 2, per Cent.	Group 3, per Cent.
Males.....	790	44.9	29.1	15.0	0.76
Females.....	993	79.6	45.5	30.3	3.8
Totals.....	1,783	64.2	38.2	23.5	2.5

INFLUENCE OF WATER SUPPLY

The examination disclosed that the numbers and proportions of different types of goiter at the various ages and sexes did not vary with the different water supplies, in spite of the fact that the water from Lake Superior must be considerably diluted, and, therefore, any chemical or active virus must be in proportionate dilution. The spring water comes from bubbling springs from five to eight miles in a crow's path due east from the shore of Lake Superior. The former flows into a lake tributary (Torch Lake) of the latter twenty miles from the intake of the Lake Superior water supply station. An adequate idea of the location and relative distances can easily be acquired by a reference to a map of the Keweenaw Peninsula of Upper Michigan. Space does not permit me at this time to mention the

results of examinations of the various water supplies, but I may add that the waters about the county, whether spring water or Lake Superior water, from various sources, have a constant factor. The relation of calcium to sodium elements is always more than 1:1, and this relationship occurs but rarely in any other water supplies in the United States. The water supply has been given the credit for carrying the positive factor of goiter but in this incident, it does not assist us any in determining it. At some future date this study will continue and further information will be presented on this phase of the subject.

Chart 1.—Outline dots indicate percentage of total goiters to number of persons in each year in the 1,783 examined. AB, mean curve of percentages.

INFLUENCE OF AGE AND SEX ON INCIDENCE OF GOITER

The occurrence of goiter in age is so differently influenced by the nature of the sex, that a comparative study of these two factors would be more advantageous. The goiters commence at the first year in about 22 to 26 per cent. of those examined at that age, both sex percentages advancing rapidly towards puberty, much steadier in the female, whose percentage of total goiters in the period from 10 to 15 years being about 94, while that of the male averages about 68.

Chart 2.—Outline dots indicate percentage of total goiters to numbers in each year in the 993 females. CD, mean curve of percentages in five year averages.

Chart 3.—Outline dots indicate percentage of total goiters to numbers in each year in the 790 males. EF, mean curve of percentages in the five year averages.

The mean curve of the goiter percentages in the female is maintained throughout life above 80 per cent., while that of the male drops very markedly to about 20 per cent. between 35 and 40 years of age, when it gradually rises to the height of 32 per cent. at 42, slipping down later with accidental fluctuations till 20 per cent. is reached near the end of life.

One can readily see that as the functions of the glands of internal secretions are more drawn on by the female at puberty, during child bearing and at the menopause, she has more reason for alteration and growth of this important gland. Therefore, the findings in the percentages demonstrate this fact very clearly. Her incidence of thyroid enlargement is maintained more steadily, not dropping as in the male, after the rise at puberty has been established. In the examination of women at confinement, more than 90 per cent. had their thyroids enlarged from just a palpable mass to a size that interfered with respiration, extending from chin to sternum and latterly bulging the sternomastoid as much as the muscles would permit. Adenomatous masses, simple goiter and normal gland tissue, under ordinary conditions of life, all became hypertrophies during pregnancy. The constant stimulating influence, coupled with the goiter belt irritation, no doubt helps to cause a permanent enlargement of the thyroid gland in these simple and adenomatous goiters.

DIFFERENT TYPES OF GOITER

An interesting fact that the tabulation and deduction of percentages of the two important groups of goiters by sex and ages has established, is that in the first half of life in both sexes, till 35 years of age, the maintenance of the large percentages of goiters is due to the simple enlargement of the gland, and that as the age arrives when growths are more prevalent, we see the adenomas and cystadenomas arriving to absolutely maintain the percentage in the female and the male. The curves show that puberty affects the growth to simple goiter earlier than the enlargement of the adenomatous masses. Therefore, the solid line declines at 16 years and the broken line declines at 19 years. Charts 4 and 5 plainly give this wonderful and startlingly clear information. The similarity in time of the appearance of growths corresponds very closely to our idea of growths in other vital parts of the human body, i. e., the cancer period commences at about 35 years of age, and fibromas of the uterus are more marked after from 32 to 35 years of age, etc. No absolute age of commencement of the growths can be established because, no doubt, there were embryonic retention nests potentially amenable to excitation of growth, growing slowly, from the very beginning.

Chart 4.—Different types of goiters in 993 females from 1 to 61 years of age inclusive. Outline dots indicate percentage of simple goiters (Group 1) and solid triangles percentage of adenomata and cystomata (Group 2) to the total females examined for each year. Solid line, mean curve for Group 1; broken line, mean curve for Group 2.

Chart 5.—Different types of goiters in 790 males from 1 to 61 years of age, inclusive. Outline dots indicate percentage of simple goiters (Group 1) and solid triangles percentage of adenomata and cystomata (Group 2) to the total males examined for each year. Solid line, mean curve for Group 1; broken line, mean curve for Group 2.

PARENTAL RELATIONSHIP OF GOITER

Out of the total numbers examined, mothers alone had goiters in 802 instances, fathers alone in twelve, and both parents 183 times. These figures are only complete as far as they go, because in some families neither the history nor observation could establish data sufficient to note whether the parent or parents had any enlargement of the thyroid.

In the families with four or more children, the family record being complete, it was found that the presence of goiter in both parents resulted in many goiters among the children. Adenomas in both parents, especially the father, meant adenoma in the children. According to Chart 6, which contains records of full families, the influence of the presence of goiter in the mother is four times as great as that in the father. The presence of goiter in both parents leaves the offspring without the smallest possible chance of not developing goiter, if they continue to live in this district.

Chart 6.—Percentage of total goiters in 242 complete families with 1,192 persons.

REPORT OF CASES

1. Family A. P. Father and mother were born in Lower Canada and have adenoma in the right lobes of the thyroid. All the children, four girls and two boys, were born here, living here always. The eldest, a girl, aged 18, has a small simple goiter, but all the other children have adenomas in the right lobes, varying in size from small to large.
2. Family P. M. Father and mother born in Canada and had nine children, eight boys and one girl, all born here, living here always. The father has a small right adenoma, the mother has large multiple adenomas, and the four older children all have from small to moderate sized adenomas, the five smaller ones having small simple goiters.
3. Family L. P. Mother and father born in Canada and had eleven children, six boys and five girls, all born here, living here always. Parents both have adenomas of the thyroid and all the children, except a boy, aged 6, who has an adenoma, have from small to moderate sized goiters.
4. Family E. C. Father and all the children born and always lived here. The mother was born in Arkansas. Mother and father have large and multiple adenomas, respectively, and the children, seven boys and five girls, all except a 2 year old girl, have goiters (three have adenomas, and the others simple goiters).

There is, no doubt, an influence in the mothers with large exuberant thyroids to give birth to infants with enlarged thyroids. Some of the latter are large enough to cause distinct pressure.

In my experience of nearly twenty years in this section, I have never seen a nongoiterous mother bear a goiterous child, but many women with goiters, whose thyroid and goiter enlarged immensely during pregnancy, bore children with distinct enlargements of the thyroid, and, furthermore, nearly all of her children were born with the same enlargement of the thyroid. We can, with reason, draw the conclusions that influences that mean enlarging active thyroids in the mother are carried through the placenta, causing a corresponding enlargement of the fetal thyroid, and also, that no doubt it is of a chemical nature acting positively or negatively. An interesting point is that these large fetal thyroids disappear in from seven to fourteen days after birth, even though the child is nursed by its mother. Therefore, this transmitted influence passes through the placenta and not in the mammary secretion, the child acquiring it later in life. Some of these children at birth have the appearance of cretins with short noses, short stubby hands and the expression of idiots.

INFLUENCE AND LIABILITY OF DEVELOPMENT OF GOITER

In reviewing histories of the numbers who suffer from certain types of enlarged thyroids, simple, adenomatous, cystic and colloid goiters, we must conclude that enlargement of the thyroid maintained by living continuously in thyroid belts will be permanent. These glands can only be treated by surgical intervention. This applies more directly to adenomas that have the potentiality of varying in size and becoming plain tumor masses and thyrotoxic.

One thousand two hundred and twenty-three persons were born here and 538 were born elsewhere. Of the latter, 341 lived here fifteen years, 54 lived here from ten to fourteen years, 68 lived here from five to nine years, and 75 from one to four years, inclusive. This makes more than 80 per cent. of the total number subjected to the same local influence by birth or by residence for fifteen years or more. Therefore, if one were born elsewhere in a non-goiterous region and moved to this district, the liability of becoming goiterous would depend on the length of residence and the age of attaining the same. Therefore, we may deduce from these figures and other observations that, being born or acquiring a residence of fifteen years or more here, would entitle one to an enlarged thyroid according to the percentages for that year (Charts 1, 2 and 3). The danger, if the individual continued his residence, increases inversely with the age of attaining the latter.

The liability of goiters developing in persons born here is as follows: Females, aged 13 years and over, 80 per cent.; males, between 13 and 35 years, 66 per cent., and males between 35 and above, 45 per cent. (Charts 2 and 3).

The liability in Group 2 is as follows: Females from 5 to 35 years, 20 per cent.; females, 35 years and above, 62 per cent.; and males from 5 years and above, 20 per cent. (Charts 4 and 5).

RELATION OF INFECTION

In analyzing those who have focal infection and develop enlargements of the thyroid, whether becoming toxic or not, I am not free to believe that infection alone, nor the infective agent, causes goiter. The presence of infected teeth, or infected hypertrophied tonsils, or contagious diseases, or other infections will cause in thyroid patients, thyroiditis, enlargements of adenomas, or toxic symptoms, occasionally. The infective agent very rarely does this directly, but the focal toxemia causes a secondary effect on the thyroid. The weight of evidence and observations leads me to conclude that except for a direct thyroiditis, which is not uncommon, thyroid enlargements or thyroid zones are not caused necessarily by direct infective agents. This is said with due respect to the modern writers on the subject who lean toward some infective agent in itself being responsible for thyroid zones. The future will settle the question whether direct infection, or intestinal toxemia, or just the lack of some element in the soil or water, or uncleanness in the handling of vegetables grown here is, or contains, the causative agent.

The large numbers in our section who are practically normal and healthy otherwise, those who lose their enlargements of the thyroid during absence from this section, and the presence of enlargements which become more marked here than elsewhere during the periods of life when the greatest metabolic changes occur—as puberty, menopause, menstruation and pregnancy—are points in circumstantial evidence that offset much in the infective theory.

Sasaki and McCarrison's experiments with the addition of sublimated potassium iodid in a dilution of 1:5,000,000 to rat feces contradict rather than strengthen the infection theory.⁵

The arguments of Kutschera and Taussig can be explained as easily by soil and water supply in susceptible persons.⁶ D. Marine and his associates have done work that is most interesting and instruc-

5. Crotti: *Thyroid and Thymus*, 1918, p. 264.

6. Crotti: *Thyroid and Thymus*, 1918, p. 265.

tive.⁷ They have found that reduction and prevention of thyroid enlargements can be obtained by the use of 2 gm. of sodium iodid taken in 0.2 gm. doses for ten days twice yearly.⁶

In the families who live here constantly, where there is crowding and plainer, simpler methods of living and poorer hygienic conditions, goiters are more prevalent. This observation has been made elsewhere and corroborated many times.

CONCLUSIONS AND SUMMARY

1. It must be recognized that in a zone in which thyroid enlargements occur, as here, there is a normal physiologic hypertrophy, and this should not be called goiter. But to appreciate the various lines of demarkation, much study and astuteness in the differential diagnosis of thyroid enlargements is needed. All adenomas, cystomas and distinct colloid goiters can be classed as nonphysiologic. Simple enlargements may be only a physiologic response to internal needs or external influences,—the latter exaggerating the former. The thyroid gland, no doubt, plays an important rôle in the endocrine hormone in maintaining the balance of metabolism in the body and being prominently located, exhibits its response more markedly than do its associates. But it must be remembered that long continued hypertrophy means permanent enlargement, and one must always keep in mind the definite pathologic potentiality of this most active tissue. When hyperplasia occurs in simple goiter, or adenoma, whether fetal or adult, true exophthalmic goiter and hyperthyroidism may follow. I need not mention the vital organ degenerations that mark their paths.

2. One thousand seven hundred and eighty-three persons, ranging in age from new-born to 61 years, were examined for enlarged thyroids. One thousand one hundred and forty-six had enlarged thyroids with 682 simple goiters, 420 adenomas and cystomata and 44 colloid.

3. The incidence curve shows that goiters increase in both sexes during puberty, dropping to a small degree after the growth of the individual is attained. The curve remains in the female for the child bearing period, going down at about 38 or 40 years, when it rises again for the menopause. In the male, the curve gradually drops till 35 or 40 years, when there is a small rise due to the growths in the glands asserting themselves, the male having no special metabolic change to influence the enlargement.

7. Kimball, Rogoff and Marine: The Prevention of Simple Goiter in Man, J. A. M. A. **73**:1873 (Dec. 20) 1919.

4. Charts 1 to 6, inclusive, demonstrate the occurrence by age and sex of the various relationships of simple goiter, adenoma and cystoma, respectively.

5. The simple goiters maintain the high percentage till 35 years is attained and the adenoma and cystoma sustain the height of the incidence curve after that age.

6. The liability table given is approximately accurate.

7. The various water supplies—spring water or Lake Superior water—influence the enlargements of the thyroids the same.

I wish to thank Mr. H. C. Kenny and assistants for their services on the charts.