# PREVENTION OF SIMPLE GOITER IN MAN

## FOURTH PAPER *

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In previous publications [1] we have outlined the plan of prevention, presented the data of the incidence of thyroid enlargements as determined by annual surveys of all new pupils in the Akron public schools, and the results of the prophylatic use of sodium iodid for nineteen months. The present paper deals with the data obtained at the fourth general examination made October 13-17, 1919, together with summaries and conclusions based on observations extending over a period of thirty months.

### ANALYSIS OF THE RECORDS OF NEW PUPILS

The general data of the clinical condition of the thyroid gland are given in Table 1. For comparison and reference the figures for the three previous examinations are also given.

The pupils included in this table are new admissions to all grades from the fifth to the twelfth, inclusive, and presumably had not previously received iodin. The figures in the first line represent the results of the original survey of all girls in grades from the fifth to the twelfth, inclusive. The figures in the second line include (1) incoming fifth grade girls, (2) girls entering grades above the fifth grade, and (3) girls of two schools that accidently lost the records of those not taking the treatment. The figures in the third and fourth lines include (1) incoming fifth grade girls and (2) girls entering grades above the fifth. The progressive increase in the percentage of normal thyroids (43.6, 47.0, 55.4 and 65.4) and the corresponding progressive decrease in the percentage of enlarged thyroids whether taken together (56.4, 53.0, 44.6 and 34.5) or as separate groups (slightly enlarged, moderately enlarged and markedly enlarged) are due to the increasing preponderance of fifth grade girls in the second, third and fourth groups. This is also shown in Table 2, where all new pupils are grouped according to ages. Fifth grade pupils average from 10 to 11 years of age, and approxi-

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1. Marine, D., and Kimball, O. P.: The Prevention of Simple Goiter in Man, J. Lab. & Clin. Med. **3**:40, 1917. Kimball, O. P., and Marine, D.: The Prevention of Simple Goiter in Man (Second paper), Arch. Int. Med. **22**:41 (July) 1918. Kimball, O. P., Rogoff, J. M., and Marine, D.: The Prevention of Simple Goiter in Man (Third paper), J. A. M. A. **73**:1873 (Dec. 20) 1919.

TABLE 1.—Analysis of the Records of New Pupils

| Date Examined | Total Cases Examined | Total New Cases | Normal | | Slight Enlargements | | Moderate Enlargements | | Marked Enlargements | | Adenomas | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Number | Per Cent. | Number | Per Cent. | Number | Per Cent. | Number | Per Cent. | Number | Per Cent. |
| April 1917..... | 3,872 | 3,872 | 1,688 | 43.6 | 1 931 | 49.9 | 246 | 6.3 | 7 | 0.2 | 39 | 1.0 |
| November 1917..... | 4,415 | 1,772 | 831 | 47.0 | 820 | 46.2 | 121 | 6.8 | | | | |
| November 1918..... | 4,277 | 1,873 | 1,037 | 55.4 | 779 | 41.6 | 53 | 2.8 | 4 | 0.2 | 6 | 0.3 |
| October 1919..... | 5,520 | 2,162 | 1,415 | 65.4 | 679 | 31.4 | 67 | 3.1 | 1 | 0.05 | 1 | 0.05 |

TABLE 2.—Summary of Age Incidence—New Pupils

| Date of Examination | Total New Cases | Age | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 10 - 12 | | 12 - 14 | | 14 - 16 | | 16 - 18 | | 18 - 20 | |
| | | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. |
| April 1917..... | 3,872 | 945 | 24.4 | 1,261 | 32.6 | 1,140 | 29.4 | 453 | 11.7 | 73 | 1.0 |
| November 1918..... | 1,873 | 766 | 40.9 | 590 | 31.5 | 406 | 21.7 | 94 | 5.0 | 17 | 0.9 |
| October 1919..... | 2,162 | 969 | 44.8 | 678 | 31.4 | 401 | 18.6 | 102 | 4.7 | 12 | 0.5 |

TABLE 3.—Relation of Age to Thyroid Condition—New Pupils—1917

| | Age | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 10 - 12 | | 12 - 14 | | 14 - 16 | | 16 - 18 | | 18 - 20 | |
| | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. |
| Normal..... | 530 | 56.1 | 521 | 41.3 | 460 | 40.3 | 156 | 34.4 | 21 | 28.8 |
| Slightly enlarged. | 394 | 41.7 | 680 | 53.9 | 578 | 50.7 | 235 | 51.9 | 44 | 60.3 |
| Moderately enlarged..... | 21 | 2.2 | 59 | 4.7 | 98 | 8.6 | 60 | 13.2 | 8 | 11.0 |
| Markedly enlarged..... | ... | .... | 1 | 0.1 | 4 | 0.3 | 2 | 0.4 | | |

TABLE 4.—Relation of Age to Thyroid Condition—New Pupils—1918

| | Age | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 10 - 12 | | 12 - 14 | | 14 - 16 | | 16 - 18 | | 18 - 20 | |
| | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. |
| Normal..... | 491 | 64.2 | 295 | 50.0 | 214 | 52.7 | 39 | 41.5 | 9 | 52.9 |
| Slightly enlarged. | 267 | 34.8 | 276 | 46.8 | 168 | 41.4 | 49 | 52.1 | 6 | 35.3 |
| Moderately enlarged..... | 8 | 1.0 | 19 | 3.2 | 24 | 5.9 | 6 | 6.4 | 2 | 11.8 |
| Markedly enlarged..... | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |

mately 95 per cent. are included in the age group from 10 to 12. Details of the relation of age to the clinical condition of the thyroid are given in Tables 3, 4 and 5.

TABLE 5.—Relation of Age to Thyroid Condition—New Pupils—1919

| | Age | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 10 - 12 | | 12 - 14 | | 14 - 16 | | 16 - 18 | | 18 - 20 | |
| | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. | Number of Cases | Per Cent. |
| Normal | 743 | 76.7 | 419 | 61.8 | 199 | 49.6 | 53 | 51.9 | 7 | 58.3 |
| Slightly enlarged. | 215 | 22.2 | 239 | 35.3 | 170 | 42.4 | 43 | 42.2 | 5 | 41.7 |
| Moderately enlarged | 11 | 1.1 | 20 | 2.9 | 31 | 7.8 | 6 | 5.9 | 0 | 0.0 |
| Markedly enlarged | 0 | 0.0 | 0 | 0.0 | 1 | 0.2 | 0 | 0.0 | 0 | 0.0 |

TABLE 6.—Analysis of Records of New Pupils—Negroes—1919

| | Age | | | | | |
|---|---|---|---|---|---|---|
| | 10 - 12 | | 12 - 14 | | 14 - 16 | |
| | Number of Cases | Per Cent. | Number of Casec | Per Cent. | Number of Cases | Per Cent. |
| Normal | 5 | 50.0 | 7 | 53.9 | | |
| Slightly enlarged | 4 | 40.0 | 5 | 38.5 | 3 | 75.0 |
| Moderately enlarged | 1 | 10.0 | 1 | 7.6 | 1 | 25.0 |

For reference and comparison the original survey of all pupils (April, 1917), is given in Table 3, while in Tables 4 and 5 are given the results of the surveys of new pupils for 1918 and 1919, respectively. It should be emphasized, that in the 1917 examination, 43.9 per cent. of the girls in the 10-12 years age group had enlarged thyroids; that in the 1918 examination 35.8 per cent. had enlarged thyroids; and that in the 1919 examination 23.2 per cent. had thyroid enlargements. This is important from the standpoint of the age at which the phophylactic treatment should be started. When this work was begun, no data of this kind were available, and the fifth grade was arbitrarily chosen as the lower limit, because our limited facilities made it necessary to confine our efforts to what seemed to be the most important age periods. We have seen only forty instances of moderately enlarged glands and no instance of marked enlargement in the 10-12 years age group, and as very striking therapeutic effects are seen in these slight hyperplasias it makes little difference in the ultimate result. If, however, one had to depend entirely on prevention it would be necessary to begin at an earlier age.

There appears to be no noteworthy difference in the incidence of thyroid enlargements between white and colored children. The data are, however, insufficient for any definite conclusion. The data on the twenty-seven colored children are given in Table 6.

### EFFECT OF PROPHYLACTIC TREATMENT

The prophylactic treatment as carried out for the past two years consists of the administration of 2 gm. sodium iodid, given in 0.2 gm. doses daily, for ten consecutive school days, repeated each spring and autumn. The general data of those pupils not taking the treatment are given in Table 7, and of those taking the treatment in Table 8. Only pupils with two or more consecutive examinations have been included in the tabulations. A considerable number of pupils, both taking and not taking the treatment, have been omitted because they missed one examination, although otherwise their records were complete. Two thousand, three hundred and five pupils are included in the tabulation

TABLE 7.—RECORD OF PUPILS NOT TAKING PROPHYLACTIC TREATMENT

| Time Under Observation, Mos. | Normal | | | | Slightly Enlarged | | | | | | Moderately Enlarged | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Unaltered | | Increased | | Unaltered | | Increased | | Decreased | | Unaltered | | Increased | | Decreased | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| 6 | 47 | 50.0 | 47 | 50.0 | 93 | 69.4 | 36 | 26.9 | 5 | 3.7 | 16 | 69.6 | 7 | 30.4 | 0 | 0.0 |
| 12 | 420 | 75.5 | 136 | 24.5 | 251 | 70.3 | 35 | 9.8 | 71 | 19.9 | 17 | 65.4 | 8 | 30.8 | 1 | 3.8 |
| 18 | 103 | 65.2 | 55 | 34.8 | 108 | 74.5 | 18 | 12.3 | 19 | 13.1 | 11 | 57.9 | 3 | 15.8 | 5 | 26.3 |
| 24 | 135 | 76.7 | 41 | 23.3 | 106 | 79.7 | 8 | 6.0 | 19 | 14.3 | 9 | 60.0 | 3 | 20.0 | 3 | 20.0 |
| 30 | 205 | 75.1 | 68 | 24.9 | 140 | 73.7 | 30 | 15.8 | 20 | 10.5 | 4 | 66.7 | 0 | 0.0 | 2 | 33.3 |

of those not taking treatment, and 2,190 in the tabulation of those taking treatment. Further, it was necessary to tabulate the results with reference to the length of time under observation. As the prophylactic treatment was given at intervals of six months, we have used this interval as the unit and grouped the pupils according to the periods under observation, 6, 12, 18, 24 and 30 months respectively. Only the results of three groups (normals, slightly enlarged, and moderately enlarged) are included because the fourth group (markedly enlarged) is too small. A comparison of the two tables brings out striking differences between those not taking and those taking iodin. These differences are manifested both in *prevention* of enlargement and in a *decrease* in the size of existing enlargements, i.e., therapeutic effect.

*Prevention.*—This effect is shown in the columns marked "unchanged" and "increased." Taking the totals for the five six month periods (Table 9) the following results were obtained. Of those that were normal at the first examination and did not take iodin, 347, or 27.6 per cent., have enlarged thyroids, while of those that were normal at the first examination and took iodin as outlined, two, or 0.2 per cent.,

have enlarged thyroids. These two instances of enlargement were investigated. The first pupil, M. T., age 16, had her thyroid examined and classified as normal May 2, 1917, Oct. 17, 1918 and Dec. 3, 1918. At the examination Oct. 15, 1919, it was classified as slightly enlarged. This girl had taken 2 gm of sodium iodid during each of the five possible periods, May, 1917, November, 1917, May, 1918, December, 1918 and May, 1919. A special examination was made Jan. 13, 1920. The enlargement of the thyroid was verified. The enlargement was acquired as opposed to congenital, as shown by the absence of a pyramidal process or thyroglossal tract. The tonsils were markedly enlarged, nearly meeting in the midline when the mouth was widely opened.

TABLE 8.—Record of Pupils Taking Prophylactic Treatment

| Time Under Observation, Mos. | Normal | | | | Slightly Enlarged | | | | | | Moderately Enlarged | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Unaltered | | Increased | | Unaltered | | Increased | | Decreased | | Unaltered | | Increased | | Decreased | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| 6 | 17 | 94.4 | 1 | 5.6 | 54 | 69.2 | 1 | 1.3 | 23 | 29.5 | 9 | 81.8 | 0 | 0.0 | 2 | 18.2 |
| 12 | 344 | 99.7 | 1 | 0.3 | 187 | 45.5 | 0 | 0.0 | 224 | 54.5 | 10 | 23.8 | 0 | 0.0 | 32 | 76.2 |
| 18 | 73 | 100.0 | 0 | 0.0 | 72 | 52.3 | 1 | 0.7 | 64 | 46.7 | 7 | 28.0 | 0 | 0.0 | 18 | 72.0 |
| 24 | 184 | 100.0 | 0 | 0.0 | 72 | 37.9 | 1 | 0.5 | 117 | 61.6 | 2 | 7.7 | 0 | 0.0 | 24 | 92.3 |
| 30 | 288 | 100.0 | 0 | 0.0 | 92 | 28.5 | 0 | 0.0 | 231 | 71.5 | 1 | 2.6 | 0 | 0.0 | 38 | 97.4 |

TABLE 9.—Summary—Records of Pupils Taking and Not Taking Prophylactic Treatment

| | Taking | | Not Taking | |
|---|---|---|---|---|
| | Totals | Per Cent. | Totals | Per Cent. |
| Normal: | | | | |
| Unchanged | 906 | 99.8 | 910 | 72.4 |
| Increased | 2 | 0.2 | 347 | 27.6 |
| Slightly Enlarged: | | | | |
| Unchanged | 477 | 41.9 | 698 | 72.8 |
| Increased | 3 | 0.3 | 127 | 13.3 |
| Decreased | 659 | 57.8 | 134 | 13.9 |
| Moderately Enlarged: | | | | |
| Unchanged | 29 | 20.3 | 57 | 64.0 |
| Increased | 0 | 0.0 | 21 | 23.6 |
| Decreased | 114 | 79.7 | 11 | 12.4 |
| Total | 2,190 | .... | 2,305 | |

They were abnormally hyperemic, and on direct questioning the pupil stated she was subject to recurrent tonsillitis. There was also slight enlargement of the lymphoid tissue at the base of the tongue and in the nasopharynx. The general impression was that of a neurotic individual with general lymphoid hyperplasia.

The second girl, aged 15, had her thyroid first examined and classified as normal Nov. 27, 1918. At the examination Oct. 16, 1919, it was classified as slightly enlarged. This girl had taken 2 gm. sodium iodid during each of the two available periods, November, 1918 and May, 1919. A special examination was made Jan. 13, 1920, and the thyroid

enlargement was verified. Careful inspection revealed the presence of Hutchinson teeth, depressed nasal arch and interstitial keratitis. We considered the case one of neglected congenital syphilis.

Passing to Group 2, or those classified as having slightly enlarged thyroids at the first examination, it is seen among those not taking the prescribed treatment that 127, or 13.3 per cent., underwent further enlargement, while of those taking the prescribed treatment, three, or 0.3 per cent., underwent further enlargement. Two of these three pupils were again examined Jan. 13, 1920. One, R. R., aged 14, was examined May 2, 1917, Oct. 12, 1917 and Nov. 26, 1918, and the thyroid classified as slightly enlarged, and at the examination Oct. 16, 1919 the gland was classified as moderately enlarged. This girl had taken the prescribed treatment only during the last three available periods, May, 1918, November, 1918 and May, 1919. A special examination was made Jan. 13, 1920 and the thyroid enlargement verified. In this case also the tonsils were enlarged and the seat of recurrent infections. The second case, V. S., aged 11, was examined Oct. 22, 1917 and Nov. 27, 1918 and the thyroid classified as slightly enlarged. At the third examination, Oct. 16, 1919, it was classified as moderately enlarged and the special examination Jan. 13, 1920, verified this finding. This girl had taken the prescribed treatment during the four available periods, November, 1917, May, 1918, December, 1918, and May, 1919. Superficial inspection failed to reveal the existence of any associated pathologic condition as was found in each of the first three cases mentioned. The fifth girl was not present for the special examination. These five cases are the only instances out of 2,190 pupils taking iodin that showed enlargement. For the group with slightly enlarged thyroids taking iodin, 447, or 41.9 per cent., remained unchanged, while of those not taking iodin, 698, or 72.8 per cent., remained unchanged.

Passing to the third group, or those classified as having moderately enlarged thyroids at the first examination, it is seen that of those taking iodin, twenty-nine, or 20.3 per cent., remained unchanged, while of those not taking iodin, fifty-seven, or 64.0 per cent., remained unchanged; of those taking iodin none increased, while of those not taking it, twenty-one, or 23.6 per cent., increased.

*Curative or Therapeutic Effect.*—Although of secondary importance, the results are just as striking as those above described under prevention. These results are shown in the column marked "decreased." Of those pupils whose thyroids were classified as slightly enlarged at the first examination, and who took iodin, 659, or 57.8 per cent., definitely decreased in size, while of those not taking the prescribed treatment, 134, or 13.9 per cent., decreased. Passing to the group

whose thyroids were classified as moderately enlarged at the first examination, 114, or 79.7 per cent., of those taking iodin showed definite decreases. In some the decrease in size was most striking and hardly to be believed had we not had actual measurements and descriptions of the condition previously. The reduction in several cases was as marked as one sees in the thyroid enlargement of young dogs, sheep or cattle following the use of iodin. It means that with similar anatomic conditions, i.e., uncomplicated hyperplasias of the thyroids, the degree of reaction is similar. Ordinarily, one does not obtain the striking therapeutic effect on human thyroid enlargements that is seen in animals. This, as pointed out in previous papers, is due, in large part, to the duration of the enlargement, the presence of adenomas, cysts, degenerations, hemorrhage, etc., which are common in all long standing human goiters, while very uncommon in the lower animals at the ages when these animals are usually observed. The therapeutic effect is a very

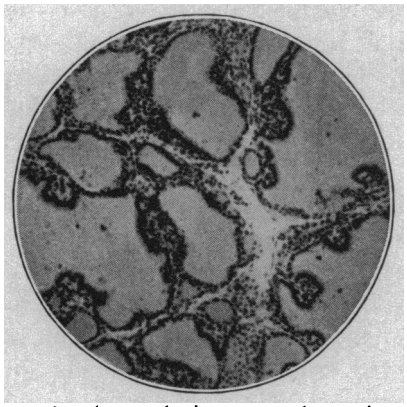

Fig. 1.—Moderate active hyperplasia; control specimen removed ten days after beginning administration of iodin (D—185a).

important supplement to prevention and makes it possible to begin prophylactic treatment in older pupils with the same practical result than would otherwise be possible.

## DISCUSSION

Our observations on the prevention of simple goiter in man have extended over a period of thirty months. The disease is as easily prevented in man as in fish or in domestic animals.

Of 2,190 pupils taking 2 gm. sodium iodid twice yearly, five have shown enlargement of the thyroid, while of 2,305 pupils not taking the prophylactic, 495 have shown enlargement of the thyroid. Of 1,182 pupils with thyroid enlargement at the first examination and who took the prophylactic, 773 thyroids have deceased in size, while of 1,048 pupils with thyroid enlargement at the first examination and who did not

take the prophylactic, 145 thyroids have decreased in size. These figures demonstrate in a striking manner both the preventive and the therapeutic effects. There is an error in the above figures in that many pupils listed as not taking iodin have taken iodin in one or another form outside the school jurisdiction. No attempt has been made to detect or estimate this error.

In the practical application of the preventive treatment, one must keep in mind the three periods when simple thyroid enlargements most commonly occur, viz., (1) fetal, (2) adolescence and (3) pregnancy.

(1) Prevention of goiter in mother and fetus is as simple as that occurring during adolescence. Practically, it would seem that it is a charge or responsibility of individual members of the medical profession supplemented with public education.

(2) The prevention of goiter of adolescence, on the other hand, should be a public health measure under state, county or municipal

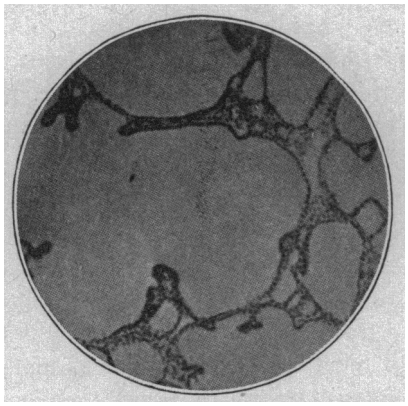

Fig. 2.—Same gland as Figure 1; specimen removed forty-four days after beginning administration of iodin.

control. The existing systems of organization of the schools, public and private, is sufficient to handle all the details without additional aid or expense. Education of the pupils would be combined with the actual administration so that after leaving school they could continue the treatment, if necessary. Physicians in industrial medicine could render an important service in this field. Thyroid enlargement is approximately six times as frequent in girls as in boys. It is a social economic question each community must decide whether it will include both sexes. Likewise, as to the age of beginning and stopping the use of iodin. In this climate probably the maximum of prevention, coupled with the minimum of effort, would be obtained by giving it between the ages of 11 and 17 years. As applied to our schools it would mean beginning with the fifth grade.

*Manner and Form of Administration.*—As previously stated, iodin is taken up by the thyroid gland when given by mouth, by inhalation, or by external application. Weith [2] reports favorable therapeutic effects from inhalation of iodin as carried out by suspending a wide mouthed bottle containing a 10 per cent. tincture of iodin in the school room. Waste and lack of control of amounts taken are the most obvious objections. Similar objections hold in case of external application. Some form of oral administration seems most practical and economical. The addition of iodin or a salt of iodin to the water supply as we have done in preventing goiter in fish might be considered. There are obvious objections to such a plan. It would entail enormous waste. It is applicable only when there are installations, i. e., in towns and cities, and depending on the chemical impurities in water interactions might throw out the iodin. The most feasible oral method would seem to be the individual administration of definite small amounts, either in solution or as tablets. The cheapest salt, sodium iodid, could be given in either form. Manufacturing pharmacists state that sodium iodid could be prepared very cheaply in tablet form protected from the action of water and light. For private use, the well known U.S.P. preparations, syrup of ferrous iodid and syrup of hydriodic acid are excellent.

*Amounts of Iodin to be Used.*—An ounce of syrup of ferrous iodid or hydriodic acid given over a period of from two to three weeks and repeated twice yearly would seem ample. As a public health measure, we have used 2 gm. of sodium iodid given over a period of two weeks and repeated twice yearly. This dosage has prevented enlargement of the thyroid in more than 99 per cent. of the children in this mildly goiterous district. It is our opinion that much smaller amounts would suffice for healthy children and healthy pregnant women, provided the period of taking was prolonged, i. e., 1 gm. sodium iodid distributed over a month would accomplish as good thyroid effects as 2 gm. given over a period of two weeks.

The prevention of thyroid enlargement in individuals with other diseases or residing in extremely goiterous districts, as in some glacial valleys of Alaska and British Columbia; certain districts in the Alps and Himalayas, might require larger amounts of iodin for normals than above indicated. Our data of the clinical condition of four of the five cases that enlarged during the administration of 2 gm. of sodium iodid, twice yearly, suggest that in infections (chronic catarrhal or suppurative tuberculosis, syphilis, etc.) and possibly also in conditions like chlorosis, osteomalacia, lymphatism and exophthalmic goiter, such amounts might not control the thyroid growth. In such conditions there

2. Weith: Goiter and Iodin in the School, Cor.-Bl. f. schweiz. Aerzte **49**: 1474, 1919.

may be a greatly increased demand for the thyroid hormone or the organism's ability to store iodin in the thyroid may be impaired. There is a great deal of clinical evidence for the first view and none at present in support of the second.

*Effect of Iodin on the Thyroid Gland.*—This is manifested in two ways (1) on the iodin store and (2) on the histologic condition. Both of these effects have been fully described in previous papers.[3]

Effect on the Store: If the thyroid gland is not saturated with iodin (i. e., contains less than 4 mg. per gm. of dried gland) it is taken up readily by the cells following its administration in any form and in any manner thus far studied. An increase in the iodin content of thyroid may be demonstrated in a few seconds following the injection of a soluble salt into the circulation.[4] Iodin thus taken up is held by the cells until elaborated into the physiologically active hormone, when any

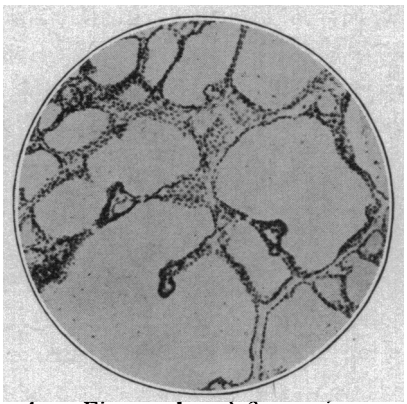

Fig. 3.—Same gland as Figures 1 and 2; specimen removed seventy-eight days after beginning administration of iodin. Total amount of iodin given, 90 mg.

excess is excreted into the follicular spaces and stored in the so-called colloid. Two factors then are concerned in the storage of iodin in the thyroid: (a) the capacity of the gland cells to take up and elaborate the

3. Marine, D.: On the Occurrence and Physiological Nature of Glandular Hyperplasia of the Thyroid (Dog and Sheep) Together with Remarks on Important Clinical Human Problems, Bull. Johns Hopkins Hosp. **18**:359, 1907. Marine, D., and Lenhart, C. H.: Colloid Glands (Goiters): Their Etiology and Physiological Significance, Bull. Johns Hopkins Hosp. **20**:131, 1909. Marine, D., and Lenhart, C. H.: Effects of the Administration or the Withholding of Iodin Containing Compounds in Normal, Colloid or Actively Hyperplastic Thyroids of Dogs, Arch. Int. Med. **4**:253, 1909. Marine, D.: Quantitative Studies on the in vivo Absorption of Iodin by Dogs' Thyroid Glands, J. Biol. Chem. **22**:547, 1915.

4. Marine, D., and Rogoff, J. M.: The Absorption of Potassium Iodid by the Thyroid Gland in vivo Following Its Intravenous Injections in Constant Amounts, J. Pharm. & Exper. Therap. **8**:439, 1916.

hormone and (b) the capacity of the colloid material to store the product. It is evident, then, that to obtain maximum thyroid effects from a minimum amount of iodin, it should be administered in amounts not to exceed the capacity of the cells at any given time to handle it. As has been shown, the elaboration of the hormone proceeds slowly [5] in the most active thyroids. Also when one recalls that from 4 to 5 mg. of iodin per gm. of dried gland, or from 25 to 30 mg., is the total storage capacity of a normal thyroid, it is clear that small amounts of iodin (a few mg.) given daily for a long period of time (a month or more) would produce optimum thyroid effects. In the school work, a compromise was found necessary, increased amounts and decreased time of administration.

Effect on Histology of the Thyroid: It has been shown that the minimum amount of iodin store necessary to maintain normal or quiescent thyroid structure is quite constant for mammals.[6] In the dog, sheep, human and pig thyroid it is approximately 1 mg. per gm. of dried gland, and immediately the percentage is reduced below the minimum, hypertrophic and hyperplastic changes begin and continue until the store of iodin has again been raised above the minimum requirements, when involution takes place. This cycle may be repeated many times in the same individual under natural or experimentally controlled conditions. In young dogs, with active hyperplasia, involution is usually complete in from fourteen to twenty-one days after beginning the administration of iodin. The histologic features of this involution have been described in detail in other papers, but for reference three microphotographs illustrating it are reproduced (Figs. 1, 2 and 3).

*Untoward Effects.*—No obvious case of exophthalmic goiter has developed, although such cases have been carefully looked for. An occasional instance of iodin idiosyncrasy (iodism), amounting to less than 0.5 per cent. of the cases, was noted. Most of the cases were very mild and the girls did not stop the treatment. As an untoward effect it is negligible.

## SUMMARY.

Observations on the prevention of simple goiter in man on a large scale have extended over a period of thirty months. The results show that it may be prevented very simply and cheaply in normal individuals. While thyroid enlargements of adolescence are more common, they are

5. Marine, D., and Rogoff, J. M.: How Rapidly Does the Intact Thyroid Gland Elaborate Its Specific Iodin Containing Hormone? J. Pharm. & Exper. Therap. **9**:1, 1916.

6. Marine, D., and Williams, W. W.: Relation of Iodin to the Structure of the Thyroid Gland, Arch. Int. Med. **1**:349, 1908. Marine, D., and Lenhart, C. H.: Further Observations on the Relation of Iodin to the Structure of the Thyroid Gland in the Sheep, Dog, Hog and Ox, Arch. Int. Med. **3**:66, 1909

not more important than those occurring in mother and fetus. Prevention of adolescent goiter is properly a public health problem, while the prevention of fetal and maternal thyroid enlargements is largely a responsibility of individual physicians. The presence of pathologic conditions may modify the result of the prophylactic treatment in individual cases. While such instances are rare they are important and merit detailed reports.