HYPERTHYROIDISM ASSOCIATED WITH PREGNANCY*

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IT IS a well-known fact that pregnancy is frequently accompanied by a hypertrophy of the thyroid gland. According to the more conservative the number of women thus affected is 40 per cent, while others place it as high as 90 per cent. These percentages vary according to whether they are taken from a goiter belt or from a seacoast community. Some refer to this condition as a physiologic enlargement of the thyroid but whether it be physiologic or pathologic is not settled, though the evidence at present would indicate it to represent a diseased thyroid state. We are referring to a primary enlargement during pregnancy and not a preexisting goiter which is aggravated by pregnancy. That excessive demands are made upon the thyroid at this time is borne out by multiparae showing evidence of thyroid enlargement during the fifth month, while primiparae do not show evidence of it until the sixth month. There are three types or stages of goiter, which include colloid, adenomatous, and exophthalmic goiter or Graves's disease. Whether these conditions represent separate diseases or stages of the continuous process is still unsettled, but Hertzler[3] has led us to believe that the different types of goiter merely represent stages in a continuous process. His work is also borne out by Rienhoff[5] and Hellwig.[2] In studying histologic sections of the thyroid in stillborn infants and in persons to eighty-nine years of age who met with accidental death, we have been forced to conclude that a correct diagnosis of thyroid diseases cannot be made from either the clinical picture or the histologic sections alone, but these must be studied together before arriving at a final diagnosis.

There are two types or stages of hyperthyroidism: (1) Adenomatous or nodular goiter. (2) Exophthalmic goiter or Graves's disease. It is essential to understand the fundamental differences in these two types or stages of hypersecretion. Some clinics go so far as to make definite clinical entities out of the above conditions, stating that they are separate diseases and not interchangeable, and that the management for one condition is different from the other, but at the present time this distinction does not seem warranted. Plummer[4] has maintained that the hyperthyroidism of exophthalmic goiter was of a different type than the hyperthyroidism of adenomatous goiter and that iodine or Lugol's solution would be beneficial in the former but contraindicated

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in the latter as a preoperative medication. Graham[1] proved that iodine was beneficial in both types preoperatively, but the quantity necessary to improve the adenomatous goiter was less than that for an exophthalmic goiter. It is very difficult to make a clinical classification which coincides with the histologic sections and one is not infrequently surprised when he has made a clinical diagnosis of adenomatous goiter with hyperthyroidism to receive a pathologic diagnosis of Graves's disease. The same holds true in typical cases of exophthalmic goiter that have received iodine therapy.

The following cases will illustrate the difficulties encountered if one relies on the history and physical findings on the one hand, or the histologic sections on the other.

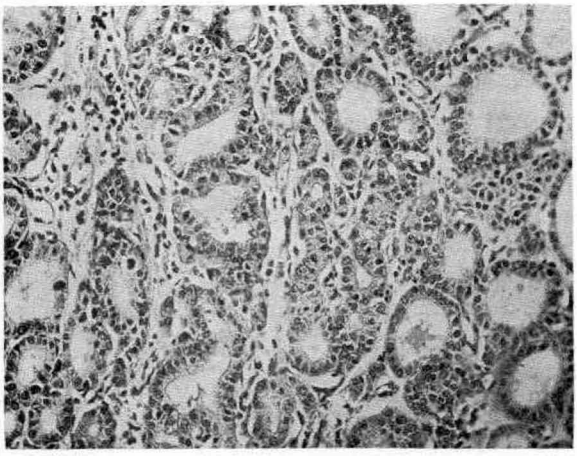

Fig. 1.—Diffuse epithelial hyperplasia with high columnar epithelium, narrow lumen with infolding and with little colloid. Active stage.

CASE 1.—Female, thirty-eight years of age, a nurse, was first seen by me on August 4, 1927; she stated that twelve years previously she had been operated upon for an adenoma of the isthmus of the thyroid. About one year after this operation she noticed a lump in the right side of her neck. This had increased slightly in size and about seven weeks before consulting me she had a gastrointestinal upset from eating sea food. Since that time she had lost 20 pounds in weight, and has had palpitation of her heart, and shortness of breath on going upstairs. Otherwise she felt well. Her menstrual periods had been scanty during the last few months. Examination: There was no evidence of exophthalmos in the right eye. The left eye had been enucleated following an accident at the age of two years. At the time of examination there was a nodular mass involving the right lobe without a thrill and her pulse was 108. A diagnosis of adenoma of the thyroid with hyperthyroidism was made. Basal metabolism on August 4 was a plus 45. The patient was advised to enter the hospital for operation, which she did, and was operated upon on August 22, 1927. She made an uneventful recovery, being discharged from the hospital on August 30, 1927. Pathologic report: Hyperplastic goiter of Graves's type, in a stage of remission at the time. See Fig. 1. This case was considered a typical adenomatous goiter with hyperthyroidism and an exophthalmic goiter was not suspected until receiving the pathologic report.

CASE 2.—Female, twenty-six years of age, was first seen by me on November 30, 1927 complaining of a swelling in her neck which she had had for one year. Friends first noticed a lump in the right side of her neck but at that time she had no symptoms referable to her goiter. Occasionally a sensation of pressure and choking were noticed but otherwise she felt perfectly well. Examination was negative, with the exception of a definite mass involving the right lobe of the thyroid. The left lobe was negative. Weight 133¾ pounds, pulse 100. Diagnosis of adenoma of the thyroid was made and basal metabolism on December 2, 1927 was plus 3. Patient was informed she had the type of goiter that could not be treated by medication, but as I had treated her sister for a colloid goiter with a satisfactory result, she demanded medication before submitting to an operation; hence she was put on thyroid extract, 1 grain t. i. d. The patient was next seen on January 18, 1928 at which time her weight was 137¼ pounds and pulse 90. She had no complaints but her neck remained unchanged and she was given thyroid extract, ½ grain t. i. d. On March 21, 1928 she returned stating she had nausea and vomiting and had been bothered with diarrhea for two weeks and was begin-

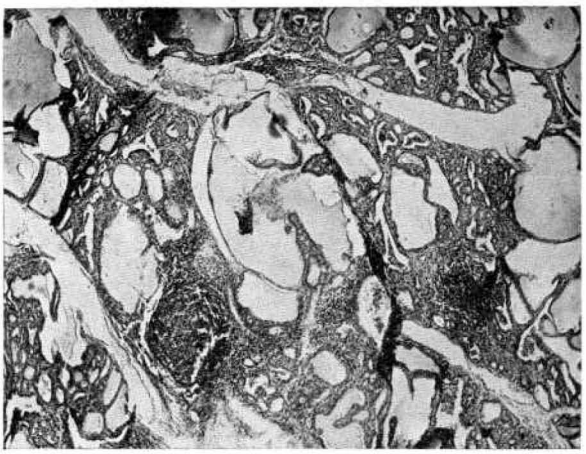

Fig. 2.—Diffuse epithelial hyperplasia. Some areas show narrow alveoli with little colloid and high epithelial lining, others contain much colloid. Numerous lymph follicles in stroma.

ning to feel ill. She complained of nervousness and palpitation and was losing weight. Examination revealed an enlargement over the thyroid region with a definite thrill over it, and a beginning exophthalmos. Diagnosis then made of exophthalmic goiter. Patient was advised to enter the hospital for observation and operation, which she did on March 22, 1928. Basal metabolism on March 26, 1928 was a plus 60. Weight was 105 pounds and pulse 160. The patient was operated upon on April 2, 1928 and made an uneventful recovery. Pathologic report: Exophthalmic goiter in the stage of remission Fig. 2. From the course of this case one can see a nodular type of goiter changed clinically to an exophthalmic goiter by thyroid medication.

CASE 3.—Female, thirty-three years of age, stated that in September, 1927 she consulted her family physician for a swelling of her left ankle and a goiter. At that time she was found to have a phlebitis of the left ankle. On communicating with Dr. Felder, her family physician, I found the patient had a colloid enlargement of her thyroid, without symptoms. The patient was not given any thyroid or iodine medication but five months later, as her mother had died from an

exophthalmic goiter, she consulted a thyroid specialist in New York, for she was rather conscious of the slight fullness in her neck. There were no symptoms referable to the thyroid at that time. Basal metabolism February 4, 1928 was a minus 1. She was informed that she had no thyroid disturbance but was given Lugol's solution 3 minims, t. i. d. Three months later she had lost 8 to 10 pounds in weight, her eyes were enlarged and she was nervous and quite irritable, and bothered with palpitation. She consulted another physician who told her she had

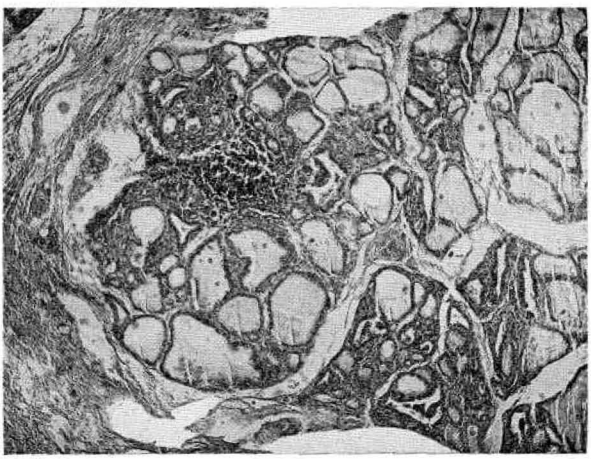

Fig. 3.—Diffuse epithelial hyperplasia with infolding, in some areas more marked than in others. Lymph follicles in stroma. Relatively low activity is shown best by increase of colloid secretion.

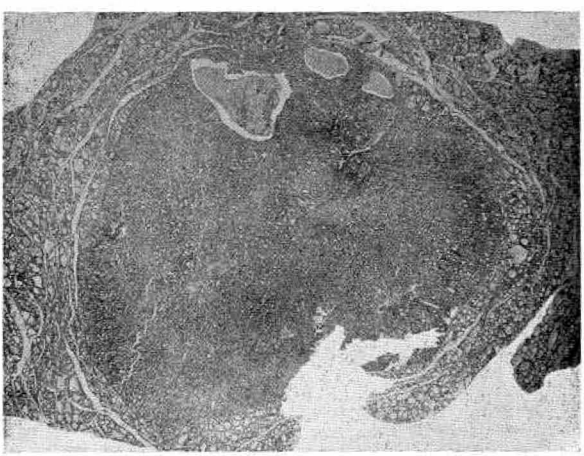

Fig. 4.—Very low magnification shows circumscribed adenoma.

Graves's disease. The patient was given 1 grain of iodide of mercury daily, and advised to have roentgen-ray therapy. She received several treatments and showed improvement but four months later, not feeling entirely well, she consulted Dr. Carter at which time her weight was 118 pounds, as against her best weight of 135 pounds. Basal metabolism on October 27, 1928 was 3 below the average normal. I saw this patient in consultation with Dr. Carter on October 28, 1928 at which time there was definite evidence of enlargement of the thyroid with a thrill over it, and it was quite apparent that the patient was suffering from an

exophthalmic goiter. Thyroidectomy was performed on November 5, 1928 by Dr. Carter. Pathologic diagnosis: Exophthalmic goiter in resting stage. (See Fig. 3.) One sees a colloid goiter which was changed into an exophthalmic goiter by iodine administration.

CASE 4.—Female, forty-five years of age, first seen June 2, 1927 complaining of nervousness, tremor of fingers, swelling of neck and protruding eyes, from which she had suffered for a period of five years. Her symptoms came on following the

Fig. 5.—Capsule of adenoma with adenoma on one side, and diffuse epithelial hyperplasia on the other.

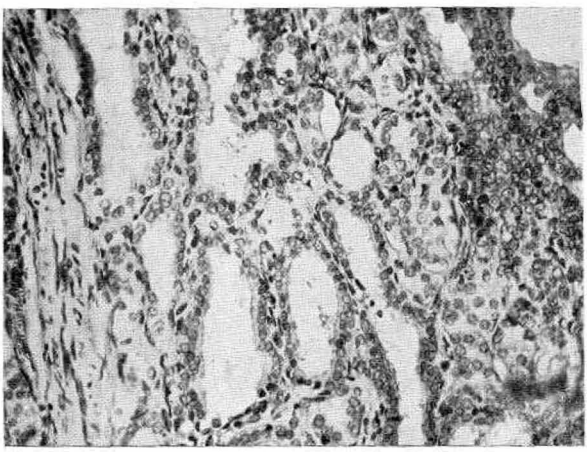

Fig. 6.—High-power magnification showing diffuse epithelial hyperplasia. Little colloid. Epithelial lining is high.

death of her daughter from pneumonia. The patient had had a cholecystectomy and appendectomy ten years previous to the time she consulted me; otherwise her history was negative. Examination revealed bilateral exophthalmos with symmetrical swelling of thyroid and thrill over it. The heart was fibrillating and the pulse could not be counted accurately. Basal metabolism on May 28, 1927 was a plus 69. Weight 157 pounds with pulse 150. The diagnosis of exophthalmic goiter was made and the patient was operated upon on June 11, 1927. Pathologic report:

Exophthalmic goiter in a resting stage, with two small adenomas. (See Figs. 4, 5, 6.) In this case the histologic sections revealed an adenomatous goiter and exophthalmic goiter in the same person which does not lead one to believe that they are separate clinical entities.

In view of the fact that the histologic findings in the above cases did not coincide with the clinical picture, we have taken sections from people whose deaths were due to accidental causes to determine whether the histologic findings are constant for different ages in life.

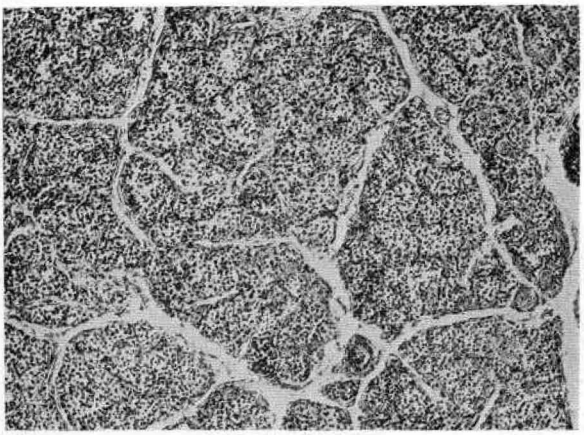

Fig. 7.

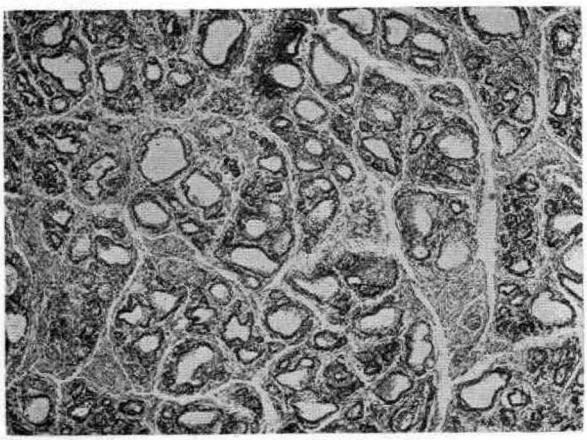

Fig. 8.

Fig. 7 is a section from a stillborn female baby, with cranial injuries. The section reveals epithelial cells divided into lobules by connective tissue and no definite formed acini. This represents what is usually found in fetal thyroids. Fig. 8, male, ten weeks of age, died from a rupture of the spleen. In this section one notes the acini well formed containing colloid with a marked amount of interacinal connective tissue. This section is so well developed that one might mistake it for an adult thyroid. Fig. 9, male, aged thirteen, cause of death

fractured skull. The section reveals very large acini containing colloid in parts of the section, while in other fields there are numerous epithelial cells closely spaced. Fig. 10, female, aged thirty-five, cause of death fractured skull. This section reveals one or two developing acini while most of the section contains dense masses of epithelial cells with connective tissue dividing the gland into lobules. The histologic picture in this section is more of a fetal type. Fig. 11, male, aged twenty-five, shot and instantly killed. This section reveals the acini large and dilated containing dense colloid material, showing a marked contrast with Fig. 10.

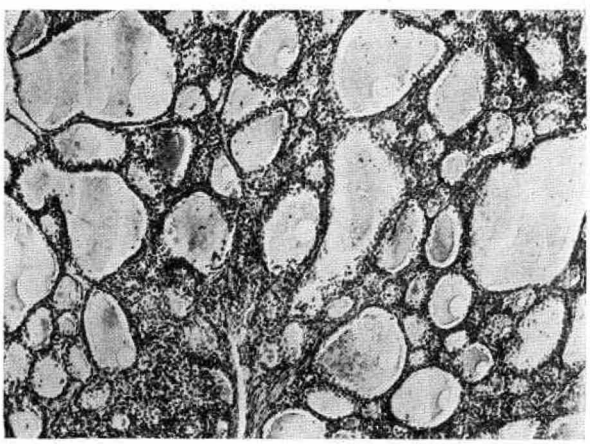

Fig. 9.

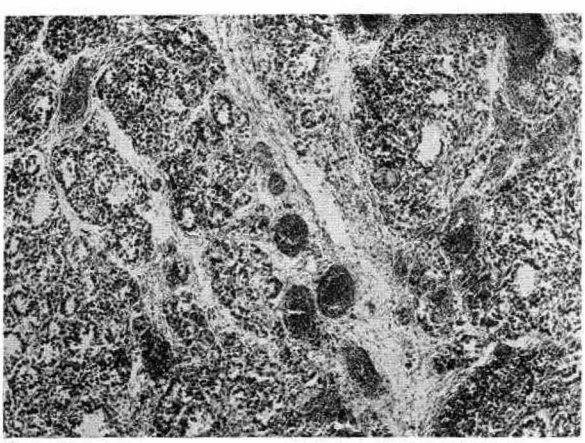

Fig. 10.

Fig. 12, female, aged sixty-one, committed suicide by strangulation. The section reveals epithelial cells closely spaced with some very small acini. The general appearance of this section is similar to that of an infant thyroid. Fig. 13, male, aged seventy-five, fractured skull and lacerated brain. This section reveals some well-developed acini containing colloid but in other parts the section reveals epithelial cells that are closely spaced with fibrous tissue forming a definite lobule. This section is more characteristic of an infant's thyroid than that of a man seventy-five years of age.

From the above sections it can be seen there is a marked variation in the histologic picture of the thyroid of people in apparently normal health who met with accidental death.

It is essential to look upon hyperthyroidism during pregnancy as one continuous process and not as separate diseases. From the above cases it can be seen how difficult it is to be certain of a diagnosis unless the

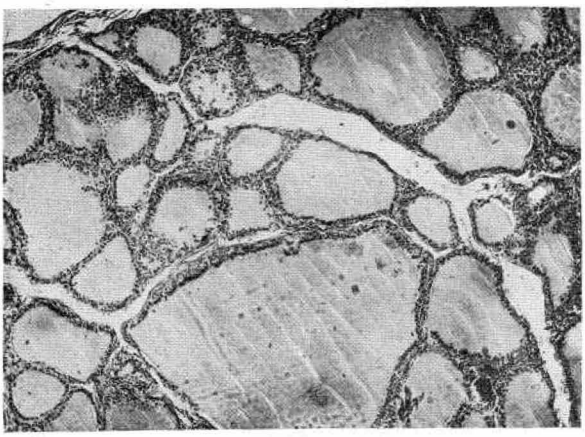

Fig. 11.

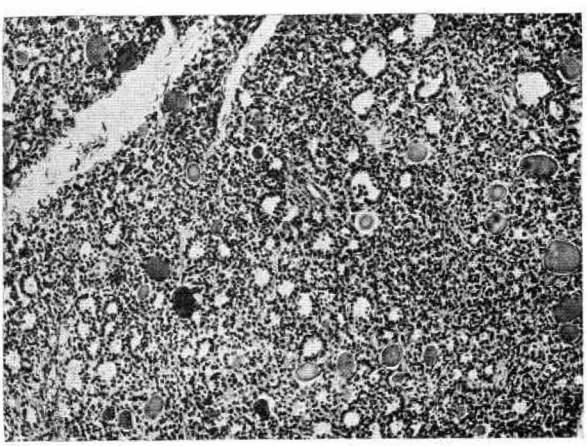

Fig. 12.

clinical findings and histologic sections are studied together, but for the clinical management of the patient it is essential to divide them into acute and chronic stages of hyperthyroidism, or exophthalmic goiter and adenomatous goiter.

Treatment.—Chronic hyperthyroidism, or hyperthyroidism from a nodular or adenomatous goiter usually occurs in women who have borne several children in rapid succession and who say an enlargement of

the thyroid was noticed after the birth of the first or second child, while the symptoms of hyperthyroidism may not develop until after the third or fourth pregnancy. What should be done in this type depends to a great extent upon the patient's condition and her desire to have more children. If the case is clinically mild with a metabolic rate not exceeding a plus 30, the patient can, in all probability, be carried through a normal pregnancy without any undue risk of permanent cardiac damage. But if the patient at the beginning of pregnancy has a high metabolic rate with a definite cardiac involvement, termination of pregnancy is advisable, and if the patient does not wish to submit to that the only alternative is a thyroidectomy after proper preoperative treatment.

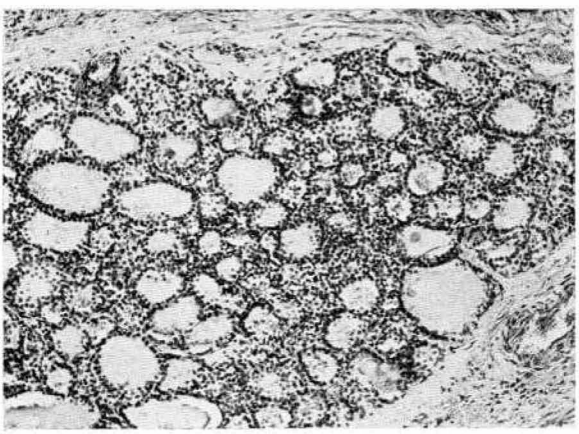

Fig. 13.

Exophthalmic goiter or Graves's disease usually develops in the early months of pregnancy, and more frequently in primiparae. The management will depend entirely upon the condition of the patient when first seen. Unless she is critically ill it is not necessary to interrupt the pregnancy but a thyroidectomy can be performed and the patient carried through a normal delivery. If the case is very mild it may be possible to carry the patient through her pregnancy on medical management and defer more radical measures until later.

Comment.—The two types of cases which need pregnancy interrupted are: First, chronic hyperthyroidism associated with the nodular or adenomatous goiter in which there is a definite myocardial degeneration; and second, cases of exophthalmic goiter or Graves's disease which are of a fulminating type and which endanger the life of the mother by allowing the pregnancy to continue. It is safe to estimate that 90 per cent of cases of hyperthyroidism associated with pregnancy can be carried to a normal delivery if properly managed.

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