

EXOPHTHALMIC GOITRE AND PREGNANCY.*

BY

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(With Chart.)

I WISH to report the following case in which the association of Basedow's disease and pregnancy led to a fatal termination.

Mrs. W. Aged twenty-four years. Menstruation began when sixteen years of age. The flow lasted six days and was normal in character. The personal history is negative to the age of twenty-one, when an operation was performed for acute appendi-

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citis. At the time of operation, the peritoneum was found to be the seat of miliary tuberculosis. In 1905 the patient became pregnant for the first time, but aborted in two and a half months. This abortion was probably due to the goitre, as the symptoms had made their appearance a few months previously. No attempt to terminate gestation had been made as the family were anxious for children.

The patient was seen by Dr. R. A. Cunliffe, to whose courtesy I am indebted for the privilege of reporting the case. The family history was negative regarding any neurotic or hereditary influences. The patient had noticed a slight bulging of the eyes, a rapid action of the heart, and an increased irritability of the nervous system for a period of eighteen months before December, 1906. Physical examination revealed a marked exophthalmus. Both Stellwag's and Graefe's signs were present. Tremor of the tongue and fingers was observed, numbering eight or ten movements to the second. The heart action was tumultuous and recorded 115 beats per minute. The enlargement of the thyroid gland was slight and confined principally to the right side. The reflexes were increased and the patient was easily excited.

A diagnosis of exophthalmic goitre was made and the woman kept in bed for varying intervals of time. The treatment consisted of rest, ice packs, and sedatives. The symptoms improved during the next few months. The appetite became normal. The stomach and bowels were acting well. The pulse averaged 90 to 100 beats per minute. The ocular signs and the enlarged gland remained stationary.

This improvement was maintained until October 8, 1907. This was the date of the last menstruation. With the advent of pregnancy, there was a slight return of the goitre symptoms, but for the first month the general condition was excellent. On December 17, 1907, the patient began to vomit incessantly and continued for eleven days. At this time, the average pulse was 130. The temperature was 100.6° F. The mother's condition grew worse every day, and I first saw her on December 28, 1907. The cardinal signs of goitre were plainly evident. The pulse varied from 160 to 170 beats per minute and was high in tension. The apex beat was located nearly an inch to the left of the nipple line and behind the sixth rib. A blowing, systolic murmur transmitted to the left and below was audible. The patient had been unable to sleep for several nights and appeared to be utterly exhausted. The muscular weakness was marked. The teeth

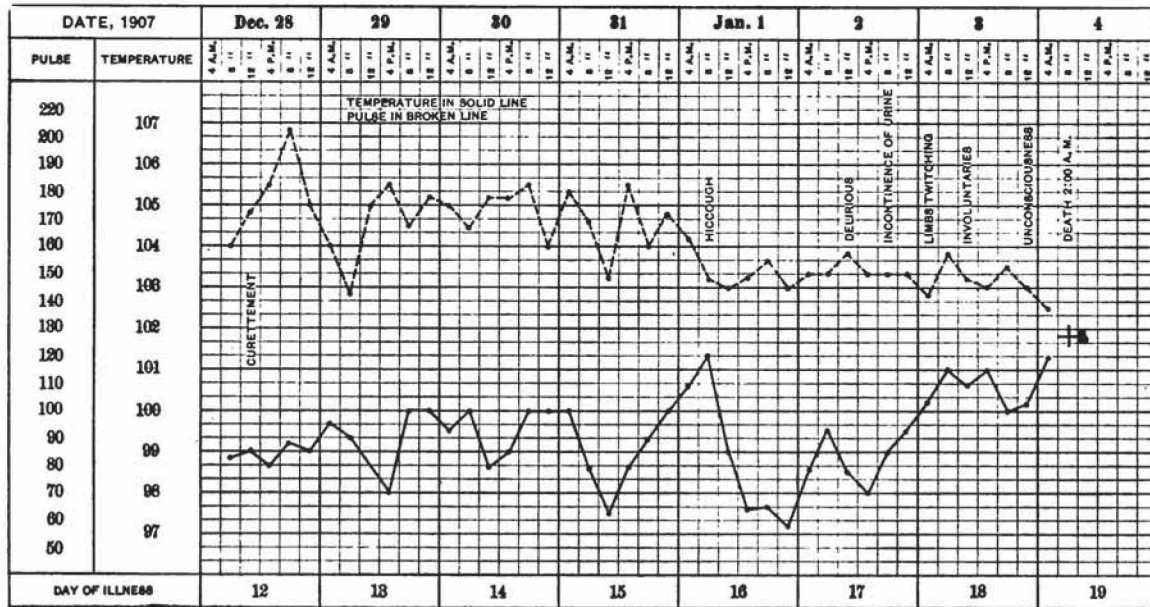


Chart of case of exophthalmic goitre and pregnancy.

were covered with sordes and the breath was foul. The ocular signs were well developed. The right lobe of the thyroid gland was slightly hypertrophied. The vomitus consisted of a large quantity of thin, glairy mucus mixed with bile. There had been a diarrhea for the past two weeks. Lately, the passages contained some blood. The woman was pregnant about ten weeks.

Examination of the urine showed the following condition: Sp. gr. 1.010; acid reaction; albumin 2 per cent.; sugar absent; chlorides, 14 per cent.; phosphates 5 per cent.; sulphate 1 per cent., total solids for twenty-four hours 15.4 grams; urea 0.6 per cent.; ammonia excreted as nitrogen 19 per cent. Traces of bile pigment and small amounts of leucin were found. Hyaline and broad granular casts were present in moderate numbers. No bacteria.

Owing to the serious condition of the patient and the rapid downward course of the disease, it was decided to empty the uterus at once. Ether was used for anesthesia. When the patient was placed in bed, the pulse was 180 and the respirations 50 and shallow.

During the next three days the vomiting ceased and the woman appeared to lie in a semistupor. The diarrhea improved, but the irritable condition of the rectum precluded the use of salines. On the following day the patient was distressed by hiccough. The pupils were dilated. The patient was stupid and drowsy, at times delirious. Incontinence of urine and feces. The abdomen was soft and relaxed, no evidence of peritonitis being present. One could notice a slight icterus. The liver dullness extended from the upper border of the fourth rib to four centimeters above the costal arch in the anterior axillary line. Small petechia appeared on the legs and thighs. Later, the patient appeared more restless and there was considerable twitching of the arms and legs. No convulsions occurred. On Friday, six days after the operation, the hiccoughing returned and the patient sank and died at two o'clock Saturday morning. No autopsy was permitted.

Basedow's disease is a rare complication of pregnancy and its relation thereto is shrouded in mystery. The fact that exophthalmic goitre may exert a pernicious influence upon the pregnant woman admits of no doubt, as many cases of this character are reported in the literature. On the other hand, many medical men believe that the association causes little disturbance in the chronic course of the disease.

While many hypotheses have been formulated regarding the etiology of goitre, the preponderance of modern opinion is in favor of the theory that the thyroid gland secretes a material that has a selective influence upon the nervous and cardiovascular systems. This material has been termed iodothylin. According to Gauthier, there are two kinds of secretion: one, normal, regulates the changes of nutrition; the other, abnormal, is capable of producing exophthalmic goitre. Both varieties are chemically identical. Mobius claims that the symptoms of goitre are due to the excess of material secreted from the diseased or abnormal thyroid gland floating in the blood. This condition is known as hyperthyroidism and is somewhat similar in action to the toxemia of pregnancy. This opinion is based upon the contrast between exophthalmic goitre and the diseases caused by atrophy of the glands, namely, myxedema and cretinism and the profound influence upon the course of the disease produced by operative interference.

Reid Hunt has recently proved that mice fed upon blood taken from exophthalmic patients were more immune to the action of acetonitrile than their controls, and accepts the fact as evidence that the blood of these patients contains thyroid secretion.

Whether this material is excreted by the emunctories or is absorbed into the general system is not certain, but it is probable, that all the organs take part in the elimination and the retained iodothylin exerts its baneful influence upon the vital centers.

The great majority of these cases show urinary changes indicating kidney lesions of a more or less severe character. Albuminuria, glycosuria and renal casts are common findings. The quantity of urine passed in twenty-four hours may be increased, but the total solids are low.

The onset of vomiting and diarrhea which may occur during the course of the disease is similiar in character to cases of obstetric toxemia. V. Graefe's patient vomited from ten to twenty times a day for a period of four weeks, but finally recovered. Eger's patient vomited for six weeks continually before she died. Bloody stools occur in the more serious cases and are due to ulceration of the intestines or to the degenerative changes in the blood-vessels. Ballet and Enriquez fed quantities of thyroid extract to dogs and found that they commonly suffered from hemorrhagic enteritis.

The skin plays a relatively large part in the excretion of toxins generally, but there seems to be but little effort to excrete the

irritative material through this channel. Profuse perspiration, erythema, urticaria, edema, and falling out of the hair are occasionally present and it is interesting to note that, according to several authors, these skin lesions have been increased when, because of the rapid pulse and other signs, the excess of iodothyrim may be presumed to exist. Hirschlaff experimented with the respiratory action in a girl of twenty-one who ultimately died of the disease. The gaseous interchange was about 77 per cent. greater than that of a normal girl of the same age and weight. During the last three weeks of life, the amount of oxygen consumed was 28 per cent. greater and 52 per cent. more carbon dioxide was given off than occurs normally.

Attention is directed to the cardiac changes secondary to Basedow's disease as bearing upon its association with pregnancy. Clinically, one finds a rapid heart action, a forcible beating of the carotids and abdominal aorta and at times visual pulsation of the capillaries. The tension is increased. The area of percussion dullness is increased as cardiac hypertrophy and later dilatation supervene. Murmurs and bruits may be heard over various portions of the heart. The arteries are sclerotic and hardened and petechiæ frequently occur toward the close of the disease. This latter condition is responsible for the cases of spontaneous abortion, premature separation of the placenta, and postpartum hemorrhage—three accidents that are predisposed to occur in the association of Basedow's disease and pregnancy. At autopsy there is found more or less hypertrophy of the left chambers of the heart. At times dilatation is also present. Fatty degeneration of the heart muscle, relative insufficiency of the valves combined with muscular weakness makes a trio of conditions that should cause us to regard the extra burden of pregnancy as a serious complication in the later stages of the disease.

The genital changes following in the course of certain cases of exophthalmic goitre have been pointed out by Cholmogoroff and Kleinwachter. In their cases the following findings were noted: Falling out of the hair; atrophy of the breasts; the mons veneris is deficient in fatty tissue; the labia are atrophic; the vulva gapes; the vagina relaxes and its anterior wall prolapses; the uterus is small, short, thin-walled and somewhat prolapsed, while the tubes and ovaries are small and pale in color. Similar changes have been pointed out by Mobius, Cheadle, Hoedemacher, and Bamours. These changes are very similiar to those occurring

at the menopause. In Foote's case, that of an otherwise healthy girl of eighteen years, menstruation ceased when the attack came on and the fully developed breasts became markedly atrophic. On the other hand, Sanger reported three cases and Hennig another one where these changes were absent. Jouin has seen forty-three personal cases of exophthalmic goitre in which uterine disease preceded the exophthalmus. When the local condition improved, the other grew worse. This author believes that both diseases start simultaneously, but that the small and insignificant signs of the goitre are masked by the uterine findings, and attention is directed to the goitre in course of time.

The influence of goitre upon pregnancy is extremely variable, although in the majority of cases the disturbance is slight. The patient may grow rapidly worse and die in the early months of pregnancy and present a clinical picture very similiar to that of the pernicious vomiting of pregnancy. In other cases, the symptoms may be held in abeyance during pregnancy and continue with their former severity after delivery. The puerperium may exert a favorable influence upon the course of the disease. In a few cases the goitre may make its first appearance at this time. d'Outrepoint, in 1828, reported a long-standing case of goitre in which the patient died when six months pregnant. Her symptoms were greatly aggravated by the gestation, and she collapsed after an attack of vomiting and bloody diarrhea. Guillot, in 1860, reported the cases of two women who developed exophthalmic goitre during their first pregnancy. Both were delivered normally of living children. Both patients, however, died during the close of the second gestation.

The recurrence of pregnancy may have a deleterious effect on the course of goitre. The condition frequently grows worse as the number of pregnancies increases and the secondary changes become more pronounced. This point is well illustrated in Pastrian's case. This woman, twenty-five years old, presented a slight enlargement of the thyroid gland during the first gestation. This enlargement remained stationary until the second pregnancy, when it increased until it had attained the size of an egg on both sides of the neck. Between the second and third pregnancies the condition was again stationary. During the third gestation the growth continued. In the fourth and last pregnancy there was an enormous enlargement of the gland with rapid pulse and exophthalmus. Joffrey's case is similiar. Simple goitre was present in the first pregnancy. Rapid growth in the second and

third, and rapid heart action, tremor, and exophthalmus in the fourth gestation. Several cases are recorded where pregnancy adds to a simple goitre the extra burden of Basedow's disease, while between the pregnancies only the simple form is present.

In both Basedow's disease and pregnancy the patient suffers more or less from a toxemia due to the retention of toxic products floating in the blood. These products are irritating, and when present in large amount or when possessed of great virulence, certain symptoms are liable to follow. In one case we find disturbances of the heart, eyes, thyroid gland, and the nervous and arterial systems. In the other, gastrointestinal disturbance is often present. The channels of elimination in both conditions are apt to be injured by the toxins, as is shown by the changes in the liver, kidneys, bowels, and skin. The patient is therefore called upon to suffer from a double toxemia—a poisoning from the abnormal secretion of the thyroid plus the products of incomplete metabolism. While every woman suffers from toxemia during pregnancy, in the great majority of cases, the activity of the excretory organs suffices to maintain the amount and virulence of the toxic products at such a low ebb that few or no symptoms arise. The same is true with regard to exophthalmic goitre. Here the thyroid gland takes the place of the fetus and placenta and pours its toxins into the blood. If the excretory organs are able to carry away this material and prevent retention, the patient is not harmed to any extent. In both conditions, the well-being of the patient depends upon the activity of the excretory organs.

If the double toxemia is too great a strain upon the excretory organs, we observe the symptoms of acute or subacute poisoning. Not only do we see the symptoms of the exophthalmic goitre become severe, especially those of the heart and blood-vessels, but the patient is prostrated by the muscular weakness and the continuous vomiting and diarrhea that frequently accompany the late stages. In the case reported, the kidneys were unable to carry off the waste products of both thyroid and fetal origin, and retention resulted until nature attempted to get rid of them by vomiting and diarrhea. The injury inflicted upon the liver and kidneys during the period of retention turned the scale against the patient and she died from the effects of both hyperthyroidism and toxemia of pregnancy.

The prognosis of exophthalmic goitre complicating pregnancy should be guarded. The former mortality of goitre in the non-

pregnant state varied from 16.6 (Buschan) to 25 per cent. (Charcot). Under modern treatment, both medical and surgical, the mortality averages from 6 to 10 per cent. When associated with pregnancy, we should consider the dangers of abortion, premature separation of the placenta, hemorrhage, and the strain on the weakened heart muscle. The rapid development of the disease in the nonpregnant state or the sudden changes for the worse during pregnancy is of grave import. The longer the disease has lasted in a mild form, the better is the outlook for life. A rapid loss of weight and strength, the presence of fever, the early appearance of a systole, and the onset of incessant vomiting and diarrhea are unfavorable signs. The prognosis depends largely upon the condition of the heart, the state of nutrition, and the action of the kidneys and intestines. If the pulse can be maintained in the neighborhood of 100 beats per minute and the arterial tension reduced, the patient will frequently gain in weight, and the outlook is favorable. If, in spite of the improvement in the heart, vomiting and diarrhea develop and are associated with fever, mental disturbance, and paralysis, the prognosis is grave.

The fetal mortality is higher than the maternal because of the danger of abortion and the complications that are apt to occur at the time of labor.

The occurrence of pregnancy during the course of exophthalmic goitre requires careful observation on the part of the attending obstetrician. Special attention is to be paid during the entire period of gestation to the heart, the nutrition, and excretion. The liability of intestinal autointoxication should be kept in mind and the alimentary canal kept in proper condition by daily evacuation of the bowels. The pulse rate should be kept in the neighborhood of 100 beats per minute by the avoidance of mental excitement and rest in bed. Anders strongly advises the use of ice packs. Osler advises the electric current for a period of from three to four months. Arterial tension should be reduced by free elimination and the administration of nitroglycerin or the nitrites. Frequent urinalysis should be made and attention given to the detection of albumin, casts, leucin and tyrosin, total solids and the nitrogen excreted as ammonia as determined by Folin's test. Thyroid extract should not be given unless there are signs of myxedema present.

If the condition of the patient can be kept within reasonable limits, the pregnancy may be allowed to continue to full term

If albuminuria is present without hypertrophy of the thyroid, iodothyryn may be given as advised by Lange.

If the condition of the patient grows worse, as shown by the high pulse rate, loss in weight, fever, pernicious vomiting, and bloody diarrhea, the pregnancy should be terminated. Artificial abortion should be done if the heart is organically diseased. It is unwise to treat any of the graver signs and symptoms by medical or expectant measures as precious time may be lost. In such cases, the patient may succumb in spite of the abortion. The essence of the treatment consists, therefore, in watching the patient closely and terminating gestation upon the appearance of any of the more serious symptoms. No attempt should be made to extirpate the gland during pregnancy, as the risks at this time are markedly increased.

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