EXOPHTHALMIC GOITER AND PREGNANCY.[1]

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ALTHOUGH this subject has in part been presented by Dr. G. G. Ward at the last meeting of our Society, I venture to reopen the question in order to elicit from the members an expression of opinion as to the best way of dealing with a pregnancy complicated by exophthalmic goiter. That such cases are somewhat out of the ordinary is probably due to the restraining influence which Graves' disease exerts upon conception. The individual observer thus deprived of sufficient personal experience must look to the accumulated experiences of other individual observers for guidance. As yet, the opinions have not become crystallized, and the views of those, who backed by the authority of Charcot and Kocher, ascribe to pregnancy a salutary influence upon exophthalmic goiter, are almost diametrically opposed to the beliefs of others, who see in the

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coincidence of these two conditions a grave danger to the life of the patient. In consequence, the therapeutic régime suggested ranges between a merely expectant attitude and a radical operative intervention.

In the case to be described presently there was, however, but little doubt left as to the safest course to pursue.

CASE I.—Mrs. W. W., aged thirty-four years, was referred to me by Dr. Walter Fischel on Sept. 2, 1910, for the repair of a complete tear of the perineum suffered at the first of her three confinements five years previously. For the last six months she has become very nervous, which she ascribed to the discomfort of incontinence of the bowels, while Dr. Fischel found in her a beginning exophthalmic goiter. Her history up to this time was unimportant. To her knowledge there has never been a case of goiter, diabetes, or psychosis in her family. Her own menstrual history was normal in every respect, nor had she noticed a swelling of the neck or a protrusion of the eyeballs. The repair of the laceration was to be performed under spinal anesthesia as an inhalation narcosis seemed to add an element of danger, but the stovain solution used was too weak and my own technic imperfect, as this was my first case of spinal anesthesia; so that the analgesia was incomplete and a small quantity of ether had to be given which was, however, well tolerated. Her recovery and the result of the operation were eminently satisfactory.

Within the next six months, however, the symptoms of Graves' disease became somewhat more pronounced although she remained under medicinal treatment. The goiter extended from the left to the right side; the tremor increased; the heart action became accelerated; there were frequent attacks of diarrhea, and she had amenorrhea from January to May, 1911.

She again consulted me at the end of November, 1912, when I found her to be pregnant about twenty weeks. While she herself claimed that her goiter was not materially larger than previously, yet her entire condition was undeniably worse. The exophthalmos was greatly pronounced, both tremor and general weakness were markedly increased, the heart tumultuous, the pulse very hard (blood-pressure tests were made but unfortunately not recorded); hands, feet and face were swollen. Loss in weight was not inconsiderable. The urine contained a large amount of sugar and had a specific gravity of 1037. Polydipsia and polyuria were marked.

In view of the change for the worse in the general condition of the patient and further considering the complication of glycosuria, it seemed best to relieve an organism already laboring under great disadvantages from the added strain of pregnancy and labor, and interruption of pregnancy was decided upon in consultation with Dr. Fischel. A few days in bed but without any particular antidiabetic diet reduced the specific gravity of the urine and brought about the disappearance of sugar without, however, affecting the thirst and polyuria or influencing the symptoms of exophthalmic goiter. The operation was performed December 10, 1912, under spinal anesthesia

with 2 c.c. of a 10 per cent. novocain solution with suprarenin, which produced complete analgesia. A typical vaginal Cesarean section was done, a fetus of about twenty-two weeks was turned and extracted, and the incision sewed up in the usual way. The bleeding was very slight, and there was absolutely no shock or pain.

The beneficial effect of the operation was startling. The swelling disappeared almost immediately; the patient while in bed looked practically normal, the exophthalmos receded, the neck became smaller, and the heart's action calmer. Polydipsia and polyuria subsided within two or three days and patient left the hospital in excellent condition twelve days after the operation.

Since then she has remained under medicinal treatment and is slowly gaining in health. Goiter and exophthalmos have not increased but the pulse rate has again gone up, and the menstruation has at the present writing, *i.e.*, four months after the operation, not yet reappeared.

In order to determine our attitude in cases such as the one described, we must needs appreciate to its fullest extent the influence which exophthalmic goiter exerts upon the entire organism. Whatever theory of the etiology of this affliction we may accept, whether we consider the true nature of the disease to be a hyperthyroidism or a hypothyroidism, this fact is indisputable that such patients suffer and die from heart disease (Moebius). It is mainly the condition of the heart which decides the possibility of a cure. Notwithstanding our total ignorance of the real character of the toxic agent, we know from thousandfold experience that the vitality of patients with Graves' disease is markedly diminished and that the extent of their general resistance against any increased demands cannot be foretold. It is this question above all others that calls for earnest consideration when an exophthalmic goiter becomes complicated by pregnancy. Now that the problem of exophthalmic goiter has received so much attention within the most recent past, we gynecologists will be in a position of acquiring valuable experience. It is well known that the disease attacks the female sex more frequently than the male. Buschau found among 980 cases 175 men and 805 women. Mannheim determined the proportion of men to women as 1:8.2, and other authors report even higher percentages. Whether or not there is a causal relationship between exophthalmic goiter and gynecologic diseases, as first claimed by H. W. Freund, I dare not decide. It so happens that practically all patients with Graves' disease whom I have observed in the last ten years had normal genital organs or else they presented conditions such as perineal lacerations or carcinoma, which certainly had no etiologic connection with the affection of the thyroid. I am as yet more inclined to believe in a coincidence of

two so frequent groups of disease. It is perhaps permissible to mention in this connection that when speaking of exophthalmic goiter we must not merely have in mind the well pronounced cases with the triad of exophthalmos, goiter, and tachycardia. W. W. Graves, of St. Louis, has only recently, and to my mind very justly, pointed out that ever so many cases which are being treated for nervousness, hysteria, gastrointestinal neuroses, functional heart disturbance, or some trivial affection in the genital sphere or other parts of the body, are in reality earliest forms of hyperthyroidism.

When seeking information regarding the problem of exophthalmic goiter and pregnancy I found practically all of the literature up to 1912 carefully considered in the comprehensive studies by Novak and Ward, both of which authors have been freely consulted for this article. While these writers admit that the disease of the thyroid may occasionally be influenced favorably by an intercurrent pregnancy, yet they insist that this is the exception rather than the rule.

In the following case, an influence of an exophthalmic goiter upon a co-existing pregnancy was unmistakable.

CASE II.—Mrs. A. B., aged forty-two years, primipara was seen in consultation with Dr. L. P. Butler, Feb. 17, 1913. She was married eight years and had presented symptoms of well-advanced Graves' disease in 1909. A year later practically all objective and subjective signs of the disease had disappeared under medicinal treatment (Dr. Butler). She was pregnant since Aug., 1912, presenting none of her former symptoms save a slight exophthalmos. In the latter part of January she developed albuminuria and increase in blood pressure, both of which conditions progressively grew worse in spite of strictest measures. Our intention of interrupting pregnancy when the fetus became viable was anticipated by the morbid process which led to the premature birth of a macerated fetus April 1, 1913. I have been told by Dr. Butler that the symptoms of Graves' disease have again made noticeable progress since the confinement.

Quite recently, Bernard v. Beck has added a contribution to the subject based on an unusually large material. He contends that pregnancy causes an increased demand upon the thyroid. Until the latter has become accustomed to this increase, there exist disturbances in the function of the gland which cause subjective symptoms in the first two or four months of gestation. Patients with Graves' disease, whose thyroids have already been functionating excessively before conception occurred, improve subjectively during pregnancy. This, he claims, is chiefly due to the absence of the menstrual cycle which, in the nonpregnant state, is one of the main causes of an increase of disturbance. Only if during the earlier months of pregnancy the nervous symptoms rapidly and persistently increase

should operative treatment in the form of strumectomy be instituted. The treatment in all other cases should consist of internal remedies. Subjective improvement usually occurs after the fifth month of pregnancy, and labor is uncomplicated. In 260 cases of Graves' disease and pregnancy he felt compelled to perform thyroidectomy only in five cases, and in no case did he find it necessary to interrupt pregnancy.

This is, indeed, a remarkable record and would relieve us of all doubts, if the conditions prevailing in Karlsruhe, where v. Beck works, could be applied to this country. v. Beck states that the German principality of Baden has a very large percentage of affections of the thyroid of all kinds (he himself has observed 1090 women with goiter within eleven years!), and I wonder whether so common an affection does not lose a great deal of its dangers. Conversely, the same disease is infrequent in this country—or at least not endemical—and consequently more severe, in analogy to other diseases that are transplanted upon a virgin soil. If this assumption is correct, it would explain the harmlessness of the complication in question in Kocher's statistics from Switzerland, another goiter country, and the opposed views of Cholmogoroff in Russia, Kleinwæchter in Poland, and others.

At any rate, in the case under consideration, the hoped-for improvement did not occur in the fifth month. On the contrary, the patient gave the impression of a very sick woman, and the clinical picture rather closely resembled that of an *acute* Basedow's disease which has been so graphically depicted by Schlesinger.

The increase in the size of the goiter was least pronounced, but the exophthalmos, the tachycardia, the gastrointestinal disturbances, the tremor, and above all the loss in weight, were distinctly aggravated. Another noteworthy feature was the appearance of sugar in the urine, which Schlesinger has also observed in a number of his cases. Glycosuria is of very common occurrence in the second half of pregnancy and as a rule only transitory. Occasionally such glycosuria develops into a true diabetes, and when as in our case there is a high specific gravity with polydipsia and polyuria we cannot pass lightly over this complication, notwithstanding the fact that in this case the sugar disappeared from the urine after a few days of rest in bed. I myself have become rather apprehensive since I have seen a case of diabetes appear under my eyes and lead to death in coma within three weeks.

After this article had been written, a paper by Seitz on the same subject appeared in print. Since this treatise represents at the pres-

ent time the most exhaustive study of the relations between exophthalmic goiter and pregnancy, at least the most important points must here be inserted. Seitz has collected in all 112 cases from his own material, from literature and from circular letters. He has carefully tabulated, of all these cases, the menstrual history, the first appearance of evidences of hyperthyroidism, the symptoms in former and in the present pregnancies, the therapy employed, and the results as far as mother and child were concerned. He found that the manifestations of hyperthyroidism were not affected in about 40 per cent. of the cases; a very small number even improved during pregnancy. On the other hand, sixty-seven out of 112 cases (= about 60 per cent.) were made distinctly worse by gestation. In about one-fourth of these sixty-seven cases a serious danger to health and life of the patients ensued. Seven patients died; in five cases therapeutic abortion and in eleven premature labor were produced, while in seven cases thyroidectomy was performed during pregnancy.

In discussing the symptomatology, Seitz found in his statistics three cases of miscarriage, three macerated fetuses and three cases of premature birth. He ascribes the intrauterine death and maceration of the fetus to toxic influences, a factor which very likely played a rôle in my second case. He also refers to a report by Clifford White of a patient with Graves diseas who had given birth to two children with congenital exophthalmic goiter.

Seitz, like all other observers, considers the effect upon the heart as the greatest danger, and while he expresses himself very conservatively throughout, yet he warns against too great an optimism as to the seriousness of hyperthyroidism in pregnancy. He has not seen any decisive results from medicinal treatment nor does he consider *x*-ray treatment as yet of definite value. More stress is laid upon a dietetic-hygienic régime by which the greater part of the cases can be kept in fairly good condition. At any rate in the first part of pregnancy an expectant treatment is more advisable than artificial abortion. Only if in later months both subjective and objective symptoms progressively grow worse, does he admit of an indication to interfere with pregnancy.

While thus an acute exacerbation of all symptoms of an exophthalmic goiter must put us on guard and warn us against subjecting the lowered vitality of the patient to any continued strain such as the remainder of pregnancy would produce, the method of relieving this strain must be equally carefully considered. For even a slight operation, a short narcosis, or a mild infection may prove

disastrous. Under these circumstances vaginal Cesarean section seemed to me, as it did to Ward, Hammerschlag, and Riessmann, the least dangerous form of intervention and preferable to the induction of labor by means of bags or the like.

The possibility of performing vaginal Cesarean section under *spinal anesthesia* marks, in my opinion, a distinct advantage. If the patient is brought to the operating table in "twilight sleep," spinal anesthesia represents the principles of anoci-association which Crile demands particularly for operations for exophthalmic goiter. As a matter of fact, there was both during and after the operation no shock whatsoever.

There is, of course, the question whether a thyroidectomy would not be preferable to interruption of pregnancy. The literature on this question is still too meager to permit of definite conclusions, but as the mortality from this operation steadily grows smaller, it may have to be considered more seriously in the future.

What should be our attitude if such patients with Graves' disease wish to marry? Exophthalmic goiter is often incurable even though the thyroid has been removed. It does not only impair the physical strength of the patient but may also exert a serious influence upon her psyche, causing various neuroses and psychoses such as hysteria, neurasthenia, hemicrania, epilepsy, melancholia and mania. Or else it may associate itself with severe vasomotor and trophoneurotic disturbances and auto-intoxications, *e.g.*, myxedema, sclerodermia, Addison's disease, diabetes insipidus and mellitus.

Furthermore, the disease has a marked tendency toward transmission to the offspring. In such instances, the exophthalmic goiter of the mother is usually inherited by the female descendants.

The following is an instructive example:

CASE III.—Mrs. H. C., para-iv, was delivered of her last child eight years ago. During her pregnancy she suffered greatly from what I then thought to be neurasthenia, but what I now, in the light of subsequent developments, recognize as early manifestations of hyperthyroidism. Labor, however, took place without further complications. About three years ago the classical symptoms of Graves' disease made their appearance, and strumectomy was performed some time later. *Quite recently the eldest three daughters, sixteen, fifteen and ten years old respectively, almost simultaneously developed signs of hyperthyroidism.*

There is, then, sufficient reason to advise against marriage if the symptoms of Graves' disease are fully established.

If the affliction appear after marriage, conception should be prevented as far as possible, and if, as in my first case, the manifestations

of the disease have become aggravated during a former pregnancy, tubal sterilization seems to me justifiable. The use of spinal anesthesia would eliminate to a great extent the objections against any surgical intervention in exophthalmic goiter.

I feel that in my first case such tubal sterilization should have been done at the time of the Cesarean section. As a matter of fact, I had obtained the consent of both husband and wife, but I was swayed in my judgment by the advice of a surgical friend who warned me against it. I would, however, not refrain from excising the tubes through the vagina, thereby prolonging the operation about ten minutes, if a similar case offers itself.

As stated in the beginning, my object in presenting this paper was to learn from the discussion. My conclusions, therefore, are merely tentative, namely,

1. The complication of pregnancy and exophthalmic goiter, while comparatively slight in some cases, may constitute a grave danger to the life of the mother.

2. If the manifestations of Graves' disease are aggravated in spite of medicinal and other conservative treatment, interruption of pregnancy is indicated without delay.

3. The quickest and therefore best method of interruption is by means of vaginal Cesarean section.

4. Spinal anesthesia is preferable to any other form of anesthesia in that it reduces the dangers from any operation on patients with exophthalmic goiter.

5. Girls with well-developed hyperthyroidism should be advised against marrying.

6. If Graves' disease has appeared after marriage, conception should be prevented.

7. If vaginal Cesarean section be performed, tubal sterilization should be added.

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