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**ORIGINAL COMMUNICATIONS.**

GOITRE IN THE MOTHER AND ITS MANIFESTATIONS  
IN THE OFFSPRING.\*

IS GRAVES' DISEASE INHERITED OR TRANSMITTED?

BY

GEORGE SCHMAUCH, M. D.,

Chicago.

(With four illustrations.)

THE cases I present to-night are of twofold interest: First, the mother with an exophthalmic goitre of the classical type; secondly, her four children, three of which show gradually increasing pathological changes in their bony system.

Discussing Graves' disease and its influence on the descendants, one has to first come to an understanding of the disease. I am an adherent of the Moebius-Rehn theory of Graves' disease as a quantitative anomaly in the secretion of the thyroid gland and not as a chemicopathological change. While generally the pathology of an organ has been cleared up by our knowledge of its physiological action, the opposite holds true in the thyroid. For a long time the gland was regarded as a superfluous organ, but we came to recognize that it has important functions which we had not understood. The contrast between Graves' disease and myxedema led Moebius to advance his theory and to advise the use of his antithyroidin. Struma and Basedow's disease have taught us that the thyroid gland belongs to that group of glands which have an internal secretion. Such glands are the thyroid, the hypophysis, thymus, suprarenal glands and the ovaries. Their influence is great and their true functions, thus far obscure.

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Most of the knowledge gained about the interrelation between these glands is based on the rather rough experiments upon animals and the clinical results obtained by successful treatment. I do not deny the connection of some of these organs with the sympathetic and the vagus, and there is no doubt that electrical treatment of the sympathetic gives good results in Graves' disease, though it is not the sovereign remedy which the French school claims it to be. Nerves doubtless influence the secretion of glands, as for instance the submaxillary, but our knowledge of their functions except as mere conductive organs is so limited that they have to be omitted in the discussion of the disease. Inasmuch as these organs, when successfully transplanted, are ready to take up their internal secretion, we can safely omit all the nervous theories from our discussion (transplantation of ovaries, Halban) (thyroid: Christiani and Kummer, Pfaeffer, Kocher). The influence of those organs on the human body must be transmitted through the circulatory system.

There is no uniform histological picture that corresponds to Graves' disease. A fatally ending case of thyroid disease presents a picture different from that of a struma removed from a patient in a less advanced stage. We find all kinds of transitional stages between a cystic struma, a colloid struma and Graves' disease struma. Clinical experience, on the other hand, shows that the symptoms of Graves' disease may appear at any time in a common struma, but the so-called "formes frustes" of the French of exophthalmic goitre show that the presence of all the three well-known symptoms of this disease is not absolutely necessary in the clinical consideration of Graves' disease. The success of our therapeutics also points to a more analytic differentiation of this disease. In a very few cases of Graves' disease iodine helps, in most of them it is of detrimental effect, while in the common struma it generally proves beneficial. In one case we see a rapid improvement under Moebius' antithyroidin; in others, again, the simple thyroid extract proves satisfactory. Therefore, all these facts point to the more analytic differentiation of this metabolic disturbance, called Graves' disease. It is not always possible to distinguish between hyper- and hypothyroidism. It is much more sensible to divide the anomalies of the thyroid secretion in the above-named way than to consider all the various disturbances, to be due to toxic or antitoxic products, secreted by the gland. This same division certainly pertains to all the other glands with internal secretions.

While hyper- and hyposecretion appeal to our reason, we must say that dysthyroidism does not. It assumes an unknown product of glandular secretion, absolutely without any parallel in any other gland in the body, and has neither a chemical, nor a histological foundation in our present knowledge. Therefore it seems wiser to refrain from the assumption of such an unknown chemicopathological product. There are so many glands with internal secretion in the human body, whose products as will be shown later, counterbalance each other that a quantitative disturbance in the output of any one of these glands is sufficient to explain the unbalanced metabolic changes, without referring to a mystic toxic secretion.

As the latest researches confirm, it is not the thyroid gland alone that causes the symptom-complex of Graves' disease. Moreover, 79 per cent. of all the operated cases that came to post-mortem showed a persistency of the thymus (Capelle). Some authors (Hart) therefore regard the thymus as the primary cause of at least one of the cardinal symptoms, *e. g.*, the tachycardia and the main effect of the Moebius antithyroidin seems to be derived from adrenalin contained therein, as shown by Hoffmann (and in a form that can be absorbed by the stomach). We will have to discuss the co-relations between the various organs with internal secretion later on; for they seem to cooperate. So much to justify the statement that Graves' disease is a metabolic disease, similar to other metabolic disorders, *e. g.*, diabetes, etc. That great success may be obtained by applying a rational dietetic treatment everyone handling such disturbances will confirm (read Alt's paper). We need not be surprised to find this disease sixteen times or even forty-six times (as Buschen claims), as frequent in women as in men, for women are physiologically subjected to greater changes in their metabolism than men, on account of the various changes, *e. g.*, menstruation, pregnancy, birth, and nursing. The organ that creates and regulates these phases in the woman's body is said to be the ovary. That there is an established relation between the thyroid and the sexual organs is not yet widely known. There was a time when the sexual disturbances were regarded as the primary cause. Charcot and his students looked upon pregnancy as nature's cure for Graves' disease. Most women, however, suffering therewith abort or give birth to a premature child, and although some women feel much better after birth, a number of them die during labor (Kleinwaechter, Stowe, Kron). The



disease itself, like any other disorder, must be aggravated during pregnancy, when the woman's organism is called upon to do the greater work for two organisms.

We notice swelling of the thyroid in puberty. There are also cases of an enlargement appearing regularly at every menstruation (Jenks, Olshausen). According to Jenks, coition also has an influence on the thyroid. He relates that the ancients regarded the swelling of the thyroid as a sign of lost virginity and measured the neck to prove the chastity of a newly married woman. Jenks, a gynegologist of the late Chicago Medical College, is one of the few older writers who recognize the connection between menstruation and goitre. The thyroid gland sympathizes with the uterus, as he states. His excellent paper, written in 1881, shows a keen observation of facts which we are just going to discover again, namely, the disappearance of the goitre in young girls when menstruation sets in, also the occasional spontaneous cure by cessation of the menses. We also find quite frequently swelling in pregnancy and eclampsia, and pregnancy is by some authors regarded as a physiological factor in this disease. Male animals deprived of their thyroid gland lose their potency (Lanz); female animals abort (Gurew). The milk production diminishes to one-third, and disappears completely in a few months (Lanz). Matthieu saw Graves' disease set in after removal of the ovaries, and I believe that this occurrence is probably much more frequent after operation for the so-called cystic ovaries than reported. Menstrual changes, and we might further say development and activity of the female sexual organs, depend on ovulation. On the other hand, we find atrophy of the sexual glands and mammæ, falling out of the hair in advanced Graves' disease (Kleinwaecheter, Foote, Wynne, and others). There is a great resemblance between the condition of a young woman with this disease to an older woman in the menopause. It is the same picture—hot flashes, that sensation of heat, palpitation, tremor of the hands, all of which are comprised under the name climacteric phenomena (Ausfallserscheinungen). Many of these symptoms are found, though less pronounced in some young women at every menstruation. I mention these facts only to show that there is a clinically established connection between these two organs, thyroid and ovaries.

The ovaries, besides their function of ovulation, by their internal secretion seem to affect the bony and connective-tissue

development in animals. The pronounced influence of the thyroid gland on all connective tissue is much better known than that of the ovaries, for extirpation of the ovaries in the young animal is followed by disease of the bones, which become weak and bent (Lanz and others). In Graves' disease we find a complete degeneration of the striped muscle of the whole skeleton (Askanazy). Insufficiency or defect of the thyroid gland causes a doughy swelling of the skin known as myxedema, caused by a myxomatous degeneration of the connective tissue. In Graves' disease we notice falling out of the hair. In the menopause, artificial or natural, we meet all those symptoms (dreaded by our women patients) as growing of a beard, a masculine appearance of the face. It is still under discussion whether there is anything like climacteric phenomena after removal of both ovaries, while recent authors differentiate between uterine and ovarian climacteric phenomena (Pankow). We do not know how many times an accessory ovary takes up the function of the removed ovaries. A. Martin reports among sixty cases, thirteen times regular menstruation. It took many years before we became convinced of Darwin's theory of evolution; it will take many more years before we learn that the animal organism is not only able to adapt itself to external conditions, but also to changes in its internal relations (Spencer's definition of life). It is fully observed clinically, that when there is a loss of such organs, the disturbances become compensated sooner or later, no matter whether the loss occurs accidentally or is surgically induced, the results are the same—compensation.

In Graves' disease the mammæ become atrophic. Extirpation of the ovaries has the same effect (a fact used by some English surgeons in treatment of inoperable carcinoma of the breast). Acromegaly is a disease attacking women much more frequently than men. As shown lately by Patellani, it affects women in the full age of puberty, and the connection with the ovaries is plainly shown by the fact that nearly all reported cases were amenorrhœic. Castration in early youth produces excessive growth, and the whole industry of caponizing rests on this fact.

Another disease, whose connection with pregnancy is evident, is osteomalacia. Fehling showed that double ovariectomy cures puerperal osteomalacia, consequently we have come to regard the whole process as caused by a hypersecretion of the ovary. The same effect accompanies cessation of menstruation (Loehlein), while the recurrence of menstruation brings on the



old pains anew (Seeligmann). Still there are a number of cases reported in which the removal of the ovaries did not stop the disease (about one-fourth of all reports). It seems to be a disease which prevails in those countries where struma is found. Hoenneck reports nineteen strumas in thirty-three cases of osteomalacia. Latzko reported five cases of osteomalacia following Graves' disease.

Seeligmann reports three cases of Graves' disease cured and improved by ovariin.

This entire discussion might seem foreign to the subject of this paper; still I had to give a short review of the facts demonstrating the complex metabolic nature of Graves' disease in order to prove the close connection between the thyroid and the ovaries, and the similarity of their influence on the connective tissue.

It is hard to define what kind of connection exists between these two organs, ovary and thyroid, whether they are synergistic (as Gauin, Florian, Hoffmann claim) or antagonistic (as Goldstein, Barchura, Bucura hold). *The whole process of internal secretion is still mystifying. A clearer understanding of these highly organized glands and their secretions will do away with the hypothesis of trophic nerves.* There are many facts pointing to an antagonism, as, for instance, the enlargement of the thyroid during pregnancy and menstruation, but as stated before the ovary seems a more complex organ than the thyroid. One fact should forever be emphasized and that is this, that a *pathologic secretion of toxic elements from any of the organs with internal secretion (so far assumed by most authors) is not necessary for the production of disturbances, which can be easily explained by a plus or minus in the activity of the gland.*

At the beginning of my paper I mentioned the fact that Hoffmann discovered the presence of adrenalin in the Moebius antithyroidin. The latter is nothing but the serum of the sheep, a herbivorous animal, deprived of his thyroid but retaining the products of the antagonistic glands. Anomalies in the pigmentation, similar to that in Addison's disease, *e.g.*, looseness of the bowels, decrease in the muscle power found in Graves' disease, suggested to Hoffmann the idea of a relative insufficiency of the adrenal glands, besides the hyperthyroidism. *We might add to these facts all the so-called subjective signs of pregnancy, further the pigmentation appearing during pregnancy, the pigmentation noticeable at puberty, arising with the beginning of the ovulation, also the abnormal condition of relaxation of the*

peripheral blood-vessels. In all these conditions we have a greater activity of the ovaries, a hypersecretion, which again leads to more or less insufficiency of the adrenal glands. One of the astonishing results, we observe in the treatment of exophthalmic goitre with the Moebius serum, is the stopping of the diarrhoea. It precedes the increase of weight in these patients. *Another phenomenon that most impressed me in the three patients whom I treated successfully by this method is the arrest of the menstruation which did not set in again until an equilibrium in the secretion in the various glands was established.* The patients grew stronger, gained in weight, were able to walk again and to do their housework, but menstruation stopped during the treatment with the serum, which seemed to suppress the activity of the ovaries and to create a relative insufficiency of the organs. All these facts point toward an antagonism between adrenal glands, thyroid, and the ovary. Hoffmann was the first to prove this antagonism, and saw the proof of his conclusions in the somewhat successful treatment of one case of osteomalacia with this serum.

It is not within the scope of this paper to go into details in regard to the connection of these glands with the nerves, also their relations to kidney, liver, pancreas, and diabetes. These things do not directly pertain to our present discussion. I also refrain from discussing the hypertrophies of some of these organs found in autopsies after the removal of analogous glands (cf. Roessle). The antagonism existing between thyroid and suprarenal glands has lately been proven again by the experiments of Bossi. Removal of one suprarenal gland in sheep, pregnant or not, brings on osteomalacia. Injection of adrenalin cures osteomalacia, also rickets as reported by other Italian physicians using this treatment on the advice of Bossi. These results substantiate Hoffmann's findings in the blood of osteomalacia. According to him, when Ehrmann's test on the frog's eye is used, the serum of osteomalacic patients shows elements antagonistic to adrenalin; they produce contraction of the pupil in the same way as in Graves' disease, while the serum in myxedema proves the hyperactivity of the adrenal bodies in dilating the pupil.

We have no proof of an antagonism between thyroid and ovaries, they are probably rather synergetic. The swelling of the thyroid in pregnancy is not caused by an inactivity of the ovary as generally understood. Although ovulation stops, the



internal secretion of the ovary through the corpus luteum is probably more active than in a condition of nonpregnancy. Every one of these three glands may, through the increased or decreased output of its specific secretion, bring on a disturbance in the physiological increase or decrease of the bony substance, and all these processes are connected with an increased or decreased elimination of phosphorus. We find in some cases of Graves' disease an enlarged excretion of phosphorus (Alt), extirpation of the testicles or ovaries diminishes the elimination of phosphorus. Feeding with ovariin tablets increases it (Curatulo and Tarulli), extracts of thyroids, fed to dogs increased the output of phosphates ten times (Ross and Buerger). Extirpation of the suprarenal glands had the same effect (Bossi). The retention of the organic phosphorus, according to these authors, brings on an accumulation of lime salts in the human body in the form of calcium and magnesium phosphates, and leads thus to a restitution of the normal solidity of the bones. *Ovaries and thyroid, on one hand, hold the balance with their antagonists, namely, the suprarenal bodies.* "Hypersecretion of one of them naturally will bring on a relative insufficiency of the antagonist. The secretive activity of the ovary rises and sinks with that of the thyroid," as Hoffmann puts it. So much for the explanation of the nature of Graves' disease. It will help us to understand the malnutrition in children born of a mother suffering therefrom.

Mrs. H., thirty-five years old, had four children; all, as I will state as a curiosity, were born in November except the last one. Her first child was born when she was twenty-six years old, the second when she was twenty-eight, the third when thirty, and the fourth when thirty-two. This boy, the object of this paper, was born on the tenth of September, 1906, about eight weeks before his time, the fifth of November.

No history of goitre in the family way back to the great-grandparents. The patient menstruated when fourteen years, a year and a half later than her younger sister; no signs of rickets except an irregularity of teeth. She learned to walk at ten months. Her labors were normal, but protracted. In the second half of her first pregnancy a swelling in the right side of her neck appeared, and this has since increased with each pregnancy. From the time she was pregnant with her second child a general weakness set in impeding her greatly in her housework. She used to vomit during the whole nine months of her gestations except in her last pregnancy. This also was the only time her bowels were regular. During the third childbirth she had some trouble from her goitre, had to sit up in a chair on account



of suffocating spells. She nursed all of her children except the last one. I saw her about thirty-six hours after her last labor. This child was born in head presentation in about three hours with the assistance of a midwife. The patient was very cyanotic, had immense edema of the entire body, was gasping for air; in short, presenting all the symptoms of an acute cardiac insufficiency. Her whole body was covered with prickly heat and she was perspiring profusely; pulse 145. Unable to lie down, she had had no sleep. Her neck measured 40 cm., and her eyes were bulging out at that time in an alarming manner. Camphor and digitalis was administered, which relieved her somewhat. Three days after labor, I put her on Moebius anti-thyroidin, one-half teaspoonful twice every second day. This dose was later on reduced to 20 drops and increased again to 50 drops. It was the only medical treatment she received except a diet free from NaCl, consisting chiefly of vegetables, eggs, and buttermilk. She improved rapidly under this treatment. Altogether she took twenty-eight bottles, equal to 280 cm. I must say, I never have seen more severe symptoms of Graves' disease than in this case. There was an extreme tremor of the hands, she could not hold anything without dropping it, also tremor of the tongue, violent headaches, profuse diarrhea, her hair came out in large quantities. Greatly excited during the day, she became delirious as soon as she fell asleep. Besides she was not able to swallow any water without choking. This condition had set in about two months before labor and kept up until three months afterward. Eight days after labor she was able to walk around in her room. On the eleventh day she went to bed for the first time; the edema disappeared rapidly. On the twenty-sixth day she was able to call at my office, the diarrhea had stopped, her bowels moved only two or three times a day. Pulse varied between 120 and 140, headaches had disappeared, the eyes did not protrude as much. She improved steadily; while she did not weigh more than 114 pounds after labor, she gained ten pounds within three months, and weighs now 138 pounds, more than she ever weighed. Her goitre went down to 37 cm., but measures now again 41 cm. Nevertheless, she has no trouble in swallowing. This shows that the latter disturbance has not been brought on so much by pressure as probably by a softening of the cartilage of larynx and trachea. She still has a distinct exophthalmus, is nervous, and has that hasty way of talking and moving about noticed in women suffering from Graves' disease. Her pulse beat varies now between 90 and 110. Her menstruation resumed six months after labor and appears in regular intervals of four weeks, but only lasts three days instead of eight days as before. From October, 1907, she was amenorrhic for four months. She has not taken any medicine for her goitre since about twenty months. According to her own statement, she is stronger and feels better now than she ever felt in the last six years, is again able to do

her own washing. However, her breasts are atrophic, her hair is very thin, the genitalia appear normal, there is no pronounced atrophy. Her undiluted blood serum applied to the frog's eye (Ehrmann test) brings on a contraction of the pupil within twenty-five minutes, a condition called by Hoffmann thyroïdosis in opposition to the adrenalin reaction. The patient in question probably suffers from hyperthyroidism, but, as Hoffmann himself states, this reaction does not prove hyperthyroidism.

In regard to the child, I must say it was somewhat neglected. The mother's condition was so serious that none took much



FIG. 1.—W. H. 5 months old. Forme fruste of myxedema. Note irregular shape of cranium, exophthalmus, myxedematous folds in skin of neck and chest, large abdomen, absence of hair except on the occiput.

interest in this little boy. He hardly weighed four pounds, was nothing but skin and bones, but appeared otherwise normal. As the mother had no milk, he was fed cow's milk one part to four parts of water with a spoon, as he was unable to take the bottle. Although not much older than thirty-two weeks, he developed nicely on this food. Five weeks after labor his eyes started to bulge out and the head as a whole seemed to grow, especially the forehead. A few days later the temporal bones began to protrude, then one side of the occiput, then the other side, then the left frontal bone in the region of the protuberance



seemed to elevate. The mother thought all these changes were brought on by the child sleeping on one side of his head. However soon afterward the right frontal bone protruded in the same way. While all this happened, the bones themselves did not soften, instead they seemed to grow harder, the sutures remained closed, the large fontanel became smaller. This whole process took about six weeks. The eyes were bulging out more and more, and at the same time small openings ap-



FIG. 2.—W. H. 5 months old. Note the open mouth, the umbilical hernia and the myxedematous folds of skin.

peared in the temporal and frontal bones, the size of half a cm., surrounded by an elevated area. All these changes had no influence on his general condition, his appetite was good, he slept well and grew. At the end of the fourth month there was still a hole in the right frontal bone, and the child's head had the form of a turret head (Thurmschaedel) and saddle head. Forehead and occiput were bulging out, while the parietal bones were sunken. This, together with the exophthalmus, gave the

child a very queer appearance (cf. picture taken at that time). The treatment of the child consisted in the administration of lemon juice. He used about two lemons a day. Later on, phosphorus oil was given in addition. When eleven months old the boy weighed 19 1/2 pounds. He always enjoyed good general health. While the other children were suffering from whooping-cough, he did not contract it. When two years old, he suffered from pneumonia, but recovered. Last summer he developed an abscess in the right gluteal region near the anus.



FIG. 3.—W. H. 27 months old. Turret and saddle head.

When opened, I was astonished to get into a perfectly calcified cavity. I thought of a dermoid and proposed extirpation. However, when I saw the child two months ago, the whole tumor had disappeared. This is another phenomenon pointing to the abnormal deposition and absorption of limy substance in the body of this boy.

He still appears abnormal. Comparing his present appearance with the photographs which were taken when he was four and one-half months old, it is evident that he has greatly improved. He looked worst when about twelve weeks old. His height is about normal, 80 cm., he weighs 35 pounds. His arms and chest are well developed, his skin has now a rosy natural color



and shows a good panniculus adiposus. The muscular power in his arms is greater than one would think. He moves a chair without much difficulty as his mother reports. His legs are not so strong, he is just starting to walk. The umbilical hernia, to be seen in one of the pictures has disappeared, also the myxedematous condition of the skin, the wrinkles on his neck and under his arms; the genitalia are well developed. The part of the child which first attracts attention is his head.



FIG. 4.—W. H. Turret and saddle head.

The measurements are:

*Circumference.*—Frontooccipital, February, 1907, 42 cm.; April, 1907, 45 cm. August, 1907, 47 cm.; February, 1909, 51 cm. Frontosuboccipital (highest part of forehead to neck), February, 1907, 41 cm.; April, 1907, 41 1/2 cm.; August, 1907, 43 cm. Mentooccipital, February, 1907, 43 1/2 cm.; April, 1907, 47 cm.; February, 1909, 53 cm.

*Diameters.*—February, 1909, Bitemporal, 14 cm.; biparietal, 12 cm.; frontomental (highest part of forehead), 19 cm.; suboccipitopregmatic 11.5.

The shape of the head has, therefore, not much changed; it reminds the obstetrician mostly of a child born in a protracted brow presentation. Still this boy was born with a perfectly

round head. You notice an immense broad forehead the temporal bones bulging out, and a saddle-shaped depression of the parietal bones. His eyes are protruding, but not half as badly as about fifteen months ago. At that time you could not see more than the upper half of the cornea. He now covers his eye-balls completely when he sleeps. Another phenomenon you will observe is that the boy keeps his mouth open all the time, and the saliva runs continually from it. There is no saddle-nose, but as in congenital myxidiocy, the large tongue sticks out continually; the palate is very high-arched, V-shaped. During the first sixteen or eighteen months he was in the habit of shrieking aloud as myxedematous children do, terrifying his mother and the whole family. His eye-brows are not developed, there is hardly any hair on the temporal region; the rest of the head is covered with coarse red hair. Primary dentition began at the age of ten months; his teeth are only half developed and already show symptoms of decay. The enamel is covered with grooves and has a greenish appearance. At the first glance at the eyes of the child, you will think of a hydrocephalus. But you can convince yourself how hard the cranial bones are. Contrary to hydrocephalus, the large fontanel was closed at the age of eight months. The sutures were never gaping, the aplasia of the cranium in this child was totally different from that found in hydrocephalus, the so-called "Lueckenschaedel." The craniotabes of rickets presents a different picture also. Rickets generally attacks the whole bony system and in the cranium the occiput is the place most frequently diseased, while in this boy the frontal and temporal bones showed defects. Besides the rarefaction, probably a premature synostosis of the parietal and sphenoidal bones took place, causing the saddle head, "Klinocephalus," according to Virchow. Syphilis may be excluded, as the child got well without any specific treatment. Clinically, the whole process in its rapid course impressed me as an osteomalacia rather than rickets. The histological difference between these two diseases has recently been denied by Schmorl, who regards the rachitis tarda as an osteomalacia. Nearly all bone diseases have one thing in common, and that is, their etiology is unknown. Syphilis and alcoholism, according to text-books, are the cause of everything. Lately, however, the opinion is more frequently expressed that every bone disease in childhood is caused by an anomaly of the thyroid (Fuchs) or analogous glands (Stoeltzner), or as we may say now of the antagonistic glands. There might have been a minor degree of hydrocephalus. The brain is that organ which is deprived of its limy substance second to the bones in rickets (H. Aron). However, the protrusion of the bulbi, the first symptom of an abnormality of this child, appeared before there were any striking changes in the rest of the cranium. In my opinion, it was not caused by the pressure of a hydrocephalus alone, but is probably the consequence of a softening of the orbital roof.



There are a small number of turret heads reported, but their etiology was so far unknown. They interest the ophthalmologist especially as sometimes an atrophy of the opticus sets in. In many of these reported cases an irregularly formed head was found, and as Velhagen states, the orbita in such patients is not a horizontal cave but round, and not so deep as normally. This causes exophthalmus. Another phenomenon, not yet described, in children like this boy, is a pronounced eosinophilic leukocytosis. His blood resembles that of a new-born with the exception of the increase in the eosinophiles.

Senator quotes Neusser as having reported the same findings in a case of osteomalacia.

When the mother first called my attention to the child it was because his eyes were bulging out in the same way as her own. There was only one opinion in his home and neighborhood and that was that the child had inherited this disease from his mother. I took this idea as a joke, I never had heard of a congenital Graves' disease (we might use this term as it appeared five weeks after labor). Still it is not so absurd. Graves' disease in children is very rare, and gives an infaust prognosis. To my knowledge there has not been a case reported which developed within the first three months of life. This little boy is good natured and you will agree with me that his eyes are bright and not those of a cretin or idiot. He talks a little and enjoys playing with his brothers. We might call his condition, according to French authors, a "forme fruste" of myxedema, combined or rather caused by osteomalacia or rickets, if you like this term better. This, however, is only a symptomatic diagnosis. What interests us obstetricians in this case is the etiology. *We have here one of the rare cases of a gradually increasing deterioration of the children of a mother afflicted with Graves' disease, increasing at the same pace as that of the mother.* The first child, a girl born while the mother acquired the disease, is apparently normal; the second, a boy, shows signs of rickets; the third, a boy, has an immense head for his age, which is five years, circumference 54 cm. Two years ago he looked very much like a cretin with his fat abdomen and large head. When one year old, he weighed 28 pounds, just as much as with two years, but could not walk. The fourth, the child described, nearly cost his mother her life. I do not think it necessary to emphasize that the mother's condition is accountable for that of her children. I purposely went into details of the complicated arrangement of the glands with internal secretion, that are comprised in Graves' disease and their influence upon the connective-tissue system. *These children reflect the various stages of their mother's disease.*

Theilhaber, one of the few gynecologists who took up the question of pregnancy in Graves' disease comes to the conclusion that women afflicted therewith should not remain pregnant, abortion should be induced; secondly, girls with this disease

should not marry; thirdly, they should not be allowed to nurse their children. In regard to the first question, I will say that in mild cases interference will be just as little indicated as in compensated valvular trouble. Pregnancy makes most cases of Graves' disease worse. This act always has to be considered. However, we have in the Moebius serum, in the different thyroid extracts, and in the ovarin means to compensate the systemic disturbance. In a more serious case, especially when there is already one child, I would not hesitate to interrupt pregnancy. This has to be done in the earlier months, as the insufficiency of the heart (Graves disease heart or struma heart) predominates in the picture. The heart of a woman with exophthalmic goitre is on account of the muscular changes often unable to do the increased work of pregnancy. Premature labor is just as useless as in heart disease. *An absolute indication for artificial abortion is the combination of Graves' disease with a persistent thymus (status thymicus) in accordance with surgical rules.* Induction of abortion will also be indicated in all those cases that show pressure symptoms on the trachea or esophagus. This will be found more frequently in cystic struma than in Graves' disease, where the vascular struma prevails. However, any form of struma might develop into an exophthalmic goitre. The woman, whose case is presented to-night, has a cystic and vascular struma. For months before and after labor she was unable to swallow any water. Induction of abortion would certainly have been justified.

I always remember a sad case observed in Berlin at Olshausen's clinic. A woman with a large struma, cyanotic and in orthopnea, was brought to the hospital in her eighth month of pregnancy. Her serious condition was said to have developed quite suddenly. There was no time to induce labor we decided for Cesarean section and strumectomy. The latter was performed under local anesthesia, followed by tracheotomy and subsequent section under general anesthesia. The woman died within four days and the child within a week. Such cases show the value of an early induced abortion. It is difficult to make strict rules when and when not to interrupt pregnancy in Graves' disease as the cases differ so much. *However, I would not allow a woman with Graves' disease to become pregnant a second time.*

Should a woman suffering from Graves' disease marry? Can she expect to have healthy children? True, there are many women with this disease that give birth to children which are not only born healthy, but remain healthy and develop well.



But the case presented here would cause us to hesitate with our consent if we should be consulted.

Two years ago I delivered another woman with exophthalmic goitre who gave birth to a strong boy. It was her fifth child, forceps after eighteen hours' labor. Her sister has the same disease. She had all the symptoms of an insufficiency of the kidneys, general edema, headache, insomnia, etc., symptoms that are so frequently falsely called pre-eclamptic. Her boy is exceptionally bright, brighter than any child I ever saw. The mother nursed him up to the age of three and one-half months, when her breasts dried up. After weaning, the child suffered from bowe trouble; in fact, it did not recover until the parents moved out into the country. The only sign of rickets in this child was he did not get his first teeth until he was fourteen months old. Genitalia well developed, no struma. When fifteen months old the boy suffered from priapismus, without apparent cause.

Schaffle reported recently a case of transmission of goitre through four generations. The two oldest children showed an enlargement of the thyroid, the six younger ones were normal. Goitre is generally recognized as an inheritable disease. Demme reported a case where all the children of a woman with goitre showed a struma until she was operated upon. The children which followed were normal. This certainly is a mere coincidence. Looking at our family, one might conclude that the youngest boy has inherited the disease, still it is merely an intrauterine acquired disorder. This question is quite important.

As soon as we accept the theory that the boy has "inherited" his disease, we admit that he can transmit his functional disorder to his descendants. In order to decide this question, I must discuss briefly our present theories of heredity.

We the product of our parents, carry with us throughout life some inherited qualities; in other words, the physical arrangement of our various organs is an heirloom received from our ancestors. The average length of our life, the average life of the different organs, everything seems to be regulated by the laws of heredity. The paternal cell, the spermatozoon as well as the maternal cell, the ovum, are without sex (Weismann). They are identical in their validity, one may substitute itself for the other (Weismann). The nuclei of both contain the germinal protoplasm and carry in their chromatin all the inheritable substance. The product of the union of these protoplasms is the new individual which, therefore, will never be a perfect likeness of one of its parents. The child is the half-brother of its father



and its mother, as Baumgarten puts it (along the lines of whose ideas the laws of heredity are discussed in this paper). Part of the germinal protoplasm is early withdrawn from general use (in building up the new individual) and is deposited in the sexual glands. This "deposited" germinal protoplasm is, therefore, not created in the sexual glands, it is there. It grows and increases from generation to generation, just as a long running root sends out sprouts that develop into new plants (Baumgarten). Father and child are derived from the same protoplasm, only at different times (v. Naegeli). We do not transmit our own product to our children, but an heirloom received from our ancestors. The consequence of this "continuity of the protoplasm" (Weismann) is that a disease cannot be inherited. A disease is always an active process and not a condition or quality (Martius). We do not inherit syphilis because the father is syphilitic; neither one of the germinal cells is syphilitic. As pointed out by Finger, before the discovery of the spirochæte, syphilis may be congenital, because the syphilitic virus is mechanically added to the fertilized ovum. In order to inherit a pathologic condition, the germinal cell, ovum, or spermatozoon, has to be afflicted in the same way, the "micellen" (v. Naegeli) of the germinal protoplasm must show the same anomaly. Upon this natural obstacle to inheriting acquired diseases rests the continuance of mankind. Adopting these laws, I have to conclude that this boy did not inherit his pathologic condition, he acquired it intrauterine. *While heredity is a physiological process (Haeckel), something we cannot escape, this child might never have been taken sick if his mother had been properly cared for.*

The fact that the last three children have rickets; furthermore, that all the children have outgrown their disease without special treatment, proves to me that the child's condition is the result of the mother's malnutritive media, but has not reached the child by way of the germinal protoplasm.

There is one exception to these laws: a noxious substance (not organized) circulating in the human system will not only prove detrimental to a certain organ, as for instance the kidney or thyroid, but might also attack the corresponding "micelle" of the germinal protoplasm, which is the anlage of that organ. A diminished resistance, a disposition toward the same illness is thereby created in this special organ (Orth). According to Orth and other pathologists, in this way an inheritable anomaly is

created. This theory is not generally recognized, it is a return to Darwin's pangenesis and doctrine of "gemmulæ."

One of the reasons why I have reviewed these laws of heredity is that a family like the one presented is apt to throw some light on this subject. We do not deal with a disease caused by an organized poison, but with changes that are the consequence of a disturbed secretive function of an organ, or rather a series of them that include the sexual glands. Moreover, this organ, the thyroid, seems to be one of the most important ones in regard to the building up of the whole organism. Indeed, we might say with Baumgarten, we are not yet fully aware of the immense influence this organ exerts upon the whole connective-tissue system.

The connection of struma with drinking water is well known, while the causes of exophthalmic goitre are still under discussion. Only lately we learned that infectious disease such as la grippe, poli-arthritis, etc., may produce an acute thyroiditis. The connection with pregnancy is also recognized. The only plausible theory given for Graves' disease, is that of Bayan who regards the changes in the thyroid as similar to those in Bright's disease. A noxious fluid, circulating in the body, brings on a lesion of the epithelium. The latter is thrown off into the lumen, but contrary to the kidney remains there, is not thrown off. The consequence is a much more lasting effect of the "noxious" substance. In accordance with this theory, *the enlargement of the thyroid in menstruation and pregnancy would be a similar process to the albuminuria and nephritis gravidarum.*

The possibility of transmission of a functional disorder, in the sense of Orth, cannot be denied; heredity by direct influence of the germinal protoplasm has to be admitted theoretically. Only observation of several generations in a family like ours would justify a positive decision one way or the other. Graves' disease is not an active process in the sense of Martius. A hypertrophic, and consequently hypersecretive gland, may as readily be inherited as a large head. Practical experience, however, contradicts this theory. Most of the children born of women afflicted with Graves' disease seem to be normal. At least there are only very few reports of serious rickets, as for instance in Theilhaber's first case. It was mentioned before that there is no proof to support the theory of a toxic secretion from a diseased gland, which could influence corresponding parts of the germinal protoplasm. In my opinion, *the rickets in the*



older children and the myxedematous condition in the youngest child are sequela of their being born of a mother suffering from secretive disturbance of the thyroid and the other glands. There was no chance for the germinal protoplasm of the father to counterbalance any defects peculiar to that of the mother. The children were born normal as far as their external appearance shows. This, however, only proves the vitality of the germinal protoplasm—the parasitic nature of the child. In many cases of Graves' disease probably other glands will compensate by their increased or lessened activity, the metabolic disturbance brought on by the enlarged thyroid. Only a seriously disturbed harmony, as existed during the last gestation of this woman, seems to be able to influence the child in a pronounced manner. We know very little as to whether the glands with internal secretion are working during the period of intrauterine life. The thyroid does not become an organ without a duct before the middle of pregnancy. The sexual glands are not active. The thymus and adrenal bodies are comparatively large organs. So far no case of congenital rickets has been reported, that could not be successfully disputed (Stoeltzner). *The child adapts his own metabolism to that of the mother, and therefore is born apparently normal.* This takes place, so to say, in the same way, as the passive immunization by protective bodies of the maternal blood.

After birth, however, when the child is growing faster, when it has to adapt itself to the outside world, when it has to depend on the function of its own glands, every disturbance in the harmony of the glands with internal secretion will more readily become apparent. More so, when a child, such as this boy, is born before time. The test of the serum of this child on the frog's eye (February, 1909) gives a different result from that of the mother; there is not a contraction, but rather a slight dilatation, a rounding of the pupil taking place within ten minutes. However, not enough to prove the presence of adrenalin as found by Hoffmann in true myxedema.

Inasmuch, as the extrauterine developed malnutrition of this boy is a consequence of maternal disorders, an appropriate treatment of the mother with struma or Graves' disease during pregnancy is indicated. According to the insufficiency, determined by tests, when possible, on the frog's eye, we should administer antithyroidin, thyroid extract, or ovariin. As long as the effect of the organotherapeutics is still widely discussed, a dietetic treatment in our old way is perfectly justifiable. *Per-*



*fect health during pregnancy is the only proof of an equilibrium of the glands with internal secretion.* Such a therapy is not indicated in order to prevent the so-called toxemia. Toxemia means nowadays everything to the obstetrician, in the same way as Peruna cures everything. Thyroid extract may prove very beneficial in some cases of pregnancy, as lately shown by Foulcrod. *Administration of thyroid extracts after a certain pattern good for every kind of toxemia, is liable to cause great damage.* We should not only individualize, but also endeavor to find out which of the organs with internal secretion causes the malnutrition through its insufficiency.

As long as women with Graves' disease bear apparently healthy children, we have no right to prohibit marriage. This boy received thyroid extract for a little while, but without any striking result. I intend, however, to put him on fresh thyroid to see what effect it will have. If no result, he will receive Moebius antithyroidin.

One question only remains to be answered, namely, should a mother with this disease nurse her children? Theilhaber says, no. I do not agree with him. We know that the mother's milk does not always prevent the appearance of rickets; however, children nursed by their mother very rarely develop serious rickets. As stated above, the child's organism adjusts itself to the disturbed maternal metabolism (simulating an inherited disorder), and there is no reason why it should not thrive and grow, as long as it is kept under the same conditions it enjoyed *in utero*. The difficulty is that these women have no milk, but as soon as the child is able to select its own food it will pick out those elements it needs to build up its system. The boy presented to-night, did not show any real improvement until put on mixed food. Although he is not yet what you call a handsome child, he is improving and may become normal, and as I believe can beget healthy children. Hence Graves' disease is not an inheritable disease. It is occasionally transmitted to the children, as in the family presented, giving rise to temporary disturbances, such as rickets and myxedema. These conditions, however, are preventable by an appropriate treatment of the mother.

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