

## HYPERTHYROIDISM COMPLICATING PREGNANCY\*

BY FREDERICK HOWARD FALLS, M.S., M.D., CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, College of Medicine,  
University of Illinois)*

**T**HE control of the function of reproduction is, like that of digestion, practically entirely under the control of the vegetative nervous system. The uterus, tubes and ovaries are all richly supplied by the sympathetic ganglia of the pelvis and will function entirely independently of the central nervous system. These functions are apparently further governed in part by the action of certain hormones or secretions of the ductless glands acting directly or indirectly through stimulation of the sympathetic nervous system.

It is not surprising, therefore, that contemplating the physiologic and pathologic changes that occur during pregnancy in the human body, deviations from the normal nonpregnant state can be found in the various ductless glands as an expression of their response to the abnormal stimulus brought about by the pregnant state. Thus it is seen that the anterior lobe of the hypophysis may be greatly enlarged, even to twice its normal size,<sup>1</sup> due to overgrowth of the chief cells which dominate the eosinophilic and basophilic cells forming about 80 per cent of the total cells. The adrenals<sup>2</sup> are less changed grossly, but there is evidence that the cortical portion is markedly increased in size and that the activity of the medullary portion is also increased. The ovary presents the unusual corpus luteum of pregnancy, and the graafian follicles fail to develop during this period. Other less evident functional changes in the interstitial cells may well be present. In addition there is evidence that the thymus, epiphysis, parathyroids, and Langerhans' islands of the pancreas are also functionally altered by the pregnant state.

\*Read at the Forty-first Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Toronto, Ont., September 10-12, 1928.

The thyroid is one of the most noticeably altered of the endocrines during pregnancy. In a large percentage of cases this enlargement can be appreciated clinically, and in some cases there appears first during pregnancy a true adenomatous growth, with symptoms of a toxic adenoma. The pathologic and clinical picture of a true exophthalmic goiter may supervene.

In reviewing the literature one is struck by the fact that no one man has had a wide experience in this type of obstetric complication, and this is one important reason for bringing the subject before this association so that a free discussion will stimulate interest in the subject and add to our information.

I wish to approach the subject from two points of view, namely, from that of the surgeon and from that of the obstetrician. The material which I have collected lends itself well to this grouping of the cases. My own material which was collected at the Research Hospital, University of Illinois, was under my supervision throughout. The other cases have been furnished by my surgical colleagues, Drs. Percy and Nadeau of the Augustana Hospital and Dr. Seed of the Surgical Department, Research Hospital, of Chicago. The pregnant woman who develops symptoms of thyrotoxicosis either may consult a surgeon primarily, whether or not she knows she is pregnant, or she may be sent to a surgeon for treatment by her obstetrician. In either event the determination of the line of treatment is left to the surgeon. Quite naturally his chief interest is in the goiter and its manifestations. Under the circumstances it is logical that he concentrate attention on the management of the goiter problem and that to a greater or lesser extent he disregard the existence of the pregnancy. On the other hand to the obstetrician the goiter and its symptoms are only one phase of the pregnancy, and the latter assumes the major importance. As a result two lines of treatment have been evolved based on these two views. In a given case of thyrotoxicosis, especially the exophthalmic type of goiter, the surgeon may advise that the patient be treated medically with Lugol's solution at bed rest for a period of one or two weeks until the clinical picture improves and the basal metabolic rate drops. He will then advise partial thyroidectomy or ligation of one or both poles to decrease the thyroid symptoms. If in accomplishing this very important desideratum the patient aborts, he regrets the incident but nevertheless feels that this is the wisest course to pursue. He feels that there may result even under the best of medical management a thyrotoxicosis which in itself will produce abortion and may result in the death of the mother whether or not she is operated.

The medical man and obstetricians on the other hand are apt to proceed as follows: The patient is put to bed and on Lugol's solution ten drops three times a day. The basal metabolic rate is carefully determined, and the progress of the case is watched under this management.

and went to spontaneous delivery at term after lobectomy, done at the fourth month of pregnancy. The second was carried through under medical management, delivered a normal baby and had a subtotal thyroidectomy twenty days postpartum. One patient with severe hyperemesis gravidarum and symptoms of thyrotoxicosis responded nicely to iodine therapy.

An analysis of the basal metabolic rates in a series of normally pregnant women and in those showing the clinical manifestations of thyrotoxicosis, has disclosed the fact that the laboratory test has backed up the clinical impression in practically all cases. It was found that in those cases showing severe symptoms of hyperthyroidism the basal metabolic rate was as a rule correspondingly higher than in those showing mild or no clinical evidence of the thyroid overactivity.

In those patients showing toxic symptoms of an exophthalmic goiter type the use of Lugol's solution in ten drop doses three times a day caused a marked improvement, and the same observation has been made by Mussey, Davis, and others. We have also noted an acute intoxication following the giving of small doses of Lugol's solution to patients with adenomatous types of goiter. Those patients falling in Group I, I described above, had no iodine. This was omitted so that the clinical picture and basal metabolic rate would not be altered thereby. In Group III there are three cases who were referred to the clinic as hyperemesis gravidarum cases which were found to have acute exophthalmic goiter with severe gastrointestinal symptoms. Davis<sup>9</sup> and Dr. Carl Harper report a similar case, and it is probable that they are much more common than we are accustomed to suppose.

I wish to report in some detail one of these cases partly because it illustrates the condition just mentioned and partly because it represents the most carefully observed case that we have studied.

The patient entered the obstetric department of the University of Illinois, Sept. 15, 1927. She was a colored primipara, thirty years old, married and a factory worker. From her features and color one would say that she was not of pure Ethiopian stock. Her last regular menstruation was April 13, 1927, but she flowed for three days beginning May 10, 1927. The latter part of June she began to vomit, at first only once a day, later progressively more frequently. She had to stop work July 11 because of weakness. About Aug. 1 she became extremely nervous and developed a marked tremor. For a month before entry she vomited day and night. Food stimulated vomiting, and it was frequently preceded by hicough. Her family history and past medical and surgical history were essentially negative. Her menses began at eleven, were regular, thirty-day type and lasted five days with the passage of some clots. Physical examination revealed a poorly nourished woman whose present weight of one hundred seven pounds contrasted with her normal weight of one hundred forty-six pounds. Her pulse was 140, respirations 32, and temperature 98.6. Her systolic blood pressure was 108, diastolic 52. The positive points in the physical examination were: Neck showed moderate enlargement of the thyroid which was firm and not nodular, and the pulsations of the vessels of the neck were marked. There was a moderate degree of exophthalmos. Her chest showed decreased expansion, respirations were shallow and rapid, breasts were small and firm. The lungs were negative for rales.

Whispered and spoken voice faint. The heart's action was rapid. The apex impulse was not strong with a slight suggestion of a thrill. There was a systolic murmur which was transmitted to the axilla. The uterus was enlarged to about the size of a six months' pregnancy. Reflexes were slightly exaggerated. Vaginal examination revealed no abnormalities. The patient appeared to be extremely toxic and exhausted and was hardly able to stand. The basal rate two days after admission was plus 49. She was seen in consultation by Dr. Seed of the Surgical Department who advised Lugol's solution ten drops three times a day and was in favor of a thyroidectomy as soon as the crisis symptoms subsided. He feared that improvement, if it occurred, would only be temporary and that operation should be done before a relapse occurred. We pointed out the danger of abortion which he admitted but felt it was slight in comparison to that of another thyroid crisis. The vomiting stopped promptly on bed rest and Lugol's solution, and the basal rate remained above normal though greatly reduced. She continued on Lugol's solution from Sept. 19, until Nov. 4, and after a rest of a few days it was commenced again and was again discontinued on Dec. 19 for five days. It was then continued until her delivery. An x-ray taken of her chest was negative for tuberculosis. A film made on Sept. 16, 1927, showed a single fetus; a similar

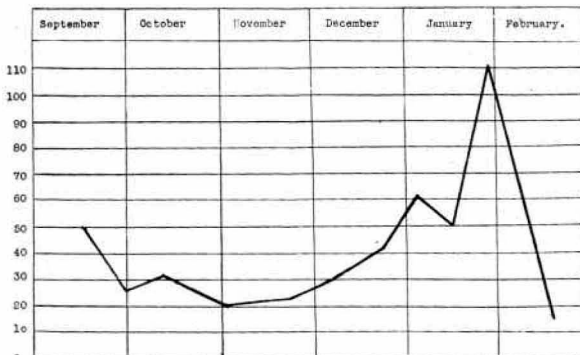


Chart I.

one taken Jan. 3, 1928, showed two babies. Chart I shows the changes of the basal metabolic rate. The red blood count was 4,650,000, leucocytes 13,600. Her general condition was so good on conservative management that we decided to defer operation until some further evidence of thyroid toxemia manifested itself. We found that the basal rate stayed only slightly above normal, that the pregnancy apparently developed normally and that the patient's general condition and nutrition continually improved. She had very little reserve strength, however, as evidenced by her weakness in attempting to get out of bed on several occasions. The iodine solution was stopped twice for a period of a few days, and this was followed each time by an aggravation of the nervous symptoms, although the vomiting did not return. We kept her under this management and in bed most of the time until February. A rather marked hydramnios developed about Jan. 15, and an x-ray picture was taken because of the possibility of a monstrosity. This picture showed two normal twin babies, presenting by the breech. Toward term she was allowed to get up for two days but seemed too weak to support much activity. A bag induction was done at term because she did not go into labor and was quite uncomfortable from the hydramnios. The duration of labor which was normal in every way was about eight hours. As soon as the first stage was completed both babies were delivered by breech extraction on February 4, 1928.

Case 8 had a plus 69.3 reading as the highest antepartum and 54.6 the lowest antepartum; the eight day postpartum reading was plus 51. This may have been due to an associated mild pre-eclamptic toxemia. The rates in general are rather low, some even well within the normal pregnancy limits, and this corresponds well with the diagnosis of a mild hyperthyroidism. It will be seen that a rate of over 30 was found in eight out of the thirteen cases. Normally in nonpregnant women it is said that a plus or minus 15 is not significant of pathologic hypersecretion. Most observers feel that normal pregnancy may raise the figure to 20 or even 30 but anything above 30 should be considered pathologic.

In those patients showing a basal rate under 25 there were in each case other symptoms upon which the diagnosis of hyperthyroidism was based. Two of the thirteen cases gave evidence of a pre-eclamptic toxemia as well as thyrotoxicosis. We were especially interested in this finding because of the statements of Ward<sup>11</sup> and others that the failure of the thyroid gland to increase its activity during pregnancy is one of the causes of eclamptogenic toxemia. Ward found that the use of saline extract of thyroid, normal human thyroid gland, seemed to affect favorably one case of hyperemesis gravidarum. He also had a patient with exophthalmic goiter who was cured by the injection of an antiserum and two years later became pregnant. She went through pregnancy perfectly normally, and on the fourth day postpartum she developed symptoms of exophthalmic goiter. He feels that the injection of saline extracts of human thyroid glands may favorably alter the metabolism in patients who have eclamptogenic toxemia or hyperemesis gravidarum.

Four of our cases displayed the clinical manifestations of toxic adenoma, Group II. The average age was thirty-one years old and all were multiparae. Two of the four had slight exophthalmos. Two had marked choking sensations and one a marked aphonia and dyspnea on lying down. Two had a 1 plus albumin in the urine and a basal rate of 50, and 105 was noted in two. This test was not made on the other two. Three of the four had symptoms of pre-eclamptic toxemia. All of the babies were born spontaneously and were normal in size and length. Weight loss was noted in one patient of the four. The apparent gain in Case 3 may have been due to pre-eclamptic toxemia with edema. Table II shows the data on these cases.

A consideration of these toxic cases, while few in number, leads us to a more conservative conclusion regarding the coexistence of thyrotoxicosis and pregnancy than that advanced by Gellhorn<sup>12</sup> who concludes that exophthalmic goiter and pregnancy constitute a serious menace for the mother. He believes that girls with a well-developed hyperthyroidism should be advised against marrying. If Graves' disease appears after marriage, conception should be prevented. The

quickest and best method of interruption is by means of a vaginal cesarean section, with tubal sterilization added. We feel that while his view may obtain for the extremely marked cases of exophthalmic goiter and especially if skilled surgical intervention is not available to the patient, we would hesitate in the light of our experience and that of others to advocate the same for all cases, particularly since it is well established that some of these patients are actually benefited by the pregnant state. We are of the opinion that every pregnant woman undergoes a readjustment of the functional activity of the ductless glands. When the readjustment results in a new balance being established, the patient is classified as a normal pregnancy. Various pathologic states may develop from a failure to establish a balance. Given, then, a patient with a disturbed balance before pregnancy begins, an adjustment more nearly to what is considered normal may be established by the pregnancy.

A review of the data in Group III shows five cases classified as exophthalmic goiter. Their average age was thirty years. Three of the five showed marked loss of weight, and four showed moderate exophthalmos. Three showed a slight trace of albumin in the urine, and one had a pressure of 176/96, with headache and epigastric pain and was thought to be a pre-eclamptic toxemia. One patient had a thyroidectomy after which she passed a blood mole. This case was transferred to us from the surgical division after the operation had been done and the abortion was in progress. Three of the five patients entered the ward with the diagnosis of hyperemesis gravidarum. The accompanying clinical manifestation of hyperthyroidism and the basal rate made the diagnosis of hyperthyroidism. Treatment directed at this condition resulted in a marked improvement of the vomiting. The babies were all well developed about term and left the hospital in good condition except one of the twins who died two days after birth in convulsions. Autopsy revealed numerous small hemorrhages in the brain. No abnormalities were noted in the thymus or in the thyroid. There were two colored women and three white women. The basal metabolic rate varied from plus 111 to plus 3 before delivery and was plus 15 and plus 8 after delivery in those cases in which a record was obtained. One of the five cases had not delivered at this writing. Table III shows the results of these cases.

An analysis of the eight cases operated on by Dr. Percy and Dr. Nadeau shows that the average age was twenty-eight years. Three of the eight had considerable loss of weight. Toxic symptoms and enlargement of the gland were present in all. There were none of the symptoms either of hyperemesis gravidarum or pre-eclamptic toxemia. One of the eight cases aborted before leaving the hospital. Four of the cases were diagnosed clinically and histologically as exophthalmic goiter, and three were toxic adenomas. The remaining case was classi-

TABLE II. TOXIC ADENOMA

CASE	AGE	RACE	WEIGHT	PARA	GOITER	EXOPHTHALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	METABOLIC RATE			BABY	REMARKS
										HIGH	LOW	POSTPARTUM		
1	28	C	120 145	IV	Enlarged adenoma	No	None	Alb. +	120 80				3240 46.5	None
2	20	C		II	Three times normal	No	Epigastric pain, edema vomiting	Alb. +	134 90				2960 50	Pre-eclamptic toxemia
3	34	W	178 203	IV	Nodular asymmetrical	Slight	Headache edema dyspnea aphonia	Neg.	154 92	+ 50	+39.4	+40 (6 da.) +29.4 (7 wk.) +24.8 (8 wk.)	3260 51	Lugol's after Oct.
4	41	W	216 196	VIII	Bilateral	Slight	Headaches vertigo aphonia epigastric pain	Alb. +	216 196	+105	+47	+26 (8 da.) +23 (7 wk.) + 8.3 (9 wk.)	3660 49	

TABLE III. EXOPHTHALMIC GOITER

CASE	AGE	RACE	WEIGHT	PARA	GOITER	EXOPHTHALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	METABOLIC RATE			BABY	REMARKS
										HIGH	LOW	POSTPARTUM		
1	31	W	95 108	II	Moderate firm	Yes	Edema	Alb. +	128 78	+ 53			3220 46.5	Mitral stenosis
2	32	W	160 215	III	Old scar	Mod.	Headache epigastric pain	Neg.	176 95	+ 34			3360 46	Pre-eclamptic
3	37	W	165 133	X	1927 thyroid	No	None	Neg.		+ 3		+ 8	Blood mole	Mitral regurgitation
4	30	C	146 107	I	Moderate	Mod.	Nausea exhaustion	Alb. +	108 52	+111	+20	+15	Twin	Hyperemesis gravidarum
5	22	C	171 129	I	Moderate firm	Mod.	Nervous pulse 140 nausea	Alb. trace	100 54	+109	+12			Not delivered hyperemesis

TABLE IV. CASES OF DRs. PERCY AND NADEAU

CASE	AGE	RACE	WEIGHT LOSS	PARA	GOITER	EXOPHTHALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	OPERATION PATHOLOGY	ANESTHETIC	BABY	REMARKS
1	30	W	60	II	Small firm enlarged		Headache	Neg.	144 60	Exophthalmic double lobectomy	Ethylene		2½ months
2	19	W	Sl.	II	Asymmetrical soft enlarged		None	Neg.	120 70	Toxic adenoma double lobectomy	Ethylene		4 months
3	37	W	19	VI	Firm enlarged		None	Neg.		Exophthalmic lobectomy	Ethylene local	Mis-carried	10 days post-operative miscarried
4	30	W	None	I	Right lobe enlarged nodular	No	None	Neg.	126 72	Toxic adenoma double lobectomy	Local		2 months
5	32	W	35	III	Bilateral enlarged		None	Neg.		Toxic adenoma double lobectomy	Local		6 weeks
6	30	W	Sl.	V	Moderate enlarged		None	Neg.		Exophthalmic double lobectomy	Local	Term twins	5 months toxic in all but 3rd
7	32		Sl.	I	Slight enlarged		None	Neg.		Exophthalmic double lobectomy	Local	Term good	2½ months
8	23			II	Marked bilateral enlarged		None	Neg.		Colloid goiter double lobectomy	Local		4 months

TABLE V. CASES OF DR. SEED

CASE	AGE	RACE	WEIGHT LOSS	PARA	GOITER	EXOPHTHALMIC	TOXIC SYMPTOMS	URINE	BLOOD PRESSURE	OPERATION PATHOLOGY	ANESTHETIC	BABY	REMARKS
1	30	W	30	II	Marked	Yes	Nervousness, dyspnea ascites	Neg.	Normal	Exophthalmic ligation double lobectomy	Local nitrous oxide	Mis-carried	6½ months
2	33	W	25	II	Marked	No	Dyspnea, tachycardia	Neg.	Normal	Adenoma double lobectomy	Nitrous oxide	Twins good	3 months



fied as a colloid goiter with toxic symptoms. The basal metabolic rate was not studied in these cases, and I am told by Dr. Percy that he relies very little on this test in handling these cases. The résumé of these cases is presented in Table IV.

A résumé of Dr. Seed's cases is seen in Table V. One was a thirty-year-old white girl who had been in St. Luke's Hospital, Chicago, for two months under medical management. He did a ligation of both superior thyroid arteries in spite of the fact that she was two months pregnant. She was advised to return in a month but waited about the sixth month and entered with marked dyspnea and cardiac decompensation, ascites, and generally poor condition. A right lobectomy was done, and she aborted at six and a half months. A second lobectomy nearly a year later was necessary, and since then she has been normal.

The second case was a thirty-two-year old para ii, with a basal metabolic rate of plus 42. She had had a marked adenomatous goiter with symptoms for several years. A thyroidectomy was done during the third month of pregnancy. She had a smooth postoperative course and delivered twins normally six months later. She lost all goiter symptoms following thyroidectomy.

It is, therefore, seen that on the whole good results are obtained from both the surgical or radical method of handling toxic goiter and the conservative or medical method. It would seem that the medical management should be used in all cases primarily. That the goiter surgeon should be called upon at any stage of the pregnancy to operate when it is evident from the basal rate and the clinical manifestations that the patient is either not improving or at least holding her own. If this intervention can be postponed until viability of the baby, so much the better. From the statistics here given it would seem that local anesthesia is most satisfactory from the surgical standpoint, and as far as contributing to abortion is concerned, it is the ideal anesthesia. The obstetrician should be ready to perform a vaginal or abdominal cesarean section, according to the indications present in the individual case. Teamwork between obstetrician and surgeon is the ideal arrangement and will give the best results.

#### CONCLUSIONS

From a consideration of these cases it would seem that the following conclusions are justified:

1. Mild hyperthyroidism as judged by the clinical manifestations and the basal metabolic rate is a not uncommon complication of pregnancy, and no special treatment is necessary.

2. Many of the nervous symptoms seen in pregnancy are probably due to abnormal activity of the thyroid gland induced by the pregnant state.