Franzén, A. (1955a). *Zool. Bidr. Uppsala*, **30**, 399.
—— (1955b). Ibid., **30**, 485.
—— (1956). Ibid., **31**, 355.
—— (1958). Ibid., **33**, 1.
Gibbons, I. R. (1961). *J. biophys. biochem. Cytol.*, **11**, 179.
Koltzoff, N. K. (1908). *Arch. Zellforsch.*, **11**, 1.
Nath, V., and Bhatia, C. L. (1953). *Res. Bull. E. Panjab Univ.*, No. 27, 33.
—— and Sharma, G. P. (1952). Ibid., No. 22, 99.
Noyes, R. W., Walton, A., and Adams, C. E. (1958). *J. Endocr.*, **17**, 374.
Panijel, J. (1951). *Métabolisme des Nucléoprotéins*. Hermann et Cie, Paris.
Retzius, G. (1906). *Biologische Untersuchungen*, **13**.
—— (1909). Ibid., **14**.
Rothschild, Lord (1961). *A Classification of Living Animals*. Longmans, Green, London.
Seshachar, B. R. (1943). *Proc. nat. Inst. Sci. India*, **9**, 271.
Sharma, G. P. (1944). Ibid., **10**, 305.
—— (1950). *Res. Bull. E. Panjab Univ.*, No. 5, 67.
Tuzet, O., and Sanchez, S. (1952). *Arch. Zool. exp. gén.*, **89**, 26.
Vasisht, H. S. (1954). *Res. Bull. Panjab Univ.*, No. 62, 169.

PREGNANCY AND THYROTOXICOSIS*

BY

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The association of thyrotoxicosis and pregnancy has received little attention in the general medical literature. It is uncommon but important because the interaction of the two conditions may lead to serious consequences for the mother and for the child.

The clinical data presented in this paper result from a study of 70 pregnant patients treated during the 15 years ending December 31, 1961, in the surgical units of the David Lewis Northern Hospital and Walton Hospital under the care of one of us (P. H.) and in the maternity units of the Liverpool Maternity Hospital and Mill Road Maternity Hospital with which H. H. F. is associated.

Physiological Considerations

One of the early effects of pregnancy in euthyroid patients is a rise in the level of the plasma thyroxine-binding protein. This removes part of the circulating free thyroxine, and the pituitary responds by increased production of thyrotropic hormone (T.S.H.). Hyperplasia of the thyroid gland follows with increased output of thyroxine (Figs. 1 and 2). These changes are reflected by an increase in the protein-bound iodine (P.B.I.) and butanol-extractable iodine of the maternal blood, and readings well within the thyrotoxic range are usual (Benson *et al.*, 1959). Concurrently with the hyperplasia, uptake of radioiodine by the thyroid gland is increased (Halnan, 1958). Elevation of the basal metabolic rate (B.M.R.) also takes place from the middle trimester onwards, and readings of +20% are to be expected towards term; this is due to increased metabolism consequent on the gravid state and is not attributable directly to thyroid overactivity (Freedberg *et al.*, 1957).

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There is good evidence of the passage of thyroxine through the placenta in the later stages of pregnancy, although only small quantities are transmitted in the first few months (Myant, 1958; Grumbach and Werner, 1956) (Fig. 3). Experimental evidence suggests that the placenta is impervious to T.S.H. (Peterson and Young, 1952; Feldman, 1960), but there may be exceptions. For example, thyrotoxic and exophthalmic babies have been born to mothers suffering from thyrotoxicosis and exophthalmos (Keynes, 1952; Levitt, 1954; Lewis and Macgregor, 1957; Riley and Sclare, 1957; Javett *et al.*, 1959). Iodides and antithyroid drugs also pass readily through the placental barrier (Freiesleben and Kjerulf-Jensen, 1947). The human foetal thyroid begins to accumulate radioiodine at the end of the first trimester (Chapman *et al.*, 1948) and thereafter ^{131}I is taken up by the foetal thyroid with even greater avidity than by the maternal gland (Halnan, 1958).

Deficiency of thyroid function may be restricted either to the maternal or to the foetal gland, or may arise simultaneously in both. According to Peterson and Young (1952) and Man *et al.* (1958), if a serious deficiency of maternal thyroxine exists the foetus is unlikely to be normal, but the extent to which the foetal thyroid can provide for the needs of the foetus in the absence of maternal thyroxine remains uncertain (*Brit. med. J.*, 1957). Examples of normal children born of myxoedematous mothers have been recorded (Osorio and Myant, 1960). The fact that clinical evidence of hypothyroidism in the athyreotic child is commonly absent for the first few weeks of life suggests that deficiency of foetal thyroxine can be offset by thyroxine secreted by the mother. When hypothyroidism follows the use of antithyroid drugs, function is depressed in *both* the foetal and maternal gland; this is a serious situation and may lead to the development of foetal goitre and cretinism (Fig. 4).

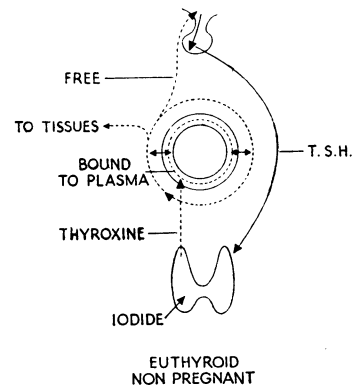

FIG. 1.—Iodide uptake and thyroxine secretion are controlled by thyrotropic hormone (T.S.H.). Free and bound thyroxine are in simple equilibrium in plasma. T.S.H. secretion is related to free thyroxine level.

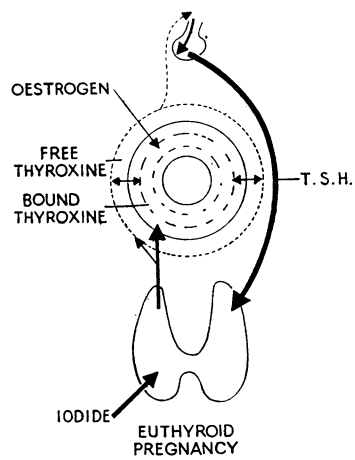

FIG. 2.—Rising oestrogen production increases thyroxine-binding protein in plasma. Free thyroxine is reduced which evokes increased T.S.H. secretion. Thyroid hyperplasia with increased iodide uptake and thyroxine output follow. Concentration of bound thyroxine (protein-bound iodine) is elevated and level of free thyroxine is restored.

Diagnosis of Thyrotoxicosis During Pregnancy

Certain clinical features, such as increased cardiac

action, accelerated peripheral circulation, enlargement of the thyroid gland, decreased heat tolerance, and anxiety states, are common to pregnancy and to thyrotoxicosis. Because of this the diagnosis may prove difficult. The more striking these clinical features the greater is the probability that the patient is suffering from thyrotoxicosis. Persistent tachycardia, high sleeping pulse rates, considerable enlargement of the thyroid, pulsation of the gland, excessive fatigue, failure to gain weight despite good appetite, excessive sweating, tremor, and, if present, exophthalmos may also provide valuable evidence.

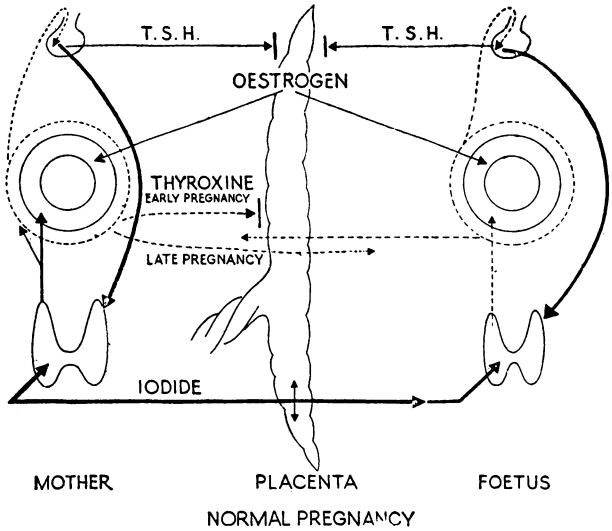

FIG. 3.—Iodides pass freely through placenta, which also acts as an iodide store. Foetal thyroid starts to take up iodides at end of first trimester. Small amounts of free maternal thyroxine are transmitted during first trimester, thereafter increasing quantities of both free maternal and foetal thyroxine traverse placenta. The placenta is impervious to maternal and foetal T.S.H.

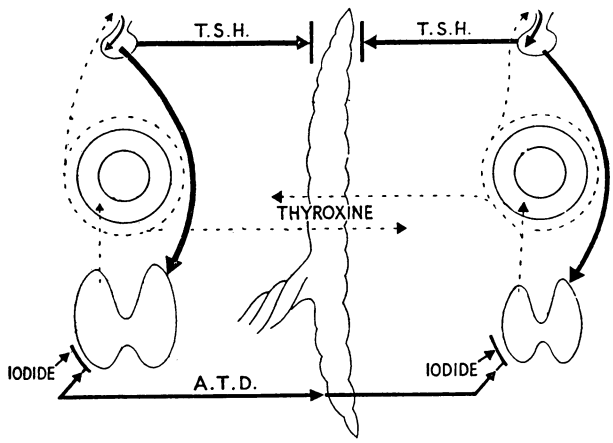

FIG. 4.—Antithyroid drugs (A.T.D.) readily pass through placenta Uptake or utilization of iodide by both maternal and foetal thyroid glands is reduced. If A.T.D. dosage is excessive, deficiency of thyroxine in foetus cannot be offset by contribution from mother. Hyperplasia of foetal thyroid results, owing to excessive foetal T.S.H.

Laboratory aids are not usually helpful in the diagnosis of thyrotoxicosis during pregnancy. The levels of serum cholesterol, B.M.R., and P.B.I., and the uptake of radioiodine are all increased in normal pregnancy; this may give rise to difficulty in the interpretation of results. During pregnancy the use of ^{131}I for diagnostic purposes may expose the foetus to danger, and is to be avoided.

Analysis of Cases and Results

A series of 70 patients is reviewed (see Table I). With a few exceptions, patients originally referred to the medical and obstetrical units were treated medically, and those directed to the thyroid clinic and surgical units were treated by subtotal thyroidectomy. No attempt was made to ensure uniform distribution, in relation to the severity of the thyrotoxicosis or to coexisting complications, between those treated medically and those treated surgically. The two groups are therefore not suitable for statistical comparison.

TABLE I.—*Analysis of the 70 Cases*

Treatment	No. of Patients	No. of Pregnancies	Thyroid Crisis	Thyrocardiac Failure	Live Births	Stillbirths	Miscarriages
Sedatives and iodides	8	9	1 (death)	0	8	0	1
Antithyroid drugs ..	29	30	1	2	26	0	4*
Subtotal thyroidectomy	33	33	0	0	32	1	0

* Two during pre-operative preparation.

Medical Group

Thirty-seven patients were treated through 39 pregnancies. Treatment with rest and sedatives was employed in nine pregnancies, and antithyroid drugs (carbimazole, methylthiouracil, and potassium perchlorate) in the remainder. With the exception of those suffering from unusually severe thyrotoxicosis or important complications such as cardiac disease the patients remained ambulant and their treatment was directed by their own physicians. This varied to some extent, but the majority followed Astwood's (1951) practice and reduced the dose during the second half of pregnancy, provided that the thyrotoxicosis appeared to be well under control. In a few instances antithyroid drugs were discontinued from about the mid-period of pregnancy.

Three patients proved exceptionally resistant to antithyroid drugs, which, despite the risk to the foetus, had to be continued up to the time of delivery. In these cases two of the babies were normal; the third proved to be a cretin. This child's mother, aged 24, was suffering from thyrotoxicosis when first seen at the 14th week of her first pregnancy. She refused treatment until she was admitted at the 26th week with severe thyrotoxicosis. It was necessary to maintain treatment with 30 mg. of carbimazole daily until labour began at 38 weeks. The thyrotoxicosis was then under control; delivery was uneventful and the baby appeared normal. The mother failed to report again until two months after leaving hospital, by which time she was suffering from a severe relapse of thyrotoxicosis. Carbimazole was again prescribed. About this time signs of hypothyroidism became obvious in the baby; a good response followed treatment with thyroxine but some mental retardation persisted. Eight months later the mother, on treatment with carbimazole, became pregnant again. Subtotal thyroidectomy was performed at four and a half months; subsequent progress was uneventful and a normal child was delivered at term.

In this series there were occasional examples of apparently spontaneous improvement of the thyro-

toxicosis as the pregnancy advanced. By contrast three patients suffered severe and unexpected exacerbation of the thyrotoxicosis about the time of delivery or soon after. One of these was mildly toxic and responded well to treatment with rest and sedatives, but premature labour at the 36th week was followed by a severe thyrotoxic reaction. The other two had thyrotoxicosis of a moderate degree which settled well on antithyroid drugs. Even when treatment was suspended during the third trimester they remained euthyroid until after delivery, but then relapsed into severe thyrotoxicosis. After further treatment with antithyroid drugs subtotal thyroidectomy was eventually successfully undertaken in both.

Thyroid Crisis

There were two examples of thyroid crisis during pregnancy.

1. The patient first developed thyrotoxicosis at the age of 33 and was successfully treated with rest, sedation, and iodide. The following year she became pregnant, and after delivery had a recurrence of thyrotoxicosis, which was treated with methylthiouracil. She next reported at the age of 38, in the 32nd week of her second pregnancy, and was admitted suffering from severe thyrotoxicosis with marked exophthalmos, breathlessness, sweating, and tachycardia (pulse 120; B.P. 175/85. Her physician advised treatment with rest and sedatives. During the next three weeks her condition improved, but early in the 36th week a very acute thyrotoxic reaction took place; this was manifested by a rapidly mounting pulse rate (130), severe restlessness, and exhaustion. The condition soon developed into an uncontrollable thyroid crisis. Emergency caesarean section was performed, but the patient died 11 hours after operation. The clinical diagnosis was confirmed at post-mortem examination. The baby was thyrotoxic for some weeks after birth, but its subsequent progress was normal.

2. This patient developed thyrotoxicosis of moderate severity soon after the delivery of her first baby, by caesarean section for contracted pelvis. Carbimazole was prescribed. Six months later, at the age of 40, she was again pregnant. Treatment was maintained until the 18th week, when it was considered safe to withdraw the drug; but after two months a serious relapse took place. On admission to the maternity unit 30 mg. of carbimazole daily was prescribed and was continued to term with considerable relief. Caesarean section was undertaken, but during the operation increasing tachycardia caused anxiety. A normal baby was delivered, but on recovery from the anaesthetic the mother passed into an acute thyrotoxic reaction with very severe restlessness, tachycardia (130), pyrexia (105° F.; 40.6° C.), sweating, and an exaggerated pulse pressure (B.P. 190/80). Despite treatment with carbimazole, heavy sedation, and hypothermia five days elapsed before the thyrotoxicosis came under control. Six months later subtotal thyroidectomy was performed for persistent thyrotoxicosis.

Cardiac Failure

Heart failure due to organic cardiac disease is a serious complication of pregnancy, and when thyrotoxicosis coexists the difficulties are substantially increased.

1. A woman aged 35 was 20 weeks pregnant when first seen in consultation. There was a history of mitral stenosis of long standing due to rheumatic fever, and of treatment of thyrotoxicosis with methylthiouracil for the previous four and a half years. During this period she suffered from recurring attacks of supraventricular tachycardia with congestive cardiac failure, for which she was treated in hospital with rest in bed, quinidine, and chlorothiazide. She was admitted to hospital when 28 weeks pregnant. As her thyrotoxicosis appeared to be well controlled methylthiouracil was discontinued in order to protect the foetus. The cardiac condition continued to give rise to anxiety, and despite treating the patient by rest in bed, digitalis, and diuretics myocardial failure always threatened. Normal delivery of a healthy baby occurred at term. The patient was allowed home on the 14th day, but recurrence of signs of heart failure and thyrotoxicosis led to her early readmission. She remains on treatment with digoxin, hydrochlorothiazide, and methylthiouracil.

2. A woman aged 30 years reported at the 12th week of pregnancy suffering from thyrotoxicosis of moderate severity which had followed a miscarriage 18 months before. She was admitted to hospital at the 16th week for treatment with methylthiouracil, 400 mg. daily, and was retained for four weeks. Readmission became necessary at the 26th week because of congestive cardiac failure and she remained in hospital for six weeks on treatment with methylthiouracil and diuretics. There was no history of previous cardiac disease. At 38 weeks admission was again necessary on account of cardiac failure with cyanosis, tachycardia, and pleural effusion. Despite treatment, cardiac decompensation was still present when labour began spontaneously at term. Her condition deteriorated alarmingly during labour and with each contraction cyanosis became extreme. A normal child was delivered by forceps with the mother in a state of cardiac failure and collapse. She unexpectedly survived. When traced two years later she was still taking methylthiouracil.

Five abortions occurred—three at the 12th week, one at the 14th week, and one at the 24th week (carbimazole 2, methylthiouracil 1, potassium perchlorate 1, potassium iodide 1).

Of the 37 patients treated medically during pregnancy, 13 were subjected to thyroidectomy at a later date for persistence or recurrence of the thyrotoxicosis.

Surgical Group

Thirty-three patients were treated by subtotal thyroidectomy during pregnancy. All suffered from primary thyrotoxicosis and 31 were thyrotoxic before pregnancy began. Twelve had already been fully investigated and were taking antithyroid drugs when they became pregnant. The remainder were pregnant and toxic when first seen, and investigation with ^{131}I was therefore omitted.

Twenty-seven patients suffering from moderate or severe thyrotoxicosis were prepared for operation with carbimazole or methylthiouracil, followed by Lugol's iodine for one to two weeks, and four patients were prepared with potassium perchlorate. Two mildly toxic patients had preoperative treatment with Lugol's iodine alone.

Operation was usually deferred until after the 12th week of pregnancy in order to avoid the period of greatest liability to abortion. Two operations were performed in the first trimester, 26 in the second, and five in the third.

Twenty-seven of the operations were undertaken by one of us. Halothane was found to be the most satisfactory anaesthetic agent. Haemostasis did not present more difficulty than might be expected in non-pregnant patients prepared with antithyroid drugs. The routine operative procedure included preliminary visualization of the recurrent laryngeal nerves and preservation of approximately 1–2 g. of thyroid tissue on either side.

There were no maternal complications such as recurrent laryngeal nerve lesions and tetany; convalescence and the subsequent course of the pregnancies

were mostly uneventful. Thirty-two women delivered normally at or about term. One child was stillborn, but this was probably not related to the thyroidectomy carried out at the 26th week of gestation. In this case abortion had threatened in early pregnancy, and the foetus, when delivered, showed multiple abnormalities incompatible with life. So far, a recurrence of thyrotoxicosis has not been seen after thyroidectomy during pregnancy. Ten patients have had one or more subsequent normal pregnancies; one other patient suffered abruptio placentae in her next pregnancy.

Following Bell and Hall's (1960) advice, as a precautionary measure against abortion we recently adopted post-operative thyroid replacement therapy as a routine measure. Nevertheless, the omission of this in 26 of the earlier cases was not followed by abortion in a single case. Although there seems to be no objection to supplementary thyroid treatment after thyroidectomy in pregnancy, it should not be continued after delivery without first reassessing the function of the patient's remaining thyroid tissue.

Discussion

Interrelationship of Thyrotoxicosis and Pregnancy

Mussey (1939) reported that only 0.5% of thyrotoxic patients attending the Mayo Clinic were pregnant, and the figure for the Lahey Clinic (0.6%) is similar (Clute and Daniels, 1930). Silver (1960) collected representative figures from the literature and reported a mean incidence of thyrotoxicosis in pregnant women of 0.047%. Figures are influenced by the fact that patients already undergoing treatment with antithyroid drugs are more likely to conceive than those with uncontrolled thyrotoxicosis. Among 700 consecutive patients treated surgically for thyrotoxicosis by one of us, 27 were pregnant. But this represents selected material. Thyrotoxicosis was recognized in 39 out of 93,033 patients delivered in our obsteric units, giving an incidence of 0.04%.

Contrary views are held on the influence of pregnancy on the course and severity of thyrotoxicosis. According to the experience of many observers (Rundle, 1951; Keynes, 1952; Levitt, 1954) adverse effects may occur, but others report no deterioration and at times amelioration of the thyrotoxicosis (Gardiner-Hill, 1929; Clute and Daniels, 1930; Astwood, 1951). Mussey and Plummer (1931) recorded that 50% of pregnancy patients suffering from toxic adenomata became worse during pregnancy as against 17% with primary thyrotoxicosis. In Joll's (1932) experience pregnancy had no adverse effects on the majority of patients but exacerbation occurred in the minority. Both he and Crile (1932) recognized the increased risk of thyroid crisis, sometimes fatal, during or immediately after delivery. Lahey (1931) likens the risk of a thyroid crisis after delivery to that which follows a major surgical procedure such as appendicectomy or cholecystectomy in patients with thyrotoxicosis. Such hazards, however, have been substantially reduced by antithyroid drugs.

Whatever influence uncontrolled thyrotoxicosis may have had in the past, under conditions of modern treatment the incidence of pre-eclampsia in pregnancy is no greater than in the non-thyrotoxic patient. Kaplan and Smith (1959) reported toxaemia in only 6.9% of patients adequately treated. Four cases of pre-eclampsia, three of which were in the medically treated group, occurred in our series of 70 patients. This incidence is no higher than might be expected in the Liverpool area, which is recorded as 8.5% in primigravidae and 4.2% in multiparae (Gemmell *et al.*, 1954).

The first reference to miscarriage associated with thyrotoxicosis must be attributed to Parry (1825). The view that uncontrolled thyrotoxicosis predisposes to abortion is supported by Gardiner-Hill (1929), Mussey *et al.* (1948), and Keynes (1952), but is not borne out by the experience of Falls (1929), Clute and Daniels (1930), and Benson *et al.* (1959). Crile (1949) related the chance of abortion to the severity of thyrotoxicosis; the influence of treatment, as well as abortive factors unassociated with thyrotoxicosis, have to be taken into account. By recognizing this Kaplan and Smith (1959) were able to reduce a gross foetal mortality of 28.1% to a figure of 8% for adequately treated patients. Although a high rate of abortion is quoted by some of the earlier workers, the more recently published figures for treated thyrotoxicosis show an abortion incidence of 10.2% (Silver, 1960). This figure approximate's to Jeffcoate's (1957) estimate of a 10% incidence of spontaneous abortion for all pregnancies in the Liverpool region. Among our series of 70 pregnancies abortion occurred five times and there was one stillbirth.

As already noted, thyrotoxicosis is only occasionally seen in the infant born of the thyrotoxic mother. There was one example in our series. In the absence of treatment with antithyroid drugs, thyrotoxicosis does not give rise to foetal goitre.

Choice of Treatment

Choice of treatment usually rests between the use of antithyroid drugs and subtotal thyroidectomy with or without preparation with antithyroid drugs. The risk to the foetus forbids the use of ^{131}I therapy (Chapman *et al.*, 1948; Werner, 1952; Russell *et al.*, 1957; Benson *et al.*, 1959), and termination of the pregnancy with its attendant risks is no longer practised (Crile, 1932; Means, 1948). Occasionally, treatment with rest and iodides alone suffices for mild attacks, although the wisdom of using iodides has recently been questioned in view of the slight danger of causing maternal hypothyroidism and foetal goitre (Bongiovanni *et al.*, 1956; Becker and Sudduth, 1959; Anderson and Bird, 1961).

Despite the very general use of antithyroid drugs during pregnancy, our experience indicates that this form of therapy is more difficult to regulate and is associated with a greater risk than it is in the non-pregnant woman. Because the clinical effects of thyrotoxicosis and pregnancy are in so many respects similar, misjudgment of the severity of thyrotoxicosis may lead to error in adjusting the dose of antithyroid drugs. The aim of treatment is to maintain the maternal B.M.R. at the raised level characteristic of a normal pregnancy. Overtreatment may endanger the foetus, inadequate treatment may lead to exacerbation of the maternal thyrotoxicosis; both situations are associated with an increased risk of foetal loss. In the interests of the foetus it is common practice to reduce antithyroid drugs during the later months of pregnancy, hoping that the control of the thyrotoxicosis will be maintained until delivery. Unfortunately, the duration of this control varies from patient to patient and an unexpectedly early relapse may occur.

The fact that antithyroid drugs pass through the placenta is a serious disadvantage. They depress the

foetal thyroid function, and this results in an increased production of T.S.H. and hyperplasia of the foetal gland. Foetal goitre, hypothyroidism, and cretinism can therefore result from treatment sufficiently intense to induce maternal hypothyroidism. In a review of the literature Piper and Rosen (1954) found that among 83 patients treated with antithyroid drugs 15 (18%) of the infants developed goitre. The thyroid enlargement usually subsided spontaneously in three to nine months, but in a few cases caused death from neonatal asphyxia. D'Abreu and Wood (1950) described the case of one infant born with a large goitre causing tracheal pressure, which required a two-stage thyroidectomy. Becker and Sudduth (1959) reported one cretin and also one neonatal death due to a large goitre in their series of 22 pregnancies in thyrotoxic women. Keynes (1952) collected records of 18 patients treated with antithyroid drugs. In 12 cases the treatment was of short duration and all the babies were normal, but in six the drug was given for a longer period, and five of these infants had goitre and two were cretins. Our series included one cretin.

A further disadvantage of giving antithyroid drugs is their excretion in the mother's milk (Williams *et al.*, 1944). Breast-feeding must therefore be avoided if the mother continues on antithyroid drug treatment after delivery.

The published results of treatment with antithyroid drugs during pregnancy vary. Astwood (1951) treated 19 patients with antithyroid drugs and substantially reduced the dosage during the second half of the pregnancy. All the resulting babies were normal and only three of the mothers required further treatment for thyrotoxicosis after delivery. Piper and Rosen (1954), using similar methods, recorded four abortions and one stillbirth among 16 pregnancies, and relapse of the thyrotoxicosis within three years in 11 of the 13 mothers treated medically. Becker and Sudduth (1959) record two examples of foetal goitre and five foetal deaths among 19 pregnancies. Our experience of patients treated medically is on the whole discouraging. Contributing factors to some of the poor results were lack of co-operation on the part of the patients and failure to employ antithyroid drugs to their best advantage. A few women responded well to rest and sedatives, others deteriorated under this regime. Most of those treated with antithyroid drugs had uneventful pregnancies but there were exceptions, and these caused considerable anxiety. A gross foetal loss of 14%, corrected to 7% by deducting two abortions which occurred too soon for antithyroid drugs to have had effect, was not excessive. Foetal goitre was not a problem, but there was one cretin. Several mothers suffered an acute exacerbation of their thyrotoxicosis.

Of the 37 patients treated medically, 13 ultimately had to be treated surgically for persistent or recurrent thyrotoxicosis. However, there are occasions when there is a definite indication for medical rather than surgical treatment during pregnancy. This arises when the patient is referred late in pregnancy in a state of uncontrolled thyrotoxicosis. One such example occurred in this series. The patient was first seen during the 35th week of pregnancy, and this was regarded as too late to permit of adequate preparation for operation before term. She was accordingly treated with antithyroid drugs. Subtotal thyroidectomy was performed six weeks after a normal delivery. Medical treatment is also to be advised on the rare occasions when pregnancy occurs in a patient suffering from recurrent thyrotoxicosis following a previous thyroidectomy. Further surgery involves a real risk to the parathyroid glands and the recurrent laryngeal nerves. We had two cases of this type; both were treated with antithyroid drugs and had normal labours at term. Since delivery the first patient, aged 20, has continued with treatment by small doses of potassium perchlorate, and the second, aged 40, has been referred for treatment with ^{131}I.

Because of the long period of treatment required and the high rate of relapse the use of antithyroid drugs in non-pregnant thyrotoxic patients is becoming less popular in this country and abroad. Certainly there is now a tendency to treat the younger thyrotoxic patients by thyroidectomy and to reserve antithyroid drugs for pre-operative preparation (Black, 1959; Greene, 1960). Despite this, these drugs continue to be recommended for the treatment of the pregnant thyrotoxic woman (Crooks and Wayne, 1960; Crooks, 1961; Martin and Hynes, 1961). Yet the special problems involved in using antithyroid drugs during pregnancy make the case for operation at this time even stronger than it is for the young non-pregnant woman. Surgery is still more strongly indicated when complications such as organic cardiac disease or diabetes are present. Joll (1932) advised medical treatment during pregnancy followed by operation after delivery, and his influence in this country was considerable. This policy was challenged by Keynes (1952) when he published impressive results of surgery combined with pre-operative treatment with Lugol's iodine. But his views were not widely accepted. The advent of antithyroid drugs may have altered the balance of opinion still further in favour of medical treatment.

Thyroidectomy during pregnancy was practised outside this country even before the discovery of antithyroid drugs (Jackson, 1924; Mussey *et al.*, 1926; Crile 1932), and the results that have been published provide good evidence of the safety of surgery for both mother and child (see Table II). Surgeons were at first reluctant to employ antithyroid drugs as pre-operative agents during pregnancy, partly because of the risk to the foetus and partly because they increased the vascularity of the thyroid gland. When used for a limited period these dangers are greatly diminished and their value in the severely toxic patient is now widely accepted.

TABLE II

Author	No. of Operations	Viable Babies	Abortions and Stillbirths	Maternal Deaths	Comments
Mussey and Plummer (1931)	31	31	1	0	One set of twins. 1 neonatal death (pyloric stenosis)
Lahey (1931)	16	15	1	0	
Crile (1949)	33	33	0	1	Maternal death at home between stages of planned 2-stage operation (pre-antithyroid drugs). 1 neonatal death (hydrocephalus)
Keynes (1952)	21	20	1	0	
Dailey and Benson (1952)	18	15	3	0	
Bell and Hall (1960):					
Series (a)	21	16	5	0	No replacement therapy
,, (b)	21	20	1	0	Routine post-operative replacement therapy
Present series	33	32	1	0	
Total ..	194	182	13	1	Includes 1 set of twins

With the exception of one unrelated stillbirth, all the babies of our mothers treated surgically were born alive and healthy. Indeed, both maternal and foetal complications were conspicuously absent. After operation the remaining months of pregnancy were remarkably free from anxiety for both patients and attendants, and apart from prophylactic replacement therapy no further treatment was necessary. There was no restriction of breast-feeding, and so far none of the women in our surgically treated group have suffered recurrences of thyrotoxicosis.

Summary and Conclusions

A study has been made of 70 pregnant patients treated in the surgical units of two general hospitals and in two obstetrical units during 15 years in regard to the association of thyrotoxicosis and pregnancy.

Treatment of thyrotoxicosis with antithyroid drugs during pregnancy involves a compromise between the interests of the mother and those of the child, and in consequence maternal and foetal complications may result. Opinions are conflicting in regard to the frequency of these complications. There is evidence that careful treatment with antithyroid drugs has substantially reduced the earlier incidence of acute thyrotoxic reactions and of foetal loss. Unfortunately these complications have not been entirely eliminated and antithyroid drugs have introduced a new problem in the form of foetal goitre. Nevertheless many regard this form of therapy as the treatment of choice.

Subtotal thyroidectomy during pregnancy appears to be a safe and efficient method provided that satisfactory surgical conditions are available. Maternal complications are rare and the subsequent course of the pregnancy is that of a euthyroid patient with little chance of recurrence of the thyrotoxicosis. Although equally good results are claimed for medical and surgical treatment, our experience is that under good conditions surgical treatment offers the better prospects. In selecting treatment, however, the severity of the thyrotoxicosis, the period of pregnancy at which the patient presents, the reliability of the patient, and the surgical facilities must be carefully assessed.

We thank the Medical Boards of the Liverpool Maternity Hospital and Mill Road Maternity Hospital for permission to use the hospital records, and to surgical colleagues who allowed us to include in the thyroidectomy series six patients on whom they had operated. We are also grateful to Professor T. N. A. Jeffcoate for his helpful advice, and to Mr. D. J. Kidd for preparing the diagrams.

REFERENCES

Anderson, G. S., and Bird, T. (1961). *Lancet*, **2**, 742.
Astwood, E. B. (1951). *J. clin. Endocr.*, **11**, 1045.
Becker, W. F., and Sudduth, P. G. (1959). *Ann. Surg.*, **149**, 867.
Bell, G. O., and Hall, J. (1960). *Med. Clin. N. Amer.*, **44**, 363.
Benson, R. C., Pickering, D. E., Kontaxis, N. E., and Fisher, D. A. (1959). *Obstet. and Gynec.*, **14**, 11.
Black, B. M. (1959). *Proc. roy. Soc. Med.*, **52**, 167.
Bongiovanni, A. M., Eberlein, W. R., Thomas, P. Z., and Anderson, W. B. (1956). *J. clin. Endocr.*, **16**, 146.
Brit. med J., 1957, **1**, 996.
Chapman, E. M., Corner, G. W., Robinson, D., and Evans, R. D. (1948). *J. clin. Endocr.*, **8**, 717.
Clute, H. M., and Daniels, D. H. (1930). *Amer. J. med. Sci.*, **179**, 477.
Crile, G. (1932). *Diagnosis and Treatment of Diseases of the Thyroid Gland*, p. 374. Saunders, Philadelphia.
Crile, G., jun. (1949). *Practical Aspects of Thyroid Disease*, edited by A. F. Rowland. p. 216. Saunders, Philadelphia.
Crooks, J. (1961). *Practitioner*, **186**, 256.
—— and Wayne, E. J. (1960). *Lancet*, **1**, 401.
D'Abreu, A. L., and Wood, B. S. B. (1950). *Arch. Dis. Childh.*, **25**, 235.
Dailey, M. E., and Benson, R. C. (1952). *Surg. Gynec. Obstet.*, **94**, 103.
Falls, F. H. (1929). *Amer. J. Obstet. Gynec.*, **17**, 536.
Feldman, J. D. (1960). Session IVd, No. 137 International Congress of Endocrinology.
Freedberg, I. M., Hamolsky, M. W., and Freedberg, A. S. (1957). *New Engl. J. Med.*, **256**, 505.
Freiesleben, E., and Kjerulf-Jensen, K. (1947). *J. clin. Endocr.*, **7**, 47.
Gardiner-Hill, H. (1929). *Lancet*, **1**, 120.
Gemmell, A. A., Logan, W. P. D., and Benjamin, B. (1954). *J. Obstet. Gynaec. Brit. Emp.*, **61**, 458.
Greene, R. (1960). *Postgrad. med. J.*, **36**, 468.
Grumbach, M. M., and Werner, S. C. (1956). *J. clin. Endocr.*, **16**, 1392.
Halnan, K. E. (1958). *Clin. Sci.*, **17**, 281.
Jackson, A. S. (1924). *Ann. clin. Med.*, **2**, 303.
Javett, S. N., Senior, B., Braudo, J. L., and Heymann, S. (1959). *Pediatrics*, **24**, 65.
Jeffcoate, T. N. A. (1957). *Principles of Gynaecology*, p. 177. Butterworth, London.
Joll, C. A. (1932). *Diseases of the Thyroid Gland*, p. 440. Heinemann, London.
Kaplan, A. L., and Smith, J. P. (1959). *Bull. Sloane Hosp. Wom. N.Y.*, **5**, 12.
Keynes, G. (1952). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 173.
Lahey, F. H. (1931). Discussion following paper by Mussey and Plummer (1931).
Levitt, T. (1954). *The Thyroid*, pp. 237, 243. Livingstone, Edinburgh.
Lewis, I. C., and Macgregor, A. G. (1957). *Lancet*, **1**, 14.
Man, E. B., Shaver, B. A., and Cooke, R. E. (1958). *Amer. J. Obstet. Gynec.*, **75**, 728.
Martin, L. C., and Hynes, M. (1961). *Clinical Endocrinology for Practitioners and Students*, 3rd ed, p. 95. Churchill, London.
Means, J. H. (1948). *The Thyroid and its Diseases*, 2nd ed., p. 437 Lippincott, Philadelphia.
Mussey, R. D. (1939). *Proc. Mayo Clin.*, **14**, 205.
—— Haines, S. F., and Ward, E. (1948). *Amer. J. Obstet. Gynec.*, **55**, 609.
—— and Plummer, W. A. (1931). *J. Amer. med. Ass.*, **97**, 602.
—— —— and Boothby, W. M. (1926). Ibid., **87**, 1009.
Myant, N. B. (1958). *Clin. Sci.*, **17**, 75.
Osorio, C., and Myant, N. B. (1960). *Brit. med. Bull.*, **16**, 159.
Parry, C. H. (1825). *Collections from the Unpublished Medical Writings of Caleb Hillier Parry*, vol. 2, p. 111. Underwoods, London.
Peterson, R. R., and Young, W. C. (1952). *Endocrinology*, **50**, 218.
Piper, J., and Rosen, J. (1954). *Acta med. scand.*, **150**, 215.
Riley, I. D., and Sclare, G. (1957). *Brit. med. J.*, **1**, 979.
Rundle, F. F. (1951). In Joll's *Diseases of the Thyroid Gland*, 2nd ed., pp. 217, 296. Heinemann, London.
Russell, K. P., Rose, H., and Starr, P. (1957). *Surg. Gynec. Obstet.*, **104**, 560.
Silver, S. (1960). *Medical, Surgical, and Gynaecological Complications of Pregnancy*, edited by A. Guttmacher and J. J. Rovinsky, p. 416. Baillière, London.
Werner, S. C. (1952). *Med. Clin. N. Amer.*, **36**, 623.
Williams, R. H., Kay, G. A., and Jandorf, B. J. (1944). *J. clin. Invest.*, **23**, 613.

"The Fifth International Congress on Leprosy, held at Havana in April, 1948, paid special attention to the very point which exercises your correspondent, having before it a resolution from patients all over the world requesting an alternative to the word leper, which has come to have undesirable associations with the idea of 'uncleanness.' The chief decisions of that Congress, as set out in the official English translation, were: (1) The disease itself will continue to be called leprosy, this being a short convenient name and quite able to convey the meaning of modern leprosy, in spite of the unfortunate linguistic confusion in the past over which we had no control. (2) It was agreed that the word 'leper' is crude and impolite and should never be used for a human being suffering from leprosy, and was recommended to be abolished in medical and general use. It was decided that if one wants to refer to a person suffering from leprosy, one should take the trouble to use the longer form and say 'a patient of leprosy,' 'a leprosy patient.' Leprosy, to use the word in its modern sense, is one of the world's major diseases. It is estimated that there are at least 15 million cases, of which 4 million are in the Commonwealth; and of these only one in five is receiving treatment." (Letter to *Daily Telegraph*, September 5, from the Chairman of the British Leprosy Relief Association.)