PREGNANCY AND THE THYROID: A CLINICAL REVIEW

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Thyroid disease is the most common pre-existing endocrine disorder occurring during pregnancy, reflecting in part a predilection for thyroid problems in women of childbearing age. Many important changes in the thyroid's physiological characteristics occur during pregnancy, and their proper understanding is essential for the effective management of thyroid diseases in pregnancy. Our review aims to provide i) an understanding of the normal physiological changes in maternal thyroid function and thyroid hormone metabolism at each stage of pregnancy, and ii) an update on the diagnosis and management of thyroid diseases in pregnancy.

FACTORS AFFECTING MATERNAL THYROID FUNCTION IN PREGNANCY

In normal pregnancy, several physiological changes can have an impact on the maternal thyroid function and thyroid hormone metabolism and may represent physiological adaptations to optimise maternal thyroid status for fetal development. A proper understanding of the nature and magnitude of these changes is essential for an appropriate interpretation of thyroid function tests in pregnancy; only then can the clinician correctly identify patients with thyroid disease from among those in whom the changes represent normal response and adaptation to pregnancy.

Increased thyroid hormone binding capacity

The majority of thyroxine (T4) and triiodothyronine (T3) circulate bound to serum proteins, whereas only 0.03% of serum total T4 and 0.3% of serum total T3, respectively, are free; these represent the metabolically active fraction. Thyroxine-binding globulin (TBG), a glycoprotein synthesised in the liver, binds approximately 70% of circulating T4 and T3. The remainder of circulating thyroid hormone is bound to thyroid-binding pre-albumin (transthyretin) and albumin. Due to the large fraction of circulating thyroid hormone that is bound to serum proteins, changes in the serum concentrations of these proteins significantly influence total hormone measurements.[1,2]

In pregnancy, serum TBG concentrations increase about 2.5 times. The elevation in TBG is seen within the first two weeks of pregnancy, peaks at the second trimester, and persists until delivery. It is oestrogen-mediated and was originally thought to result from increased TBG synthesis. However, recent studies have shown that oestrogen stimulates increased sialylation of TBG. The sialylated variants are cleared from the circulation more slowly, as fully sialylated TBG has a circulating half-life as long as three days, compared to a circulating half-life of 15 minutes for desialylated TBG.[2,3] The affinity of sialylated TBG for T4 is apparently normal. For the woman to remain euthyroid, serum total T4 and total T3 concentrations increase in parallel with the elevated TBG levels, but the concentration of free hormones remains approximately unchanged.

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Thyroid stimulation by human chorionic gonadotropin (hCG)

Both human chorionic gonadotropin (hCG) and thyroid stimulating hormone (TSH) are glycoproteins which are composed of a common alpha-subunit and a non-covalently linked hormone-specific beta-subunit. Recent investigations have clarified the structural homology not only in the hCG and TSH molecules, but also in their G-protein coupled receptors. This homology suggests the basis for cross-reactivity of hCG with the TSH receptor.[4] Data have now accumulated that indicate hCG has weak thyroid-stimulating activity, approximating $1/10^4$ that of TSH. The thyrotropic potency of hCG is influenced by the metabolism of the hCG molecule itself, including variations of peptide linkage, glycosylation, or sialylation in the hCG molecule.[5,6] In particular, truncated hCG isoforms, in which the β subunit is deglycosylated and desialylated, show increased thyrotropic potency. Besides its contribution to hyperthyroidism in patients with trophoblastic tumours, the clinical significance of the thyrotropic action of hCG is now also recognised in normal pregnancy and hyperemesis gravidarum.[4]

Relative iodine deficiency

Pregnancy is accompanied by a decrease in the availability of iodide for the maternal thyroid, due to its increased renal clearance and active transport across the placenta.[7] The thyroid gland enlarges during pregnancy when iodine intake is borderline or low, but studies show no significant thyroid enlargement in normal pregnant women living in iodine-replete areas.[8] Therefore, what was previously described as physiological goitre of pregnancy is a misnomer, as it represents goitrous compensation resulting from iodine deficiency in pregnant women living in regions with inadequate iodine availability.

Pregnancy-induced immune suppression

An interesting phenomenon in pregnancy is the state of relative immune suppression in the mother which explains why the fetus, which has foreign paternal antigens, is not rejected by the mother. The overall suppression of immune function, as observed in late pregnancy and into the early post-partum period, has a significant bearing on patients with autoimmune disease in general and autoimmune thyroid disease in particular.[9] This explains the paradoxical finding that maternal Graves' disease or Hashimoto's thyroiditis often run a favourable course during pregnancy, only to relapse postpartum.

Role of the placenta

The human placenta is intricately involved in the regulation of maternal-fetal thyroid function.[7] The placenta is permeable to thyrotropin-releasing hormone (TRH), but not to TSH. The transfer of thyroid hormone itself across the placenta has been the subject of great controversy. Although T4 and T3 do not cross the placenta freely, it is now believed that placental transfer of maternal thyroid hormone may be particularly important in early pregnancy before the fetal thyroid is functional. The significance of early placental transfer of thyroid hormone is supported by the findings that in contrast to infants with congenital hypothyroidism, infants from mothers with endemic hypothyroidism show neurologic deficits (endemic cretinism) and fail to improve with early levo-thyroxine treatment.[10] This finding suggests that maternal T4 transfer may be particularly important when fetal thyroid function is compromised, as in congenital hypothyroidism.

The placenta is also an active site for degradation of thyroid hormones by type III 5-deiodinase enzyme, however its contribution to thyroidal economy is currently unclear.

Another characteristic of the human placenta is its high permeability to iodide, fetal thyroid has been demonstrated to trap iodide by 10-12 weeks of gestation.[7] Because iodide is actively transported across the placenta, the fetus is susceptible to iodine-induced goitre and hypothyroidism when the mother is given pharmacological amounts of iodine (Wolf-Chaikoff effect). This may occur with many intravenous, oral, or topical iodine compounds, including those dyes used in amniography.

Changes in thyroid hormone profile during pregnancy

Interpretation of thyroid function studies in pregnancy must therefore be provided with due knowledge of the alterations in the production, circulation and clearance of thyroid hormone. It is also important to recognise that many of these factors have variable influences at different stages of pregnancy. The changes in thyroid hormone profile in normal pregnancy are summarised in Figure 1.

In the first trimester, circulating hCG levels rise progressively and peak at 8-12 weeks of gestation. This is accompanied by a corresponding mild increase in serum free T4 and T3 concentrations, whereas serum TSH declines by approximately 1 mU/L below the non-gravid levels. The decline in circulating TSH is associated with a blunted TSH response to thyrotropin (TRH) stimulation, suggesting thyroid hormone excess and resulting hypothalamic-pituitary suppression. At peak hCG elevation, serum TSH is found by sensitive assay methods to be suppressed below normal in 15% of normal pregnancies. Serum TBG rises in a nearly linear fashion and reaches a twofold elevation compared to non-gravid levels by 20 weeks of pregnancy. It remains elevated at these levels until delivery, and then returns to normal by 4-6 weeks postpartum. Serum total T4 and T3 concentrations show a similar profile to changes observed in TBG levels throughout pregnancy.[2,7,11]

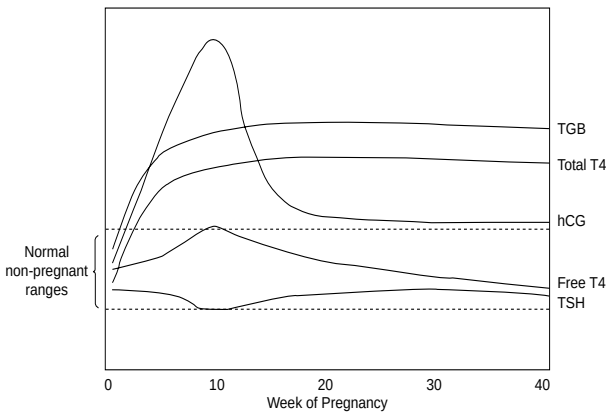

FIGURE 1
Changes in thyroid function and human chorionic gonadotropin (hCG) concentration during pregnancy.

In the third trimester, women who are clinically euthyroid show a decline in both serum free T4 and T3 concentrations. The normal ranges for free thyroid hormone during this stage of pregnancy overlap with that which represent hypothyroidism in the non-pregnant subjects.[12] This resetting of the 'thyrostat' may well be a physiological adaptation to conserve energy for labour and lactation.

THYROID DYSFUNCTION IN PREGNANCY

Hyperemesis gravidarum and gestational thyrotoxicosis

Nausea and vomiting of mild to moderate severity are especially common manifestations from early pregnancy until about 12 weeks. Hyperemesis gravidarum is the most severe form of this order, occurring in about 1-3% of pregnancies, and can be accompanied by dehydration, ketonuria, and weight loss (>5%). The diagnosis of hyperemesis gravidarum excludes other causes of vomiting, such as primary hyperthyroidism, gastroenteritis, systemic infections, or trophoblastic disease.[13,14]

Despite conflicting data, most investigators believe in the putative role of hCG in cases of hyperemesis and hyperthyroidism.[15] In some studies, high circulating hCG levels were found to correlate significantly with the severity of the hyperemesis and the degree of thyroid stimulation.[13,16,17] Circulating free T4 and free T3 levels were frequently elevated in hyperemetic pregnancies, suggesting a relationship between the severity of hyperemesis and the biochemical evidence of hyperthyroidism. The relationship between circulating hCG levels and thyroid function indices, however, remains conflicting.[15] Kimura and co-workers reported similar serum hCG concentrations in women with hyperemesis compared to those without emesis, but they found increased serum thyroid stimulating activity in the hyperemesis group. They hypothesised that hyperemetic patients produced molecular variants of hCG with increased thyroid stimulating activity.[18]

Apart from fluid and electrolyte replenishment, commonly used anti-emetics such as promethazine, metoclopromide and prochlorperazine can be used. HCG antagonists are not available and indeed their therapeutic usage would be restricted as they would adversely affect placental development.

The term gestational thyrotoxicosis refers to a subset of hyperemetic patients with clinical and biochemical hyperthyroidism in early pregnancy. Women with gestational thyrotoxicosis may be differentiated from those with Graves' disease by the absence of goitre and negative antithyroid antibodies whose titre decreases from the mid trimester

onwards but are still present with clinically active disease. As gestational thyrotoxicosis is mediated by hCG, no thyroid antibodies should be present. Hyperthyroidism is transient and self-limiting in this condition, and specific antithyroid treatment is not necessary.[18] Although women with hyperemesis have similar demographic characteristics and pregnancy outcomes as compared to the general obstetric population, adverse outcomes such as low birth weight, antepartum haemorrhage and preterm delivery may occur in selected mothers with long-term malnourishment and significant weight loss.[14]

Gestational trophoblastic disease

The precise prevalence of hyperthyroidism in patients with trophoblastic tumours is unknown. Thyroid stimulation results from the excessive levels of circulating hCG produced by the trophoblastic tissue: both hydatidiform moles and choriocarcinomas. In patients with hyperthyroidism caused by trophoblastic tumours, serum hCG levels usually exceed 300 U/mL, whereas the peak concentration noted in pregnant women at 10-12 weeks' gestation is around 100 mU/L[6,19] However, thyrotropic potency of hCG varies among its different isoforms, which explains why some patients with trophoblastic tumours and very high serum hCG levels do not manifest hyperthyroidism.[6]

The diagnosis of hyperthyroidism is established by finding elevated serum free T4 and T3 levels, and suppressed TSH concentration. Most laboratories would use either a second or third general TSH assay with a reported functional sensitivity of 0.1-0.01 mU/L respectively: each laboratory should establish its own sensitivity limits. Thyroid radioactive iodine uptake (RAIU) is markedly increased, as in Graves' disease. In most instances, patients with molar pregnancy have mild hyperthyroidism with a small goitre, and hyperthyroidism resolves rapidly after surgical removal of the hydatidiform mole. Conversely, patients with choriocarcinoma who manifest hyperthyroidism usually have a large tumour mass, and antithyroid therapy may be required in addition to appropriate chemotherapy for the tumour.[19]

Graves' disease in pregnancy

The prevalence of hyperthyroidism in pregnancy is reported in the range of 0.1-0.2%. The majority of patients have Graves' disease while other causes of hyperthyroidism occur much less frequently (Table 1).

It is an autoimmune disease characterised by a diffuse goitre, with or without infiltrative eye signs, that often remits in mid-trimester and recurs after delivery. However, clinical diagnosis may be difficult as many of the symptoms and signs of hyperthyroidism reflect those of normal pregnancy. Ultimately, biochemical parameters of thyroid function must be measured frequently and interpreted according to clinical situation and pregnancy-specific reference ranges.[20,21]

This condition, if untreated, can lead to a significant morbidity and mortality in both mother and fetus. Treatment with antithyroid drugs is the preferred therapy. Both propylthiouracil and carbimazole (or its active metabolite, methimazole) are similarly effective in blocking thyroid hormone synthesis.[20,22] Propylthiouracil appears to have some advantages over carbimazole: it also inhibits the peripheral conversion of T4 to T3, and it is less readily secreted in breast milk (propylthiouracil is 75% bound to plasma proteins, whereas carbimazole is not appreciably bound). However, few studies had reported on the pharmacodynamics of both drugs in pregnancy. Propylthiouracil is believed to cross the placenta to a lesser extent, however the only evidence supporting this is derived from a study reported by Merchant and co-investigators in 1977.[23] The investigators gave a single oral dose of radiolabelled propylthiouracil, carbimazole or methimazole to nine normal pregnant women two hours before a therapeutic abortion, and they demonstrated a reduced placental transfer of propylthiouracil compared to carbimazole or methimazole.

Thionamides should be administered in the lowest possible dose (generally ≤ 150 mg/day of propylthiouracil or ≤ 15 mg/day of carbimazole) to target maternal serum free T4 concentrations in the upper limit of normal, as both drugs cross the placenta, and can cause fetal goitre and hypothyroidism. Block-replacement regimen should not be used in pregnancy as levothyroxine crosses the placenta less freely compared to antithyroid drugs. The patient should be followed closely (at least four-weekly intervals) with frequent thyroid testing. Dosage of thionamides should be reduced progressively in anticipation of the customary steady amelioration in the disease as pregnancy advances, and treatment can eventually be discontinued in approximately 30% of patients.[20,22,24]

Propylthiouracil is the preferred drug as it is believed to cross the placenta less readily, and lesser quantities of it are secreted in breast milk.[23,25] However, there are no references to our knowledge proving it to be more effective in the outcome of pregnancy. As both drugs are effective and safe in the treatment of hyperthyroidism during pregnancy, women on carbimazole at time of conception need not switch over to propylthiouracil therapy. Moreover, carbimazole may be more acceptable because of its once-daily dosing. The only neonatal complication reported with the use of carbimazole but not with propylthiouracil is

TABLE 1
Causes of hyperthyroidism in pregnancy.

Primary thyroid disease
Graves' disease*
Multinodular goitre
Toxic adenoma
Pregnancy-related hyperthyroidism
Gestational thyrotoxicosis*
Trophoblastic tumours
Hydatidiform mole
Choriocarcinoma
Destructive thyroiditis
Subacute thyroiditis
Exogenous
Treatment with excessive thyroid hormone*
Thyrotoxicosis factitia
Others
TSH-secreting pituitary tumour
Struma ovarii

*denotes the commoner causes

aplasia cutis, i.e. congenital absence of skin in the parietal area of the scalp, characterised by a small, ulcer-like lesion that usually heals spontaneously.[25] In the general population, aplasia cutis congenital occurs in 0.03% of newborns, comparable in incidence to infants born to mothers on carbimazole.[26]

Beta-adrenergic blockers are effective in controlling hypermetabolic symptoms and may be used in combination with thionamides until the symptoms abate. However, their prolonged use is not advisable because of potential neonatal morbidity. They are generally safe although spontaneous labour may occasionally ensue. They are not associated with infantile asthma.

Surgery is reserved for patients who are not responding to antithyroid drugs because of non-compliance or allergy to both drugs, or the unusual case of a large goitre which requires large amounts of antithyroid drugs. Thyroidectomy can be safely performed in the second trimester.

Radioactive iodine therapy is contraindicated in pregnancy, because of potential congenital malformations and congenital hypothyroidism.[27]

Both maternal and fetal outcome is directly related to the control of hyperthyroidism. If poorly controlled, maternal morbidity includes a higher incidence of toxaemia, premature delivery, *abruptio placentae*, heart failure, and 'thyroid storm'. Neonatal morbidity includes intrauterine growth retardation, low birth weight infants, and prematurity.[21,28] Neonatal Graves' disease occurs in approximately 2% of mothers with Graves' disease during pregnancy. This is caused by the transplacental passage of maternal thyrotropin receptor stimulating antibody (TSAb), and is a transient condition that usually resolves within 3-12 weeks. Neonatal Graves' disease is likely if the maternal TSAb concentration is > 500% of control values.[29,30] Therefore, measurement of TSAb level near term is useful in women with active Graves' disease, or in those who had undergone thyroid surgery or radioactive iodine ablation for Graves' disease. Rarely, transient hypothyroxinaemia may occur in infants born to a mother with poorly controlled Graves' disease. These infants are believed to have transient suppression of pituitary-thyroid axis secondary to increase transplacental passage of T4 during late pregnancy.[31] Weak maternal TSAb activities and/or differences in sensitivity of fetal thyroid gland to TSAb may contribute to this unique disorder.

Hypothyroidism in pregnancy

About 0.05% of pregnant women has clinical hypothyroidism, while the incidence of subclinical hypothyroidism (associated with elevated TSH but normal free T4 levels) is about 2% of pregnant women.[32,33] The majority has elevated serum TSH concentration that antedated pregnancy. Most cases are the result of Hashimoto's thyroiditis or post-ablative therapy for Graves' disease, but other less common causes of hypothyroidism may be responsible (see Table 2). Women with autoimmune thyroid disease who are euthyroid in early pregnancy carry a significant risk of developing subclinical hypothyroidism as the pregnancy advances, despite a marked reduction in antibody titres. This results from the reduced ability of the gland to adjust to changes in thyroidal economy associated with pregnancy.[34]

Untreated hypothyroidism is associated with infertility, whereas pregnancy may be complicated by pre-eclampsia and premature delivery in those still hypothyroid near term.[35] However, early fetal loss and reduced intellectual capacity in the offspring appear to correlate with the presence of thyroid antibodies rather than thyroid status in the mother.[36,37] In view of the difficulty in making the diagnosis of hypothyroidism on clinical grounds alone, routine screening of certain high-risk groups is advocated. These include women with previous therapy for hyperthyroidism or high-dose neck irradiation, previous postpartum thyroiditis, the presence of a goitre, family history of thyroid disease, amiodarone use, and type 1 diabetes mellitus. Serum TSH is the most sensitive test to diagnose primary hypothyroidism before the clinical symptoms and signs manifest.

Levothyroxine is the drug of choice to treat hypothyroid women. Euthyroidism must be reached and maintained in a timely fashion to ensure good maternal and fetal outcome. The notion that thyroxine dosage is unlikely to be changed during pregnancy should be corrected, as recent studies showed that this increases in 75% of pregnant women with primary hypothyroidism in whom it was adequate before pregnancy.[38] Most women require a 50% dose increment (approximately 50 mg levothyroxine) to achieve normal serum TSH concentrations during pregnancy. It is important to caution the patients that drugs commonly used in pregnancy – iron, sucralfate and aluminium hydroxide – interfere with oral thyroxine absorption and should not be taken at the same time as thyroxine. Patients should be followed up during each trimester with thyroid function assessment, targeting serum TSH concentrations within the lower half of normal range.[38,39]

TABLE 2
Causes of hypothyroidism in pregnancy.

Chronic autoimmune thyroiditis*	
	Goitrous variant (Hashimoto's thyroidosis)
	Atrophic variant
Transient hypothyroidism	
	Subacute thyroiditis
	Silent thyroiditis
Post thyroid ablation*	
	Radioiodine ablation
	Thyroidectomy
	External irradiation
Drug-induced*	
	Thionamides (overtreatment of Graves' disease)
	Iodine
	Amiodarone
	Lithium
Congenital hypothyroidism	
	Thyroid agenisis/dysgenesis
	Thyroid dyshormonogenesis
Secondary hypothyroidism	
	Pituitary or hypothalamic disease

*denotes the commoner causes

Thyroid nodular disease in pregnancy

Thyroid nodules are detected in about 2% of pregnant women.[40] In regions with borderline dietary iodine intake, women with previous pregnancies have a higher prevalence of nodular disease, likely contributed to by accentuated iodine deficiency during pregnancies.[41] Although most thyroid nodules are benign and do not cause thyroid dysfunction, some women may exhibit a marked increase in nodular growth during the course of pregnancy.[42] The investigative workup is similar to that in nonpregnant patients, except that radionuclide scans are contraindicated. Fine needle aspiration cytology remains to be the most effective diagnostic tool for clinically palpable thyroid nodules in pregnancy. Thyroidectomy can be safely performed during the second trimester for malignant lesions and aspiration cytological findings suspicious of papillary cancer. Surgery may be deferred to early postpartum period for patients with low risk characteristics or those with cytological findings suspicious of follicular neoplasm.[40,43]

Postpartum thyroiditis (PPT)

PPT is an autoimmune condition that occurs in approximately 5% of women during the first year postpartum. The clinical presentation is characterised by a hyperthyroid phase occurring in the first three months postpartum, followed by a hypothyroid phase between 3-6 months after delivery, with spontaneous recovery in the majority of patients.[44,45] However, about half of the patients present with hypothyroidism without clinically apparent preceding thyrotoxicosis, and 25-30% of hypothyroid subjects eventually develop permanent hypothyroidism.[46] PPT can also occur in patients with Graves' disease or Hashimoto's thyroiditis.[47]

Symptoms during hyperthyroid phase include tachycardia, excessive sweating, and rapid post-pregnancy weight loss. Thyrotoxicosis in PPT is usually mild and self-limiting (2-8 weeks' duration), and is distinguished from relapsing Graves' disease by a low RAIU (study contraindicated if the mother is breast feeding). β-blockers can be administered if symptoms are severe. Antithyroid drugs are not useful in PPT because thyrotoxicosis is secondary to hormone release from the damaged gland. Observation is important because many patients become hypothyroid before recovering normal thyroid function.[44-46]

The duration of hypothyroid phase is variable and symptoms may include depression, fatigue, lethargy, inability to lose weight, and emotional lability. Painless goitre is a common finding. In symptomatic patients with biochemical evidence of hypothyroidism, treatment with levothyroxine is indicated. Patients who recover from PPT should be warned of the increased risk of recurrence with future pregnancies, and of developing permanent hypothyroidism in the future.[44-46]

Antibodies against thyroglobulin (Tg) or thyroperoxidase (TPO) have been reported in about 75% of patients with PPT. Although there is no consensus, systematic screening of thyroid autoimmunity in the early stages of gestation may allow specific monitoring of susceptible individuals, as approximately 50% of women with a positive test for thyroid antibodies subsequently develop PPT.[48] In a large prospective study, women with positive anti-TPO antibodies detected during antenatal screening at 16-week gestation were found to have increased prevalence of thyroid-related symptoms in the postpartum period compared to the antibody-negative group. Interestingly, thyroid-related symptoms were present in both groups of thyroid antibody-positive women with and without thyroid hormone abnormalities, suggesting that symptoms may appear well before biochemical abnormalities become apparent.[49]

Other causes of postpartum thyroid dysfunction

About half the women with Graves' disease suffer a relapse after delivery. Relapse of Graves' disease in the postpartum period accounts for the remaining 10-15% of cases of postpartum hyperthyroidism.[50] From a clinical standpoint, it may be difficult to distinguish hyperthyroidism caused by Graves' disease from an episode of PPT, and both conditions may occur in the same individual. In the majority of cases, hyperthyroidism due to Graves' disease occurs later in the postpartum period (between 3-6 months) as compared with the transient thyrotoxicosis of destructive thyroiditis. Affected mothers who breast-feed their infants should preferentially use propylthiouracil as less than 0.1% of the ingested dose is secreted in the breast milk. Nonetheless, propylthiouracil should be given in divided doses after each feeding, and the infants monitored closely with frequent thyroid function testing. Similarly, radioactive iodine treatment is contraindicated in nursing mothers.[51]

Hypothyroidism in the postpartum period may occasionally be contributed to by postpartum pituitary failure, which results from pituitary apoplexy (Sheehan's syndrome) or lymphocytic hypophysitis.[52,53] In these situations other pituitary hormones are usually affected, and serum TSH is not elevated in the presence of low thyroid hormones.

CONCLUSION

The diagnosis of thyroid diseases in pregnancy is complicated by physiological changes in metabolism and alterations of laboratory values observed in pregnancy. In general, measuring free T4 and TSH remain as good indicators of thyroid function as well as adequacy of therapy in pregnancy. Although few therapies for thyroid disease are contraindicated in pregnancy, clinicians should always be mindful of the potential fetal effects as medications may cross the placenta. The goal in treating hyperthyroidism is to use the minimal dose of thionamides that is required to achieve maternal euthyroidism, whereas hypothyroidism should be adequately replaced with levothyroxine to maintain serum TSH levels in the low-normal range. The use of radioactive iodine or radionuclide scans are contraindicated in pregnancy. Finally, it is important to realise that many thyroid conditions and treatments may directly affect the fetus, and monitoring is thus required for the fetus as well as the neonate.

Summary of new concepts and key points:

- **TBG elevation in pregnancy results from an increase in sialylated TBG variants that are cleared from the circulation more slowly than normal TBG.**
- **'Physiological' goitre of pregnancy is a misnomer as it occurs only in mothers with relative iodine deficiency.**
- **'Gestational thyrotoxicosis' describes patients with hyperemesis gravidarum with clinical and biochemical hyperthyroidism. This is characterised by the absence of goitre and thyroid antibodies, and its spontaneous resolution in the latter half of pregnancy. It is believed to arise from circulating hCG with high biological activity.**
- **Graves' disease is the commonest cause of hyperthyroidism in pregnancy. It can be safely and effectively treated with thionamides. The advantage of propylthiouracil over carbimazole is empirical rather than proven.**
- **Measurement of TSAb concentration in women with active Graves' disease in late pregnancy, or with previous ablative therapy for Graves' disease, is useful to predict neonatal Graves' disease.**
- **In hypothyroid women, thyroxine requirement increases by approximately 50% during pregnancy. Drugs commonly used in pregnancy (e.g. iron, sucralfate, and aluminium hydroxide) may interfere with oral thyroxine absorption and should not be taken at the same time as thyroxine.**
- **Mothers with thyroid disease should be monitored closely within the first year postpartum because of the tendency for relapse.**
- **Systematic thyroid autoimmunity screening in the early stages of gestation may improve obstetric outcome and identify women at risk of PPT.**

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