

# Thyroid disease and pregnancy



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**Thyroid disease may affect all aspects of obstetrics and gynaecology, from fertility to fetal outcome. The recognition of these conditions and their practical impact on obstetrics is discussed in the following brief review.**

## Normal pregnancy

Normal pregnancy is associated with a 50 per cent increase in thyroid hormone production which is required to maintain normal free T3 and T4 levels in the presence of an increase in thyroid binding globulin. The fetal thyroid does not become functional until around 12 weeks gestation and does not produce significant amounts of hormone until 18 to 20 weeks gestation. Prior to that time, the fetus is completely dependant upon transplacental transfer of maternal thyroid hormone. Later in pregnancy, maternal thyroid hormone contributes approximately 20 to 30 per cent of fetal thyroid hormone levels, but even this small contribution appears to be critical for fetal development.

Normal pregnancy is associated with potential iodide deficiency secondary to increased renal excretion of iodide. If iodide deficiency occurs, as had been demonstrated in a number of studies in Australia, there may be both maternal and fetal consequences. These include goitre, subclinical or clinical hypothyroidism and even fetal cretinism. Recommended iodide intake for pregnant women or women planning pregnancy is 150 to 250 µg daily. A number of standard pregnancy vitamin supplements now include iodide and these should be recommended, especially when the intake of iodised salt is low.

Even in iodide replete women, the thyroid gland may be palpable due to increased vascularity. The investigation of goitre in pregnancy should be limited to thyroid function tests (specifically requesting at least TSH and free T4) and ultrasound of solitary nodules or multinodular goitre if not previously investigated. In some cases, fine needle biopsy of the dominant nodule may be indicated if any of the nodules are > 10 mm in diameter, especially solid compared with cystic nodules. Nuclear thyroid scanning is contraindicated at all stages of pregnancy. Thyroid cancer is

uncommon and the prognosis does not appear to be adversely affected by pregnancy.

A significant number of women (around ten per cent) will have circulating antithyroid antibodies, particularly to thyroid peroxidase, which even in the absence of clinical or biochemical thyroid dysfunction have been associated with adverse outcomes in pregnancy. Negro et al demonstrated an association between positive antithyroid antibodies and both miscarriage and preterm delivery, even in euthyroid women. These events were reduced by the administration of thyroxine.

## Hypothyroidism

Inadequate circulating thyroid hormone may lead to amenorrhoea, reduced libido and subsequent sub- or infertility. If pregnancy does occur, there is an increased incidence of miscarriage, hypertension and placental abruption. Fetal complications include: fetal distress, preterm delivery, low birth weight, and fetal/perinatal death. Treatment with thyroid hormone replacement has been demonstrated to reduce these risks, including miscarriage. The risk of these complications is greatest in women with overt hypothyroidism compared with subclinical hypothyroidism. Of most concern is the increasing data supporting an association between maternal thyroid deficiency during pregnancy and problems with neuropsychological development of the offspring. Such problems can occur even with milder degrees of thyroid deficiency. Although theoretically adequate thyroid replacement therapy should reduce these risks, currently there is little evidence to support this.

## *'Normal pregnancy is associated with a 50 per cent increase in thyroid hormone production'*

Despite these findings, screening of asymptomatic pregnant women is not recommended, although a TSH measurement would appear to be a sensible precaution prior to conception if feasible. In women with overt or subclinical hypothyroidism, serum TSH should be measured as soon as possible after a positive pregnancy test. Dose adjustments or initiation of therapy is made with increments of 50 to 100 µg/day of thyroxine based on maintaining the free T4 in the upper half of the normal range and the TSH within the lower end of the normal range. This should be rechecked six weeks after any change in dose or at least once each trimester. Another approach recommended by one group is to increase the dose by about 30 per cent as soon as pregnancy is confirmed, with further dose changes as above. In women with previous thyroid cancer, the dose should be adjusted to maintain TSH levels below 0.5 µU/ml. The dose can be reduced to pre-pregnancy levels after delivery but serum

TSH should be measured four to six weeks later to confirm that the reduction was appropriate.

## Thyrotoxicosis

Most thyrotoxicosis predates pregnancy and diagnosis during pregnancy may be difficult as the symptoms overlap closely with normal pregnancy. Uncontrolled thyrotoxicosis is associated with an increased risk of miscarriage, maternal weight loss, maternal cardiac dysfunction, pre-eclampsia, low birth weight, thyroid storm, preterm delivery and placental abruption. If thyrotoxicosis is treated adequately, these complications are not increased. Antibody mediated fetal or neonatal thyroid disease, including goitre and thyrotoxicosis, is rare.

Treatment of thyrotoxicosis is predominantly with antithyroid drugs, although surgery may be required in rare cases. Propylthiouracil (PTU) is the drug of choice, predominantly because of its protein binding which leads to less transplacental transfer. The dosage (usually between 50 to 300 mg/day in divided doses) is based on maintaining the free T4 and T3 in the upper end of the normal range. Normalisation of the TSH level may lag many months behind the normalisation of free T4 and T3 and is not used for monitoring therapy in this setting.

Graves' disease frequently improves during pregnancy and it is often possible to reduce or even withdraw treatment by 20 weeks gestation. Postpartum, the dose may need to be increased. Women on moderate doses of antithyroid drugs (<20 mg carbimazole, <300 mg/day PTU) may breastfeed. Therapeutic doses of radioiodine are contraindicated in pregnancy and women are advised to avoid pregnancy for six months following its administration. If pregnancy occurs within this period, appropriate counselling should be offered.

## Postpartum thyroiditis

This condition presents as hypothyroidism (~40 per cent), hyperthyroidism (~30 per cent) or hyperthyroidism followed by hypothyroidism during the first 12 months postpartum. Again, as in pregnancy, symptoms may be misdiagnosed as postnatal depression or physiological tiredness. Risk factors include: previous thyroid disease, Type 1 diabetes, and positive thyroid peroxidase antibodies. Hypothyroidism may be permanent in up to 30 per cent and there is a significant risk of hypothyroidism in the remaining women over the next seven years. Screening of thyroid function during subsequent pregnancies is warranted.

The recurrence risk in subsequent pregnancies is high. Treatment includes thyroxine for symptom relief with an attempt to withdraw after three to six months. The thyrotoxic phase may be brief and beta-blockers alone may be adequate, although occasionally antithyroid drugs are warranted.

## Conclusion

Appropriate assessment and management of thyroid disease in pregnancy is generally associated with an excellent outcome and is achievable in almost all cases.

## References

1. Negro R, Formoso G, Mangieri T et al. Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: effects on obstetrical complications. *J Clin Endocrin Metab* 2006; 91(7): 2587-91.
2. LaFranchi S H, Haddow J E and Hollowell J G. Is Thyroid Inadequacy During Gestation a Risk Factor for Adverse Pregnancy and Developmental Outcomes? *Thyroid* 2005; 15(1): 60-71.

**Table 1: Interpreting thyroid function tests**

TSH	Free T3	Free T4	Diagnosis	Comment
↓	N	N	20 per cent of women in T1 due to HCG effect	TSH usually normalises by 16-20 weeks
↓	↑	↑	Thyrotoxicosis	Mostly Graves disease (+ TrAb in most cases), DD toxic adenoma, autonomous thyroid nodule, excessive thyroxine replacement, thyroiditis.
↓	↑	↑	Gestational thyrotoxicosis	HCG effect associated with hyperemesis gravidarum, usually normalises by 16-20 weeks, negative TrAb DD molar pregnancy
↓	N	N	Recovery from thyrotoxicosis	TSH may lag by many months
↑	↓	↓	Hypothyroidism	Mostly Hashimoto's DD thyroiditis, post-thyroidectomy, post radioiodine, iodide deficiency
↑	N	N	Subclinical hypothyroidism	As for hypothyroidism
N	N	N	Normal Goitre-multinodular or smooth	