Lothian Guidance for Diagnosis and Management of Thyroid Dysfunction in Pregnancy.

Early diagnosis and good management of maternal thyroid dysfunction is essential to ensure minimal adverse effects on fetal development. The following are suggestions for the use of thyroid function tests in Primary Care and are derived from the UK guidelines, modified to take into account local practice.

Diagnosis and Management of Thyroid Disease in Pregnancy

This requires close liaison between the GP, Community Midwife, Endocrinologist and Obstetrician. Much of the thyroid function testing is likely to be undertaken by the Community Midwives. However, the initial set of thyroid function tests done for screening purposes or to check thyroid status in patients with established thyroid disorders is more likely to be done by the GP.

General Points

Maternal FreeT4 (FT4) and Free T3 (FT3) rather than total hormone concentrations must be measured in pregnancy. This is because Total T4 and Total T3 increase in pregnancy due to increased serum concentrations of thyroid hormone binding proteins. It is only the FT3 and FT4 fraction (not the bound fraction) than can enter cells and modify metabolism. Trimester-specific reference ranges for FT3 and FT4 need to be applied for diagnosis as their concentrations fall during pregnancy (see below).

	First trimester	Second Trimester	Third Trimester
FT4 pmol/L	10–18	9-16	8-14
FT3 pmol/L	3.4-6.6	3.2- 6.2	3.2-5.6
TSH mU/L	<0.01 –3.4	1.3-3.3	1.2-3.5

Screening for thyroid disorders in pregnancy

The following categories of patient should be screened for thyroid disease using TSH and FT4 preferably prior to conception or if not at booking

- Type 1 and Type 2 diabetes, Gestational Diabetes
- Other autoimmune disorders eg ceoliac disease etc
- Previous history of thyroid disease
- Current thyroid disease
- Family history of thyroid disease (1st degree relative)
- Goitre or other features of thyroid disease

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Hypothyroidism and Pregnancy

Overt untreated hypothyroidism is associated with fetal loss, gestational hypertension, placental abruption, poor perinatal outcome and severe neurodevelopmental delay. The developing fetal brain requires optimal thyroxine levels from early in the first trimester of pregnancy. The fetus relies on maternal thyroxine until 12 weeks gestation when its own thyroid gland develops and in pregnancy there is an increased requirement for T4[1,2,3]. The offspring of women whose free thyroxine levels are in the lowest 10% of the reference range in the first trimester of pregnancy have significant neurodevelopmental delays at the age of two years [4].

There is an increase in serum free thyroxine (FT4) levels in women early in normal pregnancy but in women with hypothyroidism this increase does not occur. It is thus very important to ensure adequate thyroxine replacement from as early as 5 weeks gestation [5]. It is recommended that patients with established hypothyroidism should have the T4 dose increased by 25 micrograms when a pregnancy is confirmed

Assessing Hypothyroidism in Pregnancy

Ideally women with hypothyroidism should be seen pre-pregnancy to ensure that they are euthyroid. They should also be encouraged to present as soon as they become pregnant in order that their thyroxine dose may be increased and TSH and FT4 are monitored regularly. For patients with established hypothyroidism the ideal monitoring regimen is thus:-

- Before conception (if possible)
- At diagnosis of pregnancy or at antenatal booking

- 2 weeks after the dose of T4 has been increased
- At least once in each trimester
- 2-6 weeks postpartum
- **Patients with a history of Graves Disease who are euthyroid or hypothyroid through radioiodine treatment or surgery must have a TSH-receptor antibodies (TRAbs) measured early in pregnancy irrespective of the thyroid function test profile.**

  If TRAbs are undetectable *they do not need to be repeated*.

  If TRAbs are positive *the patient will need to be seen by a consultant endocrinologist. The consultant obstetrician should also be informed. It is likely that further measurements of TRAbs will be required in these patients during pregnancy. Patients should be advised to deliver in hospital and the paediatricians should be informed at delivery. Additional ultrasound scans may be required and TSH/FT4/Total T3 on cord blood may be required (see "Managing Hyperthyroidism" section below).*

T4 Replacement and Pregnancy

Expect T4 requirements to increase by up to 50% by 20 weeks and then plateau. If TFTs are poorly controlled, growth scans should be performed in the third trimester

- ***Patients with established hypothyroidism***, the daily T4 dose should be increased by 25 micrograms when the pregnancy is confirmed. Thyroid function tests should be re-checked after approximately 2 weeks to ensure that a satisfactory FT4 level has been achieved (Free T4 16-21pmol/L with ideally TSH of less than 2 mU/L). A further increase in T4 dose may be required to achieve this "ideal" thyroid function test profile.
- ***Patients newly diagnosed with hypothyroidism whilst pregnant***, should have T4 treatment commenced immediately **with a starting dose of 100 microgram daily**. A further assessment of thyroid function tests should be performed after 2 weeks to ensure FT4 is ideally 16-21 pmol/L; TSH should be less than 2 mU/L. Further changes in T4 dose, followed by repeat thyroid function tests may be required to achieve this "ideal" biochemical profile.
- As a minimum, patients should have thyroid function tests performed once each trimester
- If TFTs are unstable refer to a Consultant obstetrician / Consultant Endocrinologist as early as possible as growth scans may be required.
- Women with stable, satisfactory thyroid function tests should be offered the opportunity to see a consultant obstetrician at some point during pregnancy.
- Reduce T4 treatment to pre-pregnancy dose at 2-6 weeks post-partum and recheck TSH/Free T4 6-8 weeks later

Hyperthyroidism and Pregnancy

Patients being treated with anti-thyoid drugs require careful monitoring during pregnancy as these drugs cross the placenta and interact with the fetal thyroid. Similarly, TSH receptor antibodies (TRAbs) in maternal blood, also cross the placenta and may give rise to intrauterine and neonatal thyrotoxicosis if present in high concentration. For these reasons it is essential to identify new cases of Graves' disease in pregnancy and also to assess TRAbs status in patients with previous Graves Disease who may be hypothyroid or euthyroid due to therapy with radioiodine, surgery or anti-thyroid drugs. All women with hyperthyroidism need to be seen by a Consultant Endocrinologist and a Consultant Obstetrician from early in pregnancy

Specialist Management of Hyperthyroidism in Pregnancy

- All women with hyperthyroidism in pregnancy should be seen by a Consultant Endocrinologist and a Consultant Obstetrician from early in pregnancy.
- Home delivery is not appropriate for women with Hyperthyroidism
- The aim is for good control of hyperthyroidism on the minimum dose of carbimazole(CBZ) / propylthiouracil (PTU) possible. For those with good control of thyrotoxicosis on doses of CBZ<15mg/day or PTU<150mg/day, the maternal and foetal outcome is usually good and unaffected by the thyrotoxicosis.
- **Any patient with active Graves Disease must have a TSH-receptor antibody (TRAbs) measurement carried out at booking (or pre-conception). irrespective of their thyroid function test profile.**

  Patients with detectable TRAbs

1. The Endocrinologist and Obstetrician should be informed of any patient with detectable TRAbs.
2. Women with detectable TRAb should be advised to deliver in hospital.
3. Further TRAbs measurements and ultrasound scans will probably be required, the frequency of which will be advised by the Endocrinologist and Obstetrician
4. Paediatricians should be informed on the woman's admission to labour ward.
5. Cord blood should be taken for TSH, FT4 and Total T3 at delivery and the baby should have a resting heart rate checked and remain in hospital for at least 24 hours. Further repeat TSH, Free T4 and total T3 in the neonate should be carried out on the advice of the Paediatricians.

CBZ/PTU therapy: Post Natal Management

- Many women will have stopped CBZ/PTU prior to delivery but if not, the baby's TFTs should be checked and the Paediatricians informed. If there are abnormalities the baby may need to remain in hospital (unlikely at doses of CBZ<15mg or PTU<150mg daily.)
- Many women will not require to return to their CBZ/PTU post-natal but all should be seen in the Endocrine Clinic 8-12 weeks post partum or sooner if they have symptoms.
- CBZ is safe in the breast feeding woman in doses at or below 15mg daily and PTU at or below 150mg daily.

Significance of an "Undetectable" TSH in Pregnancy

Some "normal" pregnancies are associated with a mild transient "physiological" hyperthyroidism during the first trimester. This is caused by very high levels of hCG, that have a mild stimulatory effect on the thyroid. In approximately 3% of pregnancies the TSH will be suppressed to <0.01mU/L and FT4/FT3 may be slightly elevated. It is essential to exclude Graves' disease in such pregnancies and as such TSH-receptor antibodies should be (TRAbs) measured and an endocrine and/or obstetric opinion sought.

Post- Partum Thyroiditis

This occurs in 5% of women within 2-6 months of delivery or miscarriage. It presents with non-specific symptoms such as tiredness, anxiety and depression. Typically the patient will initially have a hyperthyroid hormone profile, which will resolve or be followed by a transient hypothyroidism. Occasionally, thyroid function may not return to normal after postpartum thyroiditis. Persistent hypothyroidism may require treatment with thyroid hormone

- If a hyperthyroid profile is found (TSH <0.01 mU/L; FT4/FT3 raised) an endocrine opinion is warranted to differentiate post-partum thyroiditis from other causes of hyperthyroidism such as Graves' disease. A TRAbs measurement will be helpful.

Post-partum patients should have thyroid function tests checked at 8 - 12 weeks if they have:-

- Symptoms of hyper or hypothyroidism
- Goitre
- Previous history of post-partum thyroiditis
- Previous history of autoimmune thyroid disease
- Positive TPOAb

References

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Dr R Hughes **Consultant Obstetrician** **Dr A D Toft** **Consultant Endocrinologist**
Dr C Calderwood **Consultant Obstetrician** **Dr G J Beckett** **Consultant Clinical Biochemist**

Action Points

Hypothyroidism

Assess thyroid status:- Preferably prior to conception or at booking in the following situations

Known hypothyroidism	Type 1, Type 2 diabetes, Gestational Diabetes
Previous history of thyroid disorder	Family history of thyroid Disease
Features of thyroid disease.	Other autoimmune thyroid disorder

Hypothyroid patients should be offered an appointment with consultant obstetrician

Measure TRAbs in <u>all</u> patients with history of Graves disease (irrespective of thyroid status)
Patients with detectable TRAbs require special management. Inform Endocrinologist/Obstetrician as soon as possible.

Patients with established hypothyroidism should have T4 dose increased by 25 micrograms as soon as a positive pregnancy test is found. Further monitoring after 2 weeks and possible further changes in T4 dose may be required to ensure FT4 is 16-21 pmol/L; TSH <2 mU/L as quickly as possible.

Further checks on thyroid function test should be made at least once in each trimester
If TFTs are not stable contact consultant obstetrician, as a growth scan may be required .

Cut back T4 dose to pre-pregnancy dose 2-6 weeks post-partum

Hyperthyroidism

All women with hyperthyroidism in pregnancy should be seen by a Consultant Endocrinologist and a Consultant Obstetrician from early in pregnancy.

Home delivery is not appropriate for women with Hyperthyroidism

Measure TRAbs in <u>all</u> patients with Graves disease at booking (irrespective of thyroid status).
Patients with detectable TRAbs require special management, irrespective of their thyroid function test profile. Inform Endocrinologist and Obstetrician as soon as possible.

The aim is for good control of hyperthyroidism on the minimum dose of carbimazole(CBZ) / propylthiouracil (PTU) possible

Post-partum Thyroiditis

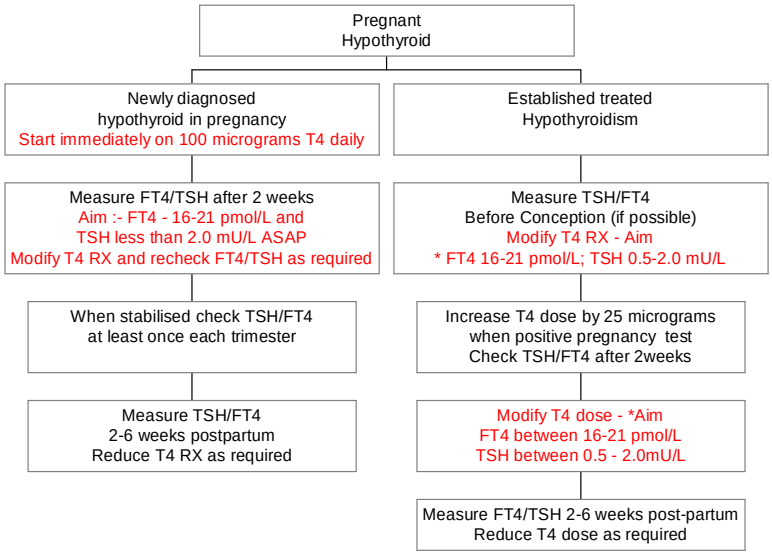
Post-partum patients should have thyroid function tests checked at 8 - 12 weeks if they have:-

- Symptoms of hyperthyroidism or hypothyroidism
- Goitre
- History of post-partum thyroiditis or thyroid disease
- Positive TPOAb

If a hyperthyroid profile is found (TSH <0.01 mU/L; FT4/FT3 raised) an endocrine opinion is warranted to differentiate post-partum thyroiditis from other causes of hyperthyroidism such as Graves' disease. A TRAbs measurement will be helpful for this.

Thyroid Disease and Pregnancy

Hypothyroidism in Pregnancy



* It is important to produce this test profile (especially a FT4 of 16-21 pmol/L) as soon as possible in the pregnancy and preferably before conception

Hyperthyroidism in Pregnancy