Clinical Guideline

THYROID DISEASE - HYPERTHYROIDISM PRECONCEPTION, IN PREGNANCY AND THE POSTNATAL PERIOD

SETTING Division of Women's and Children's Services / Division of Medicine

FOR STAFF Obstetricians, Endocrinologists & Midwives

PATIENTS Women preconception, in pregnancy and the postnatal period with thyroid disease

GUIDANCE

HYPERTHYROIDISM

Background

Hyperthyroidism complicates 1 in 500 pregnancies. Thyroid stimulating Hormone (TSH) levels usually fall in early normal pregnancy (due to an increase in hCG) and Free Thyroxine (fT4) may increase. Free Triiodothyronine (fT3) remains in the normal non-pregnant range.

This physiological "gestational hyperthyroidism" may be necessary to address the needs of the fetus and patients are seldom symptomatic and thus only very rarely need treatment. TSH and fT4 levels tend to stabilise in the second and third trimesters. TSH levels should not be used in isolation in pregnancy and should include assays of fT4 and fT3, as needed.

The Bristol laboratories agreed **normal trimestral reference ranges** in pregnancy in a woman without any pre-existing thyroid condition as follows:

	1st Trimester	2nd Trimester	3rd Trimester
TSH (mIU/L)	0.02-3.7	0.2-3.7	0.27-4.2
fT4 (pmol/L)	12.1-19.6	9.6-17.0	8.4-15.6

Hyperemesis gravidarum is commonly associated with transient biochemical thyrotoxicosis. This rarely needs treatment and typically resolves as the symptoms of hyperemesis settle. If concerns, please discuss with maternal medicine or endocrinology clinicians.

The majority of cases of hyperthyroidism in pregnancy are due to Graves' disease (an autoimmune condition caused by secretion of TSH receptor stimulating antibodies (TRAb)). Untreated women with hyperthyroidism have an increased rate of miscarriage, intra uterine growth restriction, pre-eclampsia, premature labour, stillbirth and perinatal morbidity. Evidence suggests that it may also lead to offspring neurodevelopmental disorders and mental health problems which become apparent later in life. For those women with good disease control, who are on anti-thyroid drugs or with previously treated Graves' disease in remission, the maternal

and fetal outcomes are usually good.

The use of anti-thyroid drugs peri-conception and in the first trimester of pregnancy to treat hyperthyroidism carries the risk of malformations. This would have been carefully discussed with women with pre-existing thyrotoxicosis by endocrinology team.

Reported malformations in Carbimazole users (3%–4%) include aplasia cutis congenital (absence of a portion of skin, often localised on the head), skull and facial malformations (choanal atresia; facial dysmorphism), defects of the abdominal wall and gastrointestinal tract (exomphalos, oesophageal atresia, omphalo-mesenteric duct anomaly), and heart defects such as ventricular septal defect. Propylthiouracil is associated with a slightly less frequent and severe congenital malformations (2%–3%) of urinary system, as well as malformations in the face and neck region (skin tags and such). For these reasons, Propylthiouracil is the drug of choice in peri-conception and in the first trimester until organogenesis is completed.

Both Carbimazole and Propylthiouracil (PTU) have the potential in high doses to cause fetal hypothyroidism and goitre.

TRAb must be assayed in all women with Graves' disease (including those not requiring any active anti-thyroid treatment during their pregnancy, as well as those previously definitively cured by surgery or radioiodine). TRAb should be measured at between 20 and 24 weeks gestation. Undetectable TRAb means that any risk to the fetus from possible trans-placental antibody transfer is negligible and these women can avoid the need for serial growth scans and fetal heart rate monitoring. Consequently these women can be discharged to community antenatal care for the remainder of their pregnancy with a standard letter explaining their results. The standard letter will be sent to GP, patient and community midwife by treating endocrinologist.

Pregnant women with active Graves' disease (on antithyroid drugs in pregnancy) and/or positive TRAb will be managed along the appropriate antenatal (fetal surveillance with USS and fetal heart rate assessment) and neonatal high risk pathway (see local neonatal guideline).

Fetal/neonatal thyrotoxicosis can occur in 1-5% of neonates as a result of trans placental passage of TRAb. A value >5 IU/L or 3 times the upper limit of normal in the mother indicates that the fetal thyroid may be strongly stimulated by TRAb passing through the placenta and hence fetal thyrotoxicosis is a possibility. If the baby is born with these antibodies, they may be hyperthyroid, a condition called neonatal Graves' disease. Symptoms typically develop within the first 2 weeks of life. This disorder lasts only a few weeks until the mother's antibodies are cleared away.

Graves' disease often improves with pregnancy, but can flare post-partum. Patients with autoimmune thyroid disease are also at increased risk of post-partum thyroiditis. Their thyroid function tests should be re-checked 6 weeks post-delivery.

Pre-pregnancy management

1. Achieve optimum control of thyrotoxicosis with the lowest dose of medication. If the patient is in remission and is not receiving any treatment she is unlikely to relapse in pregnancy.

2. Replace Carbimazole with PTU (5mg Carbimazole= 50mg PTU).

3. 'Block and replace' therapy is contraindicated in women who are planning pregnancy. Titration therapy with PTU should be used.

4. Avoid pregnancy for at least 6 months after treatment with radioiodine.

Antenatal Management

1. GP or Endocrinologist referral to the Joint Endocrine Antenatal Clinic.

2. Change to PTU ASAP if on Carbimazole in the first trimester (5mg Carbimazole= 50mg PTU). Women should be advised of a possible increased risk of hepatotoxicity with PTU and the option of switching to Carbimazole after the first trimester should be discussed.

3. Check TSH/ fT4 levels as soon as pregnancy is diagnosed. Aim to maintain TSH in the low normal range and fT4 at upper range of the reference range.

4. TRAb should be assayed in all women with a history of Graves' disease not requiring any active anti-thyroid treatment during their pregnancy, as well as those previously definitively cured by surgery or radioiodine, between 20 and 24 weeks gestation. Subsequently women should be reviewed in the endocrine ANC with the results to allow an endocrinology explanation and any outstanding obstetric issues to be addressed. If there are no other concerns then women with undetectable TRAb can be discharged to community or consultant antenatal care as appropriate for the remainder of their pregnancy.

5. Pregnant women with active Graves' disease (on antithyroid drugs in pregnancy) and/or positive TRAb will require assessment of fetal growth by ultrasound scan at around 28 and 36 weeks gestation (if uncontrolled hyperthyroidism/high TRAb titre refer to FMU to check for fetal goitre).

6. Pregnant women with active Graves' disease (on antithyroid drugs in pregnancy) and/or TRAb will require assessment for fetal tachycardia (with hand held Doppler or CTG) at 36 weeks gestation and weekly thereafter. Please refer to DAU if fetal heart rate is 160 beats per minute or more as this may indicate fetal thyrotoxicosis and early delivery may be advised.

7. If maternal hyperthyroidism is well controlled and there are no fetal concerns, await spontaneous labour/ induction of labour for post-maturity as per protocol for uncomplicated women.

Intrapartum Management

1. Routine management of labour

2. Inform Neonatologists after delivery (Babies of mothers with Graves' disease will be either medium or high risk and will need neonatal follow-up as per ***"protocol for infant of mother with thyroid disease"***)

Postpartum Management

1. Women who are not thyrotoxic in pregnancy, but are antibody positive, are at a higher risk of recurrence following delivery, and are sometimes advised commencing on Carbimazole 5 mg or PTU 50 mg once a day once the baby is born.

2. Women taking anti-thyroid medications prior to conceiving should be advised to revert to pre-pregnancy dose of anti-thyroid medication after delivery.

3. It is safe to breastfeed on PTU <200 mg/day and Carbimazole <20 mg/day.
4. Check TSH/fT4 at 6 weeks with GP
5. Follow up with Endocrinologist/ GP as appropriate

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Consultation Process
Antenatal working party

Ratified by Antenatal Working Party
Date: 20.5.2021
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RELATED DOCUMENTS

Neonatal Hyperthyroid Protocol: [redacted]

References

The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase (MD): The Endocrine Society; 2012
2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. THYROID Volume 27, Number 3, 2017. Severn Regional Consensus Group – Thyroid disease in Pregnancy 2017

SAFETY If patient is unwell or experiences acute symptoms, discuss with the Obstetric Registrar on call (contact via switchboard)

QUERIES Inpatient and ANC Matron ext [redacted]