Investigation and Management of babies born to mothers with thyroid disease

Please use this guideline in conjunction with the UHW obstetric guideline for the management of thyroid disease in pregnancy.

**Fetal Thyroid Physiology:** The fetal thyroid begins to concentrate Iodine at 12 weeks gestation and thereafter thyroid hormone concentrations increase with advancing gestation until 36 weeks. Both maternal thyroid hormones and anti thyroid drugs (ATD) can cross the placenta. Hence, a congenitally hypothyroid neonate is often protected from overt hypothyroid features due to transplacental passage of maternal hormone. However, inadequately treated maternal hyperthyroidism can result in fetal thyrotoxicosis and overtreatment with maternal anti thyroid drugs (ATD) may result in iatrogenic fetal hypothyroidism.

Inadequately treated maternal hypothyroidism is associated with adverse neonatal outcomes such as preterm birth and low birth weight. Also, thyroid hormones are known important factors for normal brain development in utero. Fetal thyrotoxicosis is rare and is associated with fetal tachycardia/cardiac failure, goitre, IUGR, low birth weight and preterm delivery.

**Maternal Hypothyroidism:** The prevalence of hypothyroidism during pregnancy is 0.3-0.5% for overt hypothyroidism (OH), with raised Thyroid Stimulating Hormone (TSH) and low T4 levels. Subclinical hypothyroidism (SCH) with raised TSH and normal T4 levels has a higher incidence of 2-3%. Thyroid autoantibodies are found in 5–15% of all women of childbearing age, and chronic autoimmune thyroiditis (Hashimotos disease) is the main cause of hypothyroidism during pregnancy. Determination of autoantibody titres, eg thyroid peroxidase antibodies (TPO-Ab) confirms the autoimmune origin of the disorder. These antibodies are not harmful to the fetus.

Other causes of maternal hypothyroidism include; post treatment for hyperthyroidism (using radioiodine ablation or surgery), surgery for thyroid tumours and hypothalamic/hypophyseal origin of hypothyroidism (rare). However, on a worldwide basis the most important cause of thyroid insufficiency remains iodine deficiency.

Babies born to mothers with Hashimoto thyroiditis are at low risk of developing transient hypothyroidism and very rarely hyperthyroidism. It is estimated that this risk may be as low as 1:180,000 or one baby every 30 years in a hospital the size of UHW. Moreover, neonates with transient congenital hypothyroidism will have a raised TSH which will be picked up by the routine neonatal blood spot screening and maternal TSH receptor blocking antibodies (TRAb) of affected neonates are usually strongly positive.

Pregnant women with a history of hypothyroidism have regular Thyroid Function Tests (TFT) to optimise therapy. TSH receptor antibodies (TRAb) are usually tested during pregnancy. Women with a history of Graves’ should have TRAbs tested.

Babies born to mothers with hypothyroidism

Check maternal autoantibodies,
   If TRAb negative (anti TPO may be positive or negative) and no history of previous treatment for Graves disease → routine newborn examination and blood spot screening only.

If a mother is TRAb positive in this or a previous pregnancy or is hypothyroid following treatment for Graves disease the neonate should be managed according to the maternal hyperthyroidism guideline.

**Maternal Hyperthyroidism:**

Maternal hyperthyroidism is common and complicates 0.1 – 0.4% of all pregnancies. Graves’ disease is the most common reason accounting for 85% of cases. Other causes include; single toxic adenoma, multinodular toxic goitre, thyroiditis, and rarely gestational hyperthyroidism and mutations in the TSH receptor. Women with Graves’ disease have TRAbs that can stimulate or inhibit the fetal thyroid. Inhibitory TRAbs may occasionally cause transient neonatal hypothyroidism in neonates of mothers with Graves’.

Pregnant women with hyperthyroidism require close observation of thyroid activity with fetal vigilance for tachycardia and goitre. Those with current Graves’ or a history of Graves’ require TRAbs measured at @36 weeks gestation. TRAbs often remain positive after treatment with radioactive Iodine or thyroidectomy. There is a positive correlation between the concentration of TRAb and the incidence of neonatal thyrotoxicosis.
Women who have a negative TRAb at 36 weeks and do not require ATDs have a very low risk of fetal or neonatal thyroid dysfunction.\textsuperscript{1,7} TRAb positive women need to be identified and the neonatal unit informed prior to delivery.

**Neonatal thyrotoxicosis (NT):** Neonatal thyrotoxicosis is mainly caused by the transplacental transfer of TSH receptor antibodies (TRAb) in Graves' and rarely Hashimoto's disease. Rarely, genetic mutations in the TSH receptor can cause neonatal hyperthyroidism—this should be suspected if there is a family history of thyrotoxicosis.

Neonatal thyrotoxicosis occurs in 1-10% of offspring of mothers with Graves'\textsuperscript{5}. However, the incidence can be as high as 20% if mothers require ATDs in the last trimester. Mortality is significant, between 12% and 20%, usually from cardiac failure. Onset is variable, from birth up to @10 days due to the effects of maternal ATDs wearing off quicker than maternal antibodies.\textsuperscript{5} Duration of neonatal thyrotoxicosis depends on the persistence of the maternal antibodies and usually remits after 8-20 weeks. Clinically, infants may have goitre, be irritable, tachycardic and have eye signs (please see Appendix 1). Neonates can be divided into a high or low risk group for developing NT.

**High risk**-Current maternal thyrotoxicosis on antithyroid medication (TRAb positive)

- Previous maternal thyrotoxicosis treated with radioactive iodine or surgery (TRAb positive)
- Family history of neonatal thyrotoxicosis? TSH receptor mutation
- Evidence of fetal thyrotoxicosis.

**Low risk**- Previous maternal thyrotoxicosis treated with antithyroid medication now off treatment and euthyroid (TRAb negative).

---

**Babies born to mothers with hyperthyroidism**

Confirm maternal TRAb status in pregnancy

- Careful examination for signs of hyperthyroidism at time of routine newborn examination or after birth if alerted by obstetric team of TRAb positive mother
- If any suspicion of clinical neonatal thyrotoxicosis (see Appendix 1) — Check TFT, TRAb and inform Consultant Neonatologist and Paediatric Endocrinologist
- If neonate well but at high risk (mother TRAb positive/TRAb unknown or FH of neonatal thyroid disease)
  - Observe for 48 hours on postnatal ward
  - Arrange for clinical examination and TFT, TRAb testing on day 5 – 10.
  - Advise parents of the signs of neonatal thyrotoxicosis and the need to contact the NNU if these develop in first 2 weeks of life and/or prior to review (see Appendix 2)
- If infant well and low risk (mother TRAb negative and no FH of neonatal thyroid disease) — No further action is required.

---

**References**

2. Ogundele M et al.: Arch Dis Child 2010; 95 When should we be conducting TFT in newborns and young infants
4. Evans C et al Ann Clin Biochem 2011: Transient congenital hypothyroidism due to thyroid stimulating hormone receptor blocking antibodies: a case series
5. Ogilvy-Stuart A L Arch Dis Child Fetal Neonatal Ed 2002;87:F165-F171 Neonatal thyroid disorders
6. David Peleg et al. 2002 Obstetrics and Gynaecology The Relationship Between Maternal Serum Thyroid-Stimulating Immunoglobulin and Fetal and Neonatal Thyrotoxicosis
Appendix 1

Features of neonatal hyperthyroidism/thyrotoxicosis

• Goitre

• CNS
  – Microcephaly
  – Jitteriness
  – Irritability, restlessness

• Eye signs
  – Periorbital oedema
  – Lid retraction
  – Exophtalmos

• CVS
  – Tachycardia,
  – Arrhythmia,
  – Congestive heart failure
  – Hypertension
  – Flushing, Sweating

• GI
  – Weight loss
  – Diarrhoea/Vomiting
  – Hepatosplenomegaly

• Haematology
  – Bruising, petechia, thrombocytopenia
  – Jaundice
PARENT INFORMATION LEAFLET

Signs of an overactive thyroid gland in your baby

If your baby develops any of the following problems in the first two weeks of life please contact the neonatal unit (telephone number 20742680).

Unsettled or irritability despite regular feeding
Jitteriness
Sweating
Staring eyes
Diarrhoea
Vomiting
Poor weight gain