Investigation and Management of babies born to mothers with thyroid disease

Please use this guideline in conjunction with the local 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 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 hyperthyroidism/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. Thyroid hormones are 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%. Autoimmune thyroiditis (Hashimotos disease) is the main cause of hypothyroidism during pregnancy. Determination of autoantibody titres, thyroid peroxidase antibodies (TPO-Ab), confirms the autoimmune origin of the disorder but does not help in guiding management of babies. 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). Worldwide 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. 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 should have regular Thyroid Function Tests (TFT) to optimise therapy. TSH receptor antibodies (TRAb) are usually tested during pregnancy at booking and 36 weeks, please see local obstetric guidelines.

**Management of babies born to mothers with hypothyroidism**

Check maternal TRAb status:

- **TRAb negative** – (anti TPO may be positive /negative) & no history of Graves disease → routine newborn examination and blood spot screening.
- **TRAb positive** – (this or previous pregnancies) or previous Graves Disease → manage according to hyperthyroidism guideline.
- **TRAb unknown** – Send TRAb (serum bottle). Contact biochemistry to request analysis as soon as possible → treat as TRAb positive until results known (This may be after discharge)

**Maternal Hyperthyroidism:**

Maternal hyperthyroidism occurs in 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. Mothers with hyperthyroidism, especially those with a current or previous history of Graves’ should have TRAbs measured at booking and at 36 weeks gestation. please see local obstetric guideline. TRAbs often remain positive after treatment with radioactive iodine or thyroidectomy. A positive TRAb at 36 weeks is associated with increased risk of neonatal thyrotoxicosis. Women who have a negative TRAb at 36 weeks have a very low risk of fetal or neonatal thyroid dysfunction. 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 Hashimotos’ 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’. 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 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 ATD (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 ATD now off treatment and euthyroid (TRAb negative).

### Management of babies born to mothers with Hyperthyroidism

1. Check maternal TRAb status

2. Careful examination at birth (if alerted as TRAb positive) or at time of newborn examination for signs of hyperthyroidism * (see Appendix 1)

<table>
<thead>
<tr>
<th>TRAb positive</th>
<th>TRAb unknown</th>
<th>TRAb negative</th>
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<tbody>
<tr>
<td>Observations for 48 hrs looking for signs of hyperthyroidism*</td>
<td>Take urgent blood for TRAb (serum sample)</td>
<td>and no family history of neonatal thyroid disease</td>
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<tr>
<td>If well after 48hrs:</td>
<td>1. Take urgent blood for TRAb (serum sample)</td>
<td>Routine newborn examination and blood spot.</td>
</tr>
<tr>
<td>1. Discharge with advice &amp; patient leaflet (see Appendix 2)</td>
<td>2. Treat as positive TRAb until result known. Contact biochemistry to request analysis as soon as possible. Result may come back after discharge. If negative and no family history of thyroid disease, follow up appointment can be cancelled.</td>
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<tr>
<td>2. Arrange clinical review and bloods (TFT &amp; TRAb (serum sample)) at 5-10 days</td>
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</tbody>
</table>

*Clinical suspicion of hyperthyroidism at any point (see Appendix 1) Take blood for TFT & TRAb (serum sample) & inform consultant Neonatologist and Paediatric Endocrinologist.
References


4. Ogilvy-Stuart A L Arch Dis Child Fetal Neonatal Ed 2002;87:F165-F171 Neonatal thyroid disorders


J Arthur and S Barr May 2016 to be reviewed May 2019
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 ……………………………).

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