Management of infants born to mothers with thyroid disease in pregnancy

Author: Dr Sadaf Kiani ST3
Supervisor: Dr Jennifer McGrath
Contact details: jennifer.mcgrath@nhs.net
sadaf.kiani1@nhs.net

Guideline History

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<td>2014</td>
<td>New guideline written by Dr S Leontiadi under supervision of Dr Peter Reynolds</td>
<td>Neonatal clinical Management group</td>
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<td>2022</td>
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Patients first • Personal responsibility • Passion for excellence • Pride in our team
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Introduction

The thyroid hormones have profound effects on growth, neurological development, metabolism and cardiovascular status.

- Under the influence of TRH, TSH stimulates thyroid to synthesise T4 & T3
- Only fT4, fT3 are active (= 1% of the total)
- fT4 is deiodinated to fT3 which is 3-4 times more potent

The thyroid gland in the fetus develops at 3 to 4 week of gestation but produces little thyroid hormone until 12 weeks. The fetus is dependent on the small amounts of T4 that can cross the placenta during the first trimester. During the second trimester the hypothalamic-pituitary axis becomes functional by 25 week of gestation and the TSH rises along with T3 from the thyroid gland. The full maturation of the hypothalamo-pituitary-thyroid feedback system happens in the third trimester. Therefore when babies are born the thyroid levels are a reflection of the fetal thyroid production.

At birth there is a TSH surge which results in high T4 and T3 levels. TSH should return to normal within 2-3 days of birth, followed by T3 and T4. TFTs should be interpreted within the clinical context and with caution, particularly within the first 3 days of life.

- Maternal TSH & T3 do not cross the placenta (poor permeability and placenta deiodinases)
- T4 crosses the placenta during the first trimester but this reduces significantly with increasing gestational age. At term only if the fetus is athyroid, a small amount of T4 can cross the placenta.
- Carbimazole, propythiouracil, thyroid stimulating immunoglobulins (TSIs) and thyroid inhibitory antibodies cross the placenta.

When discussing with parents

When exploring the maternal history of thyroid disease, it is important to delineate which infants are at risk. If the answer to any of the following are positive, then the infant should be considered high risk:

- “Have you ever been treated with radioiodine or had your thyroid removed?”
- “Have you ever been given treatment to lower the level of your thyroid hormone?”
- “Have you ever been told you have an overactive thyroid or had tests for this?”

Maternal Hypothyroidism

- Establish the aetiology (e.g. history, maternity badger notes, Winpath or contact GP)
- Maternal hypothyroidism:
1. **Secondary to congenital aplasia/ hypoplasia**,  
There is only a slightly increased risk of hypothyroidism to the baby.  

*Blood spot test will suffice.*

2. **Secondary to Hashimoto thyroiditis**  
Maternal inhibiting antibodies (& rarely stimulating antibodies) can cross the placenta.  

Infant can develop transient hypothyroidism and rarely hyperthyroidism  

*Clinical review (Face to face/Telephone consultation) / TFTs on day 10-14 (usually in Neonatal Rapid Access Clinic after phlebotomy clinic)*

3. **Secondary to treatment for Graves’ disease**  
Maternal Thyroid stimulating immunoglobulins (TSIs) continue to be produced even after ablation or radioiodine and cross the placenta.  

*Infant is at risk of thyrotoxicosis and should be managed as below.*

### Maternal Hyperthyroidism

- The prevalence of Graves’ disease in pregnant women is 2/1000.  
- Neonatal Graves’ disease develops in approximately 1 to 5 % of infants born to mothers with Graves hyperthyroidism and is caused by transplacental passage of maternal stimulatory thyrotropin receptor antibodies (TRAbs).  
- In babies who are exposed to high titres of TRAbs, hyperthyroid symptoms typically present at birth.  
- However, the infant may instead have hypothyroidism following delivery, depending on the balance of the maternal stimulatory TRAbs and maternal antithyroid drug (if given).  
- Neonatal Graves’ hyperthyroidism resolves spontaneously within 3-12 weeks after birth as the maternal TRAbs disappears from the infant’s circulation.

Neonatal Graves’ disease can range from mild and self-limiting to severe and life-threatening. Graves’ disease can occur in infants born to mothers who have previously had Graves’ disease but have had definitive treatment for this in the past.

TRAbs crosses the placenta and measuring cord TRAbs level is worthwhile as cord TRAbs levels correlates with the risk of developing hyperthyroidism in the neonatal period.

- Negative or undetectable TRAbs conversely indicate an extremely low risk of developing neonatal Graves disease.
Measuring cord TFTs at birth however does not correlate with thyroid function in the neonatal period, therefore it is not recommended to monitor TFTs before day 3 of life.

The pattern of hyperthyroidism in preterm infants is like that of their term counterparts and a similar pattern of monitoring at risk preterm infants is advised.

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**Infants at high risk include those with:**

- Positive maternal TRAbs in pregnancy
- Hyperthyroidism with unknown TRAbs (mother currently hypo/hyper/euthyroid)
- Family history of TSH receptor mutation
- Current or previous antenatal Graves disease
- Signs of neonatal thyrotoxicosis

**Signs and symptoms of neonatal thyrotoxicosis**

- Background history of foetal tachycardia, advanced bone age, foetal goitre
- Irritability, jitteriness and restlessness
- Small fontanelle, warm/moist skin, hyperthermia
- Poor feeding, poor weight gain, increased frequency of bowel movements
- Tachycardia and arrhythmia (can lead to cardiac failure)
- IUGR, goitre and non-immune hydrops.
- Systemic and pulmonary hypertension
- Eye signs (staring, lid retraction) may be present in the absence of maternal exophthalmos.
High risk infants should be managed as below (also see flowchart)

At birth:
- Cord blood should be sent for TRAbs after delivery.
- If negative, infant is considered low risk and routine newborn care is advised.

On day 1 of life:
- If cord blood for TRAbs was not sent, then send infant TRAbs
- Assess the infant to look for signs/symptoms of hyperthyroidism.
- At-risk babies who are well can be discharge home after 48 hours of observation including HR, temperature, RR and feeding.
- Parents must be advised of the signs and symptoms of thyrotoxicosis and an information leaflet should be given to parents and following follow up plan put in place.
- Consider a face-to-face review on D3-5 if felt to be clinically required.

On day 10-14 of life:
- In babies with positive TRAbs: TFTs in phlebotomy clinic (Monday am) on day 10-14.
- This should be followed by a face-to-face review in the NRAC clinic the following day (Tuesday pm) where the results of the blood tests can be shared with the parents and the baby can be clinically reviewed.

(ALTERNATIVELY: instead of the face-to-face review in NRAC clinic, a phone review by the ‘clinic registrar’ can occur on the Tuesday pm where the blood test results can be discussed and the wellbeing of the baby ascertained by phone.)

If the infant tests positive for TRAbs with normal TFTs:
- They will need further review at 2-3 months in neonatal consultant clinic and repeat TFTs if symptomatic at any point.

If TFTs demonstrate hyperthyroidism:
- Discuss with Consultant. The infant should be admitted for cardiovascular and temperature monitoring as well as feeding support.
- Treatment with Carbimazole may be indicated if signs/symptoms of neonatal hyperthyroidism exist. Discuss with paediatric endocrinologist
Management of high risk infants: flowchart

At birth
Please send cord TRAbs

Day 0-1 of life
NIPE/physical examination and send TRAbs if cord blood not sent. Monitor for 48 hours prior to discharge.

Day 10-14

TRAbs positive: TFTs in Phlebotomy clinic and physical review in NRAC clinic the following day.
Consider NRAC phone consultation as alternative.

Abnormal TFTs- Discuss with consultant.
Arrange admission of the baby for observations and monitoring.

Positive TRAbs and normal TFTs at D10-14:
-Neonatal consultant outpatient clinic review at 2 months.

If abnormal TFTs or clinical manifestations of thyrotoxicosis at any point, discuss with attending / HDU or TC

If negative cord or infant TRAbs, this is now a low risk infant.
Breastfeeding

Should be recommended and supported for women on thyroxine or any antithyroid medication. Women may safely breastfeed on doses of carbimazole below 15 mg/day or PTU below 150 mg/day. Discuss if they are on higher doses.
2. **Supporting References**

1. A L Ogilvy-Stuart, Neonatal thyroid disorders; ADC Neonatal Ed 2002
2. Shiri B et al, Neonatal thyroid function; neoReviews 2010
5. British Thyroid Association, UK guidelines for the use of thyroid function tests, July 2006
3. Supporting relevant trust guidelines

4. Guideline Governance

a. **Scope**

   This guideline is relevant to all staff caring for babies across neonatal intensive care, transitional care and maternity.

b. **Purpose**

   i. This guideline aims to facilitate a common approach to the management of babies admitted under neonatal care. At times deviation from the guideline may be necessary, this should be documented and is the responsibility of the attending consultant.

   ii. This guideline is subject to regular review to ensure ongoing evidence based practice.

c. **Duties and Responsibilities**

   It is the responsibility of health care professionals involved in the care of newborn patients to be familiar with the contents of this guideline.

d. **Approval and Ratification**

   This guideline will be approved and ratified by the Neonatal Guidelines Group.

e. **Dissemination and Implementation**

   i. This guideline will be uploaded to the trust intranet ‘Neonatal Guidelines’ page and thus available for common use.

   ii. This guideline will be shared as part of ongoing education within the Neonatal Unit for both medical and nursing staff.

   iii. All members of staff are invited to attend and give comments on the guideline as part of the ratification process.

f. **Review and Revision Arrangements**

   a. This policy will be reviewed on a 5 yearly basis.

   b. If new information comes to light prior to the review date, an earlier review will be prompted.

   c. Amendments to the document shall be clearly marked on the document control sheet and the updated version uploaded to the intranet. Minor amendments will be ratified through the Neonatal Guidelines Group. A minor amendment would consist of no major change in process, and includes but is not limited to, amendments to documents within the appendices.
### g. Equality Impact Assessment

#### Background
- Who was involved in the Equality Impact Assessment

#### Neonatal guidelines group

#### Methodology
- A brief account of how the likely effects of the policy was assessed (to include race and ethnic origin, disability, gender, culture, religion or belief, sexual orientation, age)
- The data sources and any other information used
- The consultation that was carried out (who, why and how?)

#### All patient and staff groups considered

#### Key Findings
- Describe the results of the assessment
- Identify if there is adverse or a potentially adverse impacts for any equalities groups

#### No evidence of discrimination

#### Conclusion
- Provide a summary of the overall conclusions

#### Guideline fit for purpose

#### Recommendations
- State recommended changes to the proposed policy as a result of the impact assessment
- Where it has not been possible to amend the policy, provide the detail of any actions that have been identified
- Describe the plans for reviewing the assessment

#### 3 Yearly reviews
h. **Document Checklist**

To be completed (electronically) and attached to any document which guides practice when submitted to the appropriate committee for approval or ratification.

**Title of the document:**

**Policy (document) Author:**

**Executive Director:**

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<td>Are local/organisational supporting documents referenced?</td>
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**Section 1 Organisational Policy**

Current Version is held on the Intranet: **December 2015**

First ratified: **December 2015**

Review date: **December 2025**

Issue: **2**

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**Committee Approval (Neonatal Guidelines Committee)**

If the committee is happy to approve this document, please complete the section below, date it and return it to the Policy (document) Owner

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<th>Name of Chair</th>
<th>M. S. Edwards</th>
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**Ratification by Management Executive (if appropriate)**

If the Management Executive is happy to ratify this document, please complete the date of ratification below and advise the Policy (document) Owner

Date: n/a