GUIDELINE

Thyroid Disorder: Care of the Infant Born to Women with Thyroid Disorders

Scope (Staff):	Midwifery, Nursing and Medical Staff
Scope (Area):	Neonatal Units KEMH and PCH, KEMH Postnatal Wards

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this disclaimer

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Aim

To outline the care of the infant born to a mother with a Thyroid disorder.

Risk

Over-production of thyroid hormones can result in life-threatening consequences and significant neuro-developmental damage.

Background

- Maternal hyperthyroidism occurs in 0.1 – 0.4% of all pregnancies (Mandel SJ et al 2001). Grave's 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.
- Neonatal thyrotoxicosis or Neonatal Grave's Disease occurs in 1-5% of women with Grave's disease (Evans C et al 2011; Weetman AP et al 2000). However, the incidence can be as high as 20% if mothers require antithyroid drugs (ATDs) in the last trimester. Onset is variable, from birth up to 10 days due to the effects of maternal ATDs wearing off faster than maternal antibodies (Evans C et al 2011).
- Duration of neonatal thyrotoxicosis depends on the persistence of the maternal antibodies and usually remits after 8-20 weeks.
- Grave's disease treatments (medical / surgical / radio-iodine ablation) render the mother hypothyroid. However, TSH Receptor Antibodies (TRAb) may still be produced and cross the placenta.
- In mothers with Grave's Disease, TRAb titres should performed antenatally by 22nd week of pregnancy to assess risk for neonatal thyrotoxicosis. (De Groot L et al 2012.) These infants are at high risk of neonatal thyroid dysfunction and require TFT's and TRAb status at birth or shortly thereafter.

Key points

- All infants born to hyperthyroid women must have early testing of TSH receptor antibodies (TRab) and Thyroid Function Tests (TFT's) to identify biochemical thyrotoxicosis. Perform on cord blood or infant blood as soon as possible after birth for TRab. TFTs are indicated on day 3-5 if TRab is positive.
- Infants considered **High Risk of neonatal Grave's disease**
  - Current maternal thyrotoxicosis treated with ATDs (TRAb +)
  - Previous maternal thyrotoxicosis treated with radioactive iodine or surgery (TRAb +)
  - Family history of neonatal thyrotoxicosis/TSH receptor mutation
  - Evidence of fetal thyrotoxicosis
  - Unknown status of maternal TRAbs

- Infants considered **Low Risk of neonatal Grave's disease**
    - Previous maternal thyrotoxicosis treated with ATDs now off treatment and euthyroid (TRAb negative).
- If the infant is hyperthyroid, anti-thyroid medication and beta-blocker therapy should be considered in consultation with the Endocrinology Consultant at PCH.

Predictors of Neonatal Grave's Disease

- Positive maternal TRAb level at 20 weeks gestation: particularly if TRAb > 3x normal (or >5IU/L) (Abeillon-du Payrat, 2014).
- Fetal US findings of hypo or hyperthyroidism (Fetal goitre- occurs in both hyper & hypothyroidism; Delayed fetal bone maturation – occurs in hypothyroidism; Fetal HR >160 -occurs in hyperthyroidism).
- Post-natal TFT: rising free T4 and free T3 in the first week, low TSH <0.90mU/L on day 3-7 (Banige, M; Research Group for Perinatal Dysthyroidism (RGPD) Study Group, 2018)

Table 1: Natural history of infant thyroid function according to maternal anti-thyroid drug (ATD) treatment in maternal Grave's disease (TRAb positive)

	No maternal ATD treatment	**Maternal ATD treatment**
In utero	○ Hyperthyroid	○ Hypothyroid
Birth – Day 7	○ Hyperthyroid	○ Euthyroid, OR ○ Hypothyroid, transient
Day 7-14	○ Hyperthyroid	○ Hyperthyroid
Up to 12 weeks	○ Monitor for TRAb clearance ○ Euthyroid by 2 weeks in low positive maternal TRAb ○ Watch for central hypothyroidism	

Neonatal Hyperthyroidism

- Neonatal thyrotoxicosis is a rare but potentially life-threatening condition. It occurs as a result of trans-placental passage of TRAb - usually due to active maternal Grave's disease and may be associated with significant morbidity and mortality if unrecognised or inadequately treated. Refer to Appendix 2: High risk of Neonatal Thyrotoxicosis Pathway

Table 2: Features of Neonatal hyperthyroidism/ thyrotoxicosis

- **Goitre**
- **Eye signs**
  - Periorbital oedema
  - Lid retraction
  - Exophthalmos
- **CVS**
  - Tachycardia,
  - Arrhythmia,
  - Congestive heart failure
  - Hypertension
  - Flushing, Sweating
- **CNS**
  - Microcephaly
  - Jitteriness
  - Irritability, restlessness
- **GI**
  - Weight loss
  - Diarrhoea/Vomiting
  - Hepatosplenomegaly
- **Haematology**
  - Bruising, petechia, thrombocytopenia
  - Jaundice

Management of Neonate at risk of Grave's Disease

- In all neonates check vital signs 6hourly and look for signs of hyperthyroidism.
- If any suspicion of clinical neonatal thyrotoxicosis (Table 2), check TFT, TRAb and inform Neonatologist.
- In High-Risk infants:
  - Check TRAb in cord blood or in the infant soon after birth.
  - Minimum 48h stay, even if asymptomatic.
  - Arrange clinical examination and TFT on day 3-5, and TFT on day 7 and day 10-14 of life.
  - Advise parents of the signs of neonatal thyrotoxicosis and the need to contact their GP if these develop in the first 2 weeks of life and/or prior to review.
  - If biochemically hyperthyroid, Paediatric endocrinologist consultation should be requested.
- In Low-risk infants:
  - Test infant TFTs and TRAbs only if clinical concerns.

Breastfeeding Advice for Mothers with Hyperthyroidism

- Mothers can breast feed with carbimazole dose <20mg/day, PTU <450mg/day; at lowest effective dose (2017 Guidelines for the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum, 2017)
- Moderate doses of carbimazole (eg. carbimazole 20-30mg daily) are also shown to be safe during breastfeeding
- If maternal carbimazole dose >20mg daily or PTU >450mg/day, check infant TFTs at 1 and 2-3 months (Seek pharmacy/endocrinology advice)

- Radio-iodine treatment is an **absolute contraindication to breastfeeding**.

Follow-up of the Neonate at Risk of Hyperthyroidism

- Regular monitoring of Free T3, FreeT4 and TSH is required for infants with congenital hyperthyroidism– normally through Endocrinology Dept, PCH.
- Infants who are clinically well and discharged early in the postnatal period can be followed up by their GP. See GP Referral Letter 'Neonate Managed for Maternal Thyroid Disorder'
- There is risk of recurrence in future pregnancies.

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Useful resources

GP Referral Letter for 'Neonate Managed for Maternal Thyroid Disorder'

This document can be made available in alternative formats on request.

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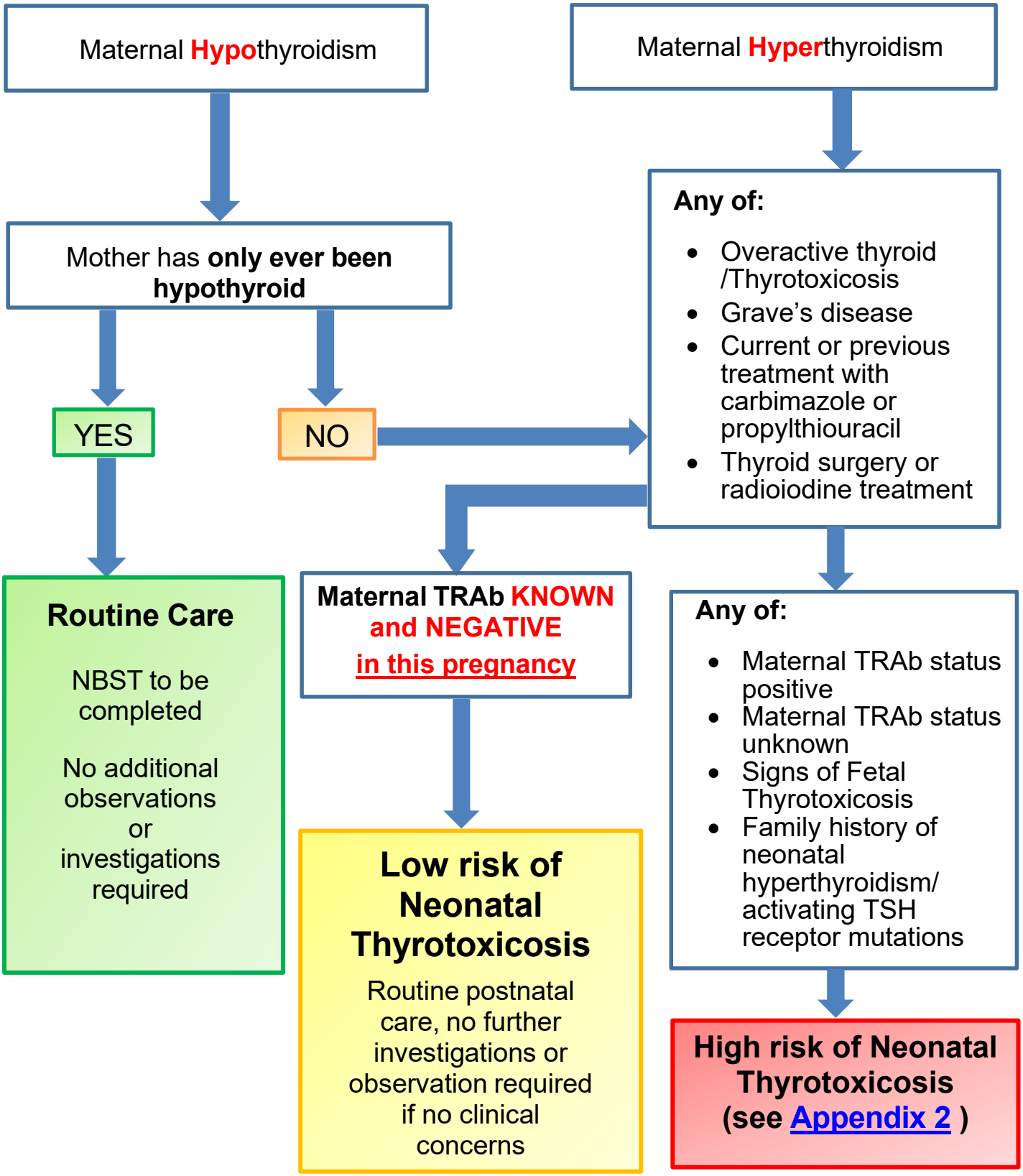
Appendix 1: Postnatal Care of Infants born to a mother with Thyroid Disease



Features of neonatal hyperthyroidism/thyrotoxicosis

Goitre; **CNS** – microcephaly, jitteriness, irritability, restlessness; **Eye** - Periorbital oedema, Lid retraction, Exophthalmos; **CVS** – Tachycardia, Arrhythmia, Congestive heart failure, Hypertension, Flushing, Sweating; **GI** - Weight loss, Diarrhoea/Vomiting, Hepatosplenomegaly; **Haematology** - Bruising, petechia, thrombocytopenia, Jaundice

Appendix 2: High Risk of Neonatal Thyrotoxicosis Pathway

- Maternal TRAb status **POSITIVE** or **UNKNOWN**
- SIGNS of **fetal thyrotoxicosis**
- FAMILY HISTORY of **neonatal hyperthyroidism / activating TSH receptor mutations**

Perform TRAb on cord blood **OR** on infant blood **ASAP** following birth. Sample must be sent in serum sample (red top) tube only.

Observe for minimum 48 hours **OR** until TRAb results available

Cord or infant **TRAb POSITIVE**

Discuss with endocrinology

Cord or infant **TRAb NEGATIVE**
Low risk infant, no further follow up required

REPEAT INFANT BLOOD TESTS:

- **Day 3-5:** TSH, fT4, fT3. If normal, discuss with endocrinology regarding discharge and follow-up
- **Day 7:** TSH, fT4, fT3
- **Day 10-14:** TSH, fT4, fT3

OBSERVE FOR:

- **RISING** fT4 and fT3: Carbimazole treatment if clinically significant hyperthyroidism
- **LOW** fT4: consider thyroxine (usually transient)