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

Contents

Aim 2
Risk 2
Background 2
Key points 2
Predictors of Neonatal Grave's Disease 3
Neonatal Hyperthyroidism 3
Management of Neonate at risk of Grave's Disease 4
Breastfeeding Advice for Mothers with Hyperthyroidism 4
Follow-up of the Neonate at Risk of Hyperthyroidism 5
Appendix 1: Postnatal Care of Infants born to a mother with Thyroid Disease 7
Appendix 2: High Risk of Neonatal Thyrotoxicosis Pathway 8

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.

References

1. Mandel SJ, Cooper JS. J Clin Endocrinol Metab 2001;86(6):2354-2359. The use of antithyroid drugs during pregnancy and lactation.
2. Evans C et al Ann Clin Biochem 2011;48(Pt 4):386-90. Transient congenital hypothyroidism due to thyroid stimulating hormone receptor blocking antibodies: a case series.
3. Weetman AP. N Engl J Med 2000;343(17):1236-1248. Graves' disease.
4. De Groot L et al J Clin Endocrinol Metab 2012;97(8):2543-65. Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline.
5. Ogilvy-Stuart AL. Neonatal Thyroid Disorders. **Archives of disease of childhood**. 2002; 87:f165-171
6. British Thyroid Association. **UK guidelines for the use of thyroid function tests**. July 2006; Extensive guidelines for the use by patients, GPs, and hospital doctors.
7. Management of Neonates Born to Mothers With Graves' Disease. van der Kaay. 4, 2016, **Pediatrics**, Vol. 137
8. Polak M, Legac I, Vuillard E, Guibourdenche J, Castanet M, Luton D. Congenital hyperthyroidism: the fetus as a patient. **Horm Res**. 2006;65(5):235–242
9. Abeillon-du Payrat, J. s.l. Predictive value of maternal second-generation thyroid-binding inhibitory immunoglobulin assay for neonatal autoimmune hyperthryoidism. **Eur J Endocrinol**, Oct 2014;171(4):451-60. doi: 10.1530/EJE-14-0254.
10. Leger. Management of Fetal and Neonatal Graves' Disease. 2017, **Horm Res Paediatr**.
11. Banige, M. Prediction of Neonatal Hyperthyroidism.; Research Group for Perinatal Dysthyroidism (RGPD) Study Group. 2018, **J Pediatrics**, p. 197:249. Epub 2018 Mar 28.
12. 2017 Guidelines for the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. **Thyroid** 2017;27(3).
13. UpToDate [Internet]. Wassner, A & LaFranchi, S. Evaluation and management of neonatal Graves disease. Available from: https://www-uptodate-com.pklibresources.health.wa.gov.au/contents/evaluation-and-management-of-neonatal-graves-disease?search=Evaluation%20and%20management%20of%20neonatal%20Graves%20disease&source=search_result&selectedTitle=1%7E9&usage_type=default&display_rank=1

Useful resources

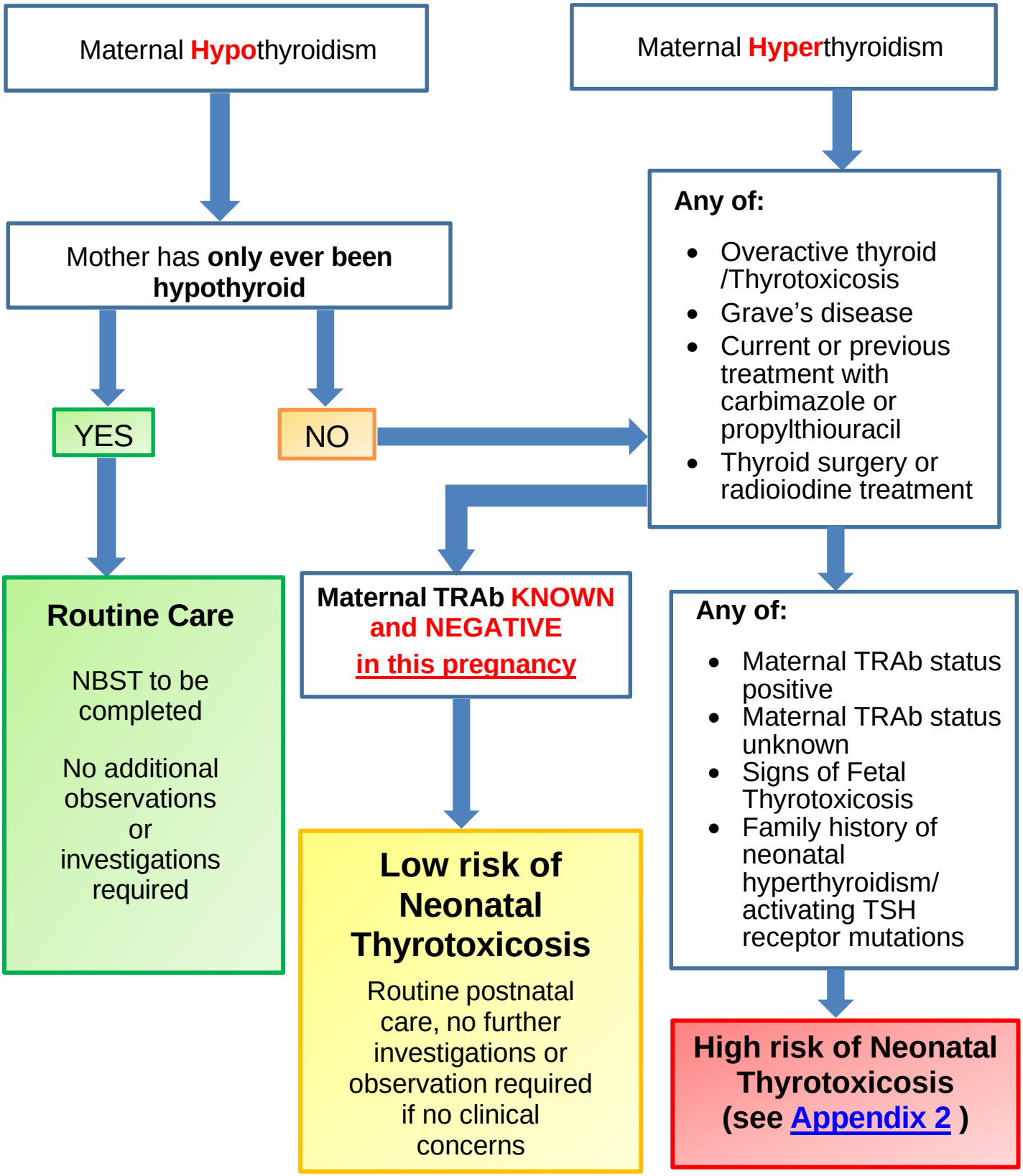
GP Referral Letter for 'Neonate Managed for Maternal Thyroid Disorder'

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

Document Owner:	Neonatology		
Reviewer / Team:	Neonatology Coordinating Group and conjunction with PCH Endocrinology		
Date First Issued:	December 2013	Last Reviewed:	April 2025
Amendment Dates:		Next Review Date:	30th April 2028
Approved by:	Neonatology Coordinating Group	Date:	30th April 2025
Endorsed by:	Neonatology Coordinating Group	Date:	
Standards Applicable:	NSQHS Standards:  Child Safe Standards: 1,10		

Printed or personally saved electronic copies of this document are considered uncontrolled

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