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

This document outlines the care of the infant born to a mother with thyroid disease.

Risk

Hormones produced by the thyroid gland affect all aspects of an infant's growth and development. Inadequate or over production of these hormones can result in life-threatening consequences and significant neuro-developmental damage. Surveillance of maternal thyroid function and antibody status, as well as neonatal thyroid function will minimise long term adverse outcomes in the infant.

Background

- Thyroid hormones (T3 & T4) are critical for brain and somatic development as well as regulation of metabolism.
- The hypothalamo-pituitary axis controls activity through sensitive feedback interactions between thyrotropin-releasing hormone (TRH), thyroid stimulating hormone (TSH) and production of T3 & T4.
- During pregnancy there is an increased demand for thyroid hormone synthesis and iodine requirements
    - Iodine is essential for normal thyroid function; however, iodine deficiency is relatively common.
- The foetus is dependent on transplacental passage of maternal iodine and T4. Maternal T3 does not cross the placenta. The foetus is able to convert T4 to T3 (through de-iodinisation), but this only really takes affect after the first trimester of pregnancy.

Conditions which may impact on neonatal thyroid status include:

- Gestational and postnatal age
- Medication
- Maternal hypothyroidism (untreated)
- Maternal iodine deficiency
- Maternal hyperthyroidism / presence of TSH-receptor antibodies
- Congenital hypothyroidism.

Term Infants

- TSH levels rise quickly after birth (60-80 mU/L), falling to around 20 mU/L at 24 hours and decline further to a steady state of 6-10 mU/L at one week of age.
- The initial surge in TSH stimulates thyroidal T4 secretion, resulting in serum T4 and T3 concentration to peak at 24-36 hours of life. T3 and T4 levels then gradually fall in the first month to that of near adult levels.

Preterm Infants

- Preterm infants follow the same pattern of TSH surge and decline, although less pronounced. Normal range levels are normally expected after the first week of age.
- In the more preterm infants (< 30 weeks), T4 falls in the first week of life before gradually rising, overlapping the normal range expected in term infants by 3-6 weeks.
    - Conditions such as Respiratory Distress and exposure to medications (glucocorticoids and dopamine) may reduce TSH production.

Key points

- Thyroid Function Tests (TFT) performed immediately after birth can be difficult to interpret, given the complexity of TSH surge in preterm and term infants.
- Newborn Blood Spot Screening Test (NBST) (previously known as Guthrie test) detects **elevated TSH** - therefore detecting only **primary hypothyroidism**.
    - Endocrinology department at PCH is advised of abnormal results.
- TFT results in preterm infants should be interpreted with caution as an immature hypothalamo-pituitary axis results in a delayed TSH surge and neonatal hypothyroidism that may only be detected after several weeks. Consultation with PCH endocrine department is advised with repeated screening.
- Treatment for neonatal hypothyroidism (with Thyroxine) should be commenced as soon as possible, as delay can result in irreversible neuro-cognitive damage.
- Neonatal thyrotoxicosis is a rare but potentially life-threatening condition. It occurs as a result of trans-placental passage of TSH receptor antibodies - usually due to active maternal Graves' disease.
    - Infants of mothers with Graves' disease should have early testing of TFT's and TSH receptor antibodies as this may identify a biochemical thyrotoxicosis. Anti-thyroid medication and beta-blocker therapy should be considered in consultation with Endocrinology Consultant at PCH.

Maternal Thyroid Disease - Hypothyroidism

Hashimoto's autoimmune thyroiditis

- Most common cause (incidence 2.5%). Presents in late childhood/early adulthood with clinical signs; presence of serum antibodies against thyroid antigens; and appearance on ultrasound.

Infant of a mother with auto-immune Hashimoto thyroiditis

- Trans-placental passage of (inhibitory) TSH receptor antibodies (Rc Ab) may produce transient hypothyroidism in the newborn.
    - Low levels of maternal TSH Rc Ab indicates low risk and screening via the NBST is sufficient.
    - If maternal titres are high or unknown, neonatal TSH / FT4 (free T4) levels should be checked at 7-10 days.

Medically / surgically treated Graves' disease (previous hyperthyroidism)

- Graves' disease treatments (medical / surgical / radio-iodine ablation) render the mother hypothyroid. However, TSH Rc Ab's may still be produced and cross the placenta. TSH Rc Ab titres should be checked in the 3rd trimester

Infant of a mother with hypothyroidism secondary to treated Graves' disease:

- These infants are at high risk of neonatal thyroid dysfunction and require TFT's and TSH Rc Ab status checked at birth or shortly thereafter.

Untreated maternal hypothyroidism

- Associated with adverse outcomes, including miscarriage, premature & still birth, poor growth and long-term neuro-cognitive impairment.
- If detected antenatally and adequately medicated with Thyroxine, there should be no foetal impact. TSH screening as part of the NBST is sufficient.

Iodine deficiency

- The commonest cause of hypothyroidism in the developing world, due to inadequate dietary intake (despite supplementation of staple foods). The World Health Organisation recommends a daily iodine intake of 150 μg/day, increasing to 200-250 μg/day during pregnancy and lactation.

Maternal congenital hypothyroidism

- Most cases are due to thyroid aplasia, ectopic thyroid tissue and dyshormonogenesis. The mother will be on regular thyroid replacement.
- If the infant inherits the condition (risk 2-5%) their TSH level will be elevated in an attempt to stimulate the absent/deficient gland.

Infant of a mother with congenital hypothyroidism

- In most cases (thyroid aplasia or ectopic thyroid tissue), NBST will detect elevated TSH (risk of hypothyroidism).
- In the rare case of hypothalamic-pituitary disorders, TSH levels will be low and will NOT be detected by the NBST. Isolated deficiency of TSH is rare.

Maternal Thyroid Disease - Hyperthyroidism

Autoimmune Graves' Disease

- Maternal hyperthyroidism is mostly caused by auto-immune Graves' disease.
  - Neonatal Graves' disease occurs in around 1-5% of babies born to mothers with Graves Disease, due to the trans-placental passage of TSH Rc Ab.
- It is recommended that all women with active Graves' disease or a history of previously medically or surgically treated Graves' disease have TSH Rc-Ab titres checked at 28-32 weeks gestation.

Infant of a mother with Graves' disease

- Infants may be hyperthyroid or hypothyroid at birth depending on the balance of maternal stimulating or inhibitory antibodies and anti-thyroid drug effect.

- **All babies born to hyperthyroid women need to have their thyroid function (TSH & Free T4) and TSH Rc Ab status checked at birth (cord blood) or shortly thereafter.**

Neonatal Thyroid Disease

Congenital Hypothyroidism

- Incidence 1:2500 to 1:4000 live births. In Western Australia, 8-12 new cases annually. Early diagnosis is critical to prevent irreversible neuro-developmental abnormalities.
- NBST will detect increased TSH levels (above 13mU/L).
  - Infants with initial TSH screening results of 13-30mU/L have a repeat NBST collected as the first step. Only those infants with a repeat TSH >8 mU/L are referred to PCH Endocrinology for follow-up.
  - Infants with initial TSH screening results > 30mU/L are referred directly to PCH Endocrinology for immediate recall and assessment (about 10%).
  - In very low birth weight and extremely low birth weight infants a second and sometime third screen at 2-4 weeks postnatal age should be performed to exclude primary hypothyroidism with a delayed TSH rise. See Newborn Blood Spot Screening Test.
- Congenital hypothyroidism is associated with an increased risk of congenital heart disease (10% vs 3% risk in normal population), particularly pulmonary stenosis, ASD and VSD.

Clinical Signs of Hypothyroidism in the Neonate

- Goitre
- Intrauterine growth restriction
- Prolonged jaundice
- Poor weight gain
- Temperature instability
- Oedema
- Large fontanelles
- Constipation
- Umbilical hernia
- Bradycardia
- Microcephaly
- Poor feeding
- Inactivity, sleepy

NOTE: Pendred Syndrome can cause congenital hypothyroidism and sensori-neural deafness arising from abnormal transport protein (pendrin) involved in iodine transport and cochlear function.

Causes of Hypothyroidism in the Neonate

Permanent causes:

- Dysgenesis (80-90%)
  - Ectopic (45-50%).
  - Agenesis (35-40%).

- Dyshormonogenesis (10-20%) - includes Pendred Syndrome.
- Other (5%) - includes TSH receptor mutations.

Transient causes:

- Exposure to iodine antiseptics.
- Maternal antithyroid medication.
- Auto-immune thyroid disease.
- Iodine deficiency / excess (maternal diet).

Management of the neonate with hypothyroidism

Neonatal hypothyroidism should be considered a medical emergency.

- Early treatment with thyroxine is essential and can prevent significant neuro-cognitive damage.
- Babies with a positive NBST screen are referred to the Endocrinology Department at PCH. TFT and antibody testing is performed.
    - Treatment with thyroxine is commenced.
    - The goal of therapy is to normalise T4 levels within 2 weeks, and TSH within 1 month.
- Periodic hearing testing is essential in infants with suspected dyshormonogenesis; family history of thyroid dysfunction; or Pendred Syndrome, as sensori-neural deafness may worsen over time.
    - The Australian Paediatric Endocrine Group suggests AABR or OAE testing at 4-8 weeks of age, and then every three months for at least the first year in such cases.

Congenital Hyperthyroidism

- Neonatal thyrotoxicosis may be associated with significant morbidity and mortality if unrecognised or inadequately treated.

Risk factors for neonatal thyrotoxicosis

- Mothers with high TSH Rc Ab titres during pregnancy (28-32 weeks). Usually due to hyperthyroidism / Graves' Disease.
- Mother on anti-thyroid treatment at the time of delivery.
- Maternal Hashimoto's Thyroiditis: Rarely produces stimulatory TSH Rc Ab antibodies.
- Activating mutation of the TSH Receptor: Suspect if maternal history of thyrotoxicosis from birth.

- Antenatal signs of thyrotoxicosis: Hydrops / tachycardia / arrhythmia; IUGR; hyperkinesis; goitre; advanced bone age (e.g. lower femoral epiphysis).

Clinical Signs of Hyperthyroidism in the Neonate

- Systemic - Tachycardia / arrhythmia, sweating, diarrhoea
- Laboratory - Jaundice, thrombocytopaenia
- Anatomical - Hydrops; IUGR; microcephaly; craniosynostosis

Management of the Neonate with Hyperthyroidism

Suspected or confirmed neonatal hyperthyroidism / thyrotoxicosis should be referred to the Endocrinology consultant on-call for PCH after discussion with the Neonatologist

- Anti-thyroid drugs should be commenced promptly in consultation with Paediatric Endocrinologist
- Carbimazole and Propylthiouracil (PTU) inhibit thyroid hormone synthesis and interaction with iodine.
    - PTU is commenced at a dose of 2.5-5mg/kg, 12 hourly.
    - Carbimazole dose is 250μg/kg, TDS.
- Free thyroxine (FT4) levels guide therapeutic dose and duration.
- Often treatment can be withdrawn in several weeks or months, with clearance of maternal antibodies (TSH Rc-Ab).
- Cessation of treatment is determined clinically and via measurements of serum TSH and FT4.
- Treatment for Graves' related hyper-stimulation is usually required for 4-8 weeks.
- A clinical response will be observed only as colloid stores are depleted.
    - Adjunct treatments include iodine containing solutions (e.g. Potassium Iodide, Lugol's solution), β-blockers, diuretics/Digoxin and Prednisolone. Glucocorticoids suppress thyroid hormone release and decrease the de-iodination of T4 to T3.
- Propranolol may be indicated for persistent tachycardia.
- Digoxin and/or diuretic may be required for cardiac failure.

Caregiver Education

- Regular monitoring of T4 and TSH is required – normally through Endocrinology Dept, PCH.
- Breastfeeding is not contraindicated if the mother is on small to moderate doses of anti-thyroid medications.

- There is risk of recurrence in future pregnancies.

Breastfeeding Advice for Mothers with Thyroid Disease

- Maternal Hypothyroidism & Thyroxine replacement: no contraindications
- Maternal hyperthyroidism**:** PTU and the active metabolite of carbimazole (methimazole) are both detectable in breast milk, however neither are contraindications to breastfeeding.
- Radio-iodine treatment is an **absolute contraindication to breastfeeding**.

Management of the Neonate at Risk of Thyroid Dysfunction

- Those infants who are clinically well and discharged early in the postnatal period can be followed up by their GP. See attached GP Referral Letter for 'Neonate Managed for Maternal Thyroid Disorder'.

Related CAHS internal policies, procedures and guidelines
Neonatology Clinical Guideline • Newborn Blood Spot Screening Test Neonatology Medication Protocols • Levothyroxine

References

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5. 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.
6. Smith L. Updated AAP guidelines on newborn screening and therapy for congenital hypothyroidism. **Am Fam Phys**. 2007; Aug (76) 3. 439-44.

Useful resources (including related forms)

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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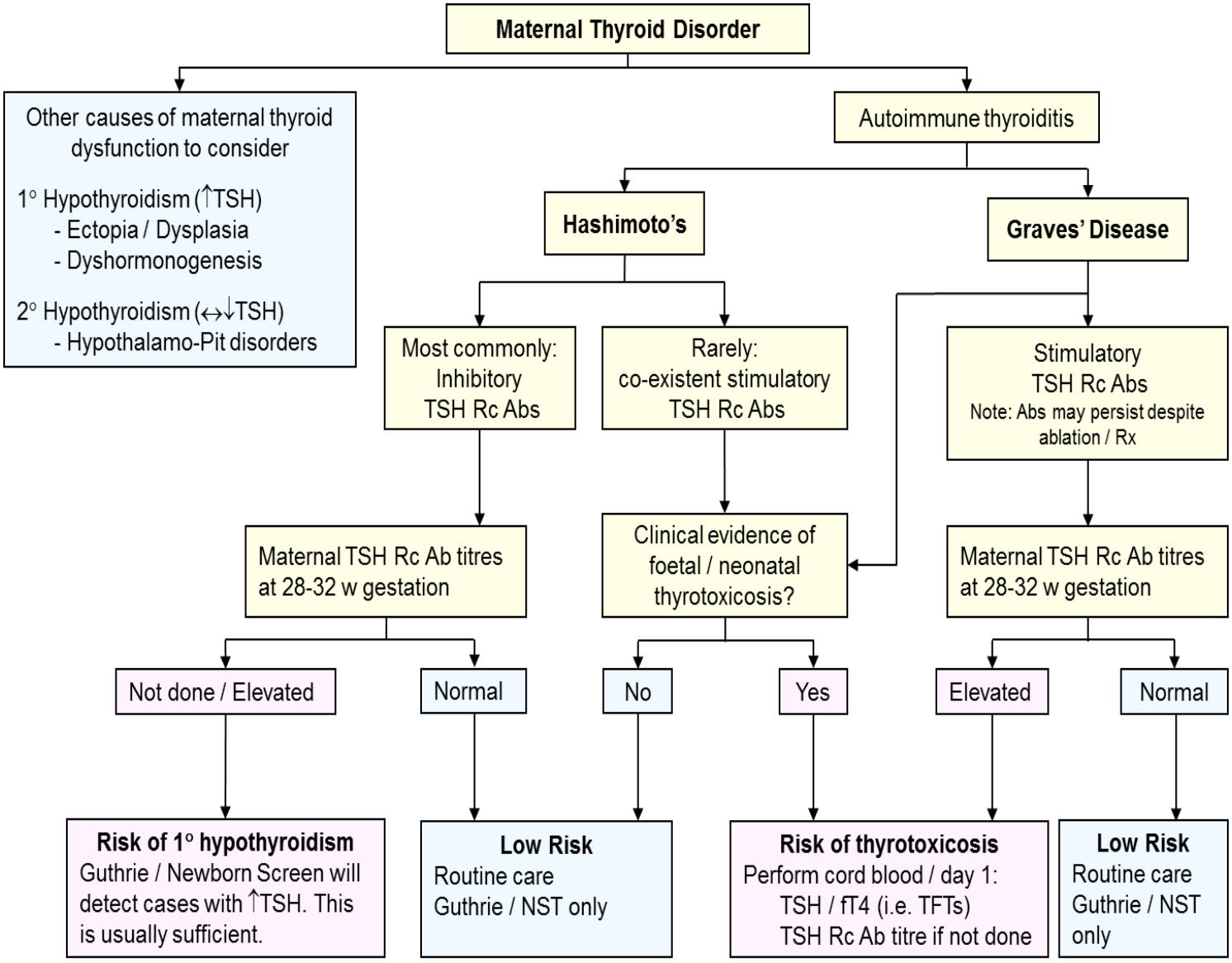
Appendix 1: Maternal Thyroid Disorder Quick Reference Guide

Quick Reference Guide



GP Letter

A GP letter template is found in 'Forms'. The letter should be completed according to the relevant scenario and given to the mother to take to the GP at next visit. It is not a medical record document but provides GPs with a brief summary of inpatient managements