Management of Neonates Born To Mothers with Thyroid Disease

Maternal Hypothyroidism
The prevalence of hypothyroidism during pregnancy is 0.3-0.5% for overt hypothyroidism, with raised Thyroid Stimulating Hormone (TSH) and low T4 levels. Subclinical hypothyroidism 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 thyroid peroxidase antibodies confirms the autoimmune origin. Pregnant women with a history of hypothyroidism should have regular Thyroid Function Tests (TFT) to optimise therapy. TSH receptor antibodies/Thyroid stimulating immunoglobulin (TRAb/TSI) are no longer routinely tested.

Babies born to mothers with Hashimoto thyroiditis are at low risk of developing transient hypothyroidism and hyperthyroidism is extremely rare. Neonates with transient congenital hypothyroidism will have a raised TSH which will be picked up by the routine neonatal blood spot screening. Therefore these babies will not require further investigations or observation after delivery.

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’ disease.

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 TRAb/TSI measured during pregnancy, please see local obstetric guideline. TRAb/TSI often remain positive after treatment with radioactive Iodine or thyroidectomy. Positive TRAb/TSI is associated with increased risk of neonatal thyrotoxicosis. Women who have a negative TRAb/TSI have a very low risk of fetal or neonatal thyroid dysfunction. TRAb/TSI positive women need to be identified and the neonatal unit informed prior to delivery.
Neonatal Thyrotoxicosis
Neonatal thyrotoxicosis is mainly caused by the transplacental transfer of TRAb/TSI in Graves’ 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 anti thyroid drugs (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. Duration of neonatal thyrotoxicosis depends on the persistence of the maternal antibodies and usually remits after 8-20 weeks. Clinically, infants may have goitre, be irritable, tachycardic and have eye signs (Appendix 2)
Type of mother’s thyroid disease

Hypothyroidism
= underactive thyroid

Are you sure about this diagnosis?

Mother’s only treatment is (and has ever been) thyroxine

Yes

Maternal TRAB/TSI status known and negative

Blood spot testing (Guthrie) only
No further investigations or observation required

Low risk of neonatal thyrotoxicosis
Routine postnatal care, no further investigations or observation required if no clinical concerns

No

Hyperthyroidism
= overactive thyroid, thyrotoxicosis
= Graves’ disease
= mother on carbimazole or propylthiouracil or had these in the past
= mother has had thyroid surgery or radio-iodine

If any of:
- Maternal TRAB/TSI status positive
- Maternal TRAB/TSI status unknown
- Signs of Foetal Thyrotoxicosis
- Family history of activating TSH receptor mutations

High risk of neonatal thyrotoxicosis
Follow high risk pathway (flow chart 2)
Wales Neonatal Network Guideline

Positive or unknown TRAb/TSI level in 2nd or 3rd trimester in the setting of maternal Graves’ disease

High risk infant

Determine TRAb/TSI in cord blood if assay available

TRAb/TSI not available or TRAb/TSI positive

Newborn day 1 of life:
- History and physical examination (careful examination is required as signs of hyperthyroidism can be subtle – see appendix 2)
- TRAb/TSI if assay available and not yet done in cord blood
- Close observation as inpatient for min. 48 hrs looking for signs of neonatal hyperthyroidism

Newborn day 5 of life
- History and physical examination
- TFT: if abnormal see Appendix 1

Newborn day 10-14 of life
- History and physical examination
- TFT: if abnormal see Appendix 1

In case of negative cord or infant TRab/TSI level:
Low risk newborn: no further follow up is required

In case of unknown or positive TRAb/TSI in an asymptomatic newborn with normal TFT:
Continue clinical follow up with Consultant at age 4 weeks and 2-3 months

Reference Number: 1
Ratified: June 2018
Authors: Dr Rainer Fortner & Dr Marcia Scheller
Review Date: June 2021
Appendix 1

Abnormal TFT result (raised T4 and suppressed TSH)

Contact local or tertiary paediatric endocrinologist for advice. Advice is likely to include:

Biochemical hyperthyroidism and no symptoms:
- Consider Methimazole: 0.2-0.5 mg/kg/d divided in 2 doses

Biochemical hyperthyroidism and symptoms:
- Start Methimazole: 0.2-0.5 mg/kg/d divided in 2 doses
- Signs of sympathetic hyperactivity: consider adding Propranolol 1 mg/kg BD for 1-2 weeks and strongly consider admission to hospital
- Adequate fluid and calorie intake

Abnormal TFT result, central or primary hypothyroidism (Low T4 and suppressed TSH)

Contact local or tertiary paediatric endocrinologist for advice. Advice is likely to include:

- Repeat TSH and T4 in 1 week
- In case of central hypothyroidism, no prior neonatal hyperthyroidism and unknown TRAb consider other pituitary deficiencies
- Before starting Levothyroxine ACTH/cortisol deficiency should be formally excluded, to avoid unintentionally inducing an adrenal crisis

One in 70 babies whose mother has Graves’ disease develops neonatal thyrotoxicosis, associated with significant morbidity and mortality. The decision of whether to treat is complex. All cases where treatment is considered must be discussed with a local or paediatric endocrinologist.
Appendix 2

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

Congratulation on the birth of your baby. You have been given this leaflet as you will have been diagnosed with an overactive thyroid gland either in the past or during this pregnancy. There is a small risk that your baby may also develop an overactive thyroid gland in the first 2 weeks of life.

Your new baby will be examined by a Paediatrician/ Advanced Neonatal Nurse Practitioner or Midwife as part of routine new born screening following delivery. They will arrange any immediate blood tests if necessary, and will also organise a clinic appointment for further blood tests on day 5 of life.

If your baby shows any of the following signs in the first 2 weeks of life please contact your local hospital and ask to speak to the on-call paediatric registrar for advice.

**Unsettled or irritable despite regular feeding, jitteriness, sweating, staring eyes, diarrhoea, vomiting, poor weight gain**

---

**TAFLEN WYBODAETH I RIENI**

**ARWYDDION O CHWARREN THYROID GORWEITHGAR YN EICH BABI**

Llongyfarchiadau ar enedigaeth eich babi. Cawsoch y dafien hon am eich bod wedi cael diagnosis o chwarren thyroid gorweithgar un ai yn y gorffennol neu yn ystod eich beichiogrwydd. Mae risg fach y gallai eich babi ddatblygu chwarren thyroid gorweithgar yn ystod pythefnos cyntaf ei fywyd hefyd.

Bydd eich babi newydd yn cael ei archwilio gan Baediatregydd/ Uwch Nyrs Ymarferydd i’r Newydd-anedig neu Fydwraig fel rhan o sgrinio arferol i fabanod ar ôl cael ei eni. Byddant yn trefnu unrhyw brofion gwaed ar unwaith os bydd angen, a hefyd yn trefnu apwyntiad clinig i wneud mwy o brofion gwaed ar ddiwrnod 5.

Os bydd eich babi’n dangos unrhyw un o’r arwyddion canlynol yn ystod ei bythefnos cyntaf, cysylltwch â’ch ysbyty lleol a gofynnwch am gael siarad â’r cofrestrydd paediatrig sydd ar alwad am gyngor.

**Gwrthod setio, neu’n aflonydd er ei fod yn cael ei fwydo’n aml, cryno, chwysu, syllu, dolor rhydd, chwydu**
References


Evans C et al Ann Clin Biochem 2011: Transient congenital hypothyroidism due to thyroid stimulating hormone receptor blocking antibodies: a case Series

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

Brown et al J Clin Endocrin Metab 1996: Incidence of transient congenital hypothyroidism due to maternal thyrotropin receptor blocking antibodies in over one million babies


Laurberg et al. TSH receptor autoimmunity in Graves’ disease after therapy with anti-thyroid drugs, surgery or radioiodine: a 5 year prospective randomised study. Eur J Endocrinol 2008;158 (1):69-75