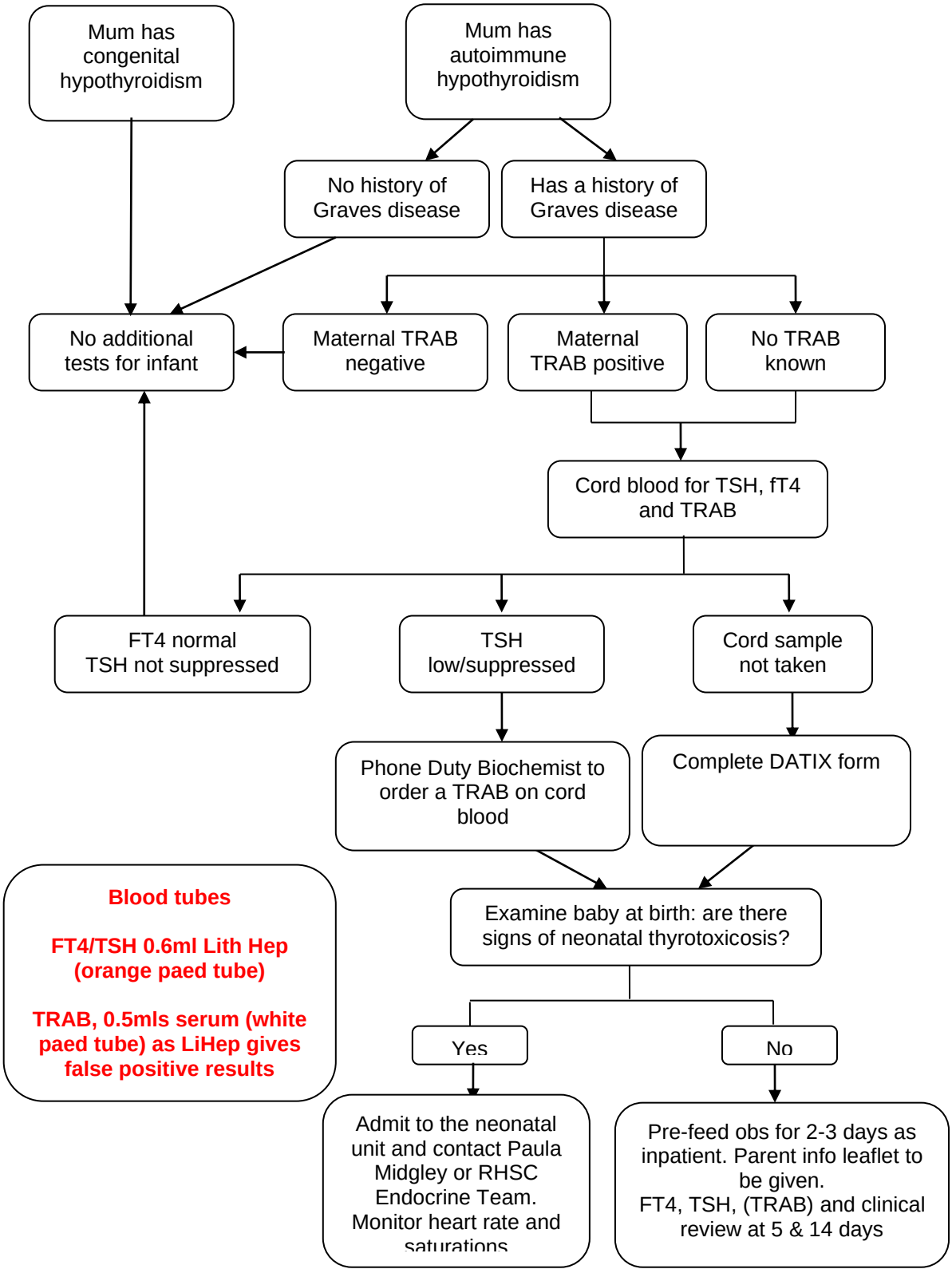
Infants Born to Mothers with Thyroid Disease

Maternal Hypothyroidism (i.e. mother is on thyroxine)

Flowchart for the investigation of the infant of a mother with hypothyroidism



Congenital Hyopthyroidism

- If the maternal hypothyroidism is secondary to congenital aplasia or hypoplasia of the thyroid gland there should be no significant increased risk to the baby of hypothyroidism and Guthrie test is sufficient.

Acquired Hypothyroidism

- This can be secondary to
    - Hashimoto's thyroiditis- the mother may be producing thyroid inhibiting so the baby may develop transient hypothyroidism. Transient hypothyroidism due to blocking antibodies should be picked up by the Guthrie screen.
    - Thyroidectomy for cancer- the infant does not require thyroid function tests (other than routine Guthrie).
    - Treatment (surgery or radioiodine) **for Graves' disease**- the baby is at risk of neonatal thyrotoxicosis and will need to be managed as for maternal thyrotoxicosis.
    - MEN (multiple endocrine neoplasia) then the child will require follow-up/screening, but not in the newborn period.

Maternal Thyrotoxicosis secondary to Graves Disease

In maternal thyrotoxicosis or history of maternal hyperthyroidism (ie. previous treatment for hyperthyroidism, thryoidectomy for Graves Disease or radio-iodine treatment), **all infants** should be examined at birth for signs of thyrotoxicosis, including resting heart rate. All mothers should be told what signs and symptoms to look for i.e. irritability, excessive feeding, poor weight gain and should receive a parent information leaflet on 'Symptoms of thryotoxicosis in my baby.'

Maternal TSH receptor antibody (TRAB) level

- Maternal TRAB negative – no additional tests required for baby
- Maternal TRAB elevated or unknown:-

1. Cord blood for fT4,TSH and TRAB. ABSOLUTELY ESSENTIAL. The endocrine biochemist should be alerted in advance, and told of anticipated delivery time so that he/she can arrange for the result to be available as soon as possible (expect fT4 and TSH result within 24 hours, TRAB not urgent). If cord blood has not been taken please ensure a Datix form is completed.
2. Examine the infant at birth for signs of thyrotoxicosis (see below).
3. Monitor the resting heart rate on the postnatal ward with pre-feed observations.
4. The infant should be monitored (resting heart rate, feeding) in hospital for 2-3 days, even if appears well, unless a normal TRAB result has been obtained from the cord or infant, in which case no further tests are required.
5. If the infant has signs of thyrotoxicosis, or is tachycardic at any time, the infant should be admitted to NNU for closer monitoring i.e. continuous heart rate and saturation monitoring.
6. There is a risk that the infant may be hypothyroid (or euthyroid) secondary to maternal treatment, but develop thyrotoxicosis as the (maternal) propylthiouracil wears off over the first week (see below)

Mother on antithyroid treatment during pregnancy

- If the mother has been on antithyroid treatment during pregnancy (carbimazole, propylthiouracil) and this has been stopped several weeks before delivery, than the infant should be managed as above (see section above 'maternal TRAB elevated or unknown').
- If the mother is on antithyroid treatment at delivery the infant may have treated hypothyroidism, and develop thyrotoxicosis over the first week of life as antithyroid drug levels fall. The infant should be managed as for elevated or unknown TRAB, and

the infant should also be reviewed clinically and have thyroid function tests done at 7 days of age. The infant should be reviewed again at 10 days of age. Further thyroid function tests will be required at 10-14 days, but the timing of these will depend on the results at 7 days, and the infant's clinical status. If in any doubt repeat thyroid function test at 10 days/discuss with Paula Midgley.

Breast feeding

- Breast feeding is NOT contraindicated in mothers treated with thionamides after delivery. Both propylthiouracil and methimazole (to which carbimazole is metabolized) are detected in breast milk but appear not to affect neonatal thyroid function if mothers dose of carbimazole is < 30 mg/day and propylthiouracil dose is < 300mg / day. Doses greater than this should be referred to the pharmacist for advice, preferably before delivery. Rare idiosyncratic reactions (eg agranulocytosis) might occur with either drug, and the infant should be watched for signs of infection and liver disease (jaundice, bruising). Monitoring of the infant's complete blood count and differential is advisable if there is a suspicion of a drug-induced blood dyscrasia.

Identification and Management of Neonatal Thyrotoxicosis

- The baby is more likely to be affected if the mother has received treatment during pregnancy
- Known TSH receptor antibody titres in pregnancy: High risk is a titre approximately five times the upper limit of normal
- Thyroid stimulating immunoglobulin levels from mothers in 3rd trimester, and the neonate correlate with risk of development of thyrotoxicosis.
- Thyroid stimulating immunoglobulin levels in neonate are predictive of the risk of hyperthyroidism (more so than maternal antibody titres but the result is not usually available in time to be of benefit to inform the neonatal management).
- Anomalies associated with the use of carbimazole (methimazole) in pregnancy are rare but include cutis aplasia, choanal atresia, gastrointestinal anomalies including oesophageal atresia, developmental delay, hearing loss, and dysmorphic facial features
- Antithyroid drugs (propylthiouracil, carbimazole or methimazole) may cross the placenta and render the fetus hypothyroid. In contrast thyroxine only crosses the placenta in small amounts.

Symptoms and signs in fetus

- Tachycardia, arrhythmias, hydrops
- Hyperkinesis
- IUGR
- Goitre picked up on fetal ultrasound scan
- Advanced bone age may be detected on ultrasound of the lower femoral epiphysis
- Preterm delivery
- Death in utero

Symptoms and signs in neonate

- Symptoms may be present at birth or delayed for several days (particularly if the mother is on antithyroid medication at time of delivery)
- Usually apparent by D10
- Can occur up to D45 after birth

Signs of hyperthyroidism:

- Goitre
- Central nervous system - Irritability, jitteriness, restlessness
- Periorbital oedema, lid retraction, exophthalmos

- Cardiovascular system – tachycardia, arrhythmia, failure
- Systemic and pulmonary hypertension
- Hypermetabolism - voracious appetite, diarrhoea, failure to thrive, flushing, sweating, tachypnoea
- Persisting acrocyanosis
- Hepatosplenomegaly, lymphadenopathy
- Thrombocytopaenia – petaechiae + bruising
- Craniosynostosis, advanced bone age, microcephaly
- Jaundice

Management of the thyrotoxic neonate

- It is not clear whether one should treat biochemical thryotoxicosis (fT4 above the normal range for age and TSH suppressed) in the absence of symptoms, but in practice most infants are treated. This is a consultant decision. Please discuss with Paula Midgley (any time of day or night). If Paula is away, then this should be discussed with the endocrine team at RHSC.

Immediate

Thionamide: The dosages as per BNFc. Lugol's Iodine solution can be given if available.

- **Thionamide:** Either Propylthiouracil or Carbimazole
- As this may take 24-48 hours to have some effect, consider blocking release of thyroid hormones with iodine eg, **Lugol's solution**
- Sympathomimetic effects may require **β-blockade**, for example Propranolol to control symptoms (beware side effects – bradycardia, hypotension and hypoglycaemia)
- **Corticosteroids** may be helpful for example Prednisolone if symptoms are severe
- **Sedatives** may be helpful
- **Heart failure** may require appropriate treatment.
- Thyrotoxicosis has been successfully treated with iodine-containing contrast media - Iopanoic acid or sodium ipodate

Medium term

- It is easy to over treat the thyrotoxic baby so beware of drug-induced hypothyroidism.
- The duration of thyrotoxicosis is determined by the persistence of maternal thyroid stimulating immunoglobulins in the baby's blood. Thyrotoxicosis usually remits after 8-20 weeks, and virtually all babies are euthyroid by 48 weeks.

Longterm

- Once thyroid function normal off treatment, no further endocrine review required
- Follow-up of growth and development may be considered
- There is a risk of recurrence in future pregnancies

Current Laboratory Reference ranges for thyroid hormones

Thyroid Stimulating Hormone (TSH)	
Age	mU/L
Neonates <3d	1.3 – 25
3d-4 weeks	0.7 – 7.4
4 weeks to 6 months	0.7 – 6
Thyroxine, Free T4	
Age	pmol/L
Neonates <7d	13 – 34
7 – 14d	12 – 26

14 – 28d	12 – 23
4wks to 1 year	11 – 19
TSH receptor antibodies (TRAB)	
All ages	< 1.6 IU/L