**Aneurin Bevan University Health Board**

# Hyperthyroidism and Hypothyroidism in Pregnancy Guideline

*N.B. Staff should be discouraged from printing this document. This is to avoid the risk of out of date printed versions of the document. The Intranet should be referred to for the current version of the document.*


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**Contents:**

## 1. Introduction/Overview

Thyroid disease is common in women of childbearing age. Optimal management of thyroid disease in pregnancy reduces maternal and fetal / neonatal morbidity and mortality.

## 2. Policy Statement

The Health Board is committed to providing evidence-based, safe care for all pregnant women, in order to optimise outcomes. This document is designed to support safe and effective practice.

## 3. Aims/Purpose

To provide support for clinical decision making.

## 4. Objectives

To ensure all of the following for women with thyroid disease in pregnancy:

- Early identification
- Optimisation of treatment
- Appropriate monitoring of thyroid function
- Appropriate monitoring of maternal and fetal wellbeing
- Provision of evidence-based information to women and their care providers

## 5. Scope

This guideline applies to all clinicians working within maternity services.

## 6. Roles and Responsibilities

All clinicians working within maternity services are responsible for ensuring implementation of this guideline for women in their care.

## 7. Guidance

### 7.1 Thyroid Physiology in Pregnancy

Hepatic synthesis of thyroid binding globulin (TBG) is increased during pregnancy. Total T4 & T3 are also increased. Levels of free T4 are less affected by pregnancy, but there is a slight increase in the first trimester, followed by a decrease in the second and third trimesters. This increase in

the first trimester is in part due to HCG, which is structurally similar to TSH and therefore has a thyrotropic (TSH-like) effect.

T4 is essential for fetal neural development. The fetal thyroid gland does not function until 12 weeks of gestation. Therefore, adequate concentrations of maternal T4 are vital, especially in the first trimester.

Sufficient iodine intake (200mcg/day) during pregnancy and lactation is necessary to meet the need for increased thyroid hormone production and provide iodine to the fetus and neonate. There is also increased excretion of iodine in the urine during pregnancy due to increased glomerular filtration rate. Dairy products and white fish are the best dietary sources of iodine so vegans are at increased risk of deficiency and should be advised to take a supplement; some pregnancy multivitamins contain iodine. In cases of iodine deficiency, the thyroid hypertrophies in order to trap more iodine, which may cause a visible goitre.

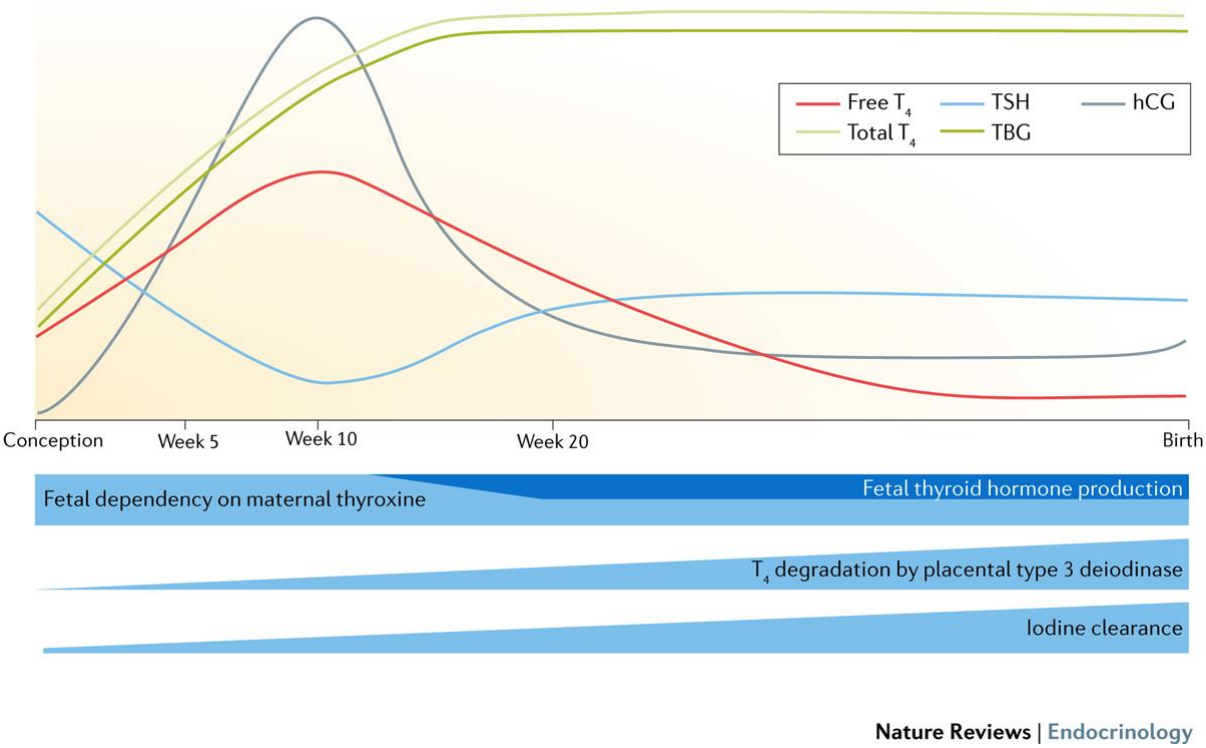


*Figure 1: Changes in Thyroid Physiology During Pregnancy*
*Korevaar, T. I. M. et al. (2017) Thyroid disease in pregnancy: new insights in diagnosis and clinical management, Nat. Rev. Endocrinol.*

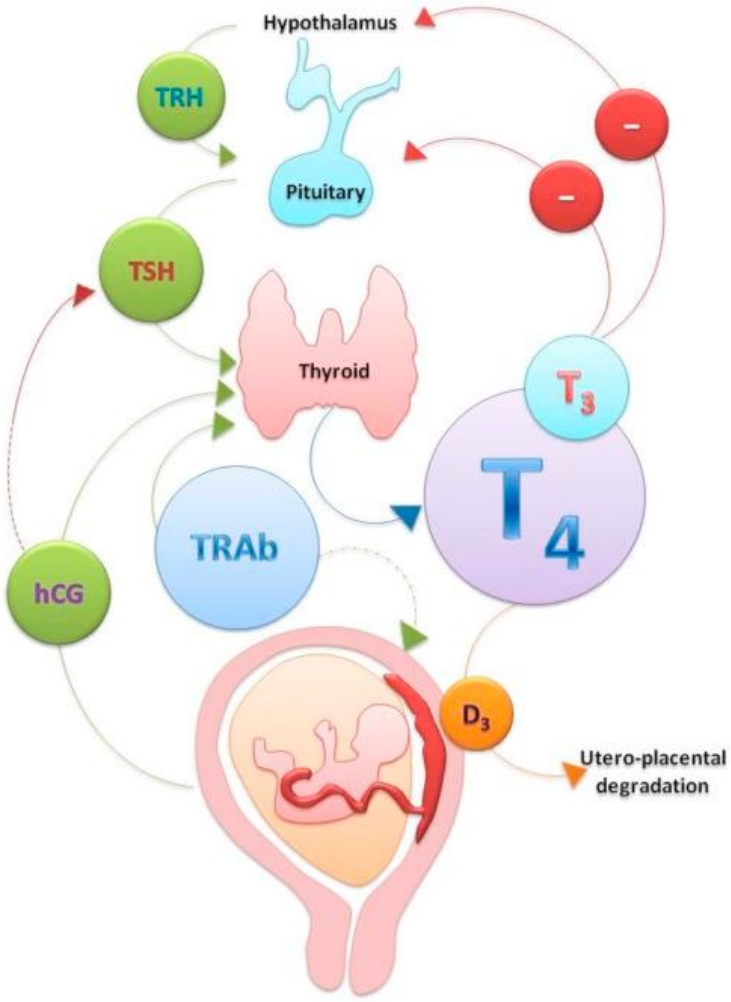


*Figure 2: Hypothalamic-Pituitary-Thyroid Axis & Pregnancy*
*Efterpi T. et al, Benign thyroid disease in pregnancy: A state of the art review, Journal of Clinical & Translational Endocrinology*

## 7.2 Thyroid Function in Hyperemesis Gravidarum

Transient biochemical hyperthyroidism (elevated T4 and low TSH) may occur in up to 11% of women in early pregnancy. This is particularly common in those with hyperemesis gravidarum due to TSH receptor stimulation by high levels of hCG. These women are rarely symptomatic and this transient hyperthyroidism has not been associated with adverse pregnancy outcomes. Treatment with anti-thyroid medications is therefore not recommended, but if symptoms are present Beta blockers can be used. This transient hyperthyroidism usually resolves by 18 weeks of pregnancy.

A detailed history should be taken for any other symptoms of hyperthyroidism and TFTs should be interpreted with caution. Patients with

transient hyperthyroidism associated with HG will usually have no history of thyroid disease & no goitre. If there is any doubt as to whether abnormal TFTs may be related to HG or Graves' disease, check TSI; this should be negative in transient hyperthyroidism and a positive result requires referral to medical ANC.

Women on Thyroxine with nausea and vomiting in pregnancy should be advised of the importance of continuing to take their Thyroxine daily, and should be prescribed antiemetic medication where necessary to achieve this.

## 7.3 Post-Partum Thyroiditis

Thyroid dysfunction in the first year after delivery affects 5-10% of women. There may be clinical features of hyperthyroidism, hypothyroidism or both. Postpartum thyroiditis is the commonest cause of thyrotoxicosis in the post-partum period. Hyperthyroidism is usually mild and short-lasting; therefore, women rarely require anti-thyroid medications, but may require Beta blockers depending on symptoms. Hypothyroidism should be treated with Thyroxine. The majority of women return to euthyroid within 1 year post-partum.

## 7.4 Hyperthyroididsm in Pregnancy

Hyperthyroidism has an incidence of 1 in 500 pregnancies. 95% of these cases are due to autoimmune thyrotoxicosis (Graves' disease). Other causes include a toxic nodule or toxic multinodular goitre. Thyroid function tests in hyperthyroidism show decreased TSH and elevated T4.

The therapeutic aim is to achieve euthyroidism as early as possible in pregnancy (or ideally, preconceptually) as this minimises the chances of maternal or fetal complications.

Presence or absence of TPO antibodies does not alter the maternal or neonatal outcome. Subclinical hyperthyroidism (low TSH with normal levels of T4) is not associated with any adverse pregnancy outcomes and treatment is not recommended.

### Maternal Risks of (Poorly Controlled) Hyperthyroidism

- Weight loss
- Palpitations
- Pregnancy induced hypertension
- 5 x increased risk of pre-eclampsia

- Placental abruption
- Thyroid storm / crisis - rare but serious
- Congestive cardiac failure

**Fetal Risks of (Poorly Controlled) Hyperthyroidism**

- Fetal anomaly if poor control in first trimester
- Miscarriage
- Transplacental transfer of maternal antibodies (TSI) causing fetal thyrotoxicosis: tachycardia, growth restriction, oligohydramnios, excessive fetal movements, goitre, high output cardiac failure
- Craniosynostosis & associated intellectual impairment
- Intrauterine growth restriction
- Prematurity
- Hydrops fetalis
- Intra uterine death
- Seizure disorders / neurobehavioural disorders later in life

**Assessment of Patient with Suspected/Confirmed Hyperthyroidism**

Check for:

- Past medical history
- Family history
- Current symptoms: palpitations, heat intolerance, weight loss, diarrhoea, vomiting (?hyperemesis gravidarum)
- Examination: maternal tachycardia, tremor in hands, eye signs (exophthalmos), goitre, brisk reflexes, fetal tachycardia

**Preconception Care**

Aim for good control on lowest dose of antithyroid medications which keeps T4 in upper end of normal range (ideally PTU but see considerations below).

**Antenatal Care**

Book into Combined Medical ANC: RGH - Monday pm; NHH - Tuesday am

TFTs should be taken at booking and at least 6-weekly thereafter. Anti-thyroid medication should be titrated to keep free T4 at the upper end of non-pregnant range.

**Thyroid Stimulating Immunoglobulin (TSI) / TSH Receptor Antibodies (TRAb)**

There are two main types of TRAb – thyroid stimulating (TSI) and thyroid blocking. TSI are the cause of Graves' disease. Our lab assays used to test for all TRAb but now screen specifically for TSI.

TSI crosses the placenta and can therefore have an effect on the fetal thyroid, potentially causing fetal thyrotoxicosis. This typically occurs at or after 20 weeks gestation. The risk of fetal thyrotoxicosis is directly proportional to antibody titre.

TSI titre should be checked at booking and 28 weeks in all women with current / history of hyperthyroidism. If TSI is positive at booking, it should also be repeated at 18-22 weeks.

For all women with a positive TSI:

- Monitor fetus for growth and goitre by serial USS
- Arrange for weekly check of fetal heart rate (due to risk of tachycardia) - can be done by community midwife
- Send neonatal alert to Dr. Sue Papworth, Neonatologist

**Ultrasound Scans in Hyperthyroidism with Positive TSI**

All women with positive TSI should have serial fetal ultrasound scans. Any of the following features on USS should raise the suspicion of fetal thyrotoxicosis:

- Fetal tachycardia > 170
- IUGR
- Fetal goitre
- Accelerated bone maturation
- Signs of congestive cardiac failure
- Hydrops fetalis

The presence of any of these features requires urgent MDT assessment and planning including input from an obstetrician, endocrinologist, fetal medicine Consultant, neonatologist and anaesthetist.

**Treatment of Hyperthyroidism**

**Anti-thyroid drugs:**

Either Propylthiouracil (PTU) or Carbimazole may be used in pregnancy. Both medications will cross the placenta and have some effect on the fetal thyroid, therefore it is important to use the lowest dose necessary (maintain maternal free T4 at upper limit of normal range).

There are pros and cons to both PTU and Carbimazole (see table below) but PTU is traditionally favoured up to at least 16 weeks of pregnancy and often continued throughout pregnancy. This is due to the increased risk of more serious congenital anomaly with Carbimazole use, particularly in the

first trimester. Therefore, usually women who conceive whilst taking Carbimazole will be switched to PTU as early as possible.

However, the most important principle is good control of hyperthyroidism; pregnancies where there is poor control are more likely to result in complications than those well controlled on either drug. The decision to start, stop or change antithyroid medication should therefore be made in consultation with the patient by an experienced Obstetrician / Endocrinologist, ideally in Medical ANC.

Many women will be able to reduce or stop their anti-thyroid medications during pregnancy as TSI, and therefore disease activity, tends to fall in the second and third trimesters, but this must be done according to TFT results and under the supervision of an experienced clinician.

**Comparison of PTU & Carbimazole**

| | PTU | Carbimazole |
|---|---|---|
| **Placental transfer** | Similar for both drugs | |
| **Risk of neonatal hypothyroidism** | Similar for both drugs | |
| **Risk of fetal anomaly** | 2-3% but usually minor, e.g. face / neck cysts | 2-3% including more serious anomalies, e.g. aplasia cutis, oesophageal atresia, choanal atresia, facial abnormalities & developmental delay |
| **Dosing** | 100-600mg/day but short half life so multiple daily doses required | 10-40mg/day in single dose |
| | When switching from Carbimazole to PTU total daily dose should be increased by factor of 10-20 (e.g. if on 10mg daily Carbimazole will require 100-200mg PTU in divided doses throughout day) | |
| **Risk of Hepatotoxicity** | Rare but can occur. LFTs must be checked every 3-4 weeks & women advised to report any new symptoms. For this reason, some clinicians recommend changing from PTU to Carbimazole after the first trimester. | No association |
| **Risk of neutropaenia / agranulocytosis** | Both PTU & Carbimazole can cause neutropenia/ agranulocytosis. Women must be advised to report symptoms such as sore throat or fever immediately. If present, urgent FBC must be done. | |
| **Breastfeeding** | Low concentration transferred in breastmilk | Significantly higher concentration in breastmilk. Although this has not been shown to have any adverse effect on breastfed infants, data is limited and there is a potential increased risk of neonatal hypothyroidism, particularly for infants of |

| | | |
|---|---|---|
| | | mothers on high dose Carbimazole. |

**Beta Blockers** (Propranolol) are used for symptom control such as tachycardia, palpitations or tremor. Long term use can lead to fetal growth restriction and this should be monitored with serial USS. However, where significant symptoms exist, benefits of beta blockade usually outweigh this risk.

**Block & Replace Treatment** (antithyroid drugs and levothyroxine used in combination): contraindicated in pregnancy & lactation.

**Thyroid Surgery** e.g. subtotal thyroidectomy can be carried out in pregnancy and if required is best done in the second trimester. It may be indicated in any of the following situations:

- Inability to achieve euthyroidism despite high doses of antithyroid drugs
- Inability to tolerate oral medication
- Non-compliance with treatment

**Radioactive Iodine** therapy for hyperthyroidism is absolutely contraindicated in pregnancy and lactation. For those who have been treated with radioactive iodine, conception should be delayed for a minimum of 6 months until euthyroid.

**Intrapartum Care**
No alterations to normal care if hyperthyroidism is well controlled. In poorly controlled hyperthyroidism there is a risk of thyroid storm / crisis, which is a medical emergency.

**Thyroid Storm** (also referred to as thyrotoxic crisis)
This is a rare, sudden and life-threatening condition in pregnancy. It could be seen in undiagnosed or poorly controlled hyperthyroidism. This sudden flare-up of symptoms can be precipitated by: labour, infection or surgery.

Symptoms and signs include: fever, tachycardia out of proportion to the fever, hypertension, high output cardiac failure, restlessness, coma, seizures, gastrointestinal symptoms: pain, diarrhoea, vomiting, and jaundice.

Thyroid storm is a medical emergency and is associated with high mortality. Rapid diagnosis and aggressive treatment are key.

Principles of Management:

- TFTs should be taken prior to treatment
- Admission to HDU or ITU setting
- Multidisciplinary care, including review by the Endocrinology Registrar / Consultant
- Treatment is with high doses of PTU or carbimazole and potassium iodide or sodium iodide (to suppress T3 & T4 production)
- High dose IV Dexamethasone (to block peripheral conversion of T4 to T3)
- Propanolol (to control tachycardia - use with caution if any suspicion of heart failure)
- Phenobarbital (to increase metabolic elimination of T4)
- Supportive therapy with IV fluids, oxygen and antipyretics should be administered
- Avoid delivery during thyroid storm where possible – stabilise patient first

**Postnatal Care**
Patients should be advised to continue their current medications and have TFTs checked via GP at 6 weeks postnatally. If antithyroid medications have been reduced or stopped in pregnancy, most women will need to restart or increase these in order to avoid a relapse.

**Neonatal Care**
Neonatal team need to be informed of delivery and should examine the baby. Baby should be observed on the ward for 48 hours and will need a blood test for TFTs at age 5-10 days.

## 7.4 Hypothyroidism in Pregnancy

Hypothyroidism affects 1% of pregnancies. Thyroid function tests show an elevated TSH and a low T4. Hashimoto thyroiditis is the commonest cause and is characterised by glandular destruction by autoantibodies, particularly antithyroid peroxidase antibodies (anti-TPO).

Subclinical hypothyroidism (elevated TSH, normal T4) is common but unlikely to progress to overt hypothyroidism during pregnancy. There is no evidence that subclinical hypothyroidism in pregnancy is associated with adverse outcomes. However, some patients may benefit from treatment particularly if they have a TSH >4.5 on more than one occasion or are symptomatic. If thyroxine is commenced in patients with subclinical hypothyroidism, monitoring and dose adjustments should be as per overt hypothyroidism guidance below.

**Maternal Risks of (Inadequately Treated) Hypothyroidism:**

- Fatigue
- Weight gain
- Anaemia
- Oedema
- Hair loss
- Goitre
- Pre-eclampsia
- Placental abruption

**Fetal Risks of (Inadequately Treated) Hypothyroidism:**

- Miscarriage
- Low birth weight
- Intrauterine death
- Impaired cognitive development
- Fetal hypothyroidism very rare (1:180000) as anti-TPO rarely cross placenta

**Preconception Care**

Adequate levels of maternal T4 are essential for normal fetal brain development, particularly in the first trimester. Check TFT to ensure Thyroxine dose is adequate (aim to achieve a TSH level of not higher than 2.5mU/l). Advise to contact GP to check TFT (free T4 and TSH) as soon the pregnancy test is positive, as the dose of Thyroxine may need to be increased if TSH >2.5mU/l.

**Antenatal Care**

At booking check TFTs and take history of thyroid disease. If the patient has a history of any of the following, check TSI and refer to Medical ANC:

- Hyperthyroidism / thyrotoxicosis / Graves' disease
- Total or partial thyroidectomy
- Radioactive Iodine treatment

Patients without the above history most likely have primary hypothyroidism and should normally be managed in the general obstetric clinics. If there is any doubt about the history, check TSI and refer to Medical ANC only if positive.

If there is a new diagnosis of hypothyroidism in pregnancy, Thyroxine treatment should be initiated urgently at 1-2microgram/kg/day then TFTs repeated in 6 weeks. TPO antibodies should also be checked.

TFTs should be checked once every trimester, and 4-6 weeks after any change in dose of Thyroxine. Thyroxine should be titrated to maintain serum TSH concentration not more than 2.5mU/l throughout all trimesters of pregnancy. Thyroxine should not be routinely increased in pregnancy without checking TFTs first, as there is some evidence that excessive thyroxine could be harmful.

**Guide to alteration of dose of thyroxine**

| Serum TSH (mU/l) | Increase in thyroxine (µg/day) |
|---|---|
| 2.5-10 | 25 - 50 |
| 10- 20 | 50 -75 |
| >20 | 100 |

There is no need for regular growth scans unless there is another clinical indication.

**Intrapartum Care**
No alterations to normal care required in labour.

**Postnatal Care**
Following delivery, the patient should be advised to resume her pre-pregnancy dose of Thyroxine (as long as hypothyroidism was well controlled prior to pregnancy). TFTs should be checked 6-8 weeks postpartum with GP.

**Neonatal Care**
In patients with primary hypothyroidism, no alterations to normal neonatal care are required. Most of these patients will not have had TSI routinely checked and should be treated as TSI negative, i.e. normal postnatal care with no additional testing for the neonate.

If patients have a positive TSI, neonatal care should be as per hyperthyroidism guidance above.

## 8. Resources

All necessary resources are already available within the Health Board.

## 9. Training

Staff are expected to access appropriate training where provided. Training needs will be identified through appraisal and clinical supervision.

## 10. Implementation

The recommendations in this guideline are already in clinical practice within the Health Board.

## 11. Further Information Clinical Documents

The evidence for this document has been checked against relevant guidelines provided by RCOG and NICE. A full list of references is included below.

## 12. Health and Care Standards Wales

This guideline complies with the Health and Care Standards Wales by providing guidance to support the provision of high-quality safe healthcare. This guideline promotes practice that is up to date, effective and consistent and can be used in day-to-day practice to encourage a consistent level of quality and safety across the Health Board. It supports a patient-centred approach, enabling women to contribute to and be involved in decisions regarding their own health and wellbeing.

## 13. Equality

This policy has undergone an equality impact assessment screening process using the toolkit designed by the NHS Centre Equality & Human Rights. Details of the screening process for this policy are available from the policy owner.

This policy promotes multidisciplinary working between all those involved in the care of women with thyroid disorders in pregnancy.

## 14. Environmental Impact

An Environmental Impact Assessment has not been carried out for this policy.

## 15. Audit

It is advised that the recommendations in this document be audited to ensure compliance by all staff.

## 16. Review

Due 3 yearly – next September 2023.

## 17. References


- Girling, J. (2008), Thyroid disease in pregnancy. The Obstetrician & Gynaecologist, 10: 237-243.
- American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Thyroid Disease in Pregnancy: ACOG Practice Bulletin, Number 223. Obstet Gynecol. 2020;135(6): e261-e274.
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- Erik K. Alexander et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid. Mar 2017. 315-389.
- Catherine Nelson-Piercy Handbook of Obstetric Medicine: Fifth Edition
- British Dietetics Association – Iodine: Food Factsheet
- Korevaar, T. I. M. et al. (2017) Thyroid disease in pregnancy: new insights in diagnosis and clinical management Nat. Rev. Endocrinol. doi:10.1038/nrendo.2017.93
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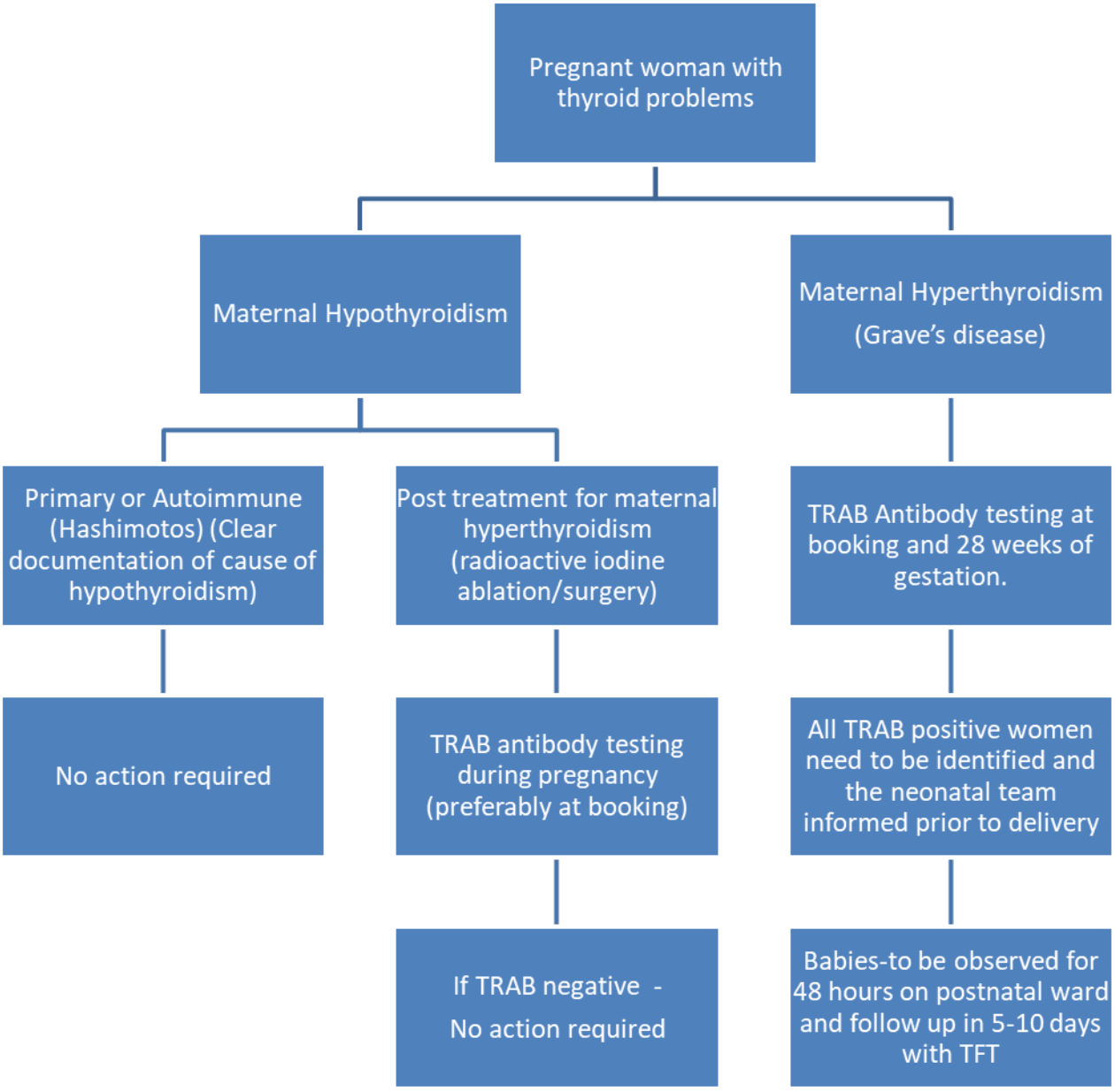
# Appendix 1:
# Management of Babies with Maternal History of Thyroid Disease



**Appendix 2:**

**Management of Patients with Suspected Hyperthyroidism**