Thyroid disorders in pregnancy

Management of antenatal hyperthyroidism and hypothyroidism

Thank you for referring your patient with an abnormal Thyroid Stimulating Hormone (TSH) measurement to the Maternity outpatient department (MOPD) of the Royal Brisbane and Women's Hospital (RBWH). The Endocrine and Obstetric Medicine Departments of the RBWH have developed the following recommendations for the management of elevated or low TSH levels measured during pregnancy. These recommendations may assist you to manage your patient without the need for referral to a specialist clinic.

Glossary of Terms

TSH - Thyroid stimulating hormone
fT4 - free T4
fT3 - free T3
Thyroid antibodies (Abs) = antithyroid antibodies = antithyroid peroxidase antibody + antithyroglobulin antibody • Present in all cases of autoimmune thyroid disease (hypo or hyperthyroidism) but also in asymptomatic patients with normal thyroid function.
TRAb - TSH receptor antibody • Typically present in autoimmune hyperthyroidism (Graves' disease).
TSI - thyroid stimulating immunoglobulin • Typically present in autoimmune hyperthyroidism (Graves' disease).
RDI - Recommended daily intake
ULN - Upper limit of normal

Changes compared with previous version include:

- Thyroxine is no longer routinely recommended for women with TSH < 2.5mIU/L who are antithyroid antibody positive. Individualise advice and/or refer for specialist input if recurrent miscarriage and positive antithyroid antibodies.
- Thyroxine is no longer recommended for women with TSH from 2.5 – 4.0mIU/L who are antithyroid antibody negative.
- Advice regarding the management of sub-clinical hyperthyroidism is provided.
- Advice regarding routine preconception/early pregnancy care is provided.
- Trimester specific recommendations for TSH interpretation/management are included.

Please manage your patient according to the below guidelines.

We have written to your patient advising them to make an appointment to see you as soon as possible.

Version 3.0 Effective: August 2022 Review: August 2025

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Routine preconception/early pregnancy advice

- **If already taking thyroxine prior to conception (pregestational hypothyroidism)**
  - Increase the total weekly dose by 30% once pregnancy is confirmed
  - Monitor every 4 weeks during the first trimester and every 6-8 weeks thereafter
  - **Target TSH 0.5-2.5 mIU/L if already taking thyroxine prior to pregnancy**
- **If known pregestational overt hyperthyroidism eg Graves' disease, toxic nodule**
  - Refer preconception or as early as possible in early pregnancy
    - If taking anti-thyroid drugs (carbimazole or propylthiouracil) – preconception advice strongly advised when possible
    - Positive TRAB and/or TSI even if euthyroid
    - T4 and/or T3 >1.5x ULN regardless of cause
- **Routine TSH measurement is currently not recommended for every pregnant patient. Check the TSH if:**
  - Current or previous treatment for thyroid dysfunction (hyper or hypothyroidism, thyroid surgery, neck irradiation)
  - Known positive antithyroid antibodies
  - > 30 years age
  - Symptoms of thyroid dysfunction and/or goitre
  - T1DM, coeliac disease, Addison's disease, pernicious anaemia
  - Family history of thyroid disease
  - BMI > 40
  - History of miscarriage, infertility or pre-term delivery
  - Recent use of amiodarone, lithium or intravenous contrast for CT scan

- **Iodine supplementation** (RDI = 220 mcg/day, maximum 500mcg daily), commercially available pregnancy multivitamin preparations contain 150mcg – 250mcg per daily dose. Iodine is a required substrate for fT4 and fT3 production in the thyroid.
- **Treatment for isolated hypothyroxinaemia** (low fT4) is not currently recommended when the TSH is normal.

Antenatal Subclinical Hyperthyroidism

<table>
<tr><th>Prior to 20 weeks gestation</th><th>From 20 weeks gestation – term</th></tr>
<tr><td>If the initial TSH is <0.1 repeat the TSH and also measure fT4, fT3 and TSH receptor antibody titre (TRAb) and/or TSH receptor stimulating immunoglobulin (TSI)</td><td>If the initial TSH is <0.4 repeat the TSH and also measure fT4, fT3 and TSH receptor antibody titre (TRAb) and/or TSH receptor stimulating immunoglobulin (TSI)</td></tr>
<tr><td colspan="2">Positive TRAb and/or positive TSI regardless of other results– refer all patients to an Endocrinology Service</td></tr>
<tr><td colspan="2">Negative TRAb and TSI</td></tr>
<tr><td>If fT4 and/or fT3 >1.5x the ULN of the laboratory reference range – REFER TO AN ENDOCRINOLOGY SERVICE</td><td rowspan="2">If fT4 and/or fT3 are above the laboratory reference range – REFER TO AN ENDOCRINOLOGY SERVICE.

If fT4 and fT3 are normal but the repeat TSH is still <0.4 - REFER TO AN ENDOCRINOLOGY SERVICE.

If the fT4 and fT3 are normal and the repeat TSH is >0.4, no further testing is needed.</td></tr>
<tr><td>If T4 and T3 <1.5x ULN of the laboratory reference range, gestational hyperthyroidism is most likely and, in most cases, will resolve spontaneously during the second trimester. Treatment is not indicated.

1. Monitor the fT4, fT3 and TSH every 4-6 weeks.

2. Refer only if the fT4/fT3 increase beyond 1.5x ULN or the TSH is persistently <0.4 after 20 weeks gestation.

3. Monitoring can cease once the fT4, fT3 and TSH are within normal range for gestation.</td></tr>
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Antenatal Subclinical hypothyroidism *_if not already prescribed thyroxine_*

A) If the initial TSH is higher than the laboratory trimester specific reference but <4.0 mIU/L

(Use default 2.5 – 4.0 mIU/l if laboratory does not provide trimester specific reference ranges)

- Repeat the TSH, FT4 and fT3, and measure antithyroid antibody (anti-thyroid peroxidase and anti-thyroglobulin) titres.

Prior to 13 weeks gestation	From 13 weeks gestation - term
If repeat TSH < 2.5 mIU/L and antibodies are negative, no further testing and thyroxine NOT required	If repeat TSH < 3.0 mIU/L and antibodies are negative no further testing and thyroxine NOT required
If repeat TSH < 2.5 mIU/L and antibodies are positive, thyroxine NOT required but at risk for progressing to hypothyroidism during pregnancy and for postpartum thyroiditis. Consider repeat TSH each trimester and refer to trimester specific guidelines. If recurrent miscarriage, may benefit from individualised advice.	If repeat TSH < 3.0 mIU/L and antibodies are positive, thyroxine NOT required but at risk for progressing to hypothyroidism during pregnancy and for postpartum thyroiditis. Consider repeat TSH each trimester and refer to trimester specific guidelines.
If repeat TSH is between 2.5 – 4.0 mIU/l and antibodies are negative - thyroxine NOT required.	If repeat TSH is between 3.0 – 4.0 mIU/l and antibodies are negative - thyroxine NOT required.
If repeat TSH > 2.5 mIU/L and antibodies are positive, **commence thyroxine 50 mcg daily.**	If repeat TSH > 3.0 mIU/L and antibodies are positive, **commence thyroxine 50 mcg daily.**
If repeat TSH 4-10 mIU/L regardless of antibodies, **commence thyroxine 50 mcg daily.**	If repeat TSH 4-10 mIU/L regardless of antibodies, **commence thyroxine 50 mcg daily.**
If repeat TSH >10.0 mIU/L regardless of antibodies, **commence thyroxine 100 mcg daily.**	If repeat TSH >10.0 mIU/L regardless of antibodies, **commence thyroxine 100 mcg daily.**

OR

B) If initial TSH 4.0 - 10 mIU/L - check antibodies and commence thyroxine 50mcg daily regardless of antibody result.

OR

C) If initial TSH >10.0 mIU/L - check antibodies and commence thyroxine 100mcg daily regardless of antibody result.

IF TREATMENT HAS BEEN COMMENCED DURING PREGNANCY, TARGET TSH 0.5 - 2.5 mIU/L AS FOR PREGESTATIONAL HYPOTHYROIDISM.

Monitoring and Titration after commencing thyroxine

1. Repeat TSH in 4 weeks:
    a. If TSH is above target, increase thyroxine dose by 25mcg per day
    b. If TSH is below target, decrease thyroxine dose by 25mcg per day

2. And then, repeat TSH **either**
    a. Every 4 weeks if dose was adjusted and continue to adjust every 4 weeks according to TSH target range

    or

    b. Every 6-8 weeks if dose is stable and continue to aim for TSH target range

Post-Partum Management

Following the birth, if prescribed thyroxine prior to pregnancy, return to the pre-pregnancy dose or if this is unknown reduce the total weekly dose by 30%.

If thyroxine was commenced during pregnancy, review the ongoing need for thyroxine according to the following suggestions:

1. If initial TSH for this pregnancy was < 4.0 mIU/L and **antibody positive**

- Stop thyroxine after birth
- Repeat TSH in 6-8 weeks
    – If TSH < 4.0 mIU/L, continue off thyroxine, check TSH in 3-6 months to screen for progressive autoimmune hypothyroidism.
    – If TSH 4-10 mIU/L, **either**
        ○ re-commence thyroxine 50mcg daily (***recommended if planning another pregnancy***)

        or

        ○ observe and retest every 3 months in the first year post-partum + then every 6 months - note increased risk for developing established hypothyroidism, ongoing monitoring required
    – If TSH >10 mIU/L, recommence thyroxine 100mcg daily, most likely established hypothyroidism and likely to require indefinite thyroxine treatment.

2. If initial TSH for this pregnancy was 4.0 - 10 mIU/L and **antibody negative**

- Stop thyroxine after birth
- Repeat TSH in 6-8 weeks
    – If TSH < 4.0 mIU/L, continue off thyroxine. Repeat TSH in 3-6 months.
    – If TSH 4-10 mIU/L, **either**
        ○ re-commence thyroxine 50mcg daily (***recommended if planning another pregnancy***)

        or

        ○ repeat again in 3-6 months - ongoing monitoring advised.

3. If initial TSH for this pregnancy was 4.0 -10 mIU/L and **antibody positive**, moderate to high likelihood of long term thyroxine requirement. Options include:

- Continue thyroxine at the reduced total weekly dose of 30% less than the late pregnancy dose, repeat TSH 6-8 weeks later and adjust dose using local laboratory TSH range for non-pregnant patients (***recommended if planning another pregnancy***)

or

- Cease thyroxine and retest TSH in 6-8 weeks. Advise patient of possible long term thyroxine requirement and need for monitoring every 3 months during the first year post-partum + every 6 months subsequently.

4. If initial TSH for this pregnancy was >10 mIU/L regardless of antibody status, continue thyroxine at the reduced total weekly dose of 30% less than the late pregnancy dose, repeat TSH 6-8 weeks later and adjust dose using local laboratory TSH range for non-pregnant patients.

PLEASE NOTE:

Patients with positive antithyroid antibodies are at risk for postpartum thyroiditis which can present with non-specific symptoms. Check TSH if a patient with positive antithyroid antibodies presents with anxiety, depression, poor sleep, palpitations and fatigue (not an exhaustive list of symptoms).

If you have any concerns about your patient's management, then please contact either:

Dr Helen Tanner	helen.tanner@health.qld.gov.au	Ph: (07) 3646 8111
Obstetric Medicine Registrar	Monday- Friday 8am-430pm	Ph: (07) 3647 0473
Obstetric Medicine Consultant	After hours and weekends	Ph: (07) 3646 8111

Yours sincerely

Dr Helen Tanner

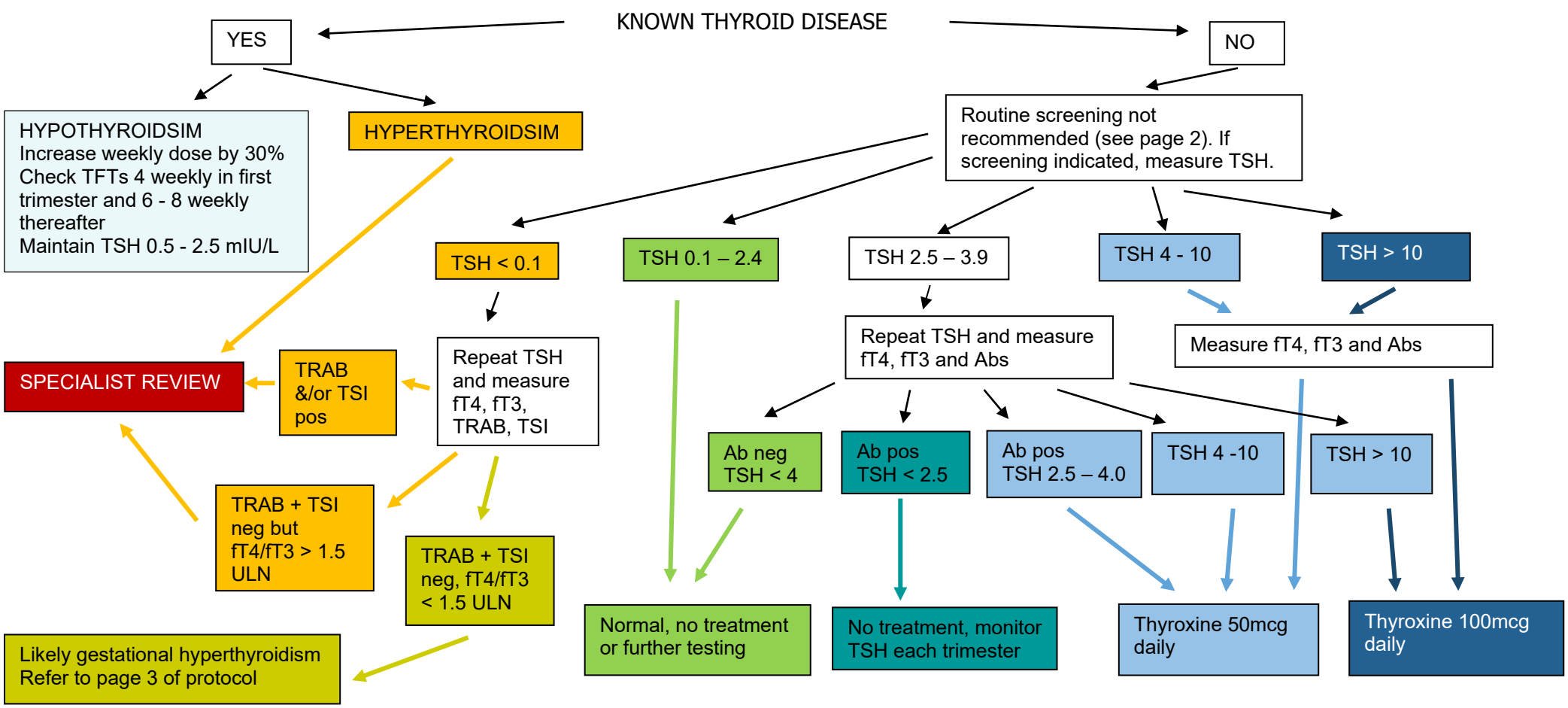
Clinical Director of Obstetric Medicine

Royal Brisbane and Women's Hospital

Reference

1. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum. DOI: 10.1089/thy.2016.0457

Management of Thyroid Disorders – prior to 13 weeks



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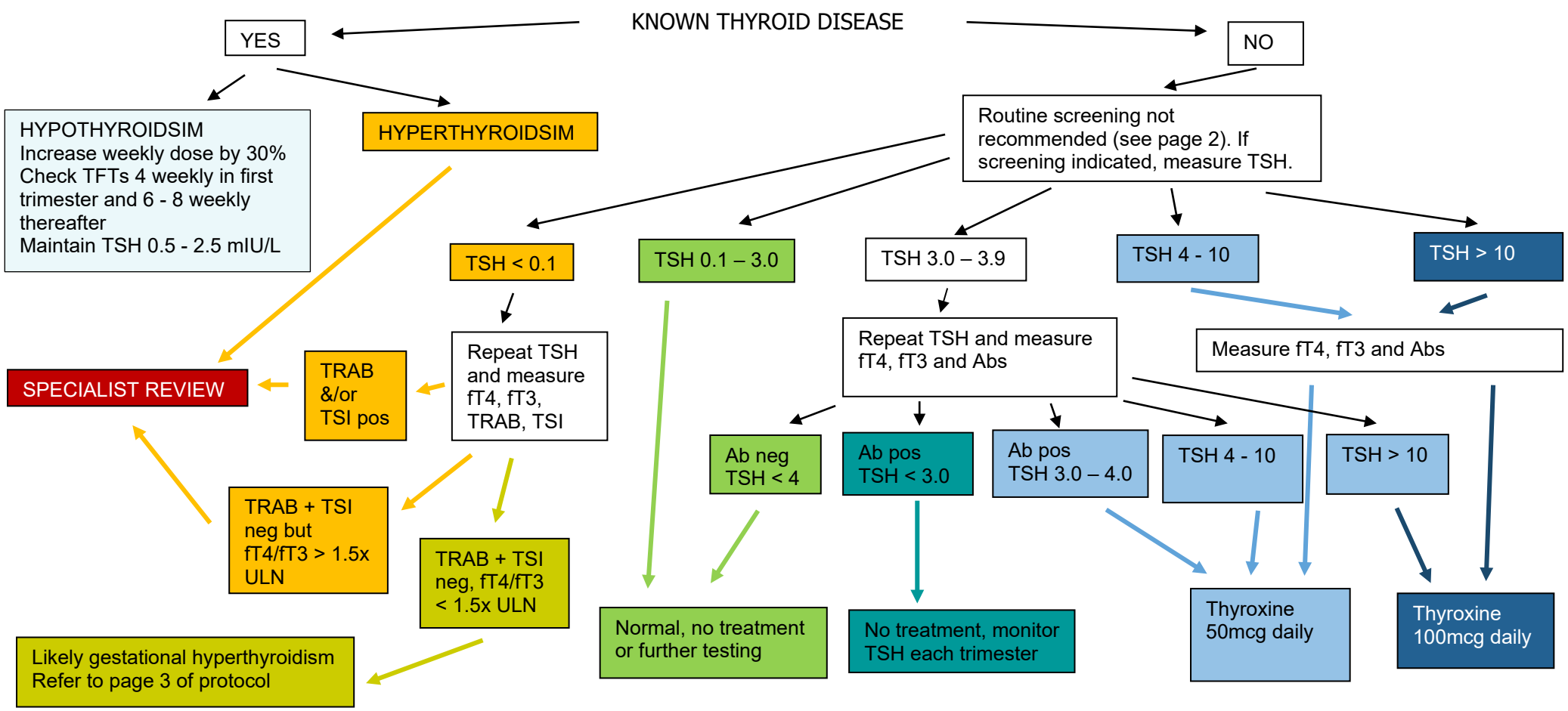
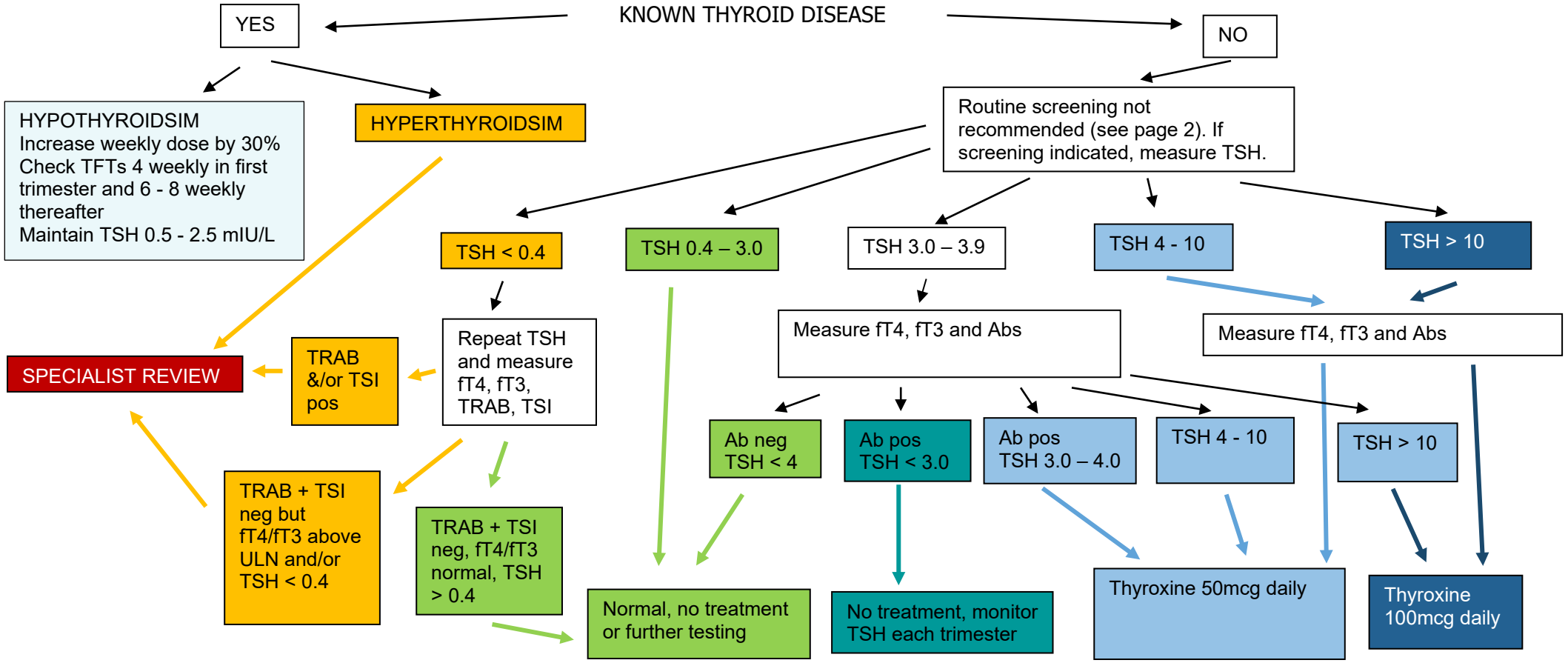
Management of Thyroid Disorders – 13-20 weeks



Management of Thyroid Disorders – after 20 weeks



Management of Thyroid Disorders – Postpartum