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

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>TSH</td>
<td>Thyroid stimulating hormone</td>
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<tr>
<td>fT4</td>
<td>free T4</td>
</tr>
<tr>
<td>fT3</td>
<td>free T3</td>
</tr>
<tr>
<td>Thyroid antibodies (Abs) = antithyroid antibodies = antithyroid peroxidase antibody + antithyroglobulin antibody</td>
<td></td>
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<tr>
<td>TRAb</td>
<td>TSH receptor antibody</td>
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<tr>
<td>TSI</td>
<td>thyroid stimulating immunoglobulin</td>
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<tr>
<td>RDI</td>
<td>Recommended daily intake</td>
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<tr>
<td>ULN</td>
<td>Upper limit of normal</td>
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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.
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>
<thead>
<tr>
<th>Prior to 20 weeks gestation</th>
<th>From 20 weeks gestation – term</th>
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</thead>
<tbody>
<tr>
<td><strong>If the initial TSH is &lt;0.1</strong> repeat the TSH and also measure fT4, fT3 and TSH receptor antibody titre (TRAb) and/or TSH receptor stimulating immunoglobulin (TSI)</td>
<td><strong>If the initial TSH is &lt;0.4</strong> repeat the TSH and also measure fT4, fT3 and TSH receptor antibody titre (TRAb) and/or TSH receptor stimulating immunoglobulin (TSI)</td>
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</tbody>
</table>

Positive TRAb and/or positive TSI regardless of other results—refer all patients to an Endocrinology Service

Negative TRAb and TSI

If fT4 and/or fT3 >1.5x the ULN of the laboratory reference range – REFER TO AN ENDOCRINOLOGY SERVICE

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.

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.
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.

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<th>Prior to 13 weeks gestation</th>
<th>From 13 weeks gestation - term</th>
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<td>If repeat TSH &lt; 2.5 mIU/L and antibodies are negative, no further testing and thyroxine NOT required</td>
<td>If repeat TSH &lt; 3.0 mIU/L and antibodies are negative, no further testing and thyroxine NOT required</td>
</tr>
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<td>If repeat TSH &lt; 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.</td>
<td>If repeat TSH &lt; 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.</td>
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<td>If repeat TSH is between 2.5 – 4.0 mIU/L and antibodies are negative - thyroxine NOT required.</td>
<td>If repeat TSH is between 3.0 – 4.0 mIU/L and antibodies are negative - thyroxine NOT required.</td>
</tr>
<tr>
<td>If repeat TSH &gt; 2.5 mIU/L and antibodies are positive, <strong>commence thyroxine 50 mcg daily.</strong></td>
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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
   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 \textit{(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

Known Thyroid Disease

Hypothyroidism
Increase weekly dose by 30%
Check TFTs 4 weekly in first trimester and 6 - 8 weekly thereafter
Maintain TSH 0.5 - 2.5 mIU/L

Hypothyroidism
Increase weekly dose by 30%
Check TFTs 4 weekly in first trimester and 6 - 8 weekly thereafter
Maintain TSH 0.5 - 2.5 mIU/L

Hyperthyroidism
Routine screening not recommended (see page 2). If screening indicated, measure TSH.

Specialist Review

TSH < 0.1
Repeat TSH and measure fT4, fT3, TRAB, TSI

TSH 0.1 – 2.4
Repeat TSH and measure fT4, fT3 and Abs

TSH 2.5 – 3.9
Repeat TSH and measure fT4, fT3 and Abs

TSH 4 - 10
Measure fT4, fT3 and Abs

TSH > 10

TRAB + TSI neg, fT4/fT3 < 1.5 ULN
TRAB + TSI neg but fT4/fT3 > 1.5 ULN
TRAB + TSI pos

TRAB &/or TSI pos

Ab neg
TSH < 4
Ab pos
TSH < 2.5
Ab pos
TSH 2.5 – 4.0

Thyroxine 50mcg daily
Thyroxine 100mcg daily

Normal, no treatment or further testing
No treatment, monitor TSH each trimester

Likely gestational hyperthyroidism
Refer to page 3 of protocol

NO

YES

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Management of Thyroid Disorders – 13-20 weeks

KNOWN THYROID DISEASE

HYPOTHYROIDISM
Increase weekly dose by 30%
Check TFTs 4 weekly in first trimester and 6 - 8 weekly thereafter
Maintain TSH 0.5 - 2.5 mIU/L

HYPERTHYROIDISM
Routine screening not recommended (see page 2). If screening indicated, measure TSH.

SPECIALIST REVIEW

TSH < 0.1
Repeat TSH and measure fT4, fT3, TRAB, TSI
Normal, no treatment or further testing

TSH 0.1 – 3.0
Repeat TSH and measure fT4, fT3 and Abs

TSH 3.0 – 3.9
Ab neg TSH < 4
No treatment, monitor TSH each trimester

Ab pos TSH < 3.0

Ab pos TSH 3.0 – 4.0

TSH 4 - 10
Ab pos
Thyroxine 50mcg daily

Ab neg
Thyroxine 100mcg daily

TSH > 10

TRAB + TSI neg, fT4/fT3 < 1.5x ULN
Likely gestational hyperthyroidism
Refer to page 3 of protocol

TRAB + TSI neg but fT4/fT3 > 1.5x ULN

TRAB &/or TSI pos

NO

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**Management of Thyroid Disorders – after 20 weeks**

**KNOWN THYROID DISEASE**

- **HYPOTHYROIDISM**
  - Increase weekly dose by 30%
  - Check TFTs 4 weekly in first trimester and 6 - 8 weekly thereafter
  - Maintain TSH 0.5 - 2.5 mIU/L

- **HYPERTHYROIDISM**
  - Routine screening not recommended (see page 2).
  - If screening indicated, measure TSH.

**SPECIALIST REVIEW**

- TRAB &/or TSI pos
- TRAB + TSI neg but fT4/fT3 above ULN and/or TSH < 0.4
- TRAB + TSI neg, fT4/fT3 normal, TSH > 0.4

**TSH < 0.4**

- Measure fT4, fT3 and Abs
- Normal, no treatment or further testing

**TSH 0.4 – 3.0**

- Repeat TSH and measure fT4, fT3, TRAB, TSI
- TRAB + TSI neg, fT4/fT3 normal, TSH > 0.4
- No treatment, monitor TSH each trimester

**TSH 3.0 – 3.9**

- Ab neg TSH < 4
- Ab pos TSH < 3.0
- Ab pos TSH 3.0 – 4.0

**TSH 3.0 – 3.9**

- TSH 4 – 10
- Ab neg
- Ab pos TSH < 3.0

**TSH > 4**

- TSH > 10
- Ab pos TSH > 10
- Thyroxine 50mcg daily
- Thyroxine 100mcg daily

**TSH > 10**

- No treatment, monitor TSH each trimester

- Measure fT4, fT3 and Abs

- Measure TRAB + TSI neg, fT4/fT3 above ULN and/or TSH < 0.4

- Measure TRAB + TSI neg, fT4/fT3 normal, TSH > 0.4
Management of Thyroid Disorders – Postpartum

**HYPERTHYROIDISM**

As per Specialist Advice. If Graves disease, flare highly likely in the first 12 months postpartum

**PRE-PREGNANCY HYPOTHYROIDISM**

- **Initial TSH > 10**
  - Recommended if planning another pregnancy
  - TSH > 10
    - Commence Thyroxine 100 mcg daily
    - Repeat TSH at 6-8 weeks and adjust thyroxine dose targeting local laboratory TSH for non-pregnant patients

- **Initial TSH 4 - 10 and Ab pos**
  - High risk of requiring ongoing treatment and of developing post partum thyroiditis
  - TSH 4 - 10
    - Commence Thyroxine 50 mcg daily

- **Initial TSH < 4.0 and Ab pos**
  - Moderate risk of requiring ongoing treatment or developing post partum thyroiditis
  - TSH < 4.0
    - Recommended if planning another pregnancy
    - Remain off treatment if Ab neg, recheck in 3-6 months and then annually. If Ab pos, recheck every 3 months in the first year then 6 monthly, at risk for short and long term thyroid dysfunction.

**THYROXINE COMMENCED DURING OR IMMEDIATELY PRIOR TO THIS PREGNANCY**

- **Initial TSH 4 - 10 and Ab neg**
  - Cease thyroxine at birth and repeat TSH 6-8 weeks post partum

- **Initial TSH > 10**
  - High risk of requiring ongoing treatment and of developing post partum thyroiditis
  - TSH > 10
    - Repeat TSH at 6-8 weeks and adjust thyroxine dose targeting local laboratory TSH for non-pregnant patients

- **Initial TSH < 4.0**
  - Moderate risk of requiring ongoing treatment or developing post partum thyroiditis
  - TSH < 4.0
    - Recommended if planning another pregnancy
    - Remain off treatment if Ab neg, recheck in 3-6 months and then annually. If Ab pos, recheck every 3 months in the first year then 6 monthly, at risk for short and long term thyroid dysfunction.

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