Recommendations for screening and treatment of hypothyroidism in pregnancy

Guidelines of the American Thyroid Association (ATA) for the diagnosis and management of thyroid disease during pregnancy and postpartum

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Pregnancy induces major changes in thyroid function[1]

During pregnancy:

- The thyroid adapts through changes in thyroid hormone and in the regulation of the hypothalamic-pituitary-thyroid axis
- Circulating total T_4 (TT_4) and T_4 binding globulin (TBG) concentrations increase by week 7 of gestation, reach a peak by approximately week 16 of gestation and remain high until delivery
- Serum FT_4 measurements are complicated by increased TBG and decreased albumin concentrations, the use of population-based, trimester-specific reference ranges remains the best way to handle this issue
- Serum TSH concentrations are for the typical patient beginning the late first trimester, week 7-12, upper reference limit of 4.0mU/L, with a gradual return towards the non-pregnant range in the second and third trimesters

Thyroid dysfunction may adversely affect the pregnancy and fetus[1]

Both overt and subclinical hypothyroidism may have adverse effects on the course of pregnancy and the development of the fetus, such as:

- An association with increased risks of adverse effects on pregnancy outcomes (pregnancy loss, fetal loss, premature birth, low birth weight)
- An association with an increased risk of adverse effects on pregnancy perinatal outcomes (pregnancy complications, premature delivery, gestational hypertension)
- An association with increased risk of detrimental effects upon fetal neurocognitive development and lower offspring IQ

Serum TSH testing is recommended if any risk factor is identified in patients seeking pregnancy or newly pregnant.[1]

- There is insufficient evidence to recommend for or against universal screening for abnormal TSH concentrations preconception, with the exception of women planning assisted reproduction or those known to have TPOAb positivity (No recommendation, insufficient evidence)
- Universal screening to detect low FT4 concentrations in pregnant women is not recommended. (Weak recommendation, moderate-quality evidence)
- Recommend pregnant women should be verbally screened at the initial prenatal visit for any history of thyroid dysfunction, and prior or current use of either thyroid hormone (LT4) or antithyroid medications (MMI, CM, or PTU), (Strong recommendation, high-quality evidence)

All patients seeking pregnancy, or newly pregnant, should undergo clinical evaluation. If any of the following risk factors are identified, testing for serum TSH is recommended (Strong recommendation moderate-quality evidence):

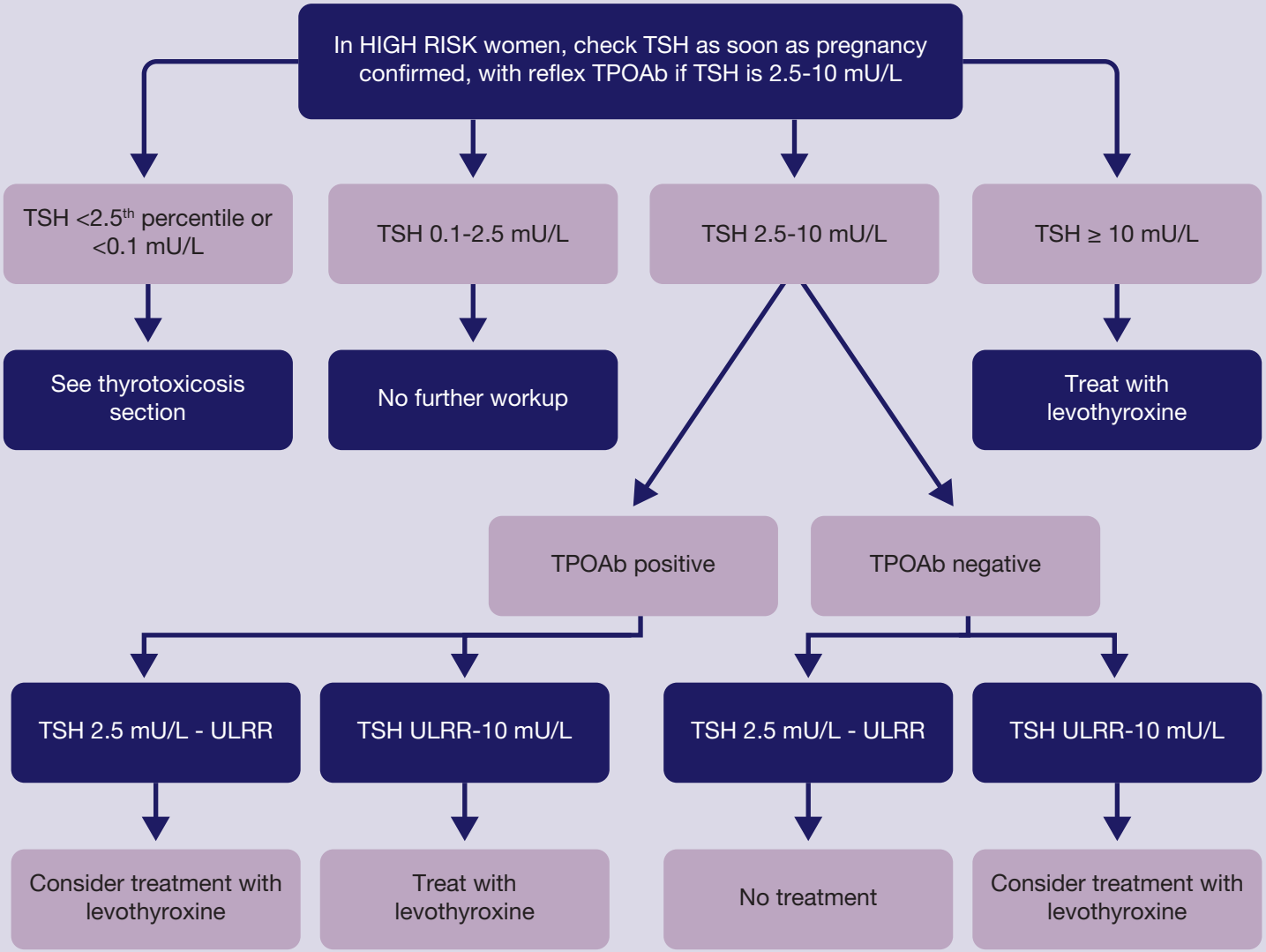
- A history of hypothyroidism/hyperthyroidism or current symptoms/signs of thyroid dysfunction
- Known thyroid antibody positivity or presence of a goiter
- History of head or neck radiation or prior thyroid surgery
- Age >30 years
- Type 1 diabetes or other autoimmune disorders
- History of pregnancy loss, preterm delivery, or infertility
- Multiple prior pregnancies (≥2)
- Family history of autoimmune thyroid disease or thyroid dysfunction
- Morbid obesity (BMI ≥40 kg/m^2)
- Use of amiodarone or lithium, or recent administration of iodinated radiologic contrast
- Residing in an area of known moderate to severe iodine insufficiency

Hormone levels of healthy pregnant women differ from those of healthy nonpregnant women[1]

In pregnant women	In nonpregnant women
The pregnancy-specific TSH reference range should be defined as follows:	The American Association of Clinical Endocrinologists classify a normal TSH range as:[2]*
• When available, population- and trimester-specific reference ranges for serum TSH during pregnancy should be defined by a provider's institute or laboratory and should represent the typical population for whom care is provided. Reference ranges should be defined in healthy TPOAb-negative pregnant women with optimal iodine intake and without thyroid illness (Strong recommendation, high-quality evidence). • When this goal is not feasible, pregnancy-specific TSH reference ranges obtained from similar patient populations and performed using similar TSH assays should be substituted. (Strong recommendation, high-quality evidence). • If internal or transferable pregnancy-specific TSH reference ranges are not available, an upper reference limit of ~4.0 mU/L may be used. For most assays, this limit represents a reduction in the nonpregnant TSH upper reference limit of ~0.5 mU/L (Strong recommendation, moderate-quality evidence).	**0.45–4.12** mIU/L

TPOAb - Thyroid Peroxidase Antibody.

Testing for thyroid dysfunction in pregnancy.[1]



ULRR - Upper Limit of the Reference Range.

Treating hypothyroidism during pregnancy[1]

Overt hypothyroidism (OH)

OH is defined as an elevated TSH (>2.5 mIU/L) in conjunction with a decreased FT_4 concentration. Women with TSH levels of ≥10.0 mIU/L, irrespective of FT_4 levels, are also considered to have OH.

Including but not limited to:

- LT4 treatment is recommended for infertile women with overt hypothyroidism who desire pregnancy (Strong recommendation, moderate-quality evidence).
- Treatment of overt hypothyroidism is recommended during pregnancy (Strong recommendation, moderate-quality evidence).

Subclinical hypothyroidism (SCH)

SCH is defined as a serum TSH between 2.5 and 10.0 mIU/L with a normal FT_4 concentration.

Pregnant women with TSH concentrations >2.5 mU/L should be evaluated for TPOAb status.

LT4 therapy is recommended for

- TPOAb-positive women with a TSH greater than the pregnancy-specific reference range (Strong recommendation, moderate-quality evidence).
- TPOAb-negative women with a TSH greater than 10.0 mU/L.

LT4 therapy may be considered for

- TPOAb-positive women with TSH concentrations >2.5 mU/L and below the upper limit of the pregnancy-specific reference range. (Weak recommendation, moderate-quality evidence).
- TPOAb-negative women and TPOAb-negative women with TSH concentrations greater than the pregnancyspecific reference range and below 10.0 mU/L. (Weak recommendation, low-quality evidence)

LT4 therapy is not recommended for

- TPOAb-negative women with a normal TSH (TSH within the pregnancy-specific reference range or <4.0 mU/L if unavailable) (Strong recommendation, high-quality evidence).

Recommended treatment of OH and SCH in pregnancy (Strong recommendation, low-quality evidence).[1]

The recommended treatment of maternal hypothyroidism is administration of oral LT4. Other thyroid preparations such as T3 or desiccated thyroid should not be used in pregnancy.

In parallel to the treatment of hypothyroidism in a general population, it is reasonable to target a TSH in the lower half of the trimester-specific reference range. When this is not available, it is reasonable to target maternal TSH concentrations below 2.5 mU/L (Weak recommendation, moderate-quality evidence).

Monitoring thyroid function in pregnant patients with treated hypothyroidism[1]

Women with overt and subclinical hypothyroidism (treated or untreated) or those at risk for hypothyroidism (e.g., patients who are euthyroid but TPOAb or TgAb positive, post-hemithyroidectomy, or treated with radioactive iodine) should be monitored with a serum TSH measurement approximately every 4 weeks until midgestation and at least once near 30 weeks gestation (Strong recommendation, high-quality evidence).

Managing LT_4 treatment in women with treated hypothyroidism.[1]

Treated hypothyroid women of reproductive age should be counseled regarding the likelihood of increased demand for LT4 during pregnancy. Such women should also be counseled to contact their caregiver immediately upon a confirmed or suspected pregnancy (Strong recommendation, high-quality evidence).

Adjusting LT_4 dosage[1]

Treated hypothyroid patients who are planning pregnancy

In hypothyroid women treated with LT4 who are planning pregnancy, serum TSH should be evaluated preconception, and LT4 dose adjusted to achieve a TSH value between the lower reference limit and 2.5 mU/L (Strong recommendation, moderate-quality evidence).

Treated hypothyroid patients who are newly pregnant

Hypothyroid patients receiving LT4 treatment with a suspected or confirmed pregnancy (e.g., positive home pregnancy test) should independently increase their dose of LT4 by ~20%–30% and urgently notify their caregiver for prompt testing and further evaluation. One means of accomplishing this is to administer two additional tablets weekly of the patient's current daily LT4 dosage (Strong recommendation, high-quality evidence).

Following delivery

- LT4 should be reduced to the patient's preconception dose. Additional thyroid function testing should be performed at approximately 6 weeks post partum (Strong recommendation, moderate-quality evidence).
- Some women in whom LT4 is initiated during pregnancy may not require LT4 post partum. Such women are candidates for discontinuing LT4. The decision to discontinue LT4, if desired, should be made by the patient and their caregiver. If LT4 is discontinued, serum TSH should be evaluated in approximately 6 weeks (Weak recommendation, moderate-quality evidence).

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- When this goal is not feasible, pregnancy-specific TSH reference ranges obtained from similar patient populations and performed using similar TSH assays should be substituted (Strong recommendation, high-quality evidence).
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In nonpregnant women

The American Association of Clinical Endocrinologists classify a normal TSH range as:[2*]

0.45–4.12 mIU/L

TPOAb - Thyroid Peroxidase Antibody.

Tell your patients to visit

thyroidsymptoms.ca and thyroid.ca

for more information about hypothyroidism during pregnancy

* TSH normal reference range may vary by lab due to analytical and biological variability. The upper limit of TSH in the literature ranges from 2.5–5.0 mIU/L.
In accordance with current ATA policies, the American College of Physicians Grading System was adopted for use in these guidelines. This grading scheme classifies the recommendations as strong or weak, and associates it with a classification of the quality of evidence supporting it i.e. high quality, moderate quality, low quality (or insufficient but only for weak recommendations).

References: 1. Alexander EK, Pearce EN, Brent GA, *et al.* 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid.* 2017 Mar;27(3):315-389.
2. Clinical Practice Guidelines for Hypothyroidism in Adults: Co-sponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Thyroid* 2012;22(12):1-36.

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