

Managing Thyroid Disease in Pregnancy

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Management of thyroid disease during pregnancy presents unique challenges due to physiologic changes that occur. These include

- Serum levels of thyroxine-binding globulin (TBG) increase along with estrogen; in turn, total thyroxine (T4) and triiodothyronine (T3) levels increase.
- Human chorionic gonadotropin (hCG) stimulates the thyroid stimulating hormone (TSH) receptors.¹

Since hCG and TSH share similar glycoprotein subunits, a transient suppression of TSH—especially around weeks 10 to 12, when hCG concentrations peak—is considered a physiologic finding. Interpretation of thyroid function testing should be made in relation to the hCG-mediated decrease in serum TSH levels.²

The following four cases will help guide your clinical management of thyroid disease in both preconception and pregnancy. Inadequately controlled thyroid dysfunction can lead to poor pregnancy outcomes for both mother and child, which will be further discussed.

CASE 1: STABLE HYPOTHYROIDISM

A 29-year-old woman with stable primary hypothyroidism calls your office to report that she is

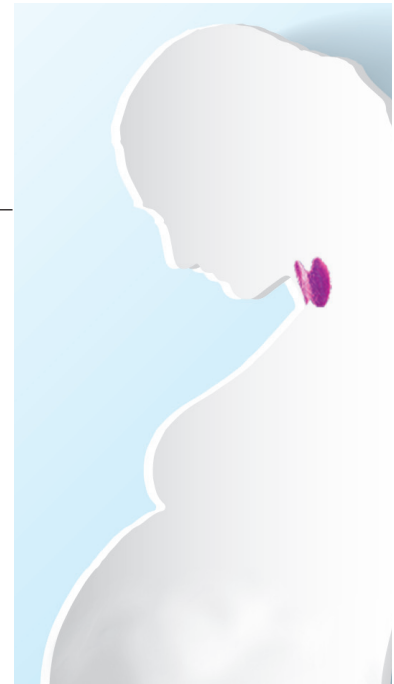
pregnant. She has taken levothyroxine (100 µg) for the past three years, and her TSH level was 1.21 mIU/L at last measurement. She denies any symptoms of hyperthyroidism or hypothyroidism. What is your next step in her management?

Recommendation

The American Thyroid Association recommends monitoring serum TSH every four weeks during the first half of pregnancy and at least once per trimester thereafter, with frequency depending on symptoms and TSH levels.³ Most women will require higher doses of levothyroxine supplementation to maintain therapeutic TSH levels.

Prior to 18 weeks' gestation, the fetus is dependent on maternal thyroid hormone. When pregnancy is confirmed, there is support in the literature for having the patient take two additional doses of levothyroxine per week until TSH can be tested.⁴ However, many endocrinology practices opt to check TSH and total T4 as soon as pregnancy is confirmed.

Since free T4 results may be unreliable during pregnancy (due to the effect of TBG), free thyroxine index (FTI) or total T4 should be monitored instead. FTI mathematically corrects free T4 for TBG levels, making it a useful marker. If total T4 is measured, it is important to remember that results will be approximately 1.5x the non-pregnancy value; thus, the refer-



ence range must be multiplied by 1.5 to calculate appropriate high and low parameters for pregnant patients.

Ideally, all women of child-bearing age should be encouraged to plan pregnancy, to ensure TSH is at target prior to conception. Maintaining a euthyroid state throughout pregnancy (starting at conception) is important to decrease risk for such adverse outcomes as spontaneous abortion, placental abruption, and gestational hypertension.² Low birth weight and respiratory distress are potential complications for newborns whose mothers have inadequately controlled hypothyroidism.

Patients should be counseled against simultaneous dosing of prenatal vitamins and levothyroxine. Prenatal vitamins contain iron, which reduces absorption of levothyroxine; therefore, it is recommended that the levothyroxine be taken four hours or more apart from prenatal vitamins.

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The Endocrine Society recommends a TSH no higher than 2.5 mIU/L for hypothyroidism diagnosed prior to pregnancy.^{2,3} After delivery, levothyroxine doses should be reduced to prepregnancy levels, with close monitoring of TSH.²

CASE 2: HISTORY OF SPONTANEOUS ABORTION

A 36-year-old G3P0 woman visits your office for a work-up after her third spontaneous abortion at 16 weeks. The patient denies history of thyroid disease but notes her maternal grandmother has Hashimoto disease. She denies symptoms of hyperthyroidism or hypothyroidism.

Recommendation

Both hyperthyroidism and hypothyroidism are associated with an increase in spontaneous abortion, premature labor, and low birth weight. Negro et al observed an increased risk for fetal loss, small-for-gestational-age fetus, premature delivery, and premature mortality in women who were TPO-antibody-positive, even if they were euthyroid. Improved fetal outcomes occurred when TPO-antibody-positive mothers received supplemental levothyroxine.⁵

However, the American Thyroid Association and the Endocrine Society state there is currently insufficient evidence to recommend universal screening of thyroid antibodies during pregnancy.^{2,3} Obtaining thyroid function studies and TPO-antibody tests could be considered as part of a work-up for women who experience multiple spontaneous abortions or have a personal or family history of autoimmune diseases.

CASE 3: CARDIOVASCULAR SYMPTOMS

A 24-year-old primigravida woman presents with complaints of palpitations and increased anxiety. She is currently 28 weeks pregnant. Her TSH level is undetectable (< 0.01 mIU/L), and her free T4 is 2.1 $\mu\text{g/dL}$ (reference range, 0.5-1.6 $\mu\text{g/dL}$). An ECG performed at your office shows sinus tachycardia with a rate of 127 beats/min.

Recommendation

Maternal hyperthyroidism increases risk for maternal congestive heart failure, uncontrolled hypertension, atrial fibrillation, and thyroid storm. Additionally, fetal hyperthyroidism can occur, especially if the mother has Graves disease. Since thyroid-stimulating immunoglobulins (TSI) can permeate the placental barrier, poor fetal growth, cardiac failure, and fetal thyrotoxicosis are severe adverse effects of in-utero TSI exposure.

To prevent further complications, antithyroid medications should be started in this case. Methimazole (MMI) carries a risk for a rare birth defect, aplasia cutis, in the first trimester and is best avoided during this time. Propylthiouracil (PTU) should be given in the first trimester and then switched to MMI in the second trimester to decrease the risk for hepatotoxicity associated with PTU. Breastfeeding mothers should be assured that low-dose MMI is generally considered safe for breastfed infants but should be taken after feeding in divided doses if possible.¹

For symptom relief, β -blockers can be used, although they do come with some risks. As pregnancy Category C drugs, β -block-

ers are associated with neonatal growth retardation, hypoglycemia, hypoxia, lower Apgar scores, and neonatal respiratory distress.⁶ Consider giving the lowest dose possible for the duration of the patient's symptoms.

Radioactive iodine (I-131) should not be given to patients who plan to become pregnant or who are pregnant.^{2,3} The Endocrine Society recommends that if a woman inadvertently becomes pregnant, she should be counseled on the risks of radiation to the fetus, which include thyroid destruction if treatment occurs/continues after the 12th week of pregnancy.² Furthermore, pregnancy should be avoided for the first six months after thyroid ablation to allow sufficient time to obtain the target maternal serum TSH level of 0.3 to 2.5 mIU/L.

CASE 4: PRECONCEPTION SCREENING

A 39-year-old G0P0 woman presents for preconception counseling. She denies family or personal history of thyroid disease and symptoms of thyroid disease. Should she be screened?

Recommendation

There is no consensus or guideline regarding preconception laboratory screening for thyroid disease. Current guidelines by the American Thyroid Association, the American College of Obstetricians and Gynecologists, and the Endocrine Society recommend targeted, not universal, screening.^{2,3,7}

The American Thyroid Association and the Endocrine Society recommend screening TSH in women who are pregnant or intend to become pregnant and

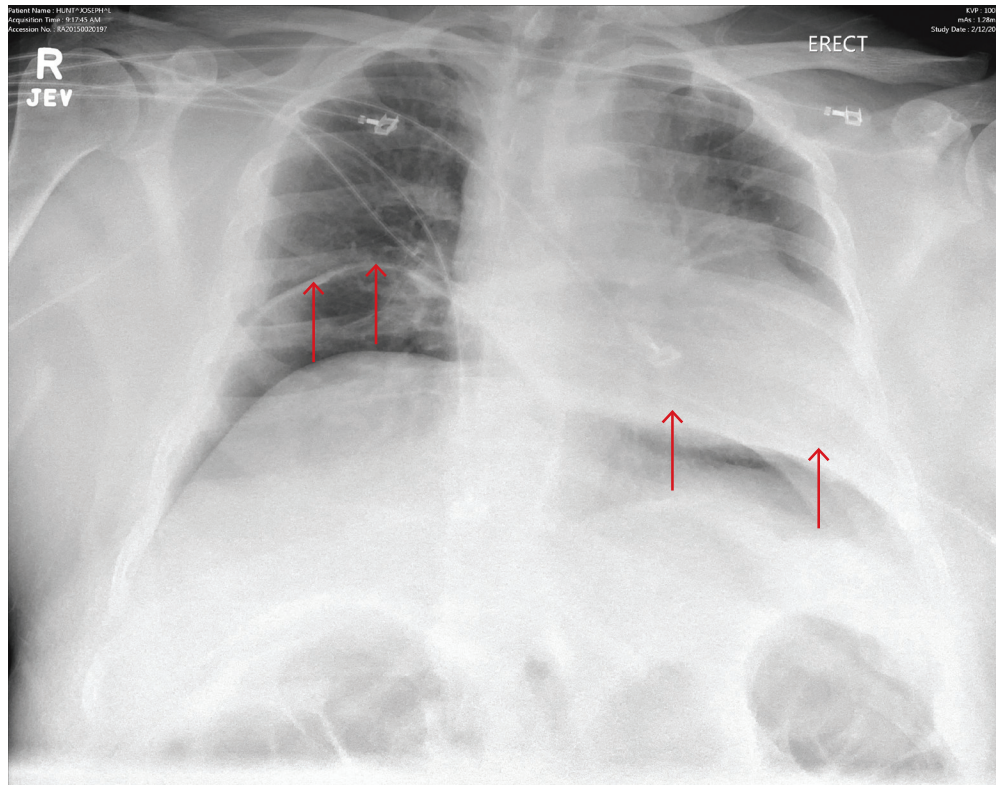
- Have a personal or family his-

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ANSWER

The radiograph demonstrates bilateral elevated diaphragm with a moderate amount of visible free air. With no history of recent abdominal procedures, the primary concern is a perforated viscus.

Urgent surgical consultation, as well as CT of the abdomen and pelvis, was obtained. The imaging confirmed the free air but provided no clear etiology. The patient underwent emergent laparotomy later that day and was found to have a perforated colon. **CR**



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tory of thyroid disease

- Are older than 30
- Demonstrate symptoms of thyroid dysfunction
- Have goiter
- Are TPO-antibody positive
- Have type 1 diabetes or other autoimmune disorders
- Have a history of miscarriage or preterm delivery
- Have a history of head or neck radiation or thyroid surgery
- Are morbidly obese (BMI > 40)
- Use amiodarone or lithium or were exposed to iodinated radiologic contrast
- Are infertile
- Live in an area with moderate to severe iodine insufficiency.^{2,3}

Rationale for targeted screen-

ing of asymptomatic women: Large-scale research has not demonstrated significantly better outcomes in those with subclinical hypothyroidism who receive treatment.⁷ Small studies² have demonstrated improved fetal outcomes when subclinical hypothyroidism is treated, but for large bodies (eg, the US Preventive Services Task Force) to recommend screening, a clear improvement in health outcomes must be established via controlled studies. Future research should evaluate the effect of treating subclinical hypothyroidism during pregnancy.

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