Northwest Perinatal Center

Perinatal Progress

Thyroid Disease in Pregnancy: An Update

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The evolving management of thyroid disease in pregnancy may present a challenge. In April 2015, the American Congress of Obstetricians and Gynecologists (ACOG) updated its 2002 publication on the topic in Practice Bulletin Number 148, *Thyroid Disease in Pregnancy*. Most of the information is the same, but there are some important facts that have changed and some that merit reiteration.[1] This issue of *Perinatal Progress* will summarize the salient features of the ACOG publication, as well as pertinent and interesting points from other sources.

Background

Overt, untreated thyroid dysfunction in pregnancy is associated with poor outcomes. Furthermore, the fetus requires normal thyroxine (T4) levels for normal brain development, especially in the first trimester before the fetal thyroid begins to produce endogenous T4. Maternal T4 crosses the placenta; therefore, it is crucial that maternal T4 levels are normal.

Indications for testing

The only currently-recommended indications for thyroid testing in pregnancy are:

- pre-existing thyroid condition;
- signs and/or symptoms of overt thyroid dysfunction; or
- women with pre-gestational diabetes who have not been screened previously, since they have an increased risk for thyroid dysfunction.

Topics for discussion

Subclinical hypothyroidism

Subclinical hypothyroidism is defined as elevated TSH with normal free T4, in the absence of clinical signs or symptoms. It occurs in 2-5% of pregnant women.[1] Data from a large randomized trial have shown that screening and treatment of women with subclinical hypothyroidism during pregnancy did not improve childhood neurodevelopmental outcomes at age three.[2] More recently, a lead presentation at the 2016 Society for Maternal Fetal-Medicine (SMFM) Annual Meeting concluded that cognitive outcomes at age five were not improved in women who were treated for subclinical hypothyroidism/hypothyroxinemia.[3]

With regard to maternal outcomes, there are also newer data that refute the association between subclinical hypothyroidism and adverse outcomes, such as preterm birth, preeclampsia, and gestational diabetes.[4,5] Thus, **there is no evidence that screening and treatment of subclinical hypothyroidism results in improved maternal/neonatal outcomes, and is therefore not recommended.**

Hyperemesis gravidarum

Increasing levels of hCG in the first trimester may stimulate TSH receptors and increase free T4, resulting in a suppressed TSH. This condition is called gestational transient hyperthyroidism. Gestational transient hyperthyroidism has not been associated with poor pregnancy outcomes, and it resolves spontaneously. **Routine measurements of thyroid function are not recommended in patients with hyperemesis gravidarum.** TSH should not be checked unless there are other overt signs of hyperthyroidism.

Screening during infertility evaluation

Although screening for subclinical hypothyroidism is no longer recommended in pregnancy, it is often done as part of infertility evaluation. Patients with subclinical hypothyroidism are treated with levothyroxine to improve fertility.[6] An abrupt discontinuation of levothyroxine in a subsequent pregnancy may be met with patient anxiety and confusion. In such cases, Northwest Perinatal Center recommends continuing the prescribed levothyroxine during the pregnancy, **but without TSH monitoring.** We recommend discontinuation of T4 therapy postpartum and checking thyroid function at the 6-8 week postpartum visit.

Thyroid testing

The initial test for thyroid disease is a thyroid stimulating hormone (TSH) level. The American Thyroid Association recommends using the following trimester-specific TSH reference ranges:[7]

Table 1: TSH Reference Ranges by Trimester

TRIMESTER	RANGE
First trimester	0.1-2.5 mIU/L
Second trimester	0.2-3.0 mIU/L
Third trimester	0.3-3.0 mIU/L

If TSH is abnormal, a free T4 level should be checked to make a diagnosis. If free T4 is normal and there is still a high suspicion for hyperthyroidism, free T3 should be checked, given the rare possibility of isolated T3 hyperthyroxinemia.

The diagnosis of thyroid disease may be made by interpreting thyroid function tests as follows:[1]

Table 2: Diagnosing Thyroid Disease in Pregnancy

DIAGNOSIS	TSH*	FREE T4
Overt hypothyroidism	↑	↓
Subclinical hypothyroidism	↑	normal
Overt hyperthyroidism	↓	↑
Subclinical hyperthyroidism	↓	normal

**trimester-specific TSH ranges*

Hypothyroidism

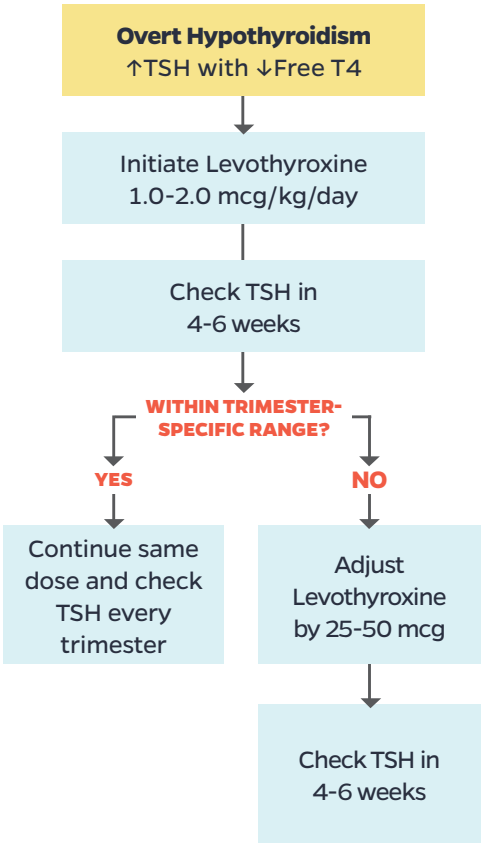
Risks

The perinatal risks of uncontrolled severe hypothyroidism in pregnancy include fetal growth restriction, miscarriage, preeclampsia, and intrauterine fetal demise. The neonatal risks are low birth weight and impaired childhood neurocognitive development.[8]

Management

The management algorithm for overt hypothyroidism in pregnancy is illustrated in Figure 1. If hypothyroidism is well-controlled, there is no indication for early delivery.

Figure 1: Management of Overt Hypothyroidism in Pregnancy



According to ACOG and the American Thyroid Association, the treatment of choice for clinical hypothyroidism is synthetic T4, or levothyroxine.[1,7] We occasionally encounter patients who use other "natural" formulations. One such product is desiccated porcine thyroid (such as Armour Thyroid and Nature-Throid), which contains both T3 and T4 in ratios that may be different from human needs. Because T3 does not cross the placenta, the American Thyroid Association recommends that T3 preparations (natural or synthetic) not be used during pregnancy.[7] We recommend transitioning patients to levothyroxine according to Figure 1, if they are amenable.

In the postpartum period, levothyroxine should be reduced to the pre-pregnancy dose and TSH checked at the 6-8 week postpartum visit.

Antenatal surveillance

We do not recommend antenatal testing, additional ultrasound surveillance, or early delivery in patients with well-controlled hypothyroidism. Fortunately, these

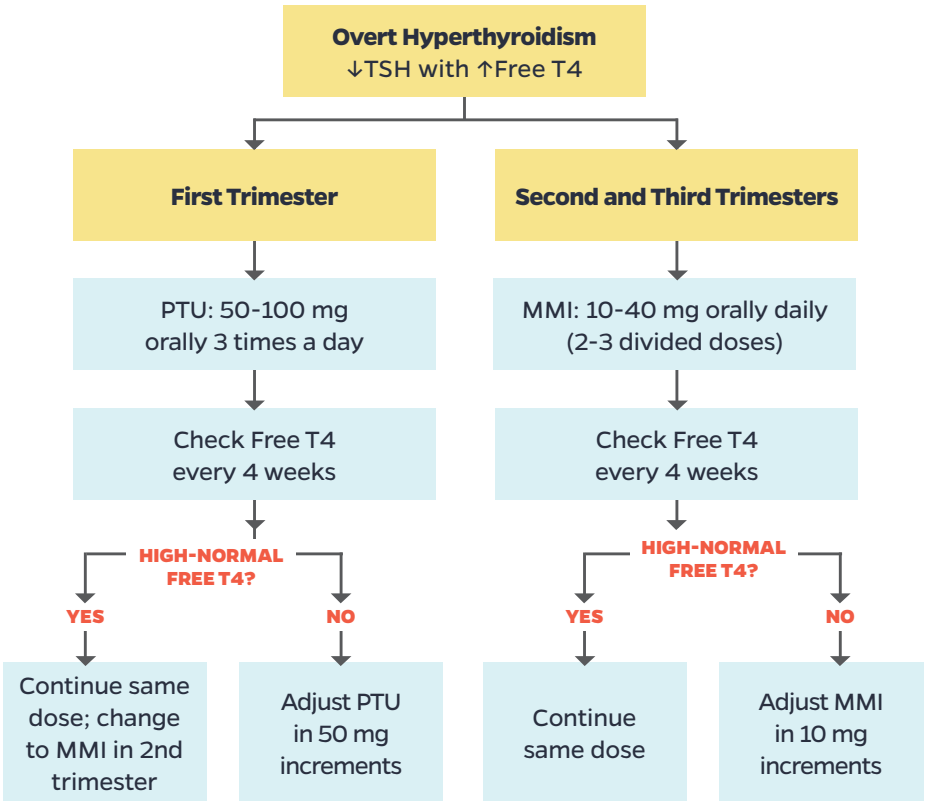
patients represent the vast majority.

Hyperthyroidism

Risks

The maternal risks of uncontrolled hyperthyroidism in pregnancy include thyroid storm and thyrotoxic heart failure, as well as severe preeclampsia. The fetal risk is related to immune-mediated hyperthyroidism (see below). The treatment for hyperthyroidism is not as simple as for hypothyroidism. **We recommend MFM consultation at the beginning of the pregnancy to coordinate surveillance and collaboration with endocrinology, if indicated.**

Figure 2: Management of Overt Hyperthyroidism in Pregnancy



Management

The management algorithm for hyperthyroidism in pregnancy is illustrated in Figure 2. The thioamides propylthiouracil (PTU) and methimazole (MMI) are used in pregnancy. PTU is no longer recommended for use in the entire pregnancy because of the risk for maternal hepatotoxicity, and MMI is not recommended in the first trimester due to risk for embryopathy. If a beta-blocker is needed for symptomatic tachycardia, propranolol (20 mg every 6-8 hours) may be used. **Free T4 (not TSH) should be checked every four weeks.** The therapeutic goal is to maintain high-normal free T4 levels, regardless of the TSH level, using the lowest possible thioamide dose. In the postpartum period, the same dose should be continued and free T4 level checked at the 6-8 week postpartum visit.

Subclinical hyperthyroidism. Subclinical hyperthyroidism is defined as a low TSH with a normal free T4, and has not been associated with adverse pregnancy outcomes.[8] As such, treatment is not recommended because antithyroid medications cross the placenta and have potential for adverse fetal effects.

Graves' disease. Most cases of hyperthyroidism are due to maternal Graves' disease, an autoimmune disease, raising concerns for neonatal Graves' disease from transplacental passage of maternal thyroid-stimulating immunoglobulin (TSI). Women who have been definitively treated for Graves' disease before pregnancy (by I-131 or thyroidectomy) are at higher risk for neonatal Graves' disease. They still produce TSI, which cross the placenta, but they do not take thioamides, which also cross the placenta and balance the effect of the TSI. Moreover, these women are often labeled as having "hypothyroidism" because they take thyroid replacement, and the fetal risk is overlooked. In the past, some experts have recommended checking levels of TSI to determine fetal risk; however, all pregnancies in women with a history of Graves' disease should be considered at risk for fetal thyrotoxicosis.

Our recommendations for fetal surveillance in women with a history of Graves' disease include ultrasound at 28 weeks to check for fetal tachycardia, growth restriction, or fetal hydrops. Audible persistent fetal tachycardia at

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Dr. Farkouh grew up in New York City. She received her undergraduate degree in biology from Union College and her medical degree from Albany Medical College as part of a six-year accelerated program. She completed her OB/GYN residency at the State University of New York in Stony Brook and her Maternal-Fetal Medicine fellowship at the University of Colorado Health Sciences Center. After completing her fellowship in 1997, Dr. Farkouh remained in Denver as a perinatologist in private practice for 16 years. She also served as the associate director of Maternal-Fetal Medicine at Presbyterian/St. Luke's Medical Center-Rocky Mountain Hospital for Children and as the medical director of the Center for Perinatal Medicine at Exempla St. Joseph Hospital, both in Denver. She is a passionate advocate for adult and childhood vaccinations, after almost losing her newborn to pertussis in 2010. She is also internationally recognized in the area of delayed-interval delivery in multifetal pregnancies.

Thyroid disease in pregnancy, con't...

office visits may be also be an indicator of fetal thyrotoxicosis. Cordocentesis for fetal thyroid studies is performed only if there is suspicion for fetal hyperthyroidism. Treatment of such is intricate and beyond the scope of our discussion here.

Antenatal surveillance

Antenatal surveillance and timing of delivery should be individualized.

References

1. Thyroid Disease in Pregnancy. ACOG Practice Bulletin No. 148. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:996-1005.
2. Lazarus JH et al. Antenatal thyroid screening and childhood cognitive function. N Engl J Med 2012;366:493-501.
3. Casey B. Effect of treatment of maternal subclinical hypothyroidism or hypothyroxinemia on IQ in offspring. Abstract presented at 2016 Society for Maternal-Fetal Medicine Annual Meeting. Am J Obstet Gynecol 2016;214:S2.
4. Cleary-Goldman J. Maternal thyroid hypofunction and pregnancy outcome. Obstet Gynecol 2008;112:85-92.
5. Casey BM, et al. Perinatal significance of isolated maternal hypothyroxinemia identified in the first half of pregnancy. Obstet Gynecol 2007;109:1129-35.
6. Subclinical hypothyroidism in the infertile female population: a guideline. Practice Committee of the American Society for Reproductive Medicine. Fertil Steril 2015;104:545-53.
7. Stagnaro-Green A, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011; 21:1081-125.
8. Casey BM, et al. Thyroid disease in pregnancy. Obstet Gynecol 2006;108:1283-92.

KEY TAKE-AWAYS

- **No universal screening for thyroid disease in pregnancy**
- **No thyroid function testing with hyperemesis gravidarum**
- **Use TSH to *screen* for thyroid disease, when indicated**
- **When TSH is abnormal, use free T4 to *diagnose* thyroid disease**
- **Use trimester-specific ranges for TSH to monitor treatment for hypothyroidism**
- **Use free T4 to monitor treatment for hyperthyroidism**
- **Recognize the risk for fetal thyrotoxicosis in patients with Graves' disease, even if definitively treated**

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