Hyperthyroidism in Pregnancy

WHAT IS THE THYROID GLAND?

The thyroid gland is a butterfly-shaped endocrine gland that is normally located in the lower front of the neck. The thyroid's job is to make thyroid hormones, which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.

WHAT ARE THE NORMAL CHANGES IN THYROID FUNCTION ASSOCIATED WITH PREGNANCY?

HORMONE CHANGES. A normal pregnancy results in a number of important physiological and hormonal changes that alter thyroid function. These changes mean that laboratory tests of thyroid function must be interpreted with caution during pregnancy. Thyroid function tests change during pregnancy due to the influence of two main hormones: human chorionic gonadotropin (hCG), the hormone that is measured in the pregnancy test and estrogen, the main female hormone. HCG can weakly turn on the thyroid and the high circulating hCG levels in the first trimester may result in a slightly low TSH. When this occurs, the TSH will be slightly decreased in the first trimester and then return to normal throughout the duration of pregnancy. Estrogen increases the amount of thyroid hormone binding proteins in the serum which increases the total thyroid hormone levels in the blood since >99% of the thyroid hormones in the blood are bound to these proteins. However, measurements of "Free" hormone (that are not bound to protein, representing the active form of the hormone) usually remain normal. The thyroid is functioning normally if the TSH and Free T4 remain in the trimester-specific normal ranges throughout pregnancy.

SIZE CHANGES. The thyroid gland can increase in size during pregnancy (enlarged thyroid = goiter). However, pregnancy-associated goiters occur much more frequently in iodine-deficient areas of the world. It is relatively uncommon in the United States. If very sensitive imaging techniques (ultrasound) are used, it is possible to detect an increase in thyroid volume in some women. This is usually only a 10-15% increase in size and is not typically apparent on physical examination by the physician. However, sometimes a significant goiter may develop and prompt the doctor to measure tests of thyroid function.

WHAT IS THE INTERACTION BETWEEN THE THYROID FUNCTION OF THE MOTHER AND THE BABY?

For the first 18-20 weeks of pregnancy, the baby is completely dependent on the mother for the production of thyroid hormone. By mid-pregnancy, the baby's thyroid begins to produce thyroid hormone on its own. The baby, however, remains dependent on the mother for ingestion of adequate amounts of iodine, which is essential to make the thyroid hormones. The World Health Organization recommends iodine intake of 250 micrograms/day during pregnancy to maintain adequate thyroid hormone production. Because iodine intakes in pregnancy are currently low in the United States, the ATA recommends that US women who are planning pregnancy, pregnant, or breastfeeding should take a daily supplement containing 150 mcg of iodine.

HYPERTHYROIDISM & PREGNANCY

WHAT ARE THE MOST COMMON CAUSES OF HYPERTHYROIDISM DURING PREGNANCY?

Overall, the most common cause of hyperthyroidism in women of childbearing age is Graves' disease (see *Graves' Disease brochure*), which occurs in 0.2% of pregnant patients. In addition to other usual causes of hyperthyroidism (see *Hyperthyroidism brochure*), very high levels of hCG, seen in severe forms of morning sickness (hyperemesis gravidarum), may cause transient hyperthyroidism in early pregnancy. The correct diagnosis is based on a careful review of history, physical exam and laboratory testing.

WHAT ARE THE RISKS OF GRAVES' DISEASE/ HYPERTHYROIDISM TO THE MOTHER?

Graves' disease may present initially during the first trimester or may be exacerbated during this time in a woman known to have the disorder. In addition to the classic symptoms associated with hyperthyroidism, inadequately treated maternal hyperthyroidism can result in early labor and a serious complication known as pre-eclampsia. Additionally, women with active Graves' disease during pregnancy are at higher risk of developing very severe hyperthyroidism known as thyroid storm. Graves' disease often improves during the third trimester of pregnancy and may worsen during the post partum period.

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WHAT ARE THE RISKS OF GRAVES' DISEASE/ HYPERTHYROIDISM TO THE BABY?

The risks to the baby from Graves' disease are due to one of three possible mechanisms:

- 1)UNCONTROLLED MATERNAL HYPERTHYROIDISM: Uncontrolled maternal hyperthyroidism has been associated with fetal tachycardia (fast heart rate), small for gestational age babies, prematurity, stillbirths and congenital malformations (birth defects). This is another reason why it is important to treat hyperthyroidism in the mother.
- 2) EXTREMELY HIGH LEVELS OF THYROID STIMULATING IMMUNOGLOBLULINS (TSI): Graves' disease is an autoimmune disorder caused by the production of antibodies that stimulate the thyroid gland referred to as thyroid stimulating immunoglobulins (TSI). These antibodies do cross the placenta and can interact with the baby's thyroid. High levels of maternal TSI's have been known to cause fetal or neonatal hyperthyroidism, but this is uncommon (only 1-5% of women with Graves' disease during pregnancy). Fortunately, this typically only occurs when the mother's TSI levels are very high (many times above normal). Measuring TSI in the mother with Graves' disease is recommended in early pregnancy and, if initially elevated, again around weeks 18-22.

When a mother with Graves' disease requires antithyroid drug therapy during pregnancy, fetal hyperthyroidism is rare because antithyroid drugs also cross the placenta and can prevent the fetal thyroid from becoming overactive. Of potentially more concern to the baby is when the mother has been treated for Graves' disease (for example radioactive iodine or surgery) and no longer requires antithyroid drugs. It is very important to tell your doctor if you have been treated for Graves' Disease in the past so proper monitoring can be done to ensure the baby remains healthy during the pregnancy.

3)ANTI-THYROID DRUG THERAPY (ATD). Methimazole

(Tapazole) or propylthiouracil (PTU) are the ATDs available in the United States for the treatment of hyperthyroidism (see Hyperthyroidism brochure). Both of these drugs cross the placenta and can potentially impair the baby's thyroid function and cause fetal goiter. Use of either drug in the first trimester of pregnancy has been associated with birth defects, although the defects associated with PTU are less frequent and less severe. Definitive therapy (thyroid surgery or radioactive iodine treatment) may be considered prior to pregnancy in order to avoid the need to use PTU or methimazole in pregnancy. When ATDs are required, PTU is preferred until week 16 of pregnancy. It is recommended that the lowest possible dose of ATD be used to control maternal hyperthyroidism in order to minimize the development of hypothyroidism in the baby. Overall, the benefits to the baby of treating a mother with hyperthyroidism during pregnancy outweigh the risks if therapy is carefully monitored.

WHAT ARE THE TREATMENT OPTIONS FOR A PREGNANT WOMAN WITH GRAVES' DISEASE/ HYPERTHYROIDISM?

Mild hyperthyroidism (slightly elevated thyroid hormone levels, minimal symptoms) often is monitored closely without therapy as long as both the mother and the baby are doing well. When hyperthyroidism is severe enough to require therapy, anti-thyroid medications are the treatment of choice, with PTU being preferred in the first trimester. The goal of therapy is to keep the mother's free T4 in the high-normal to mildly elevated range on the lowest dose of antithyroid medication. Addition of levothyroxine to ATDs ("block-and-replace") is not recommended. Targeting this range of free hormone levels will minimize the risk to the baby of developing hypothyroidism or goiter. Maternal hypothyroidism should be avoided. Therapy should be closely monitored during pregnancy. This is typically done by following thyroid function tests (TSH and thyroid hormone levels) monthly.



FURTHER INFORMATION

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In patients who cannot be adequately treated with anti-thyroid medications (i.e. those who develop an allergic reaction to the drugs), surgery is an acceptable alternative. Surgical removal of the thyroid gland is safest in the second trimester.

Radioiodine is contraindicated to treat hyperthyroidism during pregnancy since it readily crosses the placenta and is taken up by the baby's thyroid gland. This can cause destruction of the gland and result in permanent hypothyroidism.

Beta-blockers can be used during pregnancy to help treat significant palpitations and tremor due to hyperthyroidism. They should be used sparingly due to reports of impaired fetal growth associated with long-term use of these medications. Typically, these drugs are only required until the hyperthyroidism is controlled with anti-thyroid medications.

WHAT IS THE NATURAL HISTORY OF GRAVES' DISEASE AFTER DELIVERY?

Graves' disease typically worsens in the postpartum period or may occur then for the first time. When new hyperthyroidism occurs in the first months after delivery, the cause may be either Graves' disease or postpartum thyroiditis and testing with careful follow-up is needed to distinguish between the two. Higher doses of anti-thyroid medications may be required during this time. As usual, close monitoring of thyroid function tests is necessary.

CAN THE MOTHER WITH GRAVES' DISEASE, WHO IS BEING TREATED WITH ANTI-THYROID DRUGS, BREASTFEED HER INFANT?

Yes. Although very small quantities of both PTU and methimazole are transferred into breast milk, total daily doses of up to 20mg methimazole or 450mg PTU are considered safe and monitoring of the breastfed infants' thyroid status is not required.

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