Thyroid During Pregnancy: Maternal Fetal Thyroid Pathology

Thyroid hormones are amine hormones produced by the thyroid gland. There are two types of thyroid hormones: triiodothyronine (T3) and thyroxine (T4). They are stored in thyroid follicles as a component of thyroglobulin. Once released in the blood, 2/3 of the hormones are transported while bound to Thyroxine-Binding Globulin.

Functions of Thyroid Hormones

The thyroid hormones generally work to increase the body’s metabolic rate by increasing the rate at which chemical reactions occur inside cells. They affect the following metabolisms:

- **Protein metabolism** stimulates protein synthesis by speeding the transcription process on the ribosome and the translation process in the nucleus. This primarily results in increased number of cellular enzymes.
- **Carbohydrate metabolism** stimulates glucose absorption from the gut and increases secretion of insulin as well as glucose uptake by body cells; it also
speeds up glycolysis and gluconeogenesis.

- **Fat metabolism** increases fatty acid concentration in the plasma by mobilizing fatty acids in the adipose tissues. This process is known as lipolysis.
- **Vitamin metabolism:** By increasing the synthesis of cellular enzymes, the thyroid hormones subsequently increase the body’s need for vitamins. Vitamins are crucial components of enzymes and co-enzymes in metabolic reactions.

Organs which are exempted from the metabolic effects of the thyroid hormones include the brain, spleen and kidneys. The thyroid hormones affect the following body systems:

- **Cardiovascular system:** Thyroid hormones directly boost the heart rate. Another way to raise heart rate is by increasing cardiac output, and cardiac output increases as a result of amplified blood flow, which, in turn, is due to increased metabolism in the body.
- **Respiratory system:** Thyroid hormones increase the body’s metabolism which, in turn, raises the demand and utilization of oxygen. Increased oxygen demand leads to higher respiratory rate and depth.
- **Central Nervous System:** The maternal levels of thyroid hormones are most important when it comes to CNS development during the perinatal period. Proper maturation of the central nervous system is highly dependable on the thyroid hormones’ saturation during the perinatal period. Low thyroid levels in the pregnant mother can lead to permanent mental retardation.
Thyroid system

Image: “Diagram of the hypothalamic-pituitary-thyroid axis. The hypothalamus secretes TRH (green), which stimulates the production of TSH (red) by the pituitary gland. This, in turn, stimulates the production of thyroxine by the thyroid (blue). Thyroxine levels decrease TRH and TSH production by a negative feedback process,” by Mikael Häggström. License:

**Thyroid stimulating hormone**

This glycoprotein hormone is produced by the thyrotope cells in the anterior pituitary. It works through the adenylate cyclase-cAMP mechanism to increase the synthesis and secretion of thyroid hormones from the follicular cells of the thyroid gland. **Thyroid releasing hormone**, produced by the hypothalamus, causes the release of thyroid stimulating hormone from the pituitary gland.

**Thyroid binding globulin**

This binding globulin has the highest affinity for thyroid hormones in the plasma. Its levels in the blood can be used to test for thyroid diseases, especially in the case of elevated endogenous thyroid hormones.
Maternal Thyroid Changes During Pregnancy

Early in pregnancy, the mother's thyroid hormone production increases by 50%.

**Estrogen** is a primary female sex hormone which also plays a major role in pregnancy. Estrogen contributes to the development of many fetal parts, mainly stimulating the fetus's adrenal glands to produce hormones. It also maintains the uterus to accommodate the pregnancy, in addition to responding to oxytocin.

One of the functions of estrogen is to cause increased levels of thyroid binding globulin synthesis and release from the **liver**. This significantly increases its blood concentration during pregnancy.

TBG has a higher affinity for T4 than T3, hence increase in the blood concentration of TBG leads to lowered levels of free T4 in the blood. This triggers a negative feedback reaction which leads to increased production of TSH from the anterior pituitary. As a result, thyroid hormone production increases. Therefore, the final effect of increased TBG is amplified production of thyroid hormones, which meets the demands of the pregnant woman's body.

Furthermore, a hormone called **human chorionic gonadotropin**, which is produced by the syncytiotrophoblast in the placenta of pregnant women, also works to stimulate the thyroid gland due to its similarity to TSH. HCG levels are the highest during the last days of the first trimester, therefore, there is a fall in TSH levels during this time.

**Increased demand of iodine and pregnancy-induced goiter**
Iodine plays a pivotal role in thyroid hormone synthesis. There’s an increased demand of iodine in pregnant women, and it is not only due to increased synthesis of thyroid hormones. Another reason is the increased glomerular filtration rate in the kidneys, which results in loss of iodine to the urine, in addition to the fetus taking a lot of maternal iodine for its own development. If the mother does not take adequate supply of iodine supplements, a **goiter** can form.

Goiter is a swelling in the lower part of the neck caused by an enlarged thyroid gland. Because of iodine deficiency, thyroid hormones cannot be synthesized in an adequate amount, which results in increased TSH concentration from the anterior pituitary as a feedback mechanism. TSH continuously stimulates the follicular cells in the thyroid gland to make more thyroid hormones; this persistent stimulation results in follicular cells growing in size and proliferating. This change in the follicular cells causes diffuse hyperplasia of the thyroid gland, which leads to goiter.

**Thyroid stimulation by hCG**

hCG can weakly turn on the thyroid because it can bind and transduce signaling from the TSH receptor (hCG and TSH are structurally very similar. High circulating hCG levels in the first trimester may result in a slightly low TSH. When this occurs, the TSH will slightly
decreased in the first trimester and then return to normal throughout the duration of pregnancy.

**Thyroid hormones and fetal brain development**

Research has proved that thyroid hormones play the most vital part in the last stages of brain differentiation. This includes formation of axons and dendrites, myelination, formation of synapses and neuronal migration.

**Thyroid Function Tests During Pregnancy**

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**Congenital Hypothyroidism**

The human fetus has two main sources of thyroid hormones: the mother's and its own. The fetus does not start synthesizing its own thyroid hormones until 12 weeks of gestation.

*Congenital hypothyroidism*, or Cretinism, causes:
Maternal hypothyroidism: Overt maternal hypothyroidism alone cannot cause Cretinism because that would usually result in infertility. However, the subclinical type of maternal hypothyroidism has been found to cause significant developmental abnormalities in the baby.

Fetal hypothyroidism: These babies do well until the mother’s supply of thyroid hormones is circulating in the body. However, sometime after birth, symptoms of hypothyroidism start manifesting.

Causes of this can be an anatomical defect in the thyroid gland, in addition to genetic or iodine deficiency in the mother. Symptoms include mental retardation, jaundice, hypotonia, decreased activity, small size of the baby and decreased weight gain. These babies also present with a large anterior fontanelle, rough facial features, macroglossia (large tongue), pale and dry skin, goiter and umbilical hernia.

Congenital hypothyroidism is diagnosed by low levels of T4 and elevated levels of TSH. Thyroid scanning can further help identify the cause of the disease. Early diagnosis is crucial for managing this condition. Levothyroxine is used as the optimal treatment.

References

Thyroid Hormones: Pregnancy and Fetal Development via arbl.cvmbs.colostate.edu
Thyroid disease and pregnancy via thyroid.org
A Cheat Sheet to Pregnancy Hormones via parents.com
Congenital Hypothyroidism via medscape.com
Iodine Deficiency via thyroid.org
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