THYROID PHYSIOLOGY IN PREGNANCY

STELLER 2.14.2015
LEARNING OBJECTIVES

- Describe the physiologic changes in thyroid function during pregnancy

Prerequisites:
- None

See also – for closely related topics
- FLAME 34B - HYPERTHYROIDISM IN PREGNANCY
- FLAME 35 - HYPOTHYROIDISM IN PREGNANCY
THYROID HORMONE FUNCTION

- Assists in regulation maternal and fetal cell growth, development, and metabolism
- Has effects on fetal brain development
  - Early second trimester: maternal thyroid function stimulates fetal neuronal multiplication and organization
    - Damage during this phase is not reversible
  - Third trimester to age 2: “Late” brain growth also affected by fetal and neonatal thyroid function
    - Damage during this phase is partially reversible
- Neonatal cooling at birth triggers a transient increase in T3 and T4, possibly assisting in post-natal thermoregulation
THE HYPOTHALAMIC-PITUITARY AXIS

- TRH secretion stimulates TSH
- TSH
  - Directly induces secretion of both the T3 and T4 forms of thyroid hormone
  - Directly induces thyroid growth and differentiation
  - Directly induces iodine uptake
- TH can cause negative feedback on both the hypothalamus & pituitary
SOURCES OF T3/T4

- 100% of T4 is formed within the thyroid, while 20% of T3 is formed in thyroid.
- Almost any tissue can de-iodinate T4 to either T3 (which is more active) or reverse T3.
  - Catabolic states favor formation of reverse T3.
- Half life of T4 is about one week; half life of T3 is one day.
- It takes about 5-6 half lives in order to see a change in the steady state concentrations (something to keep in mind when changing the dose of a patient’s levothyroxine).
Increased maternal metabolic demands (such as ↑ basal metabolic rate, ↑ cardiac output, ↑ O₂ consumption) during a normal pregnancy result in changes in thyroid function to meet these demands

- Estrogen and human chorionic gonadotropin (hCG), help mediate these changes
- The placenta becomes a major source for localized T3 production in the 3rd trimester
ESTROGEN’S EFFECT

- Estrogen increases thyroxine-binding globulin (TBG) levels by decreasing TBG clearance and increasing hepatic TBG production (up to 2x)
  - TBG is the major transport protein for thyroid hormones
  - TBG binds free thyroid hormones and lowers available T4/T3
- By binding up more TH, this stimulates a positive feedback loop that increases TH production (thus Total T4 increases, but Free T4 level is maintained)
HCG’S EFFECT

- hCG stimulates thyrotropin (TSH) receptors
  - hCG has weak thyroid-stimulating activity due to its structural similarity to TSH
  - Causes a transient increase in T4/T3 production during weeks 8-14 and thus a transient suppression of TSH
    - Mild hyperthyroidism in the first trimester does NOT require treatment
IODINE REQUIREMENTS

- Plasma iodide levels decrease during pregnancy due to fetal theft of iodide and increased renal clearance
  - Associated with noticeable increase in thyroid gland size in 15% of women that returns to normal after birth
- ACOG recommends 220 mcg of iodine daily during pregnancy
  - In only some (minority) of prenatal vitamins
- Other sources of iodine include vegetables, fruits with color, seafood, seaweed, and salt (not sea salt)
Worldwide, about 1-1.2 billion people have iodine-deficient diets.

Effects of iodine deficiency:
- Reduction in maternal thyroxine production and placental transfer of thyroxine
- May lead to delayed fetal neurodevelopment and shorter stature
EVALUATING THYROID FUNCTION

- Recommended thyroid function tests (TFTs)
  - TSH for screening
  - TSH + free T4 for diagnosis
- ACOG does NOT recommend universal screening
  - Indications: personal hx thyroid disease, symptoms of thyroid disease, “significant” goiter, thyroid nodule
- TSH reference ranges by trimester (lab dependent)
  - First trimester: 0.1 – 2.5 mU/L (may be as low as 0.03 mU/L)
  - Second trimester: 0.2 – 3.0 mU/L
  - Third trimester: 0.3 – 3.0 mU/L
Inhibiting T4 to T3 conversion:
- Steroids, beta-blockers
- Inhibit T4 and T3 binding to binding proteins
  - Salicylates, sulphonylureas
- Inhibit GI absorption of thyroid hormones
  - Iron, aluminum containing antacids, cholestyramine
- Amiodarone
  - 3% develop thyrotoxicosis due to reduced T3 clearance
  - 20-25% will experience hypothyroidism due to persistent elevations in TSH
  - Except in iodine deficient regions, where the occurrence of hyperthyroidism predominates
REFERENCES

- ACOG Practice Bulletin Number 148, April 2015
- ACOG Guidelines for Perinatal Care, March 2013
- UpToDate: Overview of thyroid disease in pregnancy
- Williams Obstetrics 24th Edition