THYROID PHYSIOLOGY IN PREGNANCY

STELLER 5.14.19

LEARNING OBJECTIVES

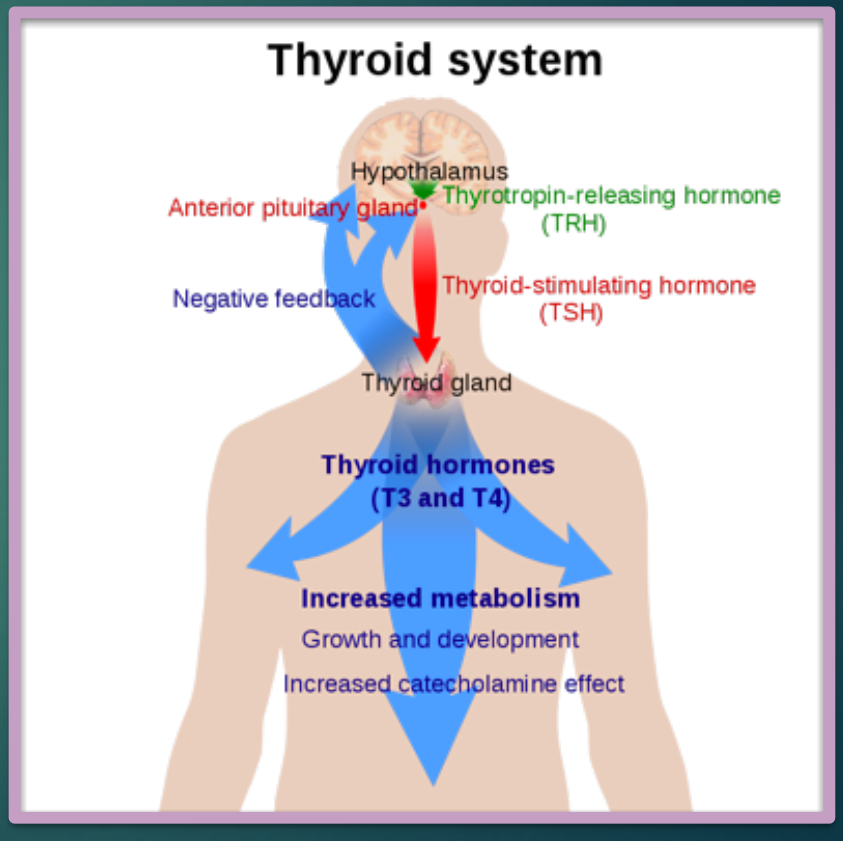
- Describe the physiologic changes in thyroid function during pregnancy
- Prerequisites:
  - None
- See also – for closely related topics
  - FLAME 34B - HYPERTHYROIDISM IN PREGNANCY
  - FLAME 35 - HYPOTHYROIDISM IN PREGNANCY

THYROID HORMONE FUNCTION

- Assists in regulation maternal and fetal cell growth, development, and metabolism
- Has effects on fetal brain development
  - Early 2nd trimester: maternal thyroid function stimulates fetal neuronal multiplication and organization
    - Damage during this phase is NOT reversible
  - 3rd trimester-to-2 years old: "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

HYPOTHALAMIC-PITUITARY-THYROID 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
- T3 & T4 can provide negative feedback on both the hypothalamus & pituitary



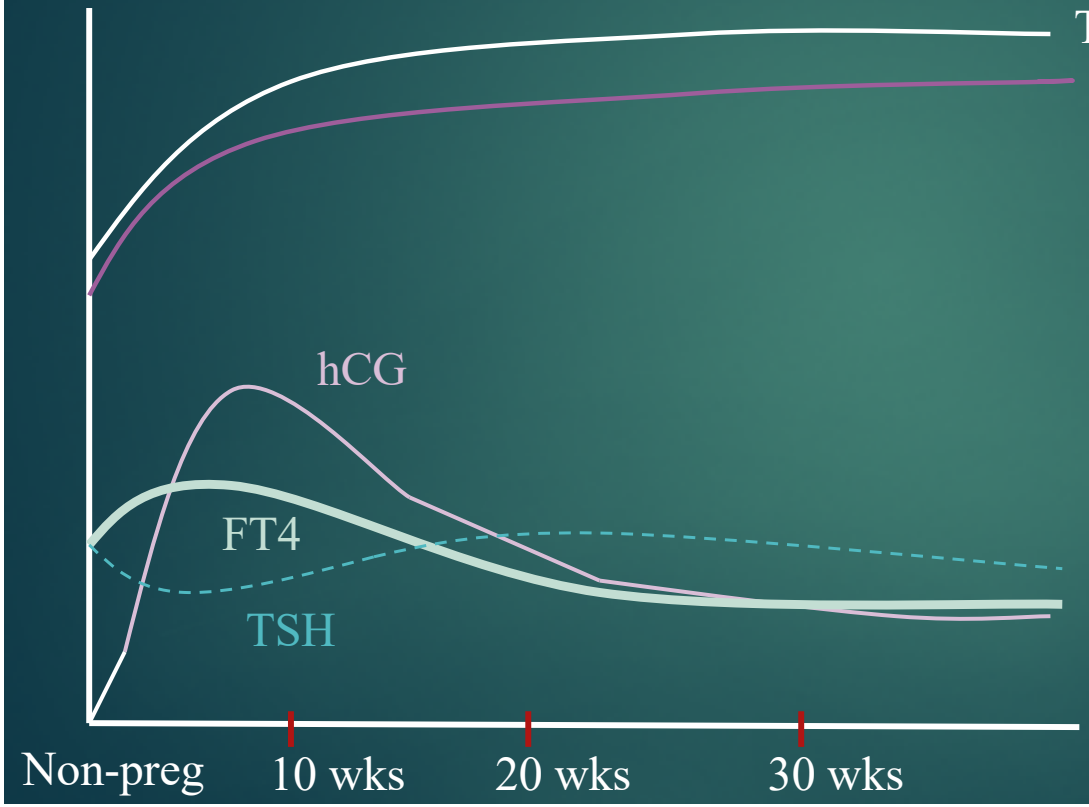
SOURCES OF T3/T4

- 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 (rT3)
  - Catabolic states favor formation of rT3
- 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
  - Keep this in mind when changing the dose of a patient's levothyroxine and re-checking levels

CHANGES IN THYROID PHYSIOLOGY DURING PREGNANCY

- Increased maternal metabolic demands (i.e ⇧ basal metabolic rate, ⇧ cardiac output, ⇧ O_2 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

CHANGES IN THYROID PHYSIOLOGY DURING PREGNANCY



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
  - Is only some (a minority) of prenatal vitamins
- Other sources of iodine include vegetables, fruits with color, seafood, seaweed, and salt (not sea salt)

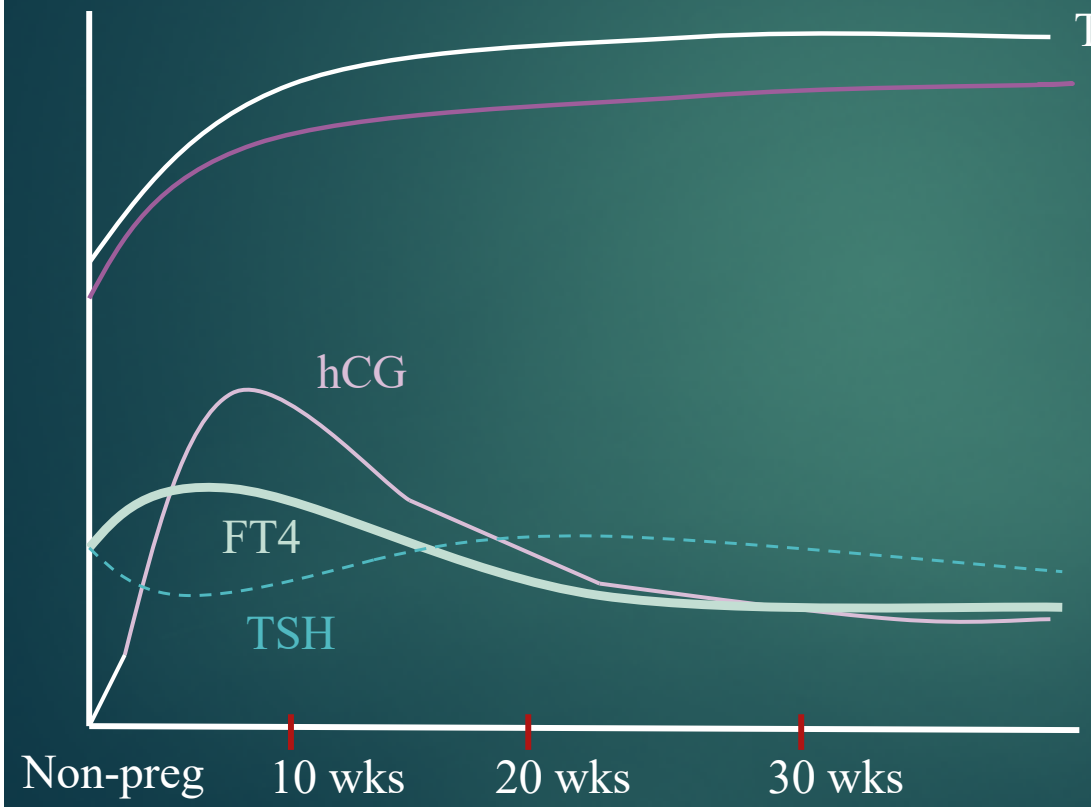
IODINE DEFICIENCY

- 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

EVALUTATING THYROID FUNCTION

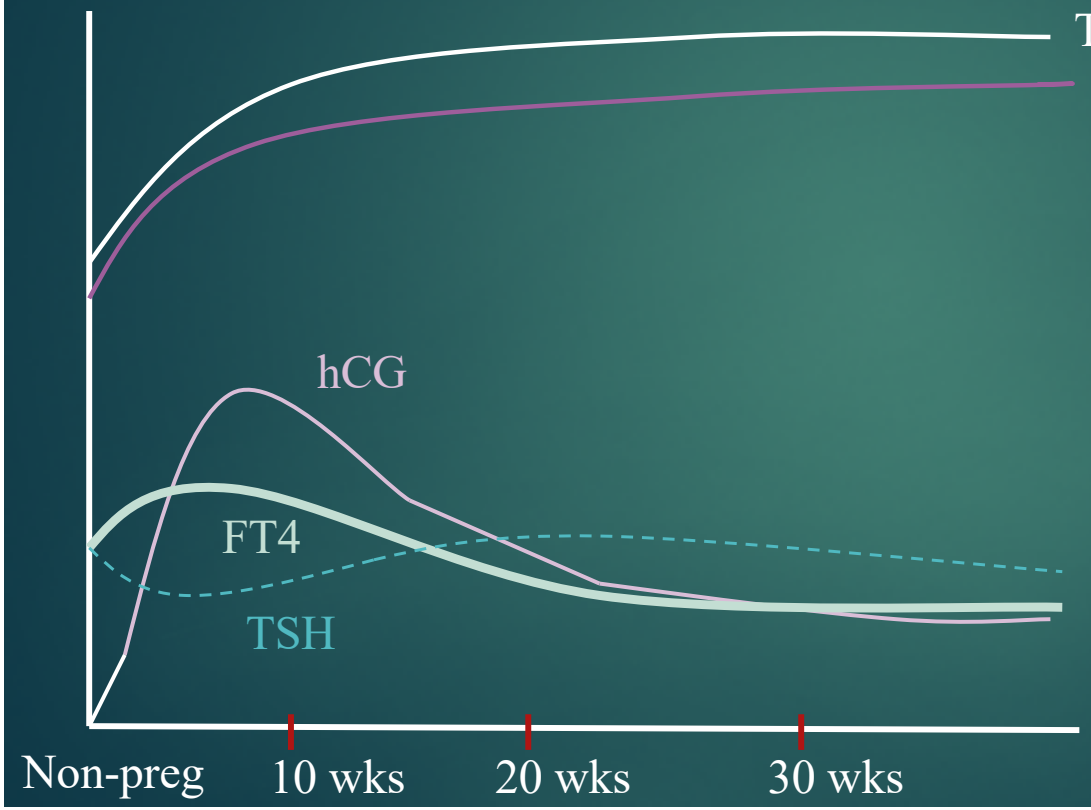
- ACOG does NOT recommend universal screening
  - Indications: personal hx thyroid disease, symptoms of thyroid disease, "significant" goiter, thyroid nodule
- Generally recommended thyroid function tests (TFTs)
  - TSH is useful for initial screening
  - TSH + reflex to free T4 (FT4) is used for diagnosis
    - It may be useful in a patients with hyperthyroidism to check a total T3 (TT3), especially if TSH is low and FT4 is relatively normal
    - Rarely do TT4 or FT3 add clinically important information to FT4 & TT3
  - As noted in the thyroid pathology FLAMEs, evaluating antibodies such as TPO, TSI, or TRAB can also help with evaluation

EVALUATING THYROID FUNCTION



- ACOG TSH range norms:
  - 1st tri: 0.1 – 2.5 mU/L (may be as low as 0.03 mU/L)
  - 2nd tri: 0.2 – 3.0 mU/L
  - 3rd tri: 0.3 – 3.0 mU/L
- MFMU Network Norms
  - TSH: 0.08-3.99
  - FT4: 0.86-1.96
- ATA TSH Norms: 0.1-3.99
- Given these discrepancies, know >4 mU/L is clearly abnormal

EVALUATING THYROID FUNCTION



- FT4 is slightly lower in 2nd and 3rd tri (~20%)
  - Thus, if TSH is low and FT4 is low, can check TT4 to guide clinical decision making
- However, note that normal TT3 and TT4 levels in preg are 1.5X the reported non-preg lab reference ranges

MEDS WITH EFFECTS ON THYROID FXN

- 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
- Casey et al. Treatment of Subclinical Hypothyroidism or Hypothyroxinemia in Pregnancy. NEJM 2017.
- Williams Obstetrics 24th Edition