

# HYPOTHYROIDISM IN PREGNANCY

FLAME LECTURE: 35

WANG/STELLER 5.14.19

# LEARNING OBJECTIVES

- ▶ Describe the pathophysiology and common causes of hyperthyroidism in pregnancy
- ▶ Describe the evaluation, diagnosis and treatment of hyperthyroidism in pregnancy
- ▶ Identify the complications of untreated hyperthyroidism in pregnancy for mother and fetus
- ▶ Describe the effects of fetal and neonatal hyperthyroidism
- ▶ Prerequisites:
  - ▶ FLAME LECTURE 34A – THYROID PHYSIOLOGY IN PREGNANCY
- ▶ See also – for closely related topics
  - ▶ FLAME LECTURE 34B – HYPERTHYROIDISM IN PREGNANCY

# ETIOLOGY OF HYPOTHYROIDISM

- ▶ Hashimoto's disease (aka. chronic thyroiditis or chronic autoimmune thyroiditis)—most common cause of hypothyroidism in developed countries
  - ▶ Due to production of anti-thyroid antibodies (thyroid peroxidase (20-30% of hypothyroid patients), thyroid anti-microsomal, and anti-thyroglobulin antibodies)
- ▶ Iodine deficiency—most common cause of hypothyroidism worldwide
- ▶ Iatrogenic—from prior treatments for hyperthyroidism (radioiodine therapy, thyroidectomy, medications e.g. lithium, amiodarone, interferon)
- ▶ Other causes: subacute thyroiditis, prior thyroidectomy or radioactive iodine treatment, pituitary or hypothalamus disorders

# EPIDEMIOLOGY

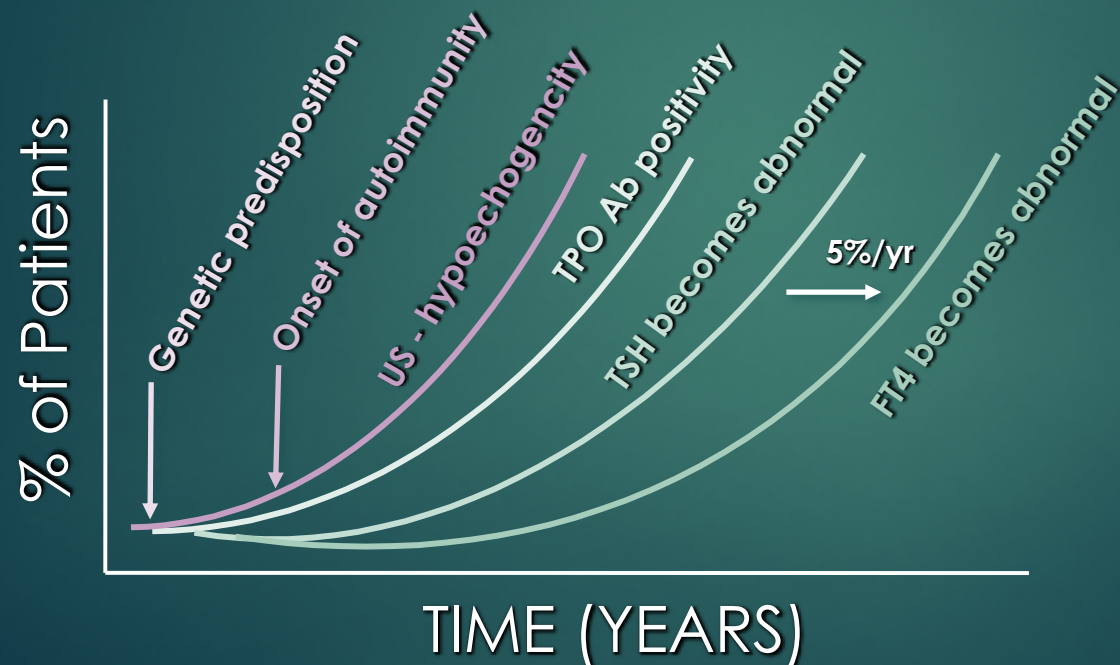
## PRIMARY

- ▶ Overt hypothyroidism: elevated TSH, low free T4
  - ▶ Rare, seen in 1-3% of reproductive-aged women
- ▶ Subclinical hypothyroidism: elevated TSH, normal free T4
  - ▶ More common, seen in 5-6% of reproductive-aged women
  - ▶ Thyroid function is inadequate, but ↑ TSH production maintains normal free T4 levels
- ▶ Combined these complicated 0.2-1.0% of pregnancies

## SECONDARY

- ▶ Central hypothyroidism: low TSH, low free T4
  - ▶ Very rare, caused by pituitary or hypothalamic disease

# TIME COURSE FOR PROGRESSION TO OVERT HYPOTHYROIDISM



# SCREENING

- ▶ Universal screening in asymptomatic pregnant women is not recommended by ACOG
- ▶ A more targeted approach is recommended for pregnant women with the following risk factors:
  - ▶ Symptoms of hypothyroidism (next slide)
  - ▶ From an endemic area of moderate-to-severe iodine insufficiency
  - ▶ Family or personal history of thyroid disease, type 1 diabetes, history of preterm delivery or miscarriage, h/o head or neck radiation
  - ▶ Morbid obesity (BMI  $\geq 40$  kg/m<sup>2</sup>), infertility, or age >30 years
- ▶ Screening is simply performed by sending a TSH

# SIGNS & SYMPTOMS

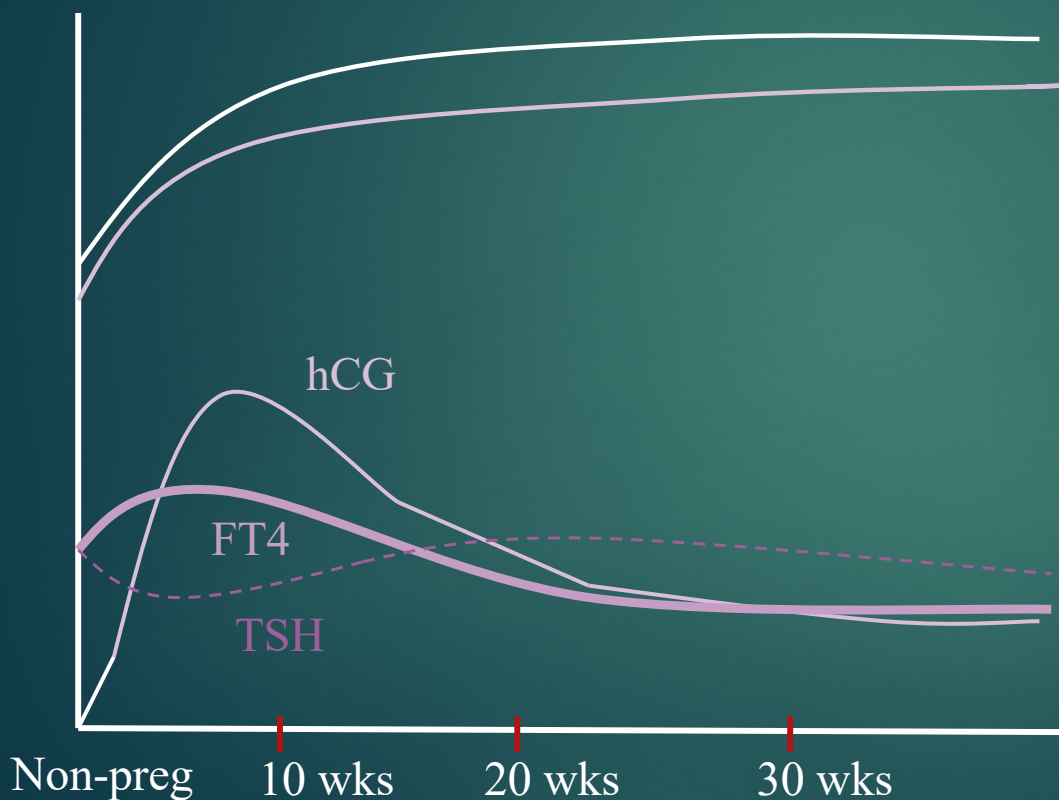
- ▶ Fatigue, constipation, cold intolerance, muscle cramps, hair loss, dry skin, prolonged relaxation phase of deep tendon reflexes, carpal tunnel syndrome
- ▶ May progress to weight gain, intellectual slowness, voice changes and insomnia
- ▶ Some nonspecific symptoms of hypothyroidism may be attributed to the pregnancy itself and may be overlooked
- ▶ Many patients are asymptomatic

# DIAGNOSIS

- ▶ High TSH levels is the most sensitive indicator of hypothyroidism
- ▶ Overt primary hypothyroidism
  - ▶ Dx based on decreased free T4 and elevated serum TSH
- ▶ Subclinical hypothyroidism
  - ▶ Dx based on normal free T4 and elevated serum TSH
- ▶ However, there is not agreement on what TSH level is considered abnormal, or better said, at what TSH level treatment is indicated to prevent fetal morbidity



# EVALUATING THYROID FUNCTION



## ▶ ACOG TSH range norms:

▶ 1<sup>st</sup> tri: 0.1 – 2.5 mU/L (may be as low as 0.03 mU/L)

▶ 2<sup>nd</sup> tri: 0.2 – 3.0 mU/L

▶ 3<sup>rd</sup> tri: 0.3 – 3.0 mU/L

## ▶ MFMU Network Norms

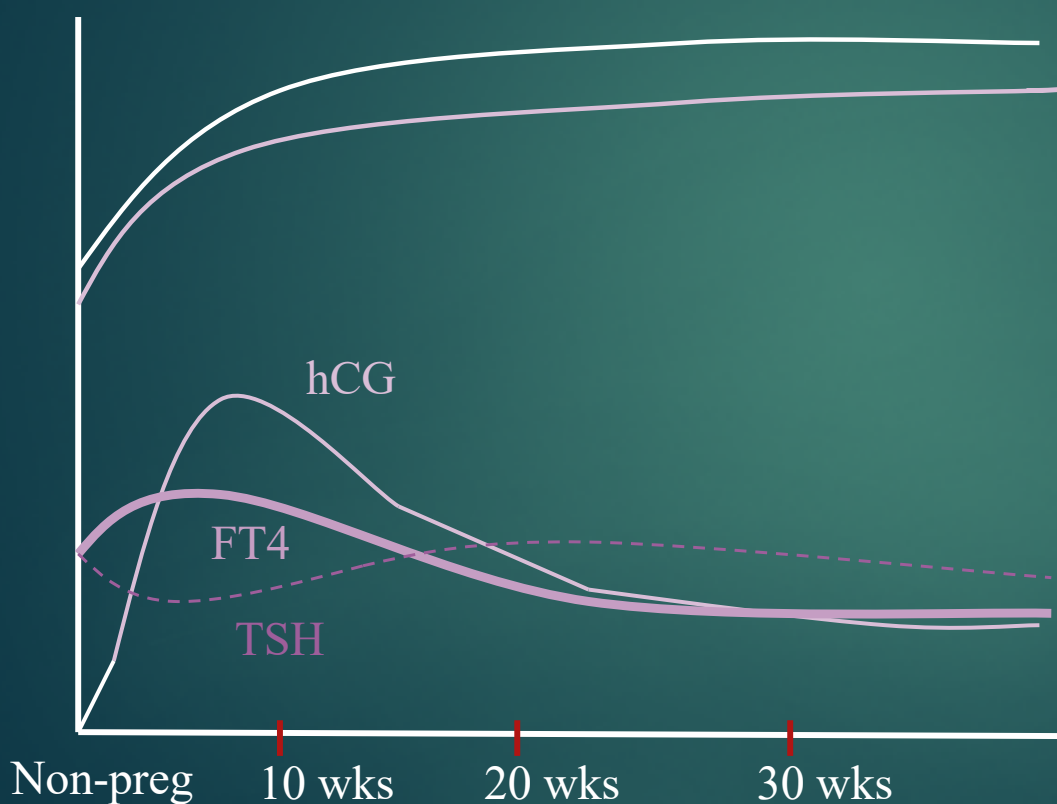
▶ TSH: 0.08-3.99

▶ FT4: 0.86-1.96

## ▶ ATA TSH Norms: 0.1-3.99

▶ Given these differences, >4 mU/L is considered abnormal and tx is indicated

# EVALUATING THYROID FUNCTION



- ▶ FT4 is slightly lower in 2<sup>nd</sup> and 3<sup>rd</sup> tri (~20%)
- ▶ Note that normal TT3 and TT4 levels in pregnancy are 1.5X the reported non-preg lab reference ranges
- ▶ FT4 levels are just slightly lower as well but the normal reference ranges can be used

# MATERNAL COMPLICATIONS

- ▶ Pregnancy loss
- ▶ Preeclampsia and gestational hypertension
- ▶ Placental abruption
- ▶ PROM
- ▶ Preterm delivery
- ▶ Increased rate of cesarean section
- ▶ Neonatal death
- ▶ Postpartum hemorrhage

# MATERNAL COMPLICATIONS

## ▶ Myxedema coma

- ▶ It is very rare for advanced hypothyroidism to the point of myxedema coma to present in pregnancy, but it is a medical emergency
- ▶ S/Sx: depressed state of consciousness, profound hypothermia, and respiratory depression
- ▶ Can be precipitated by trauma, infection, cold exposure, narcotics
- ▶ Treat with both IV T4 AND T3 (add hydrocortisone to tx refractory hypotension)
  - ▶ High mortality rate even with treatment

# FETAL COMPLICATIONS

- ▶ Low birth weight
- ▶ Fetus dependent upon maternal T4 in first trimester
  - ▶ Starts concentrating iodine to make T4 at 10-12 weeks and is independent by 16-18 weeks
- ▶ Congenital cretinism
  - ▶ Pregnant women with iodine-deficient hypothyroidism are at significant risk of having babies with congenital cretinism
  - ▶ Causes fetal growth failure, mental retardation, and other neuropsychological deficits
  - ▶ Prevent with iodine treatment in first and second trimesters

# TREATMENT

- ▶ Overt primary hypothyroidism (TSH  $>4$ , low free T4)
  - ▶ Treatment of choice is the same as for non-pregnant patients: levothyroxine (T4)
- ▶ Subclinical hypothyroidism (high TSH, normal free T4)
  - ▶ Insufficient evidence for or against tx of women with subclinical hypothyroidism, especially those with TSH between 2.5-4.0 mU/L
    - ▶ Consider treatment with levothyroxine (T4) if patient has positive TPO antibodies, develops goiter, hypercholesterolemia, sx of hypothyroidism
    - ▶ However, even in the absence of these, the risks of treatment are low, and treatment can be considered (especially in 1<sup>st</sup> trimester)

# T4 DOSING

- ▶ Levothyroxine (T4): taken PO once daily, usually in the morning on an empty stomach
- ▶ Goal of T4 replacement: restore euthyroidism as soon as possible
  - ▶ Mild hypothyroidism (TSH <10 mU/L): start on 1 mcg/kg daily
  - ▶ Moderate to severe hypothyroidism: start on 1.6 mcg/kg daily
- ▶ Maintain TSH levels within trimester-specific ranges:
  - ▶ First trimester: 0.1 to 2.5 mU/L
  - ▶ Second trimester: 0.2 to 3 mU/L
  - ▶ Third trimester: 0.3 to 3 mU/L

# T4 MONITORING

## ▶ Monitoring

- ▶ TSH levels should be measured every 4 weeks during the first half of pregnancy for dosage adjustments
- ▶ Once dose is optimized, can monitor less frequently, but at least 1X/trimester
- ▶ Pregnant women with preexisting hypothyroidism will most likely need a higher levothyroxine dose (up to 50% increase)

## ▶ Adjustments

- ▶ If TSH remains above normal ranges, increase levothyroxine (T4) dose by 12 to 25 mcg/day until a normal TSH level is reached



# Sources

- ▶ ACOG PB 148. Thyroid Disease in Pregnancy. 2015
- ▶ UpToDate: Overview of thyroid disease in pregnancy
- ▶ UpToDate: Hypothyroidism during pregnancy: Clinical manifestations, diagnosis, and treatment
- ▶ UpToDate: Clinical features and detection of congenital hypothyroidism
- ▶ Maraka et al. Subclinical hypothyroidism in pregnancy: a systematic review and meta-analysis. *Thyroid*. 2016.
- ▶ Plowden et al. Subclinical hypothyroidism and thyroid autoimmunity are not associated with fecundity, pregnancy loss, or live birth. *JCEM* 2016.
- ▶ Casey et al. Treatment of subclinical hypothyroidism or hypothyroxinemia in pregnancy. *NEJM*. 2017.