

# HYPERTHYROIDISM IN PREGNANCY

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# 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:
  - ▶ THYROID PHYSIOLOGY IN PREGNANCY
- ▶ See also – for closely related topics
  - ▶ HYPOTHYROIDISM IN PREGNANCY

# HYPERTHYROIDISM IN PREG

- ▶ **Incidence:** occurs in 0.2% of pregnancies
- ▶ **Common causes:**
  - ▶ Graves disease (95% of hyperthyroidism cases)
  - ▶ hCG-mediated hyperthyroidism (peaks at 10-12 weeks)
    - ▶ "Gestational transient thyrotoxicosis"
    - ▶ Associated with hyperemesis, multiple gestation, molar pregnancy
    - ▶ Benign and self-limited, treat only for severe or prolonged symptoms
- ▶ **Less common causes:**
  - ▶ Familial gestational hyperthyroidism
  - ▶ Thyroiditis
  - ▶ Toxic multinodular goiter
    - ▶ Which can increase in size during pregnancy
  - ▶ Toxic adenoma

# PATHOPHYSIOLOGY OF GRAVES DX

- ▶ Maternal antibodies (TSI or TRAB) bind to thyrotropin (TSH) receptors on the thyroid gland causing release of T3 and T4, and reflex suppression of the pituitary
- ▶ Maternal risks of poor control
  - ▶ Thyroid storm, cardiac failure, severe pre-eclampsia
- ▶ Fetal risks of poor control
  - ▶ SAB, preterm delivery, low birth weight
- ▶ Fetal/neonatal risks due to maternal antibodies
  - ▶ Immune-mediated hypo- or hyperthyroidism in neonate
  - ▶ Fetal thyrotoxicosis → tachycardia, IUGR, hydrops fetalis
    - ▶ Risk persists despite h/o maternal thyroid ablation/excision, due to maternal antibodies crossing the placenta

# GRAVES DX IN PREGNANCY

## ▶ Diagnosis:

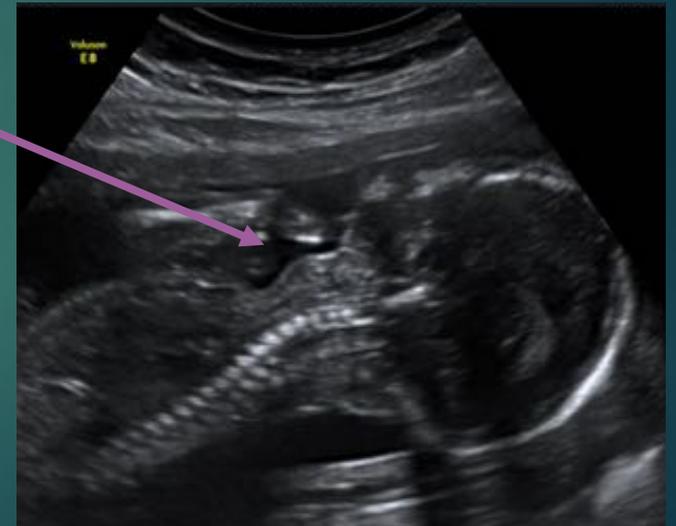
- ▶ Signs & symptoms: tachycardia, heat intolerance, anxiety, insomnia, weight loss, palpitations, hypertension, widened pulse pressure, lid lag, hoarseness, fine tremor, dry skin, frequent stools
- ▶ Graves' specific findings: diffuse goiter, exophthalmos, pretibial myxedema

## ▶ Laboratory evaluation:

- ▶ TSH levels are typically suppressed/undetectable ( $<0.01$  mU/L)
- ▶ Free T4 is usually elevated
  - ▶ Free T3 doesn't need to be checked unless patient has suppressed TSH with normal free T4 levels (T3 thyrotoxicosis is rare)
- ▶ Thyrotropin receptor antibody (TRAb), thyroid stimulating immunoglobulins (TSI) can be evaluated if diagnosis uncertain

# GRAVES DISEASE MGMT

- ▶ **Fetal Monitoring:** Begin biweekly antepartum testing whenever diagnosed after  $\geq 28$  weeks and fetal growth scans q4 weeks in all Grave's patients regardless if controlled
  - ▶ Maternal antibodies still present  $\rightarrow$  risk to fetus/neonate, thus if testing suggests fetal thyrotoxicosis:
    - ▶ US to check for hydrops, fetal goiter
    - ▶ If diagnosis uncertain, PUBS for fetal thyroid tests (rare)
- ▶ Check maternal **free T4** every 2-4 weeks
- ▶ **Goal of therapy:** maintain FT4 near or slightly above upper limit of normal throughout pregnancy, using lowest dose of thioamides to minimize fetal exposure



# GRAVES DISEASE MGMT

- ▶  $I^{131}$ : Contraindicated in pregnancy
  - ▶ Can destroy fetal thyroid tissue (case reports of stillbirth<sup>1</sup>)
- ▶ **Surgical therapy**: relatively contraindicated
  - ▶ Thyroid is more vascular → increased surgical risks
- ▶ **Medical therapy**: thioamides (PTU and MMI) inhibit the thyroid uptake of iodide and T4/T3 synthesis (PTU also inhibits the peripheral conversion of T4 to T3)

# GRAVES DISEASE MGMT

- ▶ Treatment varies by trimester in order to decrease fetal and maternal morbidity from medications
- ▶ Propylthiouracil (PTU)
  - ▶ Crosses placenta less freely than MMI
  - ▶ Still there is a rare, but increased, risk of maternal hepatotoxicity relative to MMI
- ▶ Methimazole (MMI)
  - ▶ Rare embryopathy (aplasia cutis and esophageal or choanal atresia)



# GRAVES DISEASE MGMT

- ▶ Both Methimazole and Propylthiouracil can also cause:
  - ▶ Maternal transient leukopenia
    - ▶ In 10%, does NOT require therapy cessation
  - ▶ Maternal acute agranulocytosis
    - ▶ It is NOT dose or treatment duration-related and so rare that there is no routine lab monitoring
      - ▶ Pts advised to stop drug immediately and call for evaluation and CBC if they develop sore throat and/or fever

# GRAVES DISEASE MGMT

▶ 0-16 weeks: Propylthiouracil 100-150mg PO q8h

▶ >16 weeks: Methimazole 10-20mg PO q12h

▶ However, there are a lot of issues with switching and titrating, and this switch runs the risk of inadequate treatment, so one may consider continuing PTU throughout pregnancy

▶ If switching therapies, PTU:MMI ~ 20:1

▶ Ex. ~300 mg PTU = ~15 mg MMI

# GRAVES DISEASE MGMT

- ▶ Monitor FT4 levels (or TT4 +/- TT3), every 4 weeks while on therapy
- ▶ Regardless of therapy used, use minimum dose to keep FT4 or TT4 at the upper limit of pregnancy range (or even slightly increased in order to keep the fetus from becoming hypothyroid
  - ▶ In some cases, may need to even tolerate some T3 thyrotoxicosis to prevent FT4 from falling
- ▶ If thyrotoxic, use  $\beta$ -blockers (atenolol, propranolol) to help control severe tachycardia and tremor
  - ▶ D/C when thioamides begin working or after 2-6 weeks of use

# POSTPARTUM GRAVES MGMT

- ▶ Both PTU & MMI appear in breast milk
  - ▶ PTU crosses into milk less well
  - ▶ Normal neurological development at 48-74 months in moms ingesting PTU 10-20 mg/day (Azizi 2003)
- ▶ If using MMI, recommend not exceeding 20 mg/day
  - ▶ If higher doses are used, infant's thyroid status should be monitored

# THYROID STORM IN PREGNANCY

- ▶ Life-threatening exacerbation of thyrotoxicosis precipitated by stress, labor, infection, preeclampsia, or C-section
- ▶ **Incidence:** 1% of pregnant patients with hyperthyroidism
- ▶ **Signs and symptoms:** fever, tachycardia, tremor, changes in mental status, nausea, vomiting, diarrhea
- ▶ **Complications of untreated thyroid storm:** shock, stupor, coma, maternal heart failure

# THYROID STORM MGMT

- ▶ IV Hydration with D5 source, cooling measures, cardiac monitoring, O2 as needed
- ▶ PTU (1,000 mg PO loading dose; then 200 mg PO q6h)
- ▶ Propranolol for tachycardia (if safe given cardiac function)
- ▶ Steroids to inhibit peripheral conversion (Dexamethasone 2mg IV q6h x 4 OR hydrocortisone 100mg IV q8hrs x 3)
- ▶ Iodides 1-2 hours after PTU (SSKI 5 drops PO q8h OR NaI 500mg-1000mg IV q8h)

# REFERENCES

- ▶ ACOG Practice Bulletin Number 148, April 2015
- ▶ UpToDate: Overview of thyroid disease in pregnancy
- ▶ UpToDate: Hyperthyroidism during pregnancy: Clinical manifestations, diagnosis, and causes
- ▶ Momotani et al NEJM 1986;315:24-8
- ▶ Berg et al Acta Onc 2008;47(1): 145