UNIVERSITY OF UTAH HEALTH SCIENCES

Diagnosis and Treatment of Hyperthyroidism in Pregnancy

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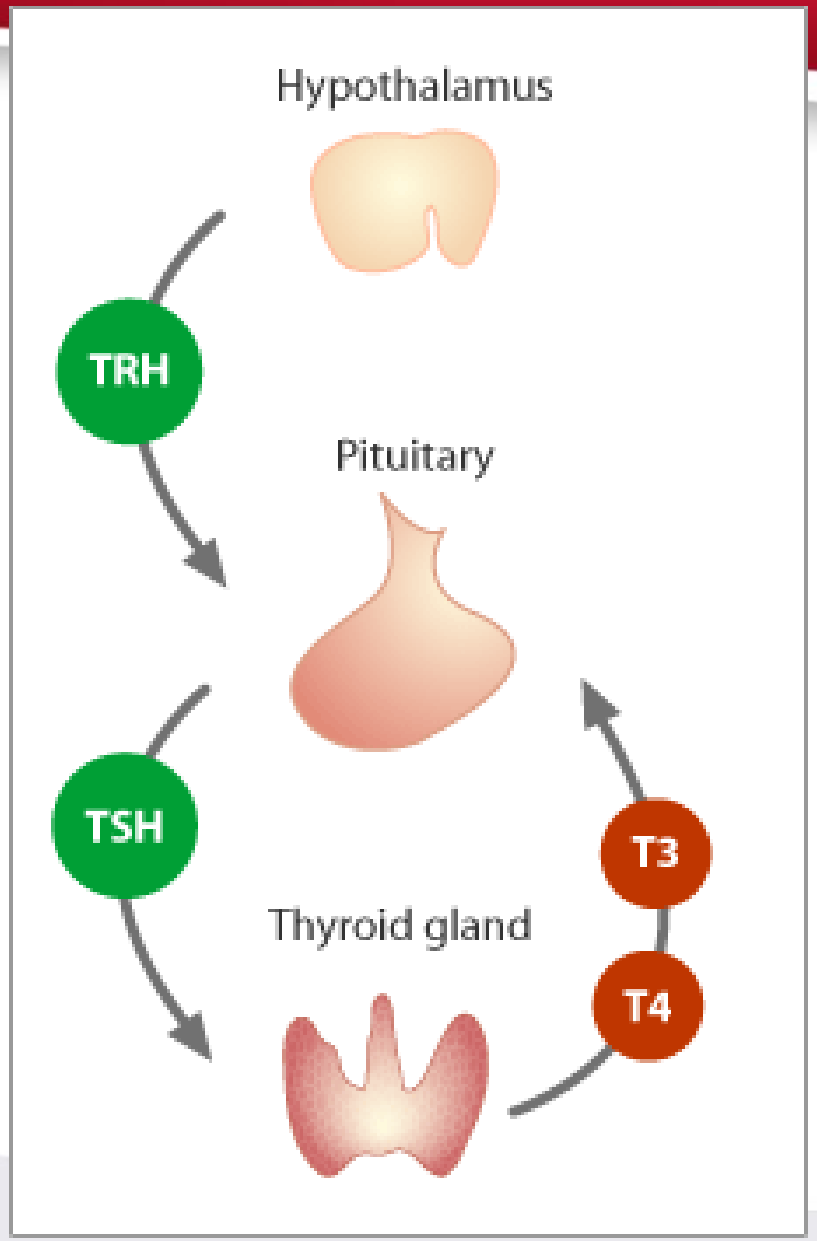
Goals

- Review thyroid physiology in pregnancy
- Discuss diagnosis of hyperthyroidism
- Outline treatment of hyperthyroidism during pregnancy
- Review thyroid storm



TRH=Thyrotropin Releasing Hormone

TSH=Thyroid Stimulating Hormone

T3=triiodothyronine

T4=thyroxine

Thyroid Changes During Pregnancy

- Serum thyroxine-binding globulin (TBG) increases by two-fold due to estrogen
  - Increased T4 and T3 overall
  - Free T4 remains stable
- Stimulation of thyrotropin (TSH) receptors by hCG (peaks at 10-12 weeks)
  - TSH is reduced – undetectable in 10-20% of normal
  - Transient mild increase free T4
- Maternal thyroid volume 30% larger by 3rd trimester

Fetal Thyroid Function

- Initially reliant on maternal production
- Fetal TSH starts at 10-12 weeks
- Hormone synthesis at 18-20 weeks
- TRH, T4, and antibodies cross placenta
- TSH minimally crosses the placenta

Hyperthyroidism in Pregnancy

- Prevalence: 0.05-0.2%
- Increased risk of preterm delivery, pregnancy loss, perinatal mortality, fetal growth restriction, preeclampsia, and maternal heart failure
- Treatment ameliorates these risks

Symptoms of Hyperthyroidism

Common in pregnancy

- heat intolerance
- diaphoresis
- fatigue
- anxiety
- emotional lability
- tachycardia
- wide pulse pressure
- nausea/vomiting

Abnormal in pregnancy

- weight loss
- pulse >100 bpm
- diffuse goiter
- tremor
- systolic HTN
- diarrhea

Clinical recommendations

- Ask about symptoms
- If suspicious:
  - Check TSH and free T4 (caution if 8-12 weeks)
  - Thyroid exam → ultrasound if nodule/goiter

Diagnosis

- GREATLY suppressed TSH
  - TSH undetectable in 10-20% of NORMAL
- If TSH <0.1 mU/mL → check free T4
  - If elevated: hyperthyroid!
  - If free T4 normal, check free T3

Causes of Hyperthyroidism

- **Graves disease**
- **hCG mediated**
- Toxic adenoma
- Toxic multinodular goiter
- Hyperemesis gravidarum
- Gestational trophoblastic disease
- TSH producing pituitary tumor
- Metastatic follicular cell carcinoma
- Exogenous T4/T3
- De Quervain thyroiditis
- Postpartum thyroiditis
- Struma ovarii

Most common is Grave's

- 90-95% of hyperthyroid pregnant women have Grave's disease
  - Clinical picture: thyrotoxicosis, thyromegaly with bruit, opthalmopathy
  - Autoimmune disease with Thyroid Stimulating Antibodies (TSIs) that activate TSH receptor
    - Present in 95% of Grave's patients

Treatment

- Always best to optimize prior to conception
- Risk of uncontrolled hyperthyroidism far outweighs risk of therapy
- Can consider no treatment if very minimal elevation of T4/T3

Treatment

Goal of therapy is control WITHOUT causing fetal or neonatal hypothyroidism

Keep free T4 in HIGH-normal range or total T4 at 1.5x upper limit of normal

Medications

- Thioamides: propylthiouricil (PTU) and methimazole (MMI)
  - inhibit synthesis of thyroid hormones
  - PTU also inhibits peripheral conversion of T4→T3

PTU vs MMI

- Both cross the placenta with equal kinetics
- Several reports of aplasia cutis with MMI
  - 0.03% = baseline risk
- Reports of choanal atresia, omphalocele, tracheoesophageal fistula
- PTU associated with reports of severe, fatal liver failure

Current Thioamide Recommendations

- Limit PTU use to first trimester only
- Switch from PTU to MMI at 13-14 weeks
  - MMI 20-30x as potent as PTU per mg
    - 300mg PTU=10-15mg MMI
- Monitor **free T4** every 4 weeks
  - When stably high normal, q trimester
- In reality, most have MMI through entire pregnancy

Thionamide Dosing

Propylthyouricil (PTU)

- Start with 50mg BID/TID
- Increase to 100mg TID
- Max 150mg TID in severe cases

Methimazole (MMI)

- Start with 5-10 mg BID
- Increase to 10-40 mg daily

Thioamide Side effects

- Agranulocytosis in 0.2-0.5%
  - Check baseline CBC
  - Counsel about risk
- Acute liver failure
- Rash, arthralgias

Other Therapies

- Beta blockers (propranolol)
- Iodides
- Radioactive ablation (contraindicated)
- Surgery)

Subclinical Hyperthyroidism

- Low TSH with normal free T4/T3
- No increased risk of pregnancy complications
- No need to follow or treat

Gestational Transient Thyrotoxicosis

- 1-3% of pregnancies
- hCG stimulation of the thyroid leads to elevated free T4
- Peaks between 8-14 weeks
- No thyromegaly
- Not associated with adverse pregnancy outcomes

Fetal and Neonatal Hyperthyroidism

- Typically due to TSIs crossing placenta
- Occurs in 1% of Grave's pregnancies
- Remember: TSIs persist after surgery or radioactive iodine ablation
- Some measure TSIs in pregnancy
  - We argue not to

Fetal Thyrotoxicosis

- Heart rate >160 bpm
- Growth retardation
- Advanced bone age
- Goiter
- Craniosynostosis

Newborn Thyrotoxicosis

- Important: notify pediatrician
- Evaluate at birth and after 48 hours

Thyroid Storm

- 2% of women undergoing treatment for hyperthyroidism
- Biggest risk factor is no treatment or incomplete treatment

Thyroid Storm Presentation

- CNS effects (agitation, delirium, coma)
- Thermoregulatory dysfunction (fever)
- GI dysfunction
- Cardiovascular problems (tachycardia, heart failure)

Thyroid Storm Precipitants

- Labor
- Delivery
- Cesarean
- Infection
- Preeclampsia

Thyroid Storm Treatment

- PTU: 600mg orally/crushed via NG tube
- Iodide (start 1 hour after PTU): 2-5 drops SSKI q8 hr
- Dexamethasone: 2mg q6hrs x4 doses
  - To block T4→T3 conversion
- Propranolol: 12mg IV q5 min for severe tachycardia plus 20-80mg PO/NG q6hr

Summary for Hyperthyroidism/Grave's

- PTU in first trimester/MMI after first trimester
- Ultrasound at 18-22 weeks for anatomy
- Growth ultrasound at 32 weeks
- Weekly NSTs at 34 weeks (optional)
- Notify pediatrician
- Postpartum follow up

References

- Belfort M, Saade G, Foley M, Phelan J, Dildy G. Critical Care Obstetrics, Fifth Edition. Wiley-Blackwell, 2010.
- Casey BM. Thyroid Disease in Pregnancy. ACOG Practice Bulletin. 2015, Number 148.
- Creasy RK, Resnik R, Iams JD, Lockwood CJ, Moore TR, Greene MF. Creasy & Resnik's Maternal-Fetal Medicine: Principles and Practice, 7th Edition. Elsevier Saunders, 2014.
- De Groot L, Abalovich M, Alexander EK, Amino N, Barbour L, et al. Management of thyroid dysfunction during pregnancy and postpartum: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2012; 97: 2543-2565.

Questions?