Thyroid Disease & Pregnancy

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A Family Practice Perspective for Management
Faculty/Presenter Disclosure

- Faculty: Dr. Nicola McLean

- Program: 51st Annual Scientific Assembly

- Relationships with commercial interests:
  - NONE
Disclosure of Commercial Support

- This program has received **NO** financial support
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- **Potential for conflict(s) of interest:**
  - **NONE**
Mitigating Potential Bias

- N/A
Objectives

- Understand normal thyroid physiology in pregnancy
- Manage pre-existing hypothyroidism
- Consider the relevance of subclinical hypothyroidism and thyroid autoimmunity
- Evaluate and manage hyperthyroidism in pregnancy
Physiologic Changes in Pregnancy

- ↑ Thyroid Binding Globulin
  - Need for ↑ Total T4/T3 to maintain Free T4/T3

- Placental Deiodination
  - ↑ T4/T3 metabolism
    - Demand for Increased T4/T3

- ↑ hCG (weak stimulator of TSH receptor)
  - Results in ↑ F T4 & reduced TSH
Importance of Physiologic Changes

- ↑ βhCG (1st trimester)
- ↓ TSH-R Abs (TSI/TBII)
- ↑ Thyroid Antibodies (post-partum)
- high fT4 & low TSH - may have mild transient thyroiditis
- Graves’ disease may improve during pregnancy
- Exacerbation of Graves’ disease - precipitation of PP thyroiditis
Casey BM & Leveno KJ. *Obstet Gynecol* 2006; 108:1283-9
Case Study 1

A 31 year old G1 woman presents at 8 weeks gestation. She has had Hashimoto’s for 4 years treated with levothyroxine 0.100 mg daily. Her TSH 3 months ago was 1.32 mIU/L
What would you do next?

1. No need to change the dose

2. Decrease to the lowest possible dose to achieve TSH < 5.00

3. Check TSH and Adjust q4 weeks until TSH is 0.1 to 2.5

4. Empirically increase levothyroxine by 2 extra pills per week and adjust q4 weeks until TSH is 0.1 to 2.5
# Normal TSH in Pregnancy

<table>
<thead>
<tr>
<th>Trimester</th>
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<tr>
<td>First</td>
<td>0.1 - 2.5 mIU/L</td>
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Thyroid Hormone dose requirements may increase by 20 - 50 % in pregnancy (J Clin Endocrinol Metab 2007, 92(8):Suppl:S1-47)

To compensate for increased demand for thyroid hormone (no fetal thyroid until after 10 - 12 weeks):

- women with functioning thyroids make extra and the gland enlarges
- women with hypothyroidism often need a dose increase.
Prospective randomized trial

- 60 pregnant women with 1º hypothyroidism on LT4, seeking pregnancy or <11 weeks pregnant

- Group A - ↑ by 2 pills/week (↑ 29%)

- Group B - ↑ by 3 pills/week (↑ 43%)

Levothyroxine dose adjusted q 4 weeks
Conclusions:

- 29% LT4 dose increase (2 extra pills/week) significantly decreased risk of maternal hypothyroidism throughout 1st trimester, without significant over treatment.

- Q 4 week adjustment better than Q 6 week to maintain target TSH.
Limitations:
- No “Standard Care” control group
- Only biochemical outcomes

But:
- There is established evidence of need for increased thyroid hormone in pregnancy
- There are meaningful consequences of hypothyroidism in pregnancy
- This study provides one practical strategy to:
  - Meet increased need
  - Maintain euthyroidism
Case Study 2

A healthy 31 y.o. F, G2A1 (previous SA at 6 weeks) presents at 9 weeks. Appropriate thyroid disease screening would be:

1. History and physical exam only
2. TSH
3. TSH, free T4
4. TSH, free T4, free T3, anti-TPO
5. TSH, anti-TPO
Screening for Thyroid Dysfunction in Pregnancy

- What is a normal TSH pregnancy?
- Gestational age-specific TSH reference range?
  - several studies, in variety of populations
  - reference ranges in non-pregnant populations are not applicable to pregnancy
28% of women > 97.5%ile of this cohort would not have been identified with TSH elevation as per assay reference value.

11% of euthyroid women (>2.5%ile) would have been incorrectly characterized as abnormal as per assay reference value.

Dashe JS et al. 2005 Obstet Gynecol 106:753-7
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Universal Screening Versus Case Finding for Detection and Treatment of Thyroid Hormonal Dysfunction During Pregnancy

Roberto Negro, Alan Schwartz, Riccardo Gismondi, Andrea Tinelli, Tiziana Mangieri, and Alex Stagnaro-Green

- 4562 women, 2 centres in Italy
- randomized to universal screening or case-finding
- stratified as high risk or low risk
- all women in universal screening group, and high risk women in case-finding group, had TSH, fT4, antiTPO
  - low risk women in case-finding group:
    - serum frozen, tested post-partum
- Rx LT4 is TSH >2.5 if +anti-TPO
- Rx antithyroid medication if hyperthyroid
Universal Screening Versus Case Finding for Detection and Treatment of Thyroid Hormonal Dysfunction During Pregnancy

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- Very few low risk women may avoid adverse outcomes with universal screening
- **Bottom Line Conclusion** - Universal screening vs. case-finding did not result in less total adverse outcomes
- i.e. the few adverse outcomes avoided in the subset of low risk women who turned out to have thyroid disease were not enough to make a relevant difference

*J Clin Endocrinol Metab 2010 95(4): 1699-707*
Antenatal Thyroid Screening and Childhood Cognitive Function


- 21,846 women age ≥ 18 with singleton pregnancies
- 10 centres in UK, 1 centre in Italy
- randomized to “screening” or “control” groups
  - screening group - TFTs tested (~12 wks GA) and if ↑TSH >97.5%ile and/or ↓fT4 <2.5 %ile - Rx LT4 (recommended starting dose 150 mcg/d, target TSH 0.1-1.0 mlU/L)
  - control group - TFTs drawn (~12 wks GA) and frozen, tested after delivery, and if ↑TSH and/or ↓fT4 - Rx LT4 post-partum

Conclusions: Antenatal thyroid screening (at median 12+3 wks GA) and maternal treatment for hypothyroidism did not result in improved cognitive function in children at 3 yrs of age
Screening Guidelines

- **Pre-pregnancy:**
  - screening not recommended
  - High risk case finding reasonable
  - Consider levothyroxine to maintain TSH < 2.5

- **Pregnant:**
  - No consensus
  - Universal screening is an option
  - High risk case finding is standard of care