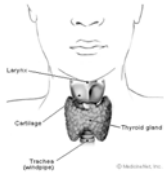


Thyroid Disease and Pregnancy: Optimizing the Maternal and Fetal Outcomes

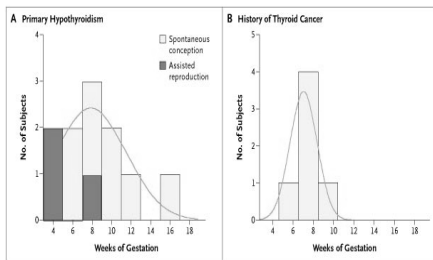


Richard T. Kloos, M.D.
The Ohio State University
Divisions of
Endocrinology
and Nuclear Medicine



Impact of Pregnancy on Pre-Pregnancy Dose of Levothyroxine

Timing and Magnitude of Increases in Levothyroxine Requirements During Pregnancy in Women with Hypothyroidism



Alexander, E. K. et al. N Engl J Med 2004;351:241-249

Timing and Magnitude of Increases in Levothyroxine Requirements During Pregnancy in Women with Hypothyroidism

- Mean levothyroxine increase was 47%
- Increase noted as early as 5 weeks and plateaued between 16-20 weeks
- Increased dose was required until delivery

Alexander, E. K. et al. N Engl J Med 2004;351:241-249

Recommendations for L-T4 Management During Pregnancy

- Alexander, NEJM – Increase L-T4 dose by two extra pills a week until TFT'S performed
- Toft, NEJM – Increase L-T4 dose by 25-50 mcg daily and obtain TFT'S in 4-6 weeks
- Stagnaro-Green, unpublished – Increase L-T4 dose to obtain pre-pregnancy TSH between 0.5 – 2.0 and obtain TFT'S as soon as pregnancy is confirmed

What are the issues for women not on L-T4? Case Presentation

A 37 year old woman is referred by her gynecologist. She is 6 weeks pregnant (first pregnancy). Her younger sister developed Hashimoto's disease 5 years ago and has a history of a preterm delivery. Knowing this history the gynecologist performed thyroid function tests on the patient with the following results: TSH – 4.3 mIU/L and positive thyroid peroxidase antibodies.

- Would you treat this woman with L-T4?

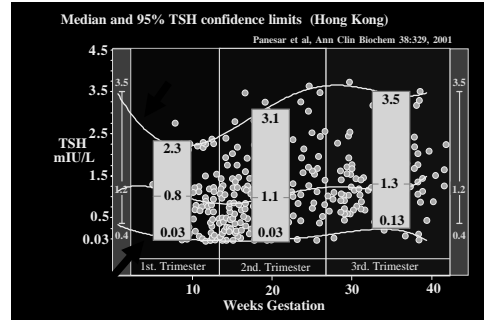
Case Presentation

The patient is an avid reader of the internet and presents with the following questions:

- Is my TSH abnormal?
- Is there a risk for pregnancy loss or pre-term delivery?
- Will there be an impact on my child's IQ?
- Am I at risk for postpartum thyroiditis?
- What can I do to decrease these risks?

TSH Levels in Normal* Pregnancies

*Did not exclude women who were TAB+

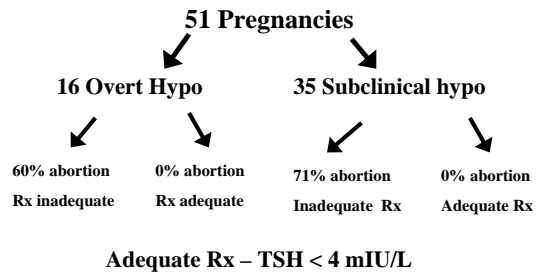


Case Presentation

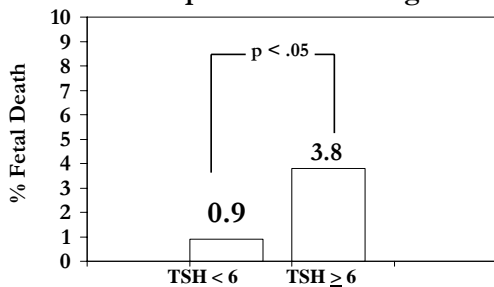
The patient is an avid reader of the internet and presents with the following questions:

- Is my TSH abnormal? Yes
- Is there a risk for pregnancy loss or pre-term delivery?

Overt and Sub clinical Hypothyroidism Complicating Pregnancy

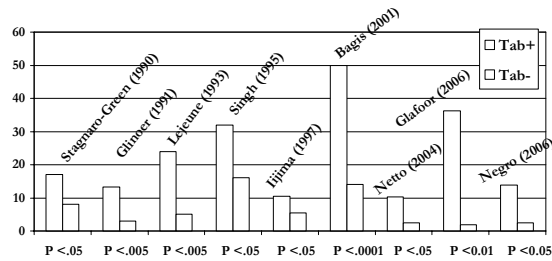


Maternal Thyroid Deficiency and Pregnancy Complications: Implications for Population Screening



Thyroid Antibodies and Spontaneous Miscarriage

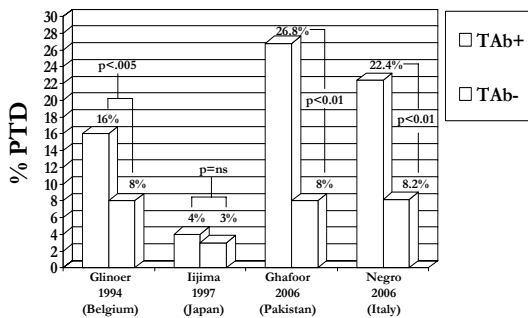
Thyroid Antibodies and Spontaneous Miscarriage



Maternal Autoimmune Thyroid Disease and Preterm Delivery

- Preterm delivery (<37 weeks gestation) – leading cause of perinatal mortality and congenital neurological disability in the U.S.
- Majority of neonatal mortality and morbidity in the United States occurs in very preterm infants (< 32 weeks gestation).
- 5000 perinatal deaths annually are due to preterm delivery

AITD and Preterm Delivery



Case Presentation

The patient is an avid reader of the internet and presents with the following questions:

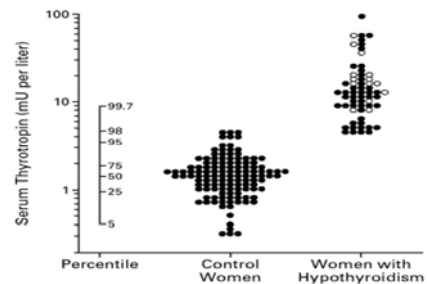
- Is my TSH abnormal? Yes.
- Is there a risk for pregnancy loss or pre-term delivery? Yes.
- Will there be an impact on my child's IQ?

Maternal Thyroid Deficiency During Pregnancy and Subsequent Neuropsychological Development of the child

- Measured TSH in 25,216 samples
- Identified 62 women with a TSH > 98th percentile and 124 matched controls
- Performed the Wechsler Intelligent Scale for offspring at 7-9 years old

Haddow et al. NEJM 1999;341:549

Maternal Thyroid Deficiency During Pregnancy and Subsequent Neuropsychological Development of the child



Haddow et al. NEJM 1999;341:549

Maternal Thyroid Deficiency During Pregnancy and Subsequent Neuropsychological Development of the child

- Full scale IQ results in ↑ TSH group
 - Overall 4 points lower (P=0.06)
 - 7 points lower in 48 untreated women (P=0.005)
 - 19% had scores of 85 or less in 48 untreated women (5% in controls, P<0.005)

Haddow et al. NEJM 1999;341:549

Case Presentation

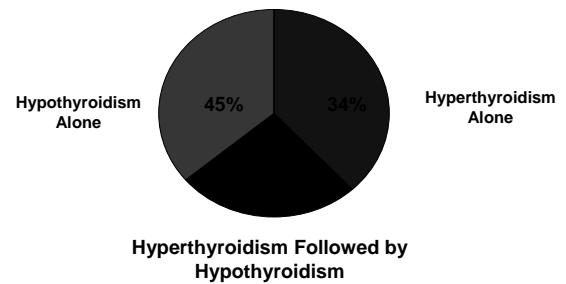
The patient is an avid reader of the internet and presents with the following questions:

- Is my TSH abnormal? Yes.
- Is there a risk for pregnancy loss or pre-term delivery? Yes.
- Will there be an impact on my child's IQ? Yes.
- Am I at risk for postpartum thyroiditis?
- What can I do to decrease these risks?

Postpartum Thyroiditis

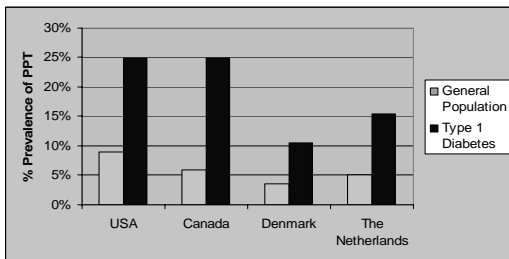
- The occurrence of transient hyperthyroidism and/or transient hypothyroidism in the postpartum period in women who were euthyroid during pregnancy.

Biochemical Presentation of Postpartum Thyroiditis



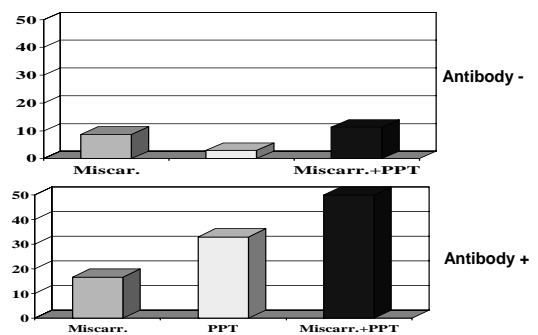
Stagnaro-Green, 2002

Prevalence of PPT in Women With Type 1 Diabetes Mellitus

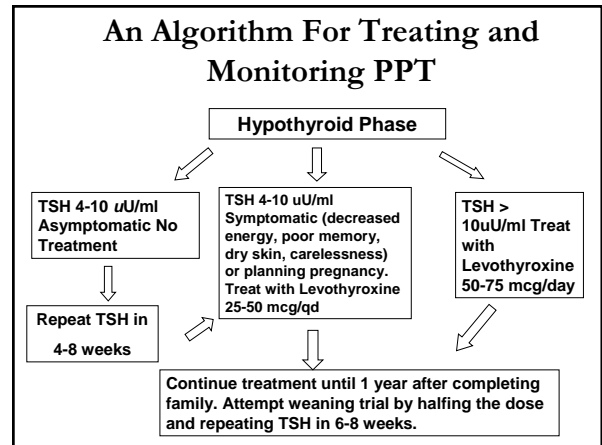
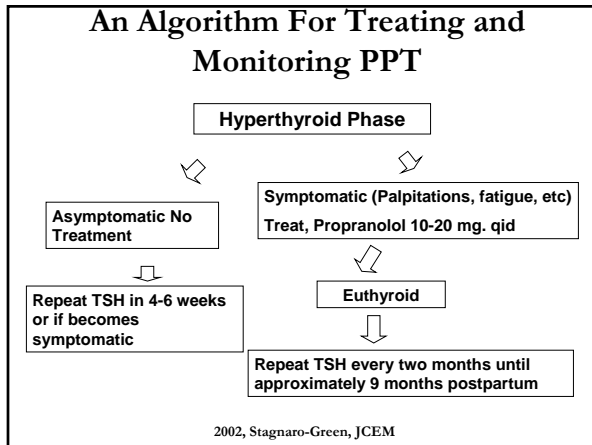
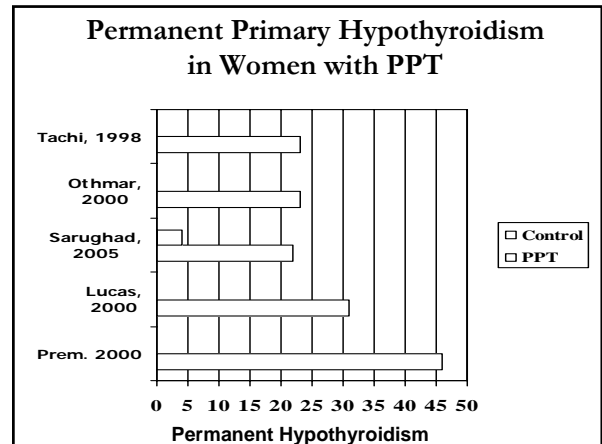
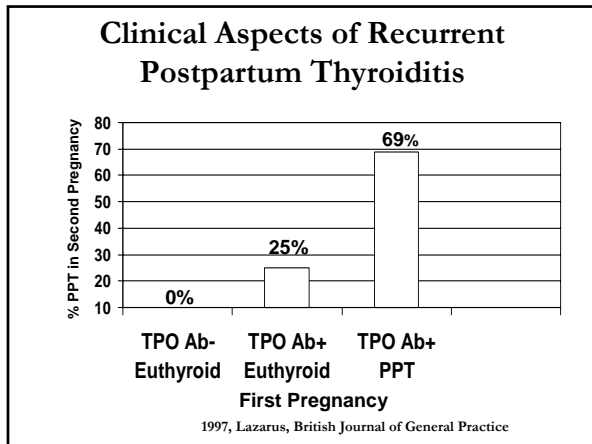


Stagnaro-Green

Outcome of Pregnancy Based On Initial Thyroid Antibody Status



Stagnaro-Green, Roman, Cobin et al, JCEM. 1992



Case Presentation

The patient is an avid reader of the internet and presents with the following questions:

- Is my TSH abnormal? Yes.
- Is there a risk for pregnancy loss or pre-term delivery? Yes.
- Will there be an impact on my child's IQ? Yes.
- Am I at risk for postpartum thyroiditis? Yes.
- What can I do to decrease these risks?

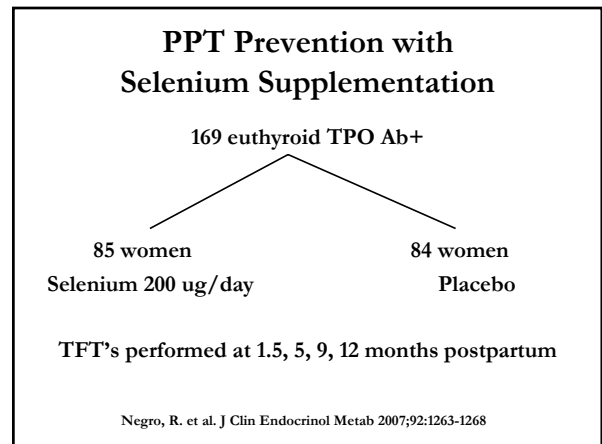
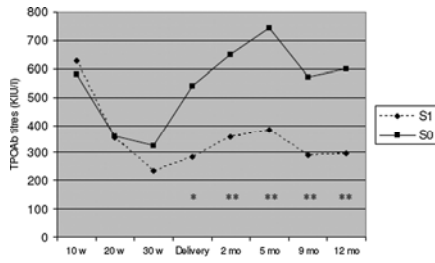


FIG. 2. Trends in TPOAb titers in TPOAb(+) women who received Se (group S1) or placebo (group S0)

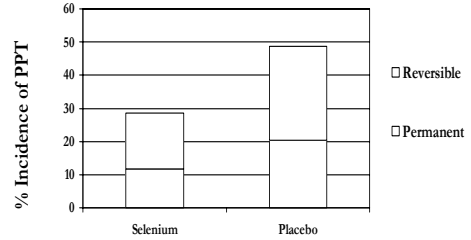


Negro, R. et al. J Clin Endocrinol Metab 2007;92:1263-1268

Copyright ©2007 The Endocrine Society

THE JOURNAL OF
CLINICAL
ENDOCRINOLOGY
& METABOLISM

PPT Prevention with Selenium Supplementation



Negro et al. J Clin Endocrinol Metab 2007;92:1263-1268

Levothyroxine in AITD During Pregnancy

Objective

- To determine if women with AITD have a higher rate of obstetrical complications.
- First randomized perspective study
- Performed in Italy

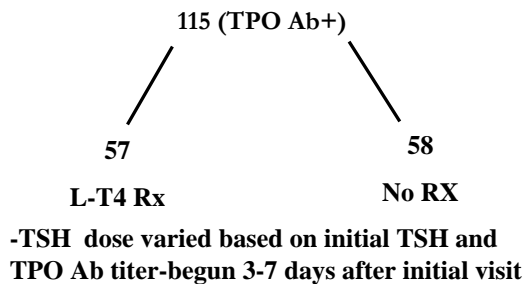
Negro et al. JCEM. 2006;91(7):2587-2591.

Methods

- 984 Woman
- TSH, and TPO Ab at first prenatal visit
- 115 women were TPO Ab+ (11.7%)
- 869 were TPO Ab- (control group)

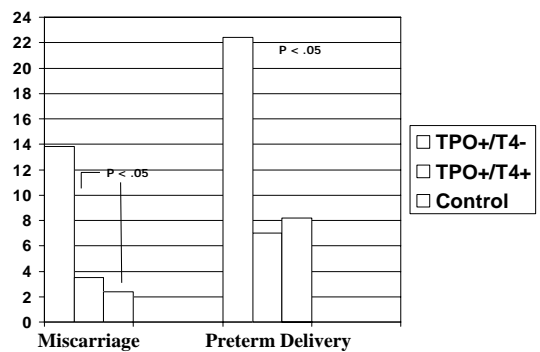
Negro et al. JCEM. 2006;91(7):2587-2591.

Methods



Negro et al. JCEM. 2006;91(7):2587-2591.

Results



Negro et al. JCEM. 2006;91(7):2587-2591.

Case Presentation

The patient is an avid reader of the internet and presents with the following questions:

- Is my TSH abnormal? Yes.
- Is there a risk for pregnancy loss or pre-term delivery? Yes.
- Will there be an impact on my child's IQ? Yes.
- Am I at risk for postpartum thyroiditis? Yes.
- What can I do to decrease these risks? L-T4 decreases miscarriage and pre-term delivery, selenium decreased post-partum thyroiditis, randomized studies regarding IQ have not been completed.

To Screen or Not to Screen the Population

1. Is thyroid disease and pregnancy common? Yes
2. Are there important associated morbidities? Yes
3. Availability of an inexpensive, available, and accurate screening test?
4. Can the morbidities be prevented?

Mild Hypothyroidism and Pregnancy

2007 Updated Guidelines
Journal of Clinical Endocrinology & Metabolism

- Case findings support screening for thyroid disease during 1st trimester of pregnancy in specific at risk populations
- Universal screening of pregnant women for thyroid disease is not yet supported by adequate studies

Abalovich M, et al. *J Clin Endocrinol Metab.* 2007 Aug;92(8 Suppl):S1-47.

Management of Thyroid Dysfunction during Pregnancy and Postpartum

2007 Updated Guidelines
Journal of Clinical Endocrinology & Metabolism

- Hypothyroidism:
 - Targeted case finding is recommended at the first prenatal visit or at diagnosis of pregnancy.
 - History of hyperthyroidism, hypothyroidism, post-partum thyroiditis (PPT), lobectomy, goiter, TPO antibodies (when known), type 1 DM, other autoimmunity, prior head and neck irradiation, miscarriage or preterm delivery.
 - Family history of thyroid disease.
 - Symptoms or signs of thyroid dysfunction, including anemia, elevated cholesterol, hyponatremia.
 - TSH should be measured during infertility evaluation

Management of Thyroid Dysfunction during Pregnancy and Postpartum

2007 Updated Guidelines
Journal of Clinical Endocrinology & Metabolism

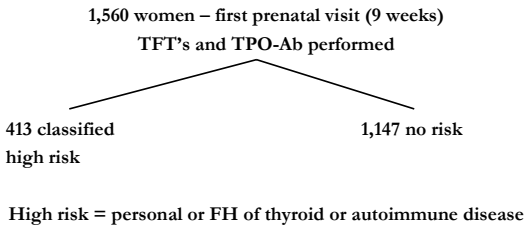
- Hypothyroidism:
 - Adjust thyroxine to reach a TSH level not higher than 2.5 uU/mL prior to pregnancy, and 3 uU/mL in the 2nd and 3rd trimester.
 - Euthyroid women with thyroid autoimmunity should be monitored for elevation of TSH above the normal range.
 - LT4 replacement recommended for subclinical hypothyroidism.

Hypothyroidism Rx During Pregnancy

- Do not take LT₄ within 4 hours of ingesting:
 - prenatal vitamins containing iron
 - iron supplements
 - soy milk
 - calcium supplements
- The American Thyroid Association recommends that women receive 150 mcg iodine supplements daily during pregnancy and lactation and that all prenatal multivitamin/mineral preparations contain 150 mcg of iodine. (read the label!)
- After delivery, reduce LT₄ to pre-pregnancy dose and recheck TSH 6 weeks postpartum

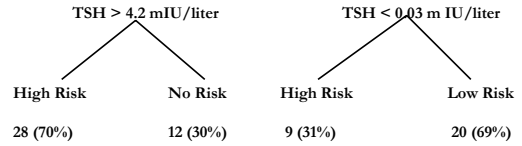
Mandel SJ. *Best Pract Res Clin Endocrinol Metab.* 2004 Jun;18(2):213-224.; Smalridge RC, et al. *J Clin Endocrinol Metab.* 2001 Jun;86(6):2349-2353.; Rashid M, Rashid MH. *Obstet Gynecol Surv.* 2007 Oct;62(10):680-8

Detection of Thyroid Dysfunction in Early Pregnancy: Universal Screening or Targeted High-Risk Case Finding



Vaidya, et al. Journal of Clinical Endocrinology & Metabolism 92:203-207,2007

Prevalence of Raised or Fully Suppressed TSH



Conclusion – Targeted case finding misses 30% (12 of 1560) of hypothyroid women and 69% of women with fully suppressed TSH

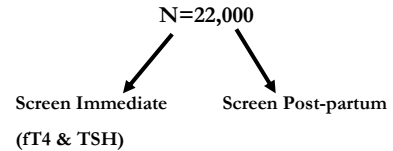
Vaidya, et al. Journal of Clinical Endocrinology & Metabolism 92:203-207,2007

To Screen or Not to Screen

1. Is thyroid disease and pregnancy common? Yes
2. Are there important associated morbidities? Yes
3. Availability of an inexpensive, available, and accurate screening test? Yes, TSH & TPO-Ab, pending cost-effectiveness analysis (e.g. 12 of 1560).
4. Can the morbidities be prevented? IQ Studies underway.

Controlled Antenatal Thyroid Study Lazarus – Cardiff Ongoing Study

Sample drawn prior to 16 weeks gestation



- > L – T4 given if fT4 < 2.5th percentile or TSH > 97.5th percentile
- > Offspring will be tested at 3 years of age



AMERICAN
THYROID
ASSOCIATION
FOUNDED 1923

<http://thyroid.org>

Acknowledgment: Alex Stagnaro-Green, Touro University College of Medicine, Chair of the ATA Thyroid Disease in Pregnancy Task Force for sharing slides for this presentation.

