

# The Presence of Thyroid Autoantibodies in Pregnancy

Dr. O'Sullivan does not have any financial relationships with any commercial interests.

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ENDORAMA

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# Chief Complaint

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**31 year-old G1P0 pregnant female** is referred to endocrine clinic at 10 + 5/7 weeks gestation for management of new-onset **hypothyroidism diagnosed during pregnancy.**

# History of Present Illness

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- Prior to pregnancy, no history of thyroid disease.
- No history of goiter. No history of radiation to the head/neck/chest.
- Pre-pregnancy TSH 3.2 (1 year prior)
- Labs at 7 wks GA: TSH 4.62 mcU/mL, + Anti-TPO Ab
- Started Levothyroxine 50 mcg daily
- +Fatigue/nausea, no notable change in symptoms after starting LT4

# Rest of History

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## PMH:

- GERD, allergic rhinitis, migraines

## PSgHx:

- s/p tonsillectomy
- s/p inguinal hernia repair (< 6 mo)

## Social Hx:

- Former smoker, quit 13 years prior.
- Teacher

## Family History:

- Sister and paternal GM w/ Hashimoto's
- Mother s/p subtotal thyroidectomy for benign nodules; h/o childhood radiation.
- Father takes LT4 prophylactically for h/o childhood neck irradiation.
- Paternal aunt with inflammatory bowel disease.

# Current Medications

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- Levothyroxine 50 mcg daily
- Prenatal vitamin (90 mcg iodine)

# Review of Systems

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General: +fatigue, but generally “feels great.” No change in weight.

HEENT: No hearing loss. No dysphagia, changes in voice or neck stiffness.

Cardiac: No chest pain or palpitations.

Pulm: No shortness of breath or wheezing.

GI: +nausea, no vomiting. +GERD. +chronic constipation.

GU: No polydipsia or polyuria.

MSK: No joint or bony pain.

Skin: No dry skin.

Neuro: +chronic numbness in hands. No headaches or weakness.

Psych: No depression

# Physical Exam

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Vitals: BP 107/61, **P 60**, R 18, Ht 5'8", Weight 166 lb (75.3 kg)

General: Well-nourished, no distress.

Eyes: Conjunctiva normal. PERRL. No increased insertions. Measurement by Hertel's exophthalmometer at base 93 mm R/L 13/13 mm.

Neck: trachea midline, no thyromegaly, no thyroid nodules.

CV: **+bradycardia**, otherwise regular. **+2/6 systolic murmur present**.

Pulm: CTAB.

Abd: No tenderness, non-distended. No hepatomegaly.

Neuro: **bicep reflexes 3+ bilaterally**, patellar reflexes 2+ bilaterally.

Skin: warm, dry, no diaphoresis.

# Laboratory Studies

	Ref. Range per EPIC	2/4/13	2/11/13	2/25/13
Gest Age		~ 7 wks	~ 8 wks	10 + 5/7 wks
TSH	0.3-4 mcU/mL	4.620	5.230	4.40
T4	5-11.6 mcg/dL	7.7		9.1
Anti-TPO	< 0.4 KU/mL	176		
Anti-Tg	< 0.4 KU/mL	< 20		
LT4 dose		None	None	50 mcg daily



# Clinical Question #1

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What is the association between antithyroid Ab positivity, hypothyroidism, and obstetric complications?

# Anti-Thyroid Antibody Positivity in Pregnancy

- Of all euthyroid women, **10-20% are antithyroid antibody positive** (TPO or Tg) in the first trimester
  - **20% of these women develop a TSH > 4 mIU/L**
- ATA Recommendations for women anti-thyroid Ab +:
  - Monitor TSH every 4 weeks during the 1<sup>st</sup> half of pregnancy and at least once between 26 and 32 weeks gestation (Level B)

Glinioer et al. JCEM. 1994

Stagnaro-Green et al. Thyroid. 2011.

# Does treatment with levothyroxine in euthyroid, anti-TPO positive women improve pregnancy outcomes?

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## **Levothyroxine Treatment in Euthyroid Pregnant Women with Autoimmune Thyroid Disease: Effects on Obstetrical Complications**

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# Does treatment with levothyroxine in euthyroid, anti-TPO positive women improve pregnancy outcomes?

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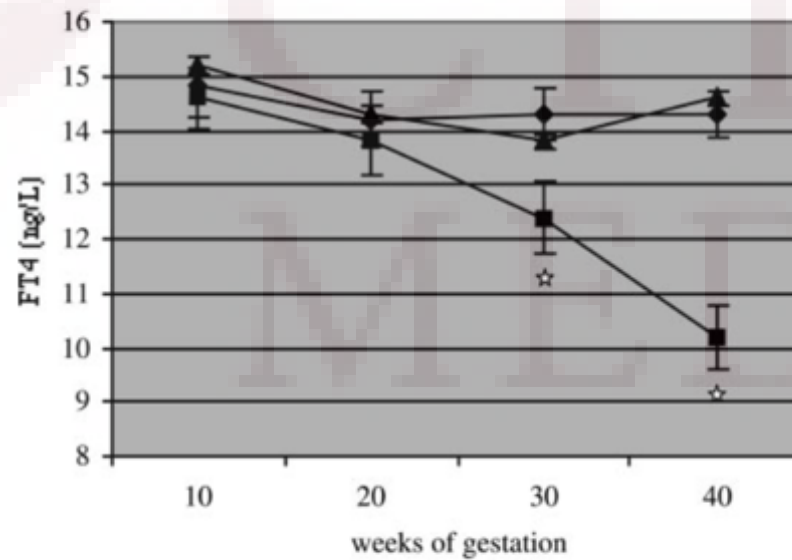
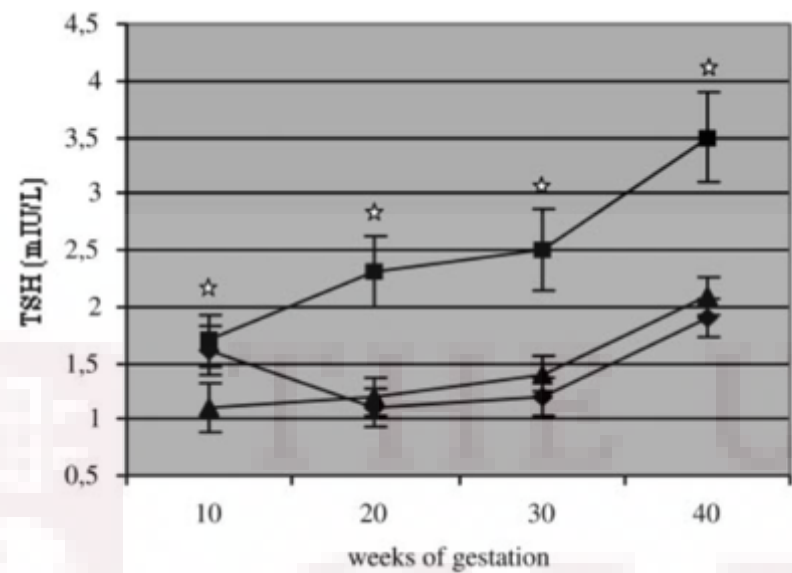
**TABLE 1.** Characteristics of patients at 10, 20, and 30 wk gestation and delivery (D)

	n	Age (yr)	TSH (mIU/liter)				FT <sub>4</sub> (ng/liter)			
			10 wk	20 wk	30 wk	D	10 wk	20 wk	30 wk	D
TPOAb <sup>+</sup> LT <sub>4</sub>	57	30 ± 5	1.6 ± 0.5	1.1 ± 0.4	1.2 ± 0.4	1.9 ± 0.5	14.8 ± 4.2	14.2 ± 3.8	14.3 ± 3.6	14.3 ± 3.2
TPOAb <sup>+</sup>	58	30 ± 6	1.7 ± 0.5	2.3 ± 0.5	2.5 ± 0.6	3.5 ± 0.7	14.6 ± 4.3	13.8 ± 4.8	12.4 ± 4.9	10.2 ± 4.5
TPOAb <sup>-</sup>	869	28 ± 5	1.1 ± 0.4	1.2 ± 0.4	1.4 ± 0.4	2.1 ± 0.6	15.2 ± 4.1	14.3 ± 4.0	13.8 ± 4.2	14.6 ± 3.8

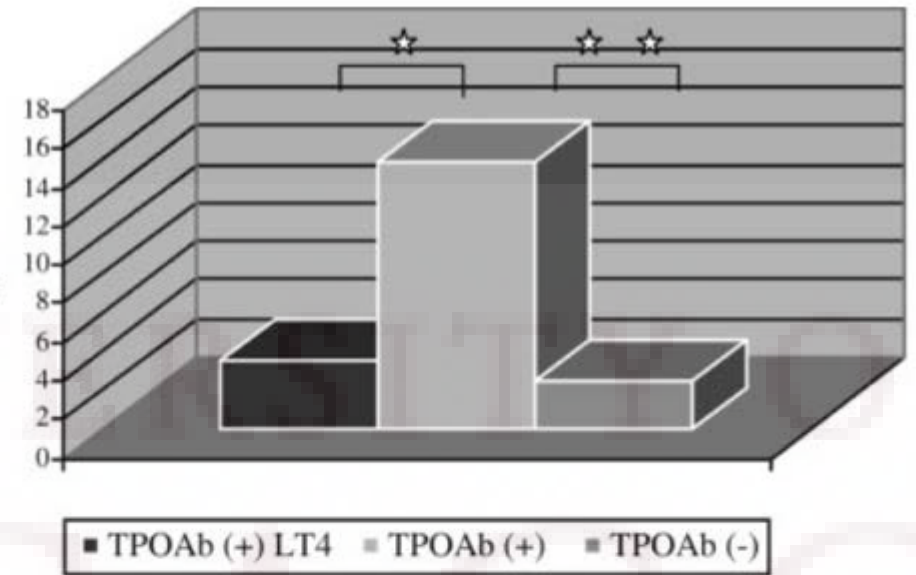
Data are expressed as mean ± SD.

C

B



Miscarriage %



Preterm delivery %

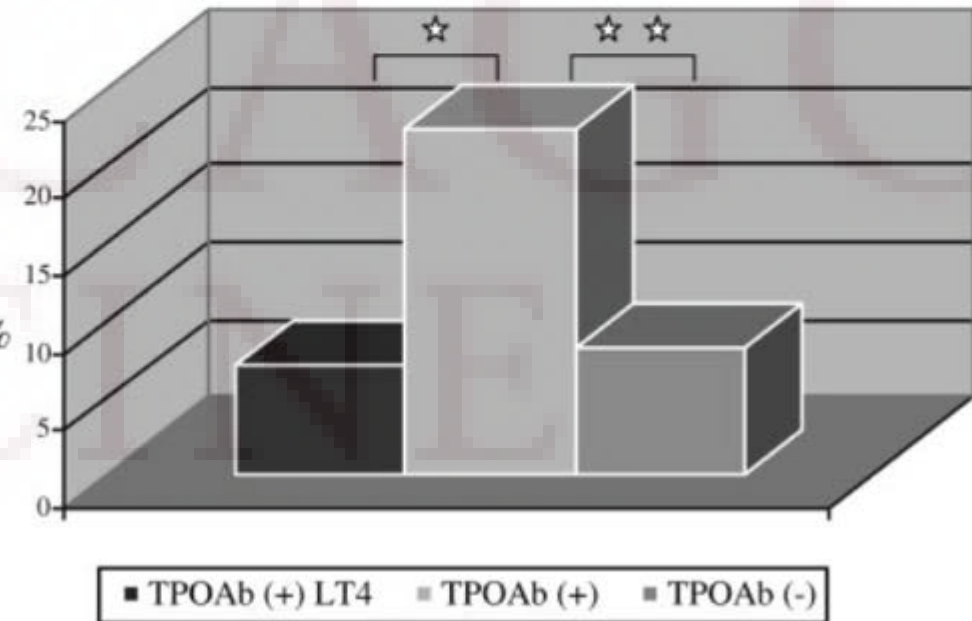


FIG. 4. Percentage of miscarriages (*top*) and premature deliveries (*bottom*) in group A (TPOAb<sup>+</sup> treated with LT<sub>4</sub>), group B (TPOAb<sup>+</sup>), and group C (TPOAb<sup>-</sup>). ☆, *P* < 0.05; ☆☆, *P* < 0.01.

# Summary of Guidelines:

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## ATA (2011)/Endocrine Society:

- No routine screening for thyroid disease in pregnancy (*ATA*)
- Antithyroid Ab + and TSH > 2.5 -> start LT4
- Start LT4 for subclinical hypothyroidism (*Endocrine Society*)
- No recommendation to start euthyroid Ab positive women on LT4

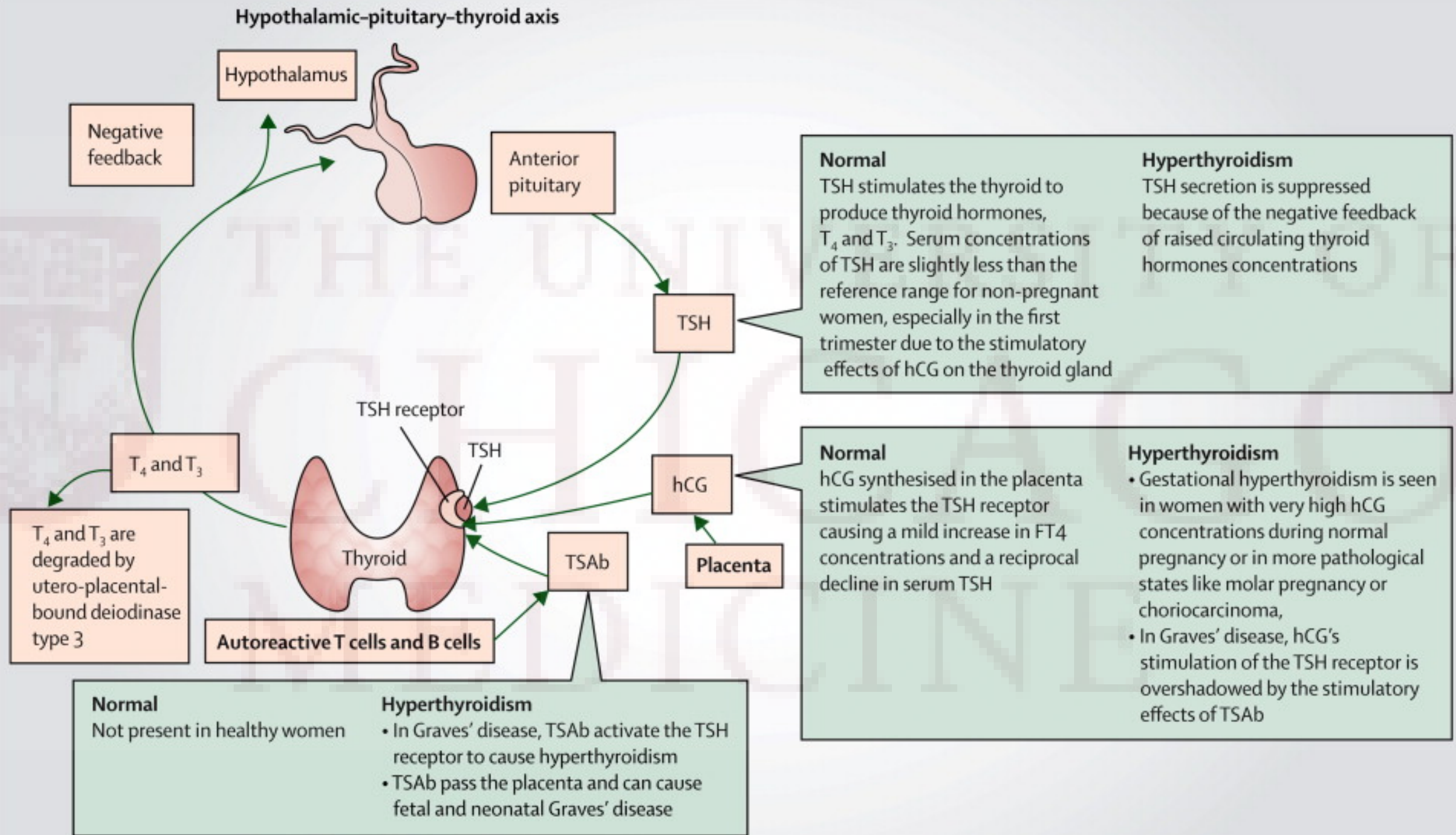
## American College of Obstetricians and Gynecologists (2015):

- No routine screening for thyroid disease in pregnancy
- No recommendation for LT4 in subclinical hypothyroidism or in euthyroid Ab positive women

## Back to the Case:

	Ref. Range per EPIC	2/4/13	2/11/13	2/25/13
Gest Age		~ 7 wks	~ 8 wks	10 + 5/7 wks
TSH	0.3-4 mcU/mL	4.620	5.230	4.40
T4	5-11.6 mcg/dL	7.7		9.1
Anti-TPO	< 0.4 KU/mL	176		
Anti-Tg	< 0.4 KU/mL	< 20		
LT4 dose		None	None	50 mcg daily







# Trimester-Specific TSH Goal in

TABLE 2. SAMPLE TRIMESTER-SPECIFIC REFERENCE INTERVALS FOR SERUM TSH

Reference	Trimester <sup>a</sup>		
	First	Second	Third
Haddow <i>et al.</i> (13)	0.94 (0.08–2.73)	1.29 (0.39–2.70)	—
Stricker <i>et al.</i> (14)	1.04 (0.09–2.83)	1.02 (0.20–2.79)	1.14 (0.31–2.90)
Panesar <i>et al.</i> (15)	0.80 (0.03–2.30)	1.10 (0.03–3.10)	1.30 (0.13–3.50)
Soldin <i>et al.</i> (16)	0.98 (0.24–2.99)	1.09 (0.46–2.95)	1.20 (0.43–2.78)
Bocos-Terraz <i>et al.</i> (17)	0.92 (0.03–2.65)	1.12 (0.12–2.64)	1.29 (0.23–3.56)
Marwaha <i>et al.</i> (18)	2.10 (0.60–5.00)	2.40 (0.43–5.78)	2.10 (0.74–5.70)

<sup>a</sup>Median TSH in mIU/L, with parenthetical data indicating 5th and 95th percentiles (13,15,18) or 2.5th and 97.5th percentiles (14,16,17).

- 1<sup>st</sup> Trimester: 0.1-2.5 mIU/L
- 2<sup>nd</sup> Trimester: 0.2-3 mIU/L
- 3<sup>rd</sup> Trimester: 0.3-3 mIU/L

# Laboratory Studies with Pregnancy Ranges

	Ref. Range per EPIC	Ref. Range 1 <sup>st</sup> Trimester	2/4/13	2/11/13	2/25/13
Gest Age			~ 7 wks	~ 8 wks	10 + 5/7 wks
TSH	0.3-4 mcU/mL	<b>0.1-2.5 mcU/mL</b>	4.620	5.230	4.40
T4	5-11.6 mcg/dL	<b>7.5-17.4 mcg/dL</b>	7.7		9.1
LT4 dose			None	None	50 mcg daily

# Results continued

	Ref. Range 1 <sup>st</sup> Trimester	Ref. Range 2 <sup>nd</sup> /3 <sup>rd</sup> Trimester	2/4/13	2/11/13	2/25/13	3/22/2013
GA (wks)			~ 7	~ 8	10 + 5/7	14 +2/7
TSH	0.1-2.5 mcU/mL	0.3-3 mcU/mL	4.620	5.230	4.40	4.43
T4	7.5-17.4 mcg/dL		7.7		9.1	11.0
LT4 dose			None	None	50 mcg daily	50 mcg + 1/wk

# Laboratory Studies with Pregnancy Ranges

	Ref. Range 2 <sup>nd</sup> /3 <sup>rd</sup> Trimester	3/22/2013	4/29/13	6/21/13	8/19/13
GA (wks)		14 +2/7	19 +5/7	27 + 2/7	35 +5/7
TSH	0.3-3 mcU/mL	4.43	2.67	2.51	2.37
T4	7.5-17.4 mcg/dL	11.0	10.6	11.4	9.5
LT4 dose		50 + 1/wk	75 mcg daily	75 + 1/wk	75 + 1/wk ~ 87 mcg/day

# Potential post-partum outcomes in antithyroid Ab positive women

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- 1) **On-going thyroid destruction resulting in hypothyroidism** for which she would require levothyroxine
- 2) **Post-partum thyroiditis** and risk for transient hyperthyroidism which would be exacerbated if she remains on levothyroxine.

# Post-Partum Thyroiditis (PPT)

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Definition: Autoimmune thyroid disease in the first year post-partum in women who were euthyroid to pregnancy, excluding Graves' Disease

## Presentations:

**Classic (22%):** Transient hyperthyroidism (1-3 mos PP) followed by transient hypothyroidism (3-9 mos PP) followed by euthyroidism

**Isolated Hypothyroidism (48%)**

**Isolated Thyrotoxicosis (30%)**

# Post-Partum Thyroiditis Risk

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Overall incidence of PPT is 5.4%

## Antibody positive (1<sup>st</sup> trimester):

- 33-50% of women TPO-Ab+ develop PPT
- Higher Ab titer, more likely to occur

## Antibody negative (1<sup>st</sup> trimester):

- Risk of PPT is “very low”

# Not to mention an increased risk in the spouse?

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## *Case Report*

### **Recurrent Episodes of Thyrotoxicosis in a Man following Pregnancies of his Spouse with Hashimoto's Thyroiditis**

**Regina Belokovskaya<sup>1</sup> and Alice C. Levine<sup>2</sup>**

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# Recommendations for LT4 Management Post-Partum:

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## ATA/Endocrine Society:

- No recommendations

## European Thyroid Association:

- Antithyroid Ab (-) women -> d/c LT4 after delivery and recheck thyroid function tests in 6 weeks.

# Laboratory Studies with Pregnancy Ranges

	Ref. Range 2 <sup>nd</sup> /3 <sup>rd</sup> Trimester	3/22/2013	4/29/13	6/21/13	8/19/13
GA (wks)		14 +2/7	19 +5/7	27 + 2/7	35 +5/7
TSH	0.3-3 mcU/mL	4.43	2.67	2.51	2.37
T4	7.5-17.4 mcg/dL	11.0	10.6	11.4	9.5
LT4 dose		50 + 1/wk	75 mcg daily	75 + 1/wk	75 + 1/wk

# Laboratory Studies with Pregnancy Ranges

	EPIC Range	8/19/13	11/14/13	2/11/14	4/16/14	7/2/14	1/15/15
GA (wks)		35 +5/7	2 mos PP	~ 5 mos PP	~ 7 mos PP	~ 10 mos PP	> 1 year PP
TSH	0.3-4 mcU/mL	2.37	3.65	4.52	10.34	4.65	3.51
T4		9.5					
Free T4	0.9-1.7 ng/dL		0.98	0.77	0.8	1.2	1.3
T3	80-195 ng/dL		76				
LT4 dose		75 + 1/wk	Off LT4 since 9/20	OFF	OFF	50 mcg	75 mcg

# What therapies can be used to prevent post-partum thyroiditis?

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- ~~Thyroid hormone~~
- ~~Iodine~~
- Vitamin D
- **Selenium???**



# The Influence of Selenium Supplementation on Postpartum Thyroid Status in Pregnant Women with Thyroid Peroxidase Autoantibodies

Roberto Negro, Gabriele Greco, Tiziana Mangieri, Antonio Pezzarossa, Davide Dazzi, and Haslinda Hassan

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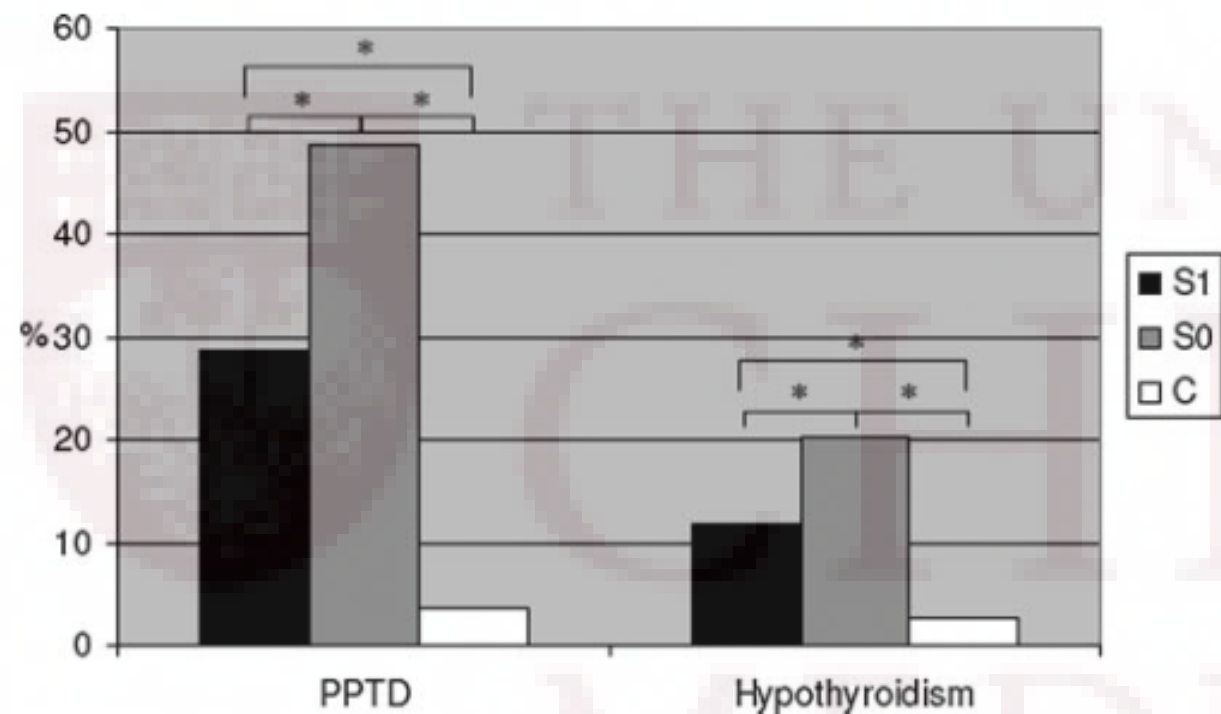


FIG. 1. Percentage of patients who had PPTD (*left*) and hypothyroidism (*right*) develop in TPOAb(+) women who received Se (group S1) or placebo (group S0), and in TPOAb(-) women (group C). \*,  $P < 0.01$ .

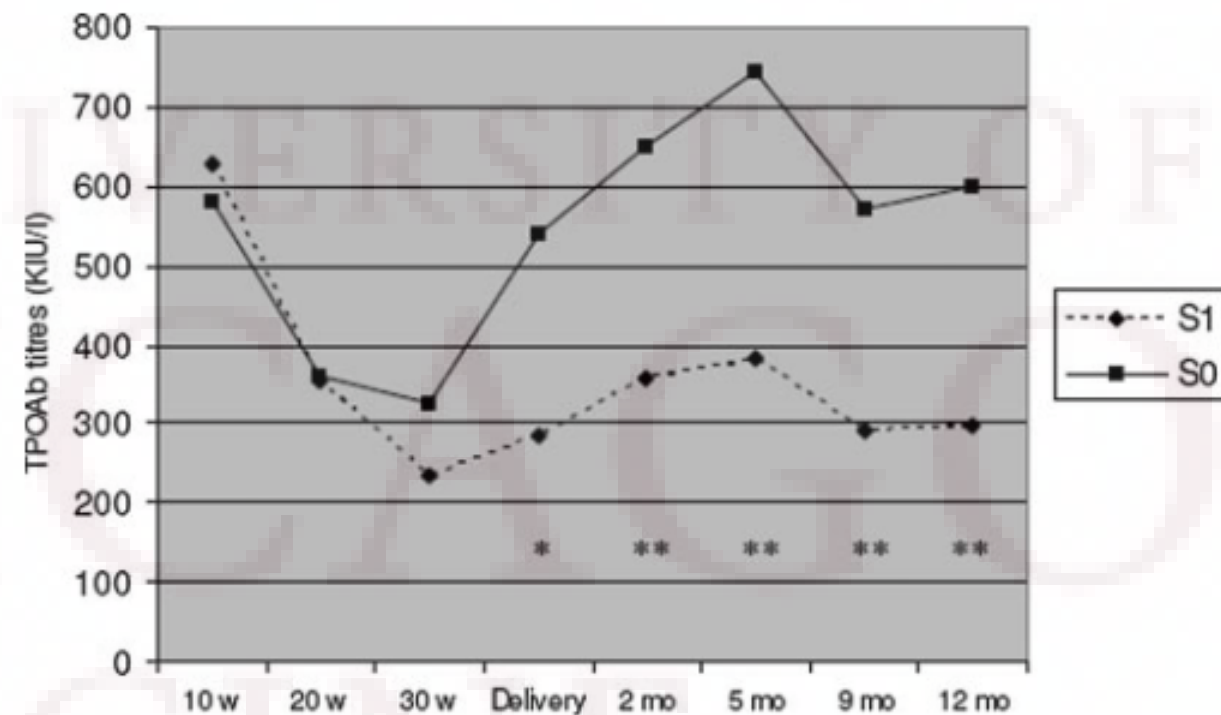


FIG. 2. Trends in TPOAb titers in TPOAb(+) women who received Se (group S1) or placebo (group S0). \*,  $P < 0.05$ . \*\*,  $P < 0.01$ . mo, Months; w, weeks.

# In Summary

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- Euthyroid women with antithyroid Ab are at high risk to develop hypothyroidism during pregnancy which may be associated with obstetric complications.
- The risk of post-partum thyroiditis in women with antithyroid Ab is high. No therapies to prevent thyroiditis are recommended, however, selenium may be beneficial.
- In women started on levothyroxine during pregnancy, there is no consensus on post-partum management; close thyroid monitoring is required.

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