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Thyroid Disorders During Pregnancy

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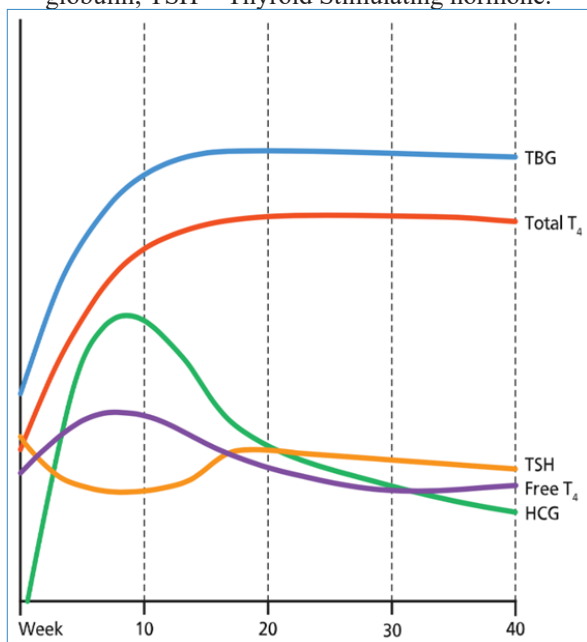
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Changes in thyroid hormones during pregnancy. Differentiation of Gestational hyperthyroidism versus Graves’ disease[1,2,3,4,5]

- Human Chorion Gonadotropin(hCG) shares a common alpha-subunit with Thyroid-stimulating hormone(TSH) and cross-reacts with the TSH receptor. TSH declines 1st trimester – nl = 0.03-2.0 mU/l. Estrogens increase Thyroid binding globulin (TBG), and Total Thyroxine and total triiodothyronine (TT4/TT3) increase with stable FT3/FT4.
- A radioactive iodine (RAI) scan is contraindicated during pregnancy
- DX of GD first during pregnancy - 0.1-0.4% - Presence of TSH receptor Antibodies, Graves ophthalmopathy, thyroid acropachy, or pretibial myxedema or hyper vascular on Doppler goiter, and continuation of symptoms beyond the first trimester of pregnancy differentiates GD during pregnancy from Gestational hyperthyroidism.
- Gestational hyperthyroidism - usually in the first 12-16 weeks of pregnancy, especially if the woman has hyperemesis gravidarum or molar pregnancy with high hCG. In 1-3% of pregnancies, complications occur. Gestational hyperthyroidism is transient..
- Previously diagnosed Graves’ disease before pregnancy usually worsens during the first trimester, with improvement thereafter during pregnancy.

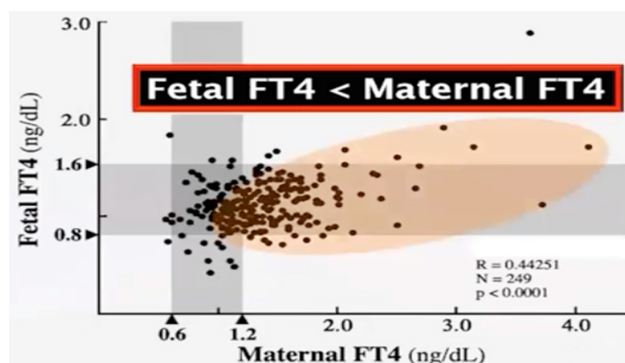
	Gestational thyrotoxicosis	Graves’
Nausea/Emesis	Yes	No
Thyrotoxic symptoms	Variable	Yes
PEx findings of Graves’ Goiter, bruit, orbitopathy	No	Yes
TRAb	No	Yes
T3/T4 ratio (ng/mcg/dl)	<20:1	>20:1
Thyroid US	Normal size Normal echogenicity Not vascular	Enlarged Heterogeneous Vascular
POC US by Endo consult team:	Thyroid normal size and echogenicity, not vascular	

Thyroid function in pregnancy. HCG = Human Chronic Gonadotropin; T₄ = Thyroxine, TBG = Thyroid binding globulin; TSH = Thyroid Stimulating hormone.



Hyperthyroid Pregnancy

- Infertility
- Spontaneous abortion
- Premature labor
- Small for age infants
- Neonatal mortality
- Maternal CHF
- Goiter
- Pulse greater than 90
- Weight loss
- Muscle weakness
- Increased frequency of bowel movements



Therapy for Maternal Hyperthyroidism

free T4 or total T4 and TSH

Monitor every 4 weeks



Rec 48b. Use lowest ATD dose to target FT4/TT4 upper limit or slightly above the reference range

Strong recommendation, high-quality evidence

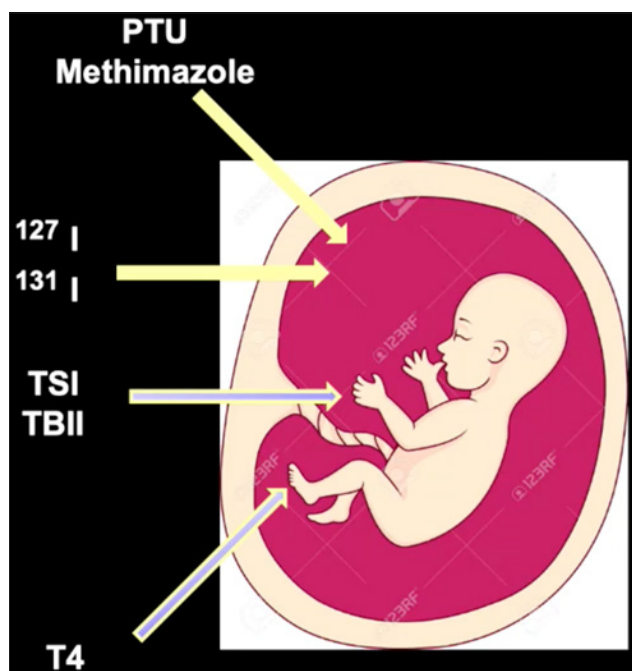
No adverse outcomes for mother or baby in SUBCLINICAL hyperthyroidism

Free T4 ranges not available

Total T4: Use reference value 1.5x nonpregnant reference range (T4 up to 18mcg/dL or 220nmol/L)

Casey, Obstet Gynecol 2006; 107:337

Maternal Fetal Transplacental Passage



Pregnancy Hyperthyroidism

- Radioiodine forbidden!
- Try to avoid surgery unless necessary!

Methimazole Embryopathy

- Choanal atresia
- Esophageal atresia / TEF
- Scalp defect (aplasia cutis)
- Omphalocele
- Omphalomesenteric duct abnormality
- Congenital heart disease (septal defects)
- Andersen et al

JCEM 2013; 98: 4373

Anti-thyroid Drug Concerns

- Neither MMI nor PTU is completely safe in 1st trimester
- PTU may be safer than MMI
- In some studies MMI + PTU may be worse than PTU alone
- Rare liver disease with PTU.
- Defects likely begin at 4 weeks gestation although most seem to occur at 6 - 10 weeks gestation.

- If high doses of ATD are necessary to control
- hyperthyroidism consider definitive therapy prior to pregnancy

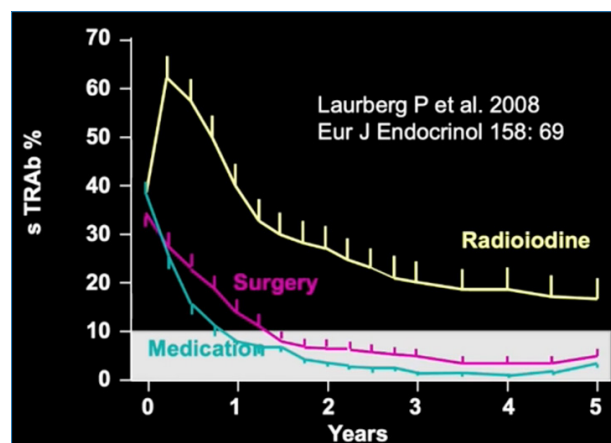
PTU Embryopathy

- Face and neck (sinuses and cysts) often requiring surgery
 - Hydronephrosis and genital abnormalities (surgery in half)
- Andersen et al
Thyroid 2014; 24: 1533

Pregnancy Guidelines for TRAb Measurements

- Euthyroid pregnant woman with prior anti-thyroid drugs for Graves' disease: TRAb measurements not necessary.
- Euthyroid pregnant woman with prior Ral or surgery for Graves' disease: Measure in early pregnancy to assess risk for fetal hyperthyroidism and late for neonatal.
- Pregnant woman on ATD for Graves: Measure TRAb in last trimester to assess for neonatal hyperthyroidism.

Change in Graves' Autoimmunity



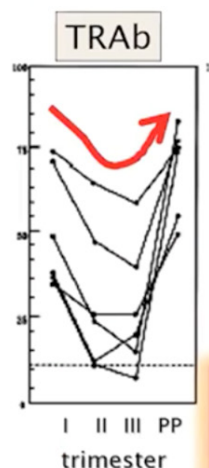
Who gets TRAb Measurement? Prediction of FETAL/NEONATAL Hyperthyroidism

Graves' on ATD Rx	Graves' after I-131 or thyrox→ on T4 Rx	Graves' in remission on NO Rx
YES	YES	NO

- Early in pregnancy → if negative DONE!
- At 18-22 weeks → fetal thyrotoxicosis
- At 30-34 weeks → neonatal thyrotoxicosis

Alexander Thyroid 2017; 27:315

Maternal TRAb and fetal thyrotoxicosis



Fetal US to assess heart rate, growth, amniotic fluid volume, and the presence of **fetal goiter**. Consultation with MFM.

Values >3x ULN are predictive of fetal thyrotoxicosis

Amino, J Clin Endocrinol Metab, 2003;88:5871; Alexander Thyroid 2017; 27:315
van Dijk Thyroid epub DOI:10.1089/thy.2017.0413

Fetal Goiter : Hyper or Hypo Look at the Mom

- Mom with active Graves' overtreated with antithyroid drugs with inappropriately "normal" or low thyroid function tests → **THINK HYPO**
- Mom with active Graves' not controlled on antithyroid drugs → **THINK HYPER**
- Hypothyroid Mom with HISTORY of Graves' after surgery or I-131 ablation → **THINK HYPER**

Luton J Clin Endocrinol Metab 2005;90:6092

What do the ATA 2017 Guidelines Suggest?

- No therapy until 12 weeks (particularly with maintenance)
- MMI dosage $\leq 5-10$ or PTU $\leq 100-200$ mg /day).
- Switch to PTU as early as possible.
- If switch to PTU first trimester consider switch back to MMI second trimester.

ATA 2017 guidelines recommendation 47

Summary

- Gestational thyrotoxicosis-- emesis, \uparrow TFTs, T3:T4 <20, no goiter, use ultrasound, TRAb
- Hyperthyroidism--PTU preferred in 1st trimester
- Mild hyperthyroidism→ withdraw Rx if TRAb negative • Use lowest dose of antithyroid drug titrated to FT4 upper normal
- Check TRAb for risk of fetal thyrotoxicosis
1st trimester TRAb positive → fu TRAb → fetal US

Iodine Requirements and Prenatal Vitamins

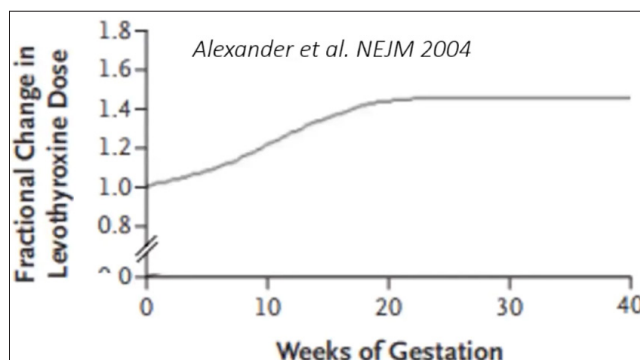
- **Iodine deficiency in pregnancy:** intellectual disability, intrauterine growth restriction, goiter

Iodine requirements increase in pregnancy

- 150 ug supplementation daily recommended (→220 ug total daily intake)

- 2013 study of urinary iodine: inadequate intake in US pregnant women

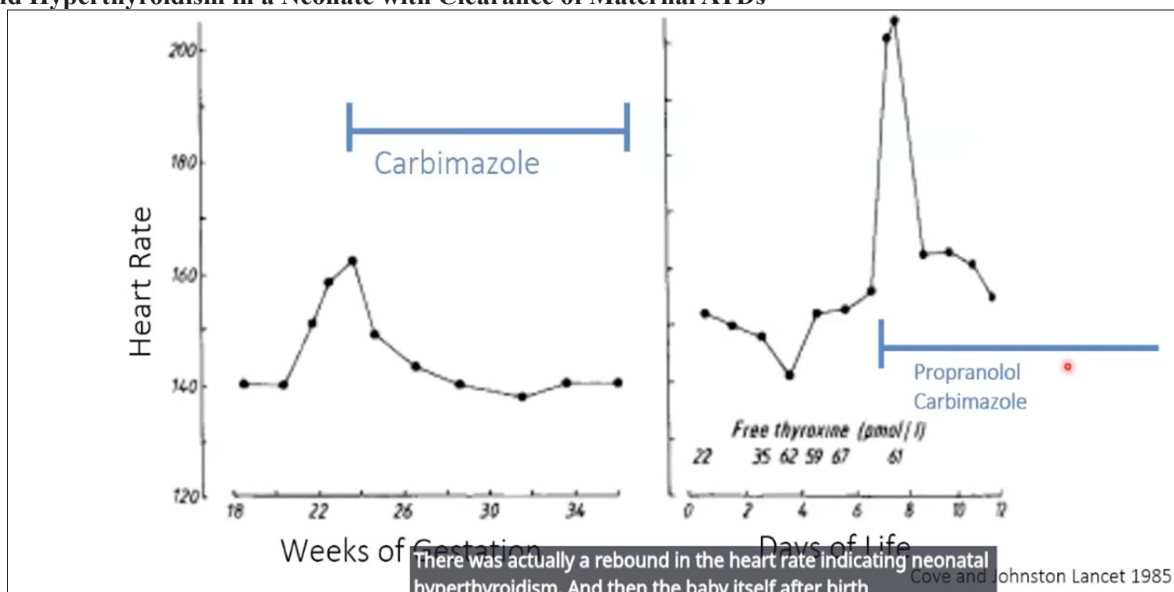
Levothyroxine requirements increase 30-50% across gestation



Add 2 pills per week with positive pregnancy test
May require 2 mcg/kg/day (vs 1.6 mcg/kg/day outside pregnancy)

Return to pre-pregnancy dose immediately after delivery

Rebound Hyperthyroidism in a Neonate with Clearance of Maternal ATDs



After delivery, if Thyroid-stimulating Immunoglobulin (TSI) in the mother is positive at 34 weeks, neonatal hyperthyroidism ensues - until 6- months Post partum- We should c/o Methimazole and beta blockers post delivery[6]

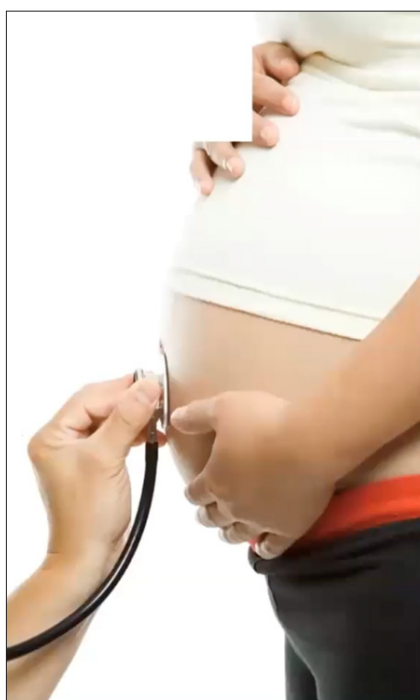
Monitoring for Fatal Thyroid Disease in Pregnants with Graves'

Check Antibodies

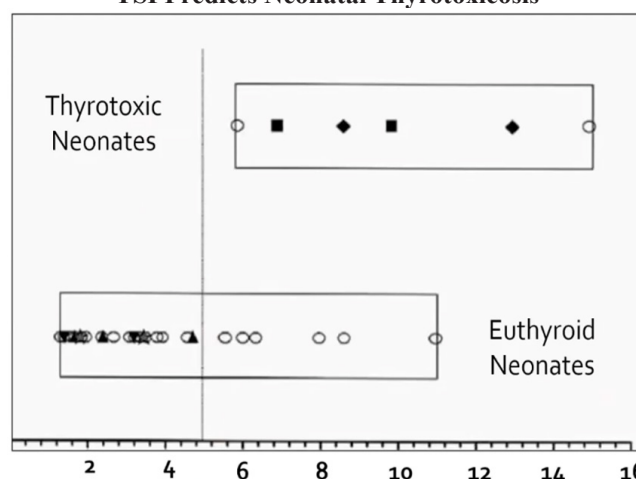
- 18-22 weeks in women s/p RAI or surgery
- 24-28 weeks in active Graves' on ATDs

Monitor (if active or +Abs >3x upper limit)

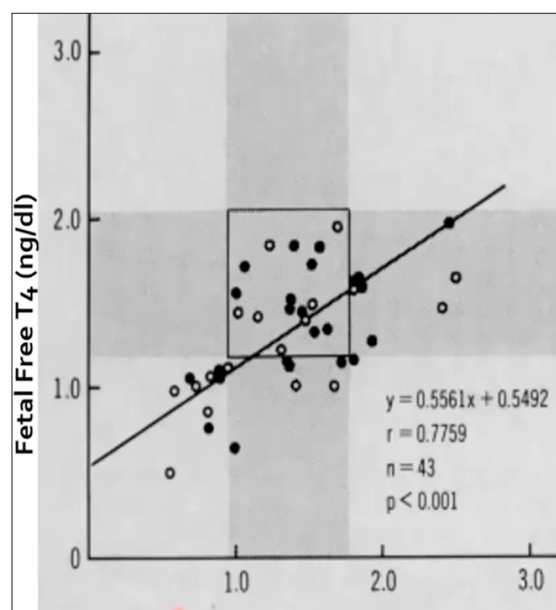
- Fetal heart rate
- Fetal growth
- Fetal thyroid



TSI Predicts Neonatal Thyrotoxicosis



TSI above 3 times nl- predicts fetal/postpartum hyperthyroid in fetus. Usually, TSI decreases with pregnancy but increases postpartum [6,7,8]



Anti Thyroid Drugs and Fetal Thyroid Function:
Maintain maternal free T4 in the upper normal or slightly high range.

Signs/Symptoms of Fetal Thyroid Disease

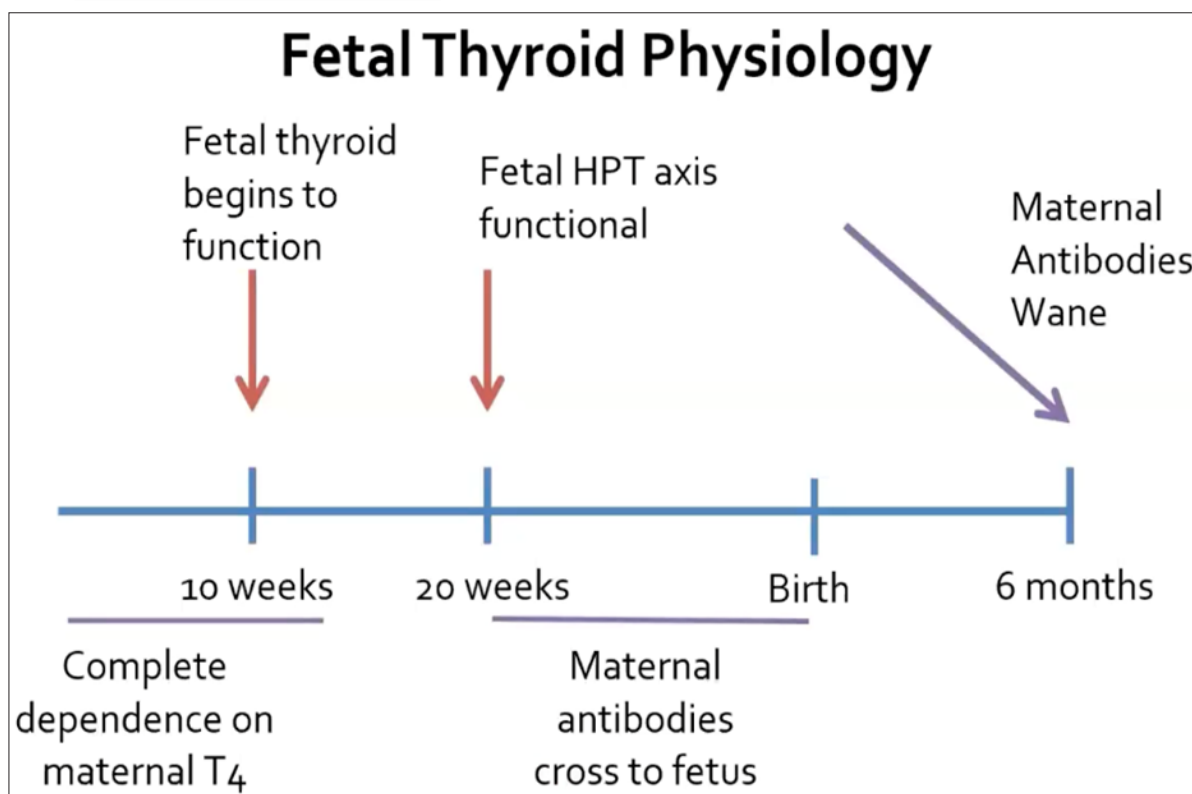
Hyperthyroidism

- Goiter
- Fetal Tachycardia
- Growth Restriction
- Hydrops
- Advanced Bone Age

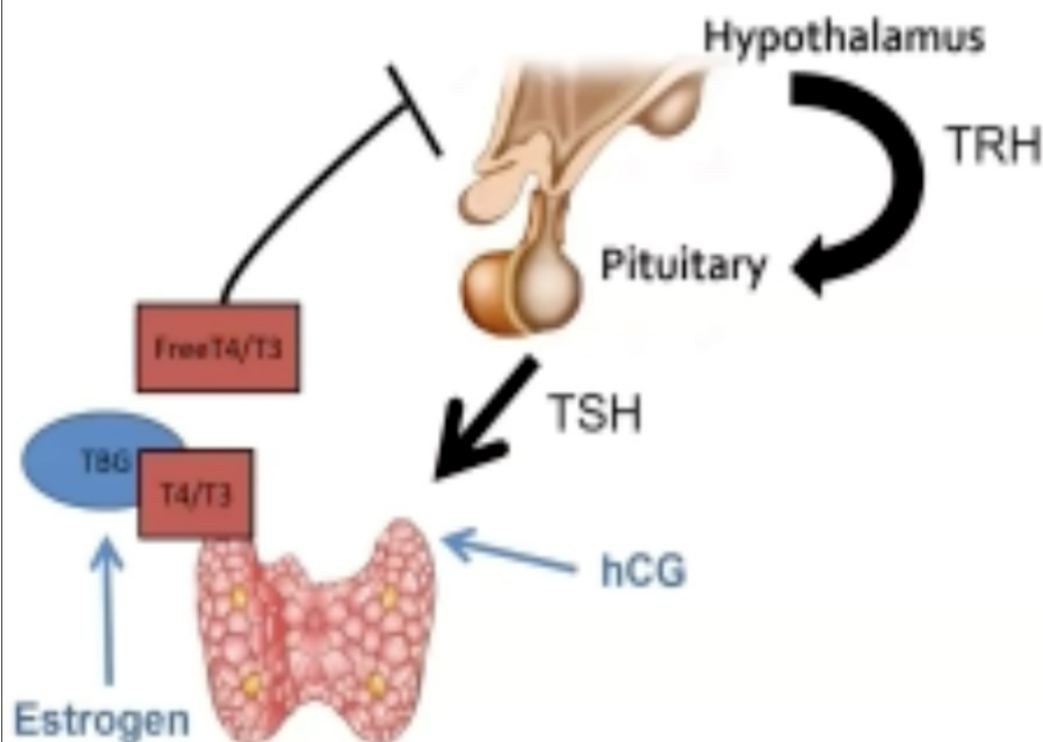


Hypothyroidism

- Goiter
- Delayed bone age
- Impaired neurologic development



Thyroid Axis in Pregnancy



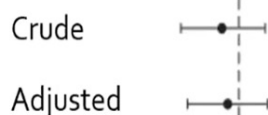
MMI/CMZ



PTU



No ATD



Reference

OR 1.0 associated with malformation, so we don't get a free pass with PTU. The malformations associated with PTU tend to be

PTU Also Associated with Malformations

Head & Neck

- preauricular and branchial sinus, fistula, cysts

Urinary

- kidney cyst
- hydronephrosis

Results of the Nazarpour Trials

levothyroxine reduced the risk of preterm delivery if TSH > 4, regardless of TPO+

	LT4: N(%)	No Rx: N (%)	P
<u>TPO+, TSH <10</u>	56	58	
Preterm Delivery	4 (7.1%)	14 (23.7%)	0.02
<u>TPO+, TSH ≥4, <10</u>	38	34	
Preterm Delivery	2 (5.3%)	10 (29.4%)	0.01
<u>TPO+, TSH <4</u>	18	24	
Nazarpour et al. EJE 2017 Preterm Delivery	2 (11.1%)	4 (16.7%)	0.69
<u>TPO-, TSH ≥ 2.5, <10</u>	183	183	
Preterm delivery	9.8%	11.5%	0.61
<u>TPO-, TSH ≥4, <10</u>	--	--	
Nazarpour et al. JCEM 2018 Preterm delivery	7.3%	12%	0.04

When they looked at, again, a subgroup analysis, take with a grain of salt and divided those individuals according to whether they had a TSH

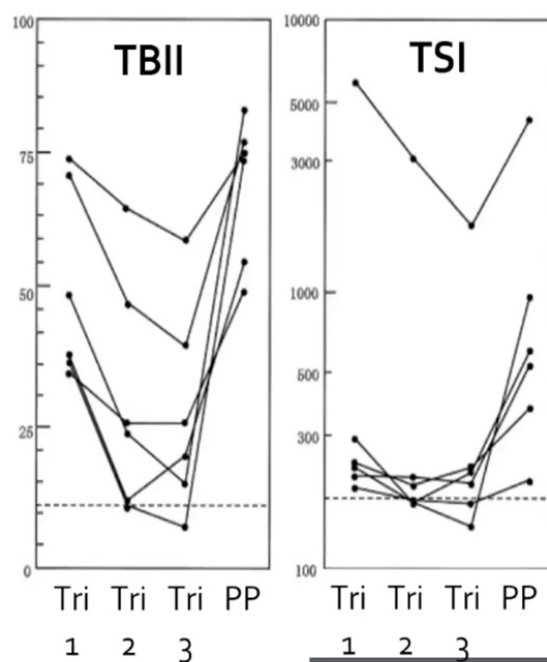
Also, the Intelligence quotient(IQ) if TSH above 10 lower of the fetus compared to no TSH[9]

Indications for TSH Receptor Antibody Assessment in Pregnancy

1. To determine cause of hyperthyroidism at diagnosis
2. In early pregnancy (1st trimester, repeat 18-22 wks if ↑)
3. To determine the risk of fetal hyperthyroidism in definitively treated maternal Graves' (s/p RAI or Surgery) With an intact gland, maternal thyroid function is the best indicator
4. To assess for Graves' remission when considering cessation of anti-thyroid drugs Opportunity to avoid risks of teratogenesis and fetal hypothyroidism!
5. In late pregnancy (30-34 weeks)

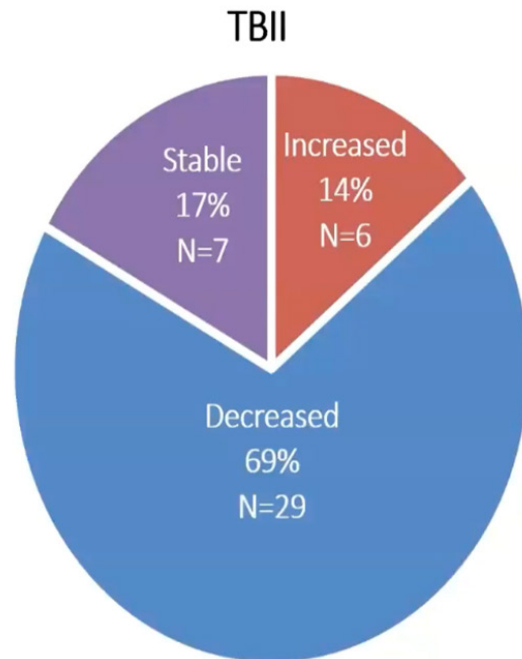
To assess risk of neonatal hyperthyroidism in maternal Graves' treated with anti-thyroid drugs Unlikely to increase if low in early pregnancy. And finally, in late pregnancy, we may test these antibodies to assess the risk apte
Lof neonatal hyper

Course of TSH Receptor Antibodies in Pregnancy



Amino et al JCEM 2003

One important thing to know is that over the course of pregnancy, TSH receptor antibodies

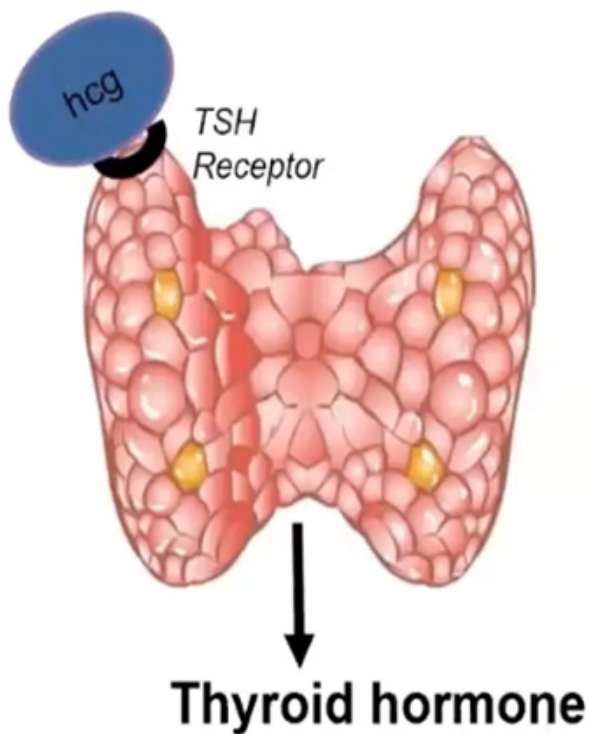


hCG-mediated hyperthyroidism

- Syndromes Described:
- Transient Gestational Hyperthyroidism
- Hyperemesis Gravidarum
- Trophoblastic Hyperthyroidism

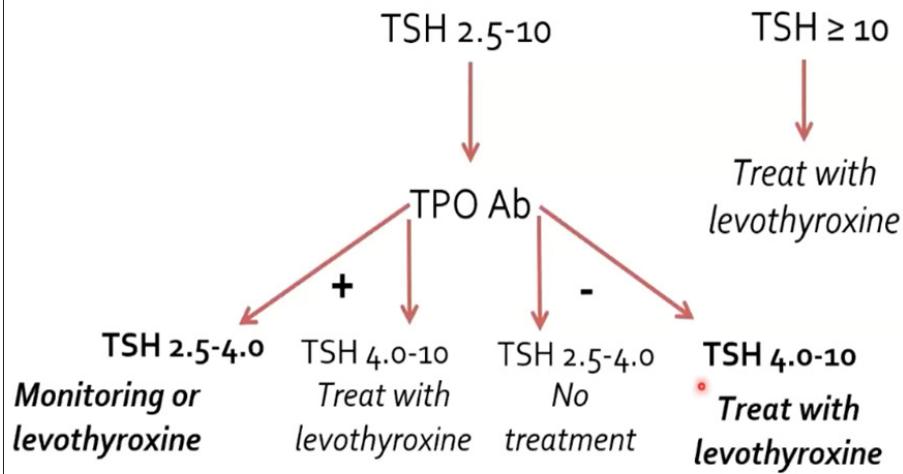
Evaluation of Hyperthyroidism in Pregnancy

Low TSH; High/Normal FT4, T4, T3



Differential Diagnosis / Use of Ultrasound	
hCG-mediated	No well-defined characteristics on u/s
Toxic nodule(s)	Rare in pregnancy, nodule(s) on u/s
Thyroiditis	Rare in pregnancy, common postpartum, decreased vascularity on u/s
Antibody-negative Graves'	Minimal fetal risk, but postpartum implications

Modified approach to hypothyroidism in pregnancy



Modified from [source] However, when the TSH is less than four, I really do rely on the TPO to help me decide what UpToDate

Most Experts Recommend if TPO Antibody is Positive and TSH is Above or Equal To 2.5, To Treat with Levothyroxine During or Before The Pregnancy

Anti Thyroid Peroxidase (TPO) Antibodies

Associated with

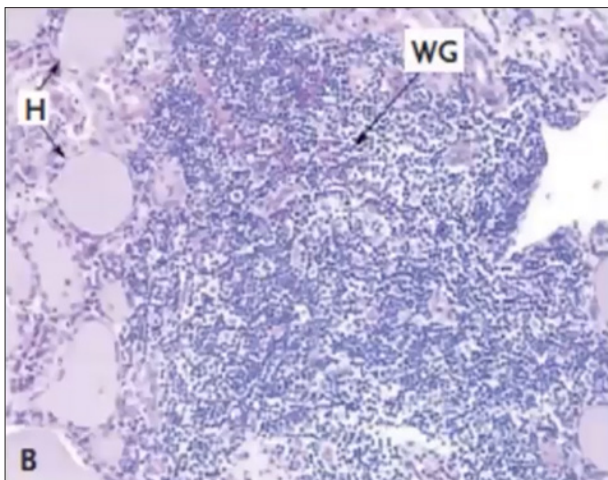
- pregnancy loss
- preterm birth
- childhood neurocognitive outcomes
- (IQ, ADHD)
- postpartum thyroiditis

Subclinical Maternal Hypothyroidism

- Pregnancy Loss?
- Preterm Birth?
- Low Birth Weight?
- Hypertensive Disorders of Pregnancy?
- Childhood Neurocognitive Outcomes (e.g. IQ)?

Overt Maternal Hypothyroidism

- Pregnancy Loss
- Preterm Birth
- Low Birth Weight
- Hypertensive Disorders of Pregnancy
- Childhood Neurocognitive Outcomes (e.g. IQ)



Thyroid Lab Values in Pregnancy*

<u>TEST</u>	<u>NORMAL RANGE</u> (if no pregnancy laboratory-specific range available)			<u>NOTE</u>
	1 st Trimester	2 nd Trimester	3 rd Trimester	
TSH	0.1-4.0 uIU/ml	Slow increase toward non-pregnant range (0.4-5.0 uIU/ml)		hCG effect
Free T4	~Non-pregnant reference range (0.9-1.8 ng/dl)			Unreliable*
Total T4	Gradual increase 7-16 wks → 1.5x non-pregnant			TBG effect
Total T3	Gradual increase 7-16 wks → 1.5x non-pregnant			TBG effect

*based on These levels actually slowly increase towards the non-pregnant reference range and the primary

*based on these levels actually slowly increase towards the non-pregnant reference range and the primary

Key Points: Thyroid Disease and Pregnancy

- In normal pregnancy, thyroid hormone requirements increase
- Treat subclinical hypothyroidism with TSH > 4.0 regardless of TPO; consider treating TSH 2.6 to 4.0 with +TPO
- Use TSH receptor antibodies to distinguish Graves' disease from hCG-mediated hyperthyroidism (usually self-limited)
- Both methimazole and PTU (1st trimester exposure) are associated with congenital malformations
- When treating overt hyperthyroidism in pregnancy, maintain mild maternal hyperthyroidism to avoid fetal hypothyroidism
- Monitor for fetal/neonatal Graves' when maternal TSH receptor antibodies are >3x the upper limit of normal

References

1. Glinioer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. *Endocr Rev.* 1997 Jun;18(3):404-33
2. Moleti M, Di Mauro M, Sturniolo G, Russo M, Vermiglio F. Hyperthyroidism in the pregnant woman: Maternal and fetal aspects. *J Clin Transl Endocrinol.* 2019 Jun;16:100190.
3. King JR, Lachica R, Lee RH, Montoro M, Mestman J. Diagnosis and Management of Hyperthyroidism in Pregnancy: A Review. *Obstet Gynecol Surv.* 2016 Nov;71(11):675-685.
4. Sharma A, Stan MN. Thyrotoxicosis: Diagnosis and Management. *Mayo Clin Proc.* 2019 Jun;94(6):1048-1064.
5. Shekhda KM, Zlatkin V, Khoo B, Armeni E. Thyrotoxicosis due to Gestational Trophoblastic Disease: Unmet Needs in the Management of Gestational Thyrotoxicosis. *Case Rep Endocrinol.* 2024;2024:5318871
6. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, Grobman WA, Laurberg P, Lazarus JH, Mandel SJ, Peeters RP, Sullivan S. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid.* 2017 Mar;27(3):315-389.
7. Thorpe-Beeston J G, Nicolaides K H, Felton C V, Butler J, McGregor A M. Maturation of the secretion of thyroid hormone and thyroid-stimulating hormone in the fetus. *N Engl J Med.* 1991;324(08):532-536. DOI: 10.1056/NEJM199102213240805
8. Pregnancy-associated changes in the thyroid-stimulating antibody of Graves' disease and the relationship to neonatal hyperthyroidism. *J Clin Endocrinol Metab.* 1983;57(05):1036-1040. DOI: 10.1210/jcem-57-5-1036.
9. Ahmed RG. Hypothyroidism and brain developmental players. *Thyroid research.* 2015;8:2. DOI: 10.1186/s13044-015-0013-7.

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