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MEDICINE &  
BIOLOGICAL  
SCIENCES

## “34 Year Old Pregnant Woman with Hyperthyroidism and Hyperemesis”

Dr. Darji does not have any relevant  
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ENDORAMA:  
34 Year Old Pregnant Woman with  
Hyperthyroidism and Hyperemesis

Monika Darji

September 27, 2018

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# Objectives

- Review the differential diagnosis and evaluation of hyperthyroidism in pregnancy
- Discuss the role of hCG in transient hyperthyroidism of hyperemesis gravidarum
- Discuss familial gestational hyperthyroidism

# Chief Complaint

34 year old G6P2032 pregnant woman at 8 weeks gestation presents with persistent nausea and vomiting

# HPI

- Patient reports worsening nausea and vomiting and inability to tolerate PO for 2 days
- Denies any triggers or new foods
- Has been having issues with N/V for last 3 weeks leading to 2 hospital admissions and 2 ER visits
- Reports 7 lbs weight loss in the last few weeks

# OB/GYN History

- G6P2032
  - 1<sup>st</sup> pregnancy in 2003 -> NSVD
  - 2<sup>nd</sup> pregnancy in 2012 -> c/b hyperemesis gravidarum, pregnancy terminated
  - 3<sup>rd</sup> pregnancy in 2013 -> NSVD
  - 4<sup>th</sup> pregnancy in 2015 c/b hyperemesis gravidarum and labs c/w hyperthyroidism, pregnancy terminated
  - 5<sup>th</sup> pregnancy in 2016 c/b hyperemesis gravidarum, pregnancy terminated
  - 6<sup>th</sup> pregnancy → current
-

# Additional history

- ROS: 7lb weight loss, palpitations, heat intolerance
  - Denies tremors, diaphoresis, diarrhea, muscle weakness, eye symptoms
- Past Medical History: asthma
- Past Surgical History: none
- Family History: thyroid disease in maternal grandmother
- Social History: married with 2 kids, works as patient care tech, denies smoking, alcohol, illicit drugs

# Additional history

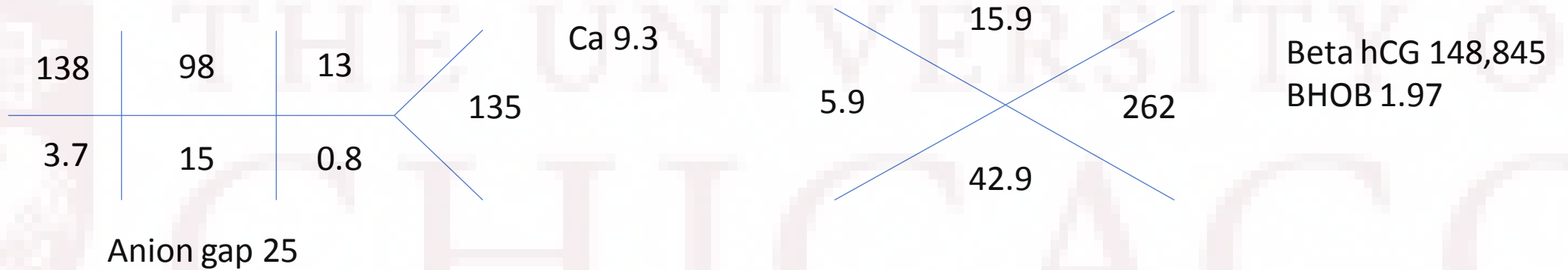
- Meds: albuterol
  - Discharged with Zofran, Compazine, Benadryl, B6, Pepcid after recent hospital stay for hyperemesis
- Allergies: Penicillin, shellfish and iodide containing products



# Physical Exam

- Vitals: 61 kg, BMI 24, Temp 98.6, HR 85, RR 18, BP 123/73, SpO2 100%
- Constitutional: no acute distress
- HEENT: EOMI, no exophthalmos, no lid lag
- Neck: supple, no thyromegaly or thyroid nodules
- Cardiovascular: regular rate and rhythm
- Pulmonary/Chest: good respiratory effort, clear to auscultation bilaterally
- Abdomen: soft, non-tender, nondistended
- Extremities: no edema
- Neurological: alert, oriented, 5/5 muscle strength in all four extremities, no tremor
- Skin: warm, dry
- Psychiatric: not agitated

# Admission Labs



Total protein 8.4      Alkaline phosphatase 42  
 Albumin 4.7            ALT 34  
 Total bilirubin 0.6     AST 29

TSH 0.01 (L)            Ref: 0.3-4.0  
 Free T4 2.3 (H)        Ref: 0.9-1.7  
 Total T4 16.5 (H)      Ref: 5-11.6  
 Free triiodothyronine 364   Ref: 230-420  
 Total triiodothyronine 149   Ref: 80-195

# Previous Labs

- Patient was admitted in 2015 during her 4<sup>th</sup> pregnancy for hyperemesis gravidarum and was found to have hyperthyroidism

TSH <0.01 (L)

Free T4 2.85 (H)

Total thyroxine 17.5 (H)

Total triiodothyronine 180

Ref: 0.3-4.0

Ref: 0.9-1.7

Ref: 5-11.6

Ref: 80-195

TSI negative

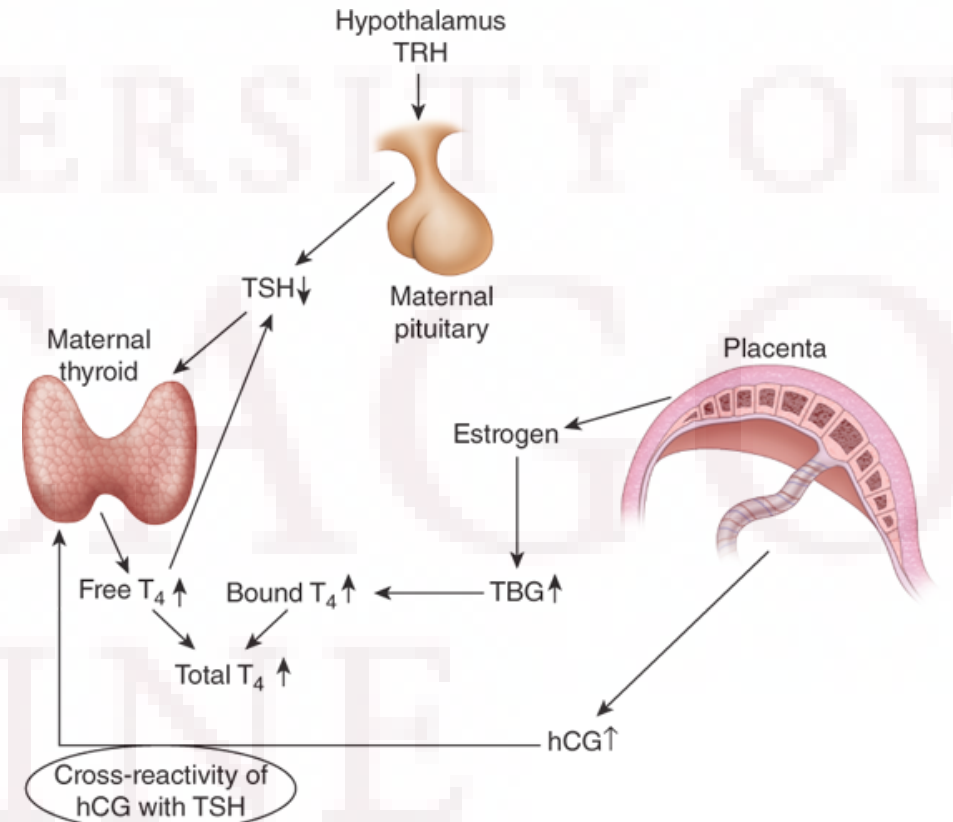
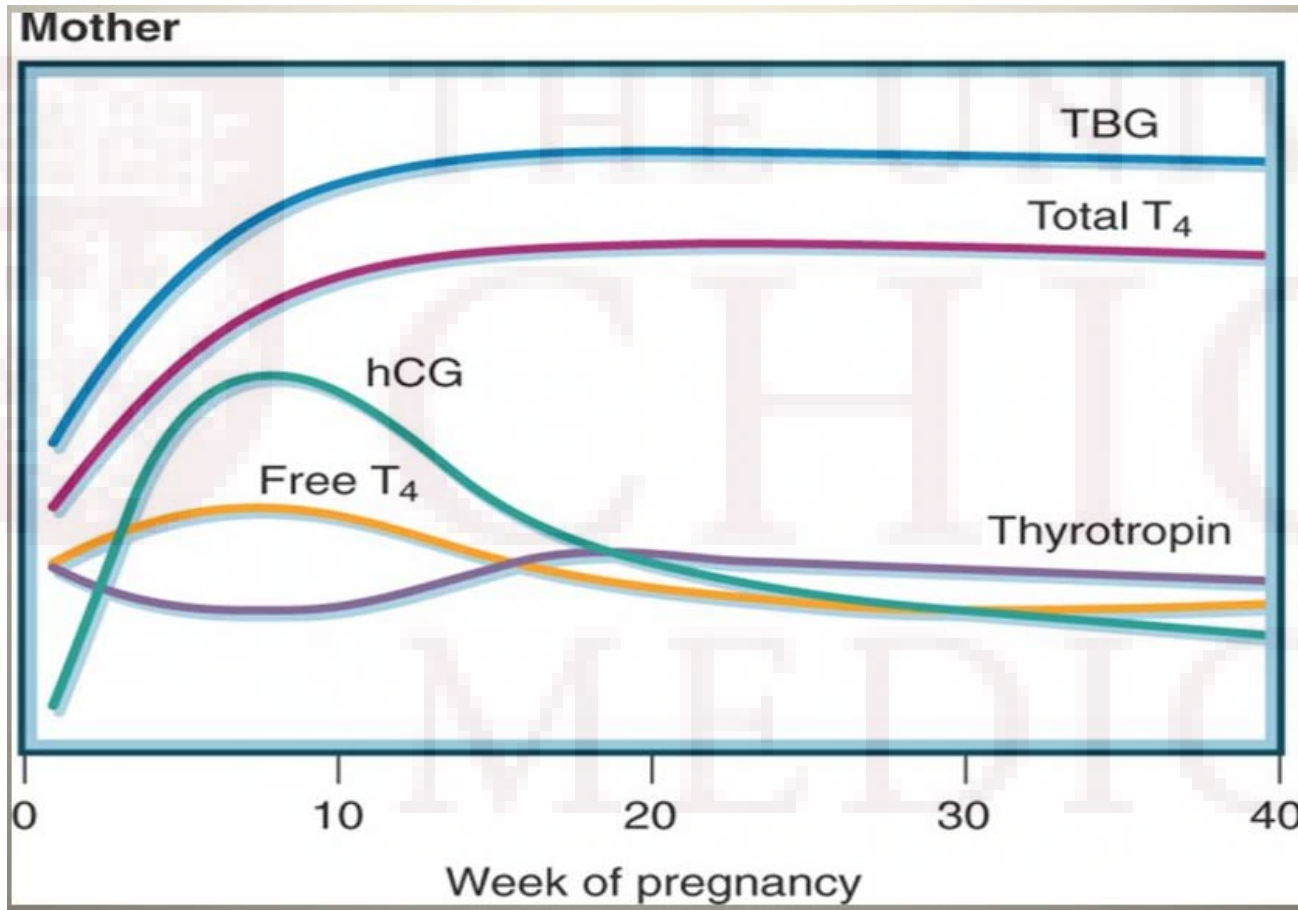
TPO antibody <0.4

Thyroglobulin antibody <0.4

# Additional history

- Patient followed up with Endocrinology in 2017 (between 5<sup>th</sup> and 6<sup>th</sup> pregnancy)
  - Asymptomatic
  - Labs showed:
    - TSH 1.04                      Ref: 0.3-4.0
    - Free T4 1.49                      Ref: 0.9-1.7
    - Triiodothyronine 112      Ref: 80-195

# Thyroid physiology in pregnancy



Source: Robert K. Silverman: Obesity Medicine: Management of Obesity in Women's Health Care [www.obgyn.mhmedical.com](http://www.obgyn.mhmedical.com)  
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# Pregnancy complications of maternal hyperthyroidism

- Fetal growth restriction
- Low birth weight
- Premature labor
- Spontaneous abortion
- Still birth
- Preeclampsia

# Diagnosis of clinical hyperthyroidism

- Clinical manifestations and lab findings
  - Suppressed TSH  $<0.01$  and free T4 and/or free T3 level or total T4 and/or total T3 exceeding the trimester specific normal range

# Etiologies

- Graves' disease
- hCG mediated hyperthyroidism
  - Gestational transient thyrotoxicosis
  - Hyperemesis gravidarum
  - Trophoblastic hyperthyroidism
  - Familial gestational hyperthyroidism
- Multinodular goiter
- Thyroiditis



# Graves' Disease – classic findings

- Presents with typical symptoms of hyperthyroidism – tachycardia, palpitations, tremors, diaphoresis, muscle weakness, weight loss, diarrhea
- Diffuse goiter
- Orbitopathy
- Presence of thyroid stimulating antibodies
- 0.1 to 1% of all pregnancies

# Hyperemesis Gravidarum

- Nausea and vomiting in early pregnancy associated with 5% weight loss
- 0.1 to 0.2% of pregnancies
- Associated with higher serum hCG and estradiol concentrations than in normal pregnant women -> transient hyperthyroidism
  - Usually does not require treatment
  - Subsides as hCG production falls

# Role of hCG

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## **The Role of Chorionic Gonadotropin in Transient Hyperthyroidism of Hyperemesis Gravidarum\***

THOMAS M. GOODWIN, MARTIN MONTORO, JORGE H. MESTMAN,  
A. EUGENE PEKARY, AND JEROME M. HERSHMAN

*Departments of Obstetrics and Gynecology and Medicine, University of Southern California (T.M.G., M.M., J.H.M.), Los Angeles, California 90033; and Department of Medicine, West Los Angeles VA Medical Center (A.E.P., J.M.H.), University of California at Los Angeles School of Medicine, Los Angeles, California 90073*

# Goodwin et al.

- Investigated the role of hCG as a casual factor for hyperthyroidism in hyperemesis patients
- 2 groups – hyperemesis group and control group, controls matched for gestational age
- Findings:
  - Hyperemesis patients differed from controls in terms of hCG, TSH, free T4
  - Significant correlation between hCG concentration and degree of thyroid stimulation

# Goodwin et al.

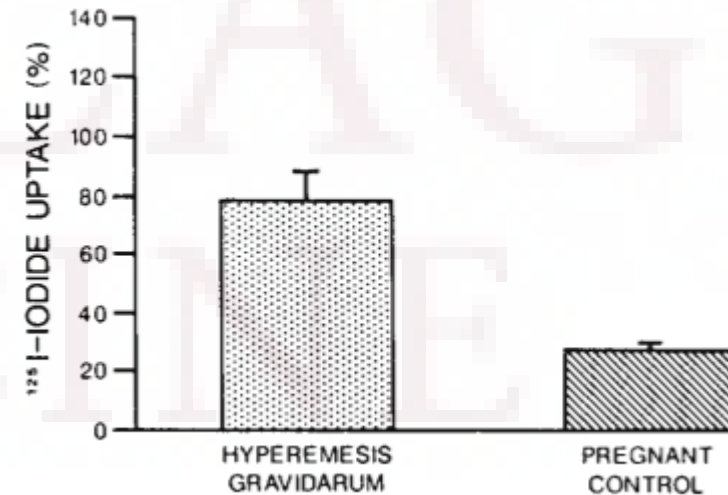
**TABLE 1.** Abnormal thyroid tests in 57 women with hyperemesis gravidarum

	n	%
TSH (mU/L)		
Undetectable <sup>a</sup>	17	30
Suppressed <sup>a</sup>	34	60
Free T <sub>4</sub> > 23.2 nmol/L	26	46
Total T <sub>3</sub> > 2.69 nmol/L	25	44
Free T <sub>4</sub> index > 13.2	33	58
Free T <sub>3</sub> index > 225	6/51	12
TSH < 0.4 or Free T <sub>4</sub> > 23.2 or Free T <sub>4</sub> index > 13.2	41	70

<sup>a</sup> Undetectable < 0.04; suppressed < 0.4.

**TABLE 2.** hCG and thyroid function in hyperemesis and controls, mean ± SE

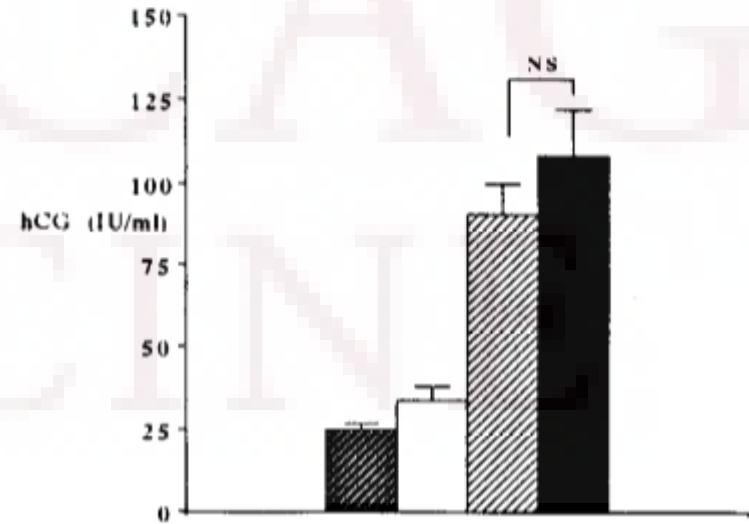
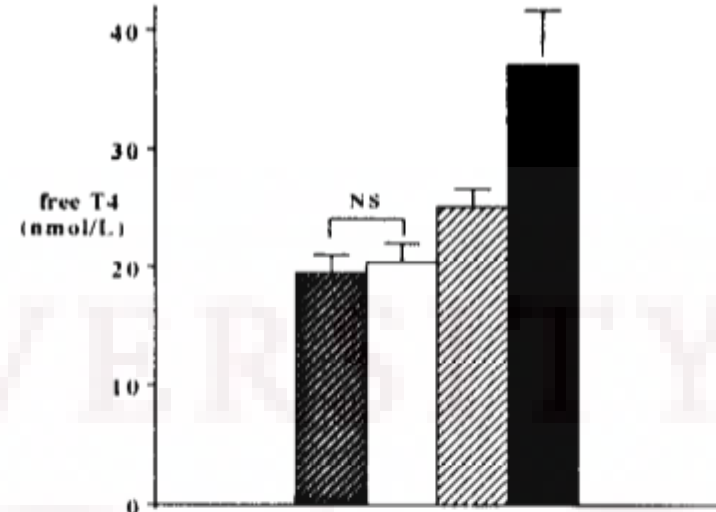
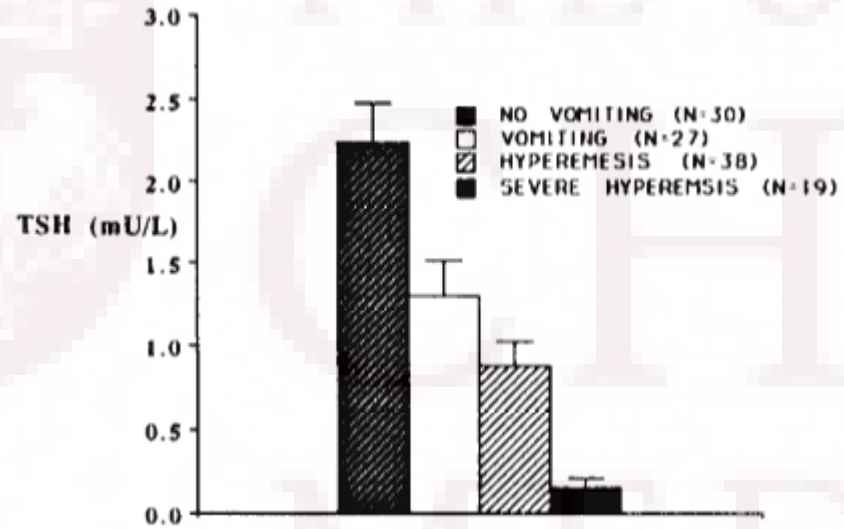
	Hyperemesis (n = 57)	Controls (n = 57)	P
hCG (IU/ml)	97 ± 8	29 ± 2	0.001
TSH (mU/L)	0.63 ± 0.10	1.79 ± 0.18	0.001
Free T <sub>4</sub> (nmol/L)	29.18 ± 1.82	20.10 ± 1.04	0.001
Total T <sub>3</sub> (nmol/L)	3.40 ± 0.31	2.29 ± 0.11	0.01
Estradiol (pmol/L)	13,256 ± 1,145	9,625 ± 679	0.04
PRL (μg/L)	180.5 ± 13.6	65.1 ± 6.4	0.001



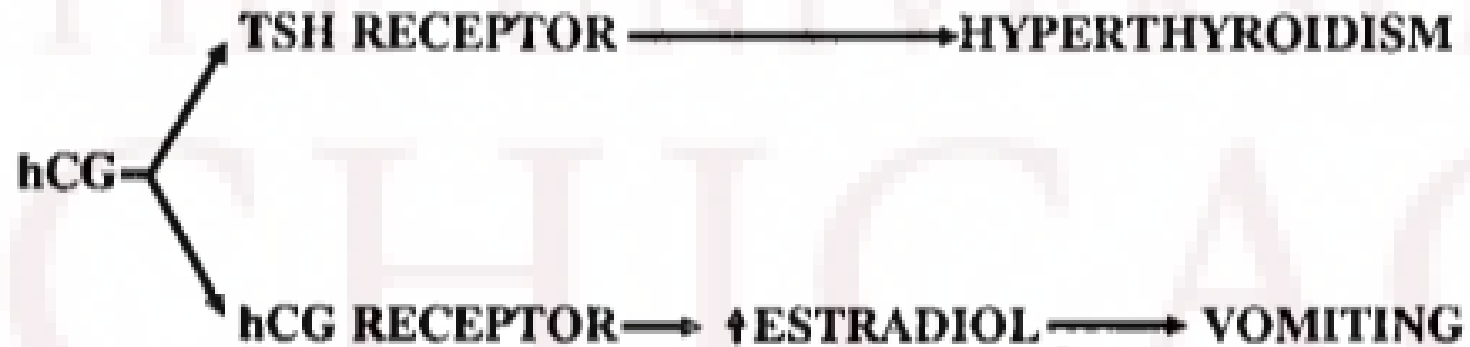
# Goodwin et al.

- The degree of thyroid stimulation and concentration of hCG varied directly with severity of hyperemesis
- More severe hyperemesis was associated with a greater degree of thyroid stimulation and higher concentration of hCG

# Goodwin et al.



# Goodwin et al.



- Estradiol found to be present in higher concentrations in hyperemesis patients
- May be related to the effect of hCG on steroidogenesis
- Hyperthyroidism -> increased SHBG -> increased estradiol



# Tan et al.

**BJOG: an International Journal of Obstetrics and Gynaecology**  
June 2002, Vol. 109, pp. 683–688

## **Transient hyperthyroidism of hyperemesis gravidarum**

**Jackie Y.L. Tan<sup>a,\*</sup>, Keh Chuan Loh<sup>b</sup>, George S.H. Yeo<sup>c</sup>, Yam Cheng Chee<sup>a</sup>**

**Objective** To characterise the clinical, biochemical and thyroid antibody profile in women with transient hyperthyroidism of hyperemesis gravidarum.

**Design** Prospective observational study.

**Setting** Hospital inpatient gynaecological ward.

**Population** Women admitted with hyperemesis gravidarum and found to have hyperthyroidism.

**Methods** Fifty-three women were admitted with hyperemesis gravidarum and were found to have hyperthyroidism. Each woman was examined for clinical signs of thyroid disease and underwent investigations including urea, creatinine, electrolytes, liver function test, thyroid antibody profile and serial thyroid function test until normalisation.

**Main outcome measures** Gestation at which thyroid function normalised, clinical and thyroid antibody

# Tan et al.

- Prospective observational study
- 53 women with hyperemesis gravidarum who were found to have hyperthyroidism
  - 9 were lost to follow up
  - 39 were diagnosed with transient hyperthyroidism of hyperemesis gravidarum
  - 5 were diagnosed with Graves' disease

# Tan et al. findings

- Clinically overt hyperthyroidism usually absent
- Thyroid antibodies usually negative
- Thyroid function normalizes by middle of second trimester without anti-thyroid treatment
  - Free T4 normalized by 15 weeks of gestation
  - TSH remained suppressed until 19 weeks of gestation

# Tan et al.

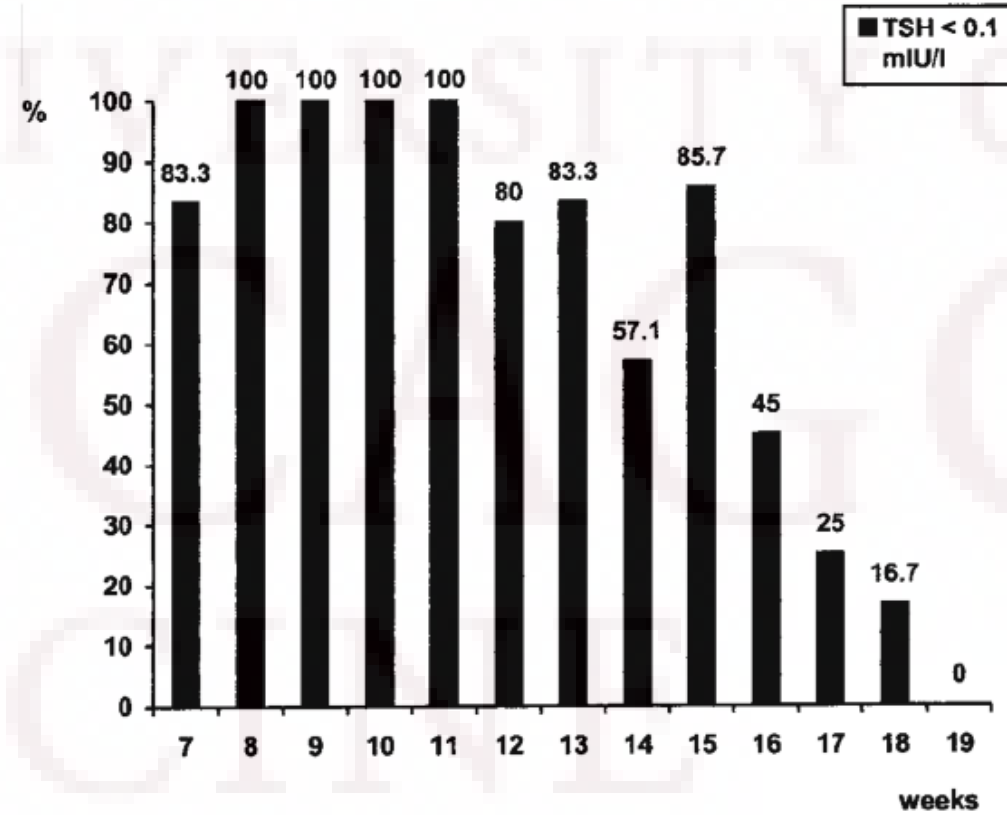
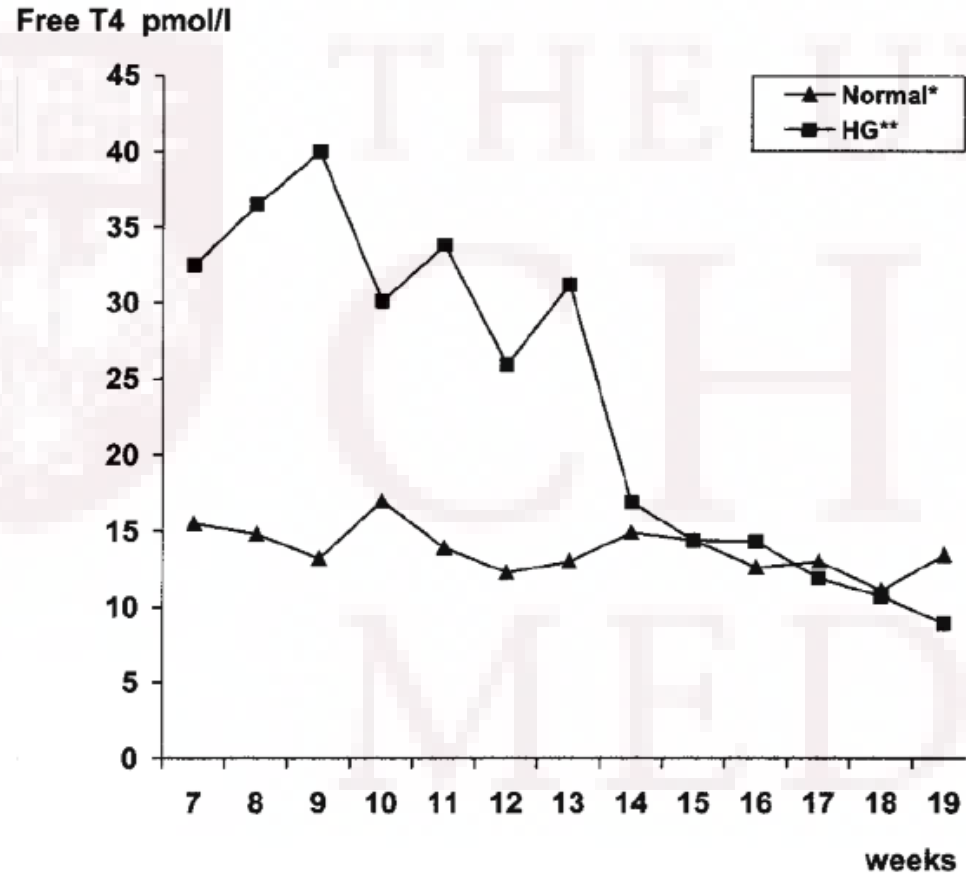


Fig. 2. Percentage of TSH < 0.1 mIU/L by gestation.

# Hyperemesis vs Graves'

- Severe vomiting with weight loss
  - Absence of goiter and ophthalmopathy
  - Absence of common signs and symptoms of hyperthyroidism like tachycardia, muscle weakness, tremor
  - Free T4 usually only mildly elevated and serum T3 usually not elevated
  - Absence of thyroid antibodies
  - Resolves by second trimester. Graves' disease can occasionally resolve during pregnancy
-

# Familial gestational hyperthyroidism

- Few case reports describing recurrent gestational hyperthyroidism  
2/2 mutant TSH receptor

Brief Report

FAMILIAL GESTATIONAL  
HYPERTHYROIDISM CAUSED BY A  
MUTANT THYROTROPIN RECEPTOR  
HYPERSENSITIVE TO HUMAN  
CHORIONIC GONADOTROPIN

PATRICE RODIEN, M.D., PH.D., CATHERINE BRÉMONT, M.D.,  
MARIE-LAURE RAFFIN SANSON, M.D.,  
JASMINE PARMA, PH.D., JACQUELINE VAN SANDE, PH.D.,  
SABINE COSTAGLIOLA, PH.D., JEAN-PIERRE LUTON, M.D.,  
GILBERT VASSART, M.D., PH.D.,  
AND LAURENCE DUPREZ, M.D., PH.D.

Clin Thyroidol 2016;28:9-10.

Clinical  
THYROIDOLOGY®

## Severe Gestational Hyperthyroidism Can Be Due to a Mutant TSH Receptor with Enhanced Sensitivity to HCG

Jerome M. Hershman

Coulon AL, Savagner F, Briet C, Vernin M, Munier M, Chabre O, Rodien P. Prolonged and severe gestational thyrotoxicosis due to enhanced hCG sensitivity of a mutant thyrotropin receptor. J Clin Endocrinol Metab. November 18, 2015;jc20153670 [Epub ahead of print].

# Familial gestational hyperthyroidism

- Rodien et al. case describes a patient with hyperemesis and signs and symptoms of hyperthyroidism
  - Recurrent gestational hyperthyroidism and hyperemesis
  - Normal hCG level for pregnancy
- Missense mutation in the extracellular domain of TSH receptor
  - Lysine replaced by arginine at position 183
  - Results in hypersensitivity of the TSH receptor to hCG despite normal hCG levels for pregnancy

# Familial gestational hyperthyroidism

- Hershman et al. similarly described a case with gestational hyperthyroidism and hyperemesis
  - Patient required treatment with antithyroid drugs
  - Hyperthyroidism persisted throughout pregnancy



# Back to our patient

- Patient was admitted for hyperemesis and started on antiemetics
  - Given IV fluids and electrolytes replaced
  - Zofran, Compazine, Tigan, Benadryl, B6, Pepcid
  - Started on methylprednisolone 16 mg q8h given minimal improvement in nausea on above regimen
- On day 3 of hospital stay, patient decided to terminate the pregnancy given severe hyperemesis, multiple admissions for hyperemesis, and other social issues

# Back to our patient

- Pt was not started on any antithyroid medications as hyperthyroidism was thought to be transient
- Considered TSH receptor mutation testing but patient deferred
- 7/23/18 – pt had surgical abortion
- No-showed to Endocrinology follow up appointment

# Conclusion

- Transient hyperthyroidism of hyperemesis gravidarum is usually mild, does not require treatment, and subsides by second trimester
- Hyperemesis is associated with higher levels of hCG which correlates with degree of thyroid stimulation
- Graves' disease can be distinguished from transient hyperthyroidism by presence of goiter, orbitopathy, thyroid antibodies, absence of severe vomiting

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