

## Hyperthyroidism and Hypothyroidism: I Heat Up, I Cool Down

David Schneider, MD, FAAFP



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## David Schneider, MD, FAAFP

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Dr. Schneider cares for the underserved in Santa Rosa, CA, serving Latino, Southeast Asian, and Eritrean populations. His professional interests include the doctor-patient relationship, clinical skills, and teaching the breadth and depth of family medicine for over 20 years. Cardiovascular system conditions are one of his specialty topics, and he points to "the growing body of evidence suggesting that lifestyle is as effective as, or more effective than, pharmacologic interventions in primary prevention." He also focuses on conditions of the endocrine system (especially thyroid), skin and dermatology, primary prevention focusing on lifestyle, and procedures. Dr Schneider is board certified not only in Family Medicine, but also in Integrative Holistic Medicine. He produces Dr. Dave's To Your Health segments for Wine Country Radio and BlogTalkRadio.com.



## Learning Objectives

1. Develop a screening protocol to identify patients with risk factors for developing hypo/hyper-thyroidism, particularly pregnant patients or those planning to become pregnant.
2. Order appropriate laboratory tests to diagnose hypo/hyper-thyroidism based on symptomatology.
3. Prescribe appropriate therapy for patients with hypo/hyper-thyroidism symptomatology and monitor patients accordingly.
4. Recognize indications for referral and possible admission and coordinate care and follow-up as necessary.



## Audience Engagement System

The image shows three sequential screenshots of the Audience Engagement System app. Step 1 is the home screen with various icons for navigation. Step 2 shows a list of CME activities, with a red arrow pointing to a specific activity. Step 3 shows the details of that activity, including the title 'CME011 Acute Coronary Syndromes: Unchain My Heart' and a description.



## Fun Thyroid Facts

- ~20 million Americans have some form of thyroid dz.
  - Up to 12% will develop some form of thyroid disease during their lifetime.
  - Up to 60% with thyroid dz are unaware of their condition.
- Thyroid receives 2% of the cardiac output, although it is only ~0.03% of body mass.
- Thyroid hormones affect function of virtually every organ & tissue in the body.

<http://www.thyroid.org/about/presence.html>; <http://www.thyroidmanager.org/>

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## AES Question



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## AES Question 1

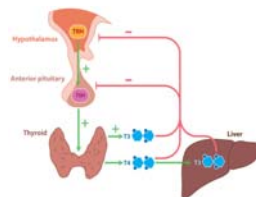
The 1<sup>st</sup> test(s) to order to diagnose thyroid disorders is/are:

- A. High sensitivity TSH
- B. TSH + Free T4
- C. TSH + Free T4 + Free T3
- D. TSH + thyroid antibodies
- E. T4 + T3 assays

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## Interpretation of TSH

- **High TSH → hypothyroid**
  - Pituitary thinks there's insufficient thyroid hormones, so it secretes more TSH.
- **Low TSH → hyperthyroid**
  - Pituitary thinks there is plenty of thyroid hormones, so it shuts down TSH production.
- There are rare exceptions.



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## Total T4 & T3

- **Total T4 (& to a lesser extent Total T3) assays are rarely clinically useful in & of themselves, and should generally only be ordered in conjunction with an estimate of free (vs bound) hormone.**
  - FT3 assays are less well validated → total T3 is often used.
  - Same is **NOT** true for T4 – use **FT4**.

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## Free Hormone Hypothesis

- **Only free hormone is available to be active in the body**, whereas hormone bound to proteins (TBG, transthyretin, albumin) is inactive.

<http://www.thyroidmanager.org/chapter/assay-of-thyroid-hormones-and-related-substances/>

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99.7 – 99.97% Protein-Bound



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## Thyroid Hormone Tests Summary

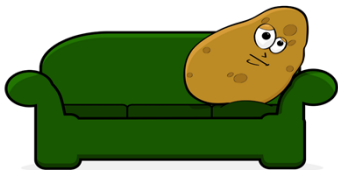
- **TSH is the single best thyroid test.**
- For most ambulatory patients, your lab's Free T4 & Free T3 assays (usually EIA or related assay) are good enough.
- In most clinical situations involving discordant FT4 and TSH results, the TSH usually provides the most reliable results.
  - Tune in later for exceptions.

<http://www.thyroidmanager.org/chapter/assay-of-thyroid-hormones-and-related-substances/>

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## General Rule of Thyroid Tests

**Do not interpret thyroid test results in a vacuum – you must look at the clinical**



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## Case 1

- A 42 y.o. woman presents to your clinic/office with fatigue.
- History reveals:
  - Depressive symptoms.
  - Anxiety symptoms.
  - Palpitations.
  - Normal appetite but ~ 10 lb wt loss over last 3 months—unintentional.
  - Diarrhea.

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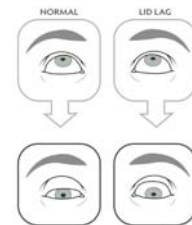
## 42 y.o. Woman w/Fatigue

- Physical exam:
  - BP 162/74, HR 104
  - 9 # wt loss since last visit 3 months ago.
  - No exophthalmos, but when she looks down you can see sclerae atop the irises.
  - Fine tremor.
  - Onycholysis of a few fingernails.

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## Lid Lag

- "...when she looks down you can see sclerae atop the irises."
- Normal: after looking up, look straight ahead → no white sclera visible above iris.
- Present in "nearly all" hyperthyroid pts.



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## Exophthalmos



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## Hyperthyroidism Diagnosis

- **TSH low.**
- Free T4 ↑.
  - FT4 may be WNL early in hyperthyroidism.
- Free T3 ↑ — may be ordered w/FT4.
  - **T3** assays: generally only in **hyper**thyroidism.
  - 5% of hyperthyroid pts have "T3 toxicosis," in which FT3 is elevated while FT4 is normal.
- If FT4 & FT3 **remain** normal while TSH **remains** suppressed, trust the TSH and follow, or refer.

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## Trust the TSH



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## AES Question



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## AES Question 2

Which of the following is FALSE about hyperthyroidism?

- A. It is more common in women.
- B. It is more common in smokers.
- C. It occurs in 1/250 individuals in the general population.
- D. Graves' dz is the most common cause in younger women.
- E. It can be treated surgically.

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## Epidemiology of Hyperthyroidism

- Women : men = 5:1.
- Overall prevalence = 1.3%.
  - 0.7% (>1/2) mild or asymptomatic.
- Prevalence in older women = 4 – 5%.
  - TMNG more common in older women.
  - Graves' more common in younger women.
- More common in smokers (OR = 2.37).

NIHANE5 01-CEM 2002;87(2):489-99;ArchivesMed 2007;167(13):1428-32

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## Signs & Symptoms of Hyperthyroidism

- Tremor
- HR increased (tachy)
- Yawning (fatigue)
- Restlessness (anxiety)
- Oligomenorrhea/amenorrhea
- Intolerance to heat
- Diarrhea
- Irritability/Insomnia
- Sweating
- Muscle wasting/wt loss

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## Signs & Symptoms of Hyperthyroidism—Short Mnemonic

- Sweating
- Tremor + Tachycardia
- Intol to heat + Irreg menses + Irritability
- Nervousness
- Goiter + GI sx (diarrhea)

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## Pretibial Myxedema



- Lumpy.
- ≤5% of Graves' pts, up to 15% of Graves' w/ophthalmopathy.
- Almost always assoc'd w/ophthalmopathy.
- May affect ankles, knees, elbows, upper back.

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Medicine (Baltimore) 1994;73(1):1-7; doi:10.1093/ajph/73.1.1. Copyright © 2008, 26-28:3-7

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## Causes of Hyperthyroidism

- Graves dz: 80% ICD-10=E05.00
  - Toxic multinodular goiter: 15% ICD-10=E05.20
  - Toxic adenoma = autonomously functioning nodule = hot nodule: 2%
  - Thyroiditis: 1%
  - Iodine load (CT, diet, amiodarone): <1%
  - Thyrotoxicosis factitia: <1%
  - Iatrogenic: variable
- Graves + TMNG = 95%.

<http://www.ncbi.nlm.nih.gov/books/br.fcgi?book=endocrin&part=A235>

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## What is the Cause of the Pt's Hyperthyroidism?

- **Radioiodine Uptake (RAIU)**
  - High uptake → increased hormone synthesis.
    - Medical treatment (antithyroid drugs) may help.
  - Low uptake → no increase in hormone synthesis in thyroid.
    - Inflammation & destruction of thyroid w/release of thyroid hormones.
      - Antithyroid meds unlikely to help.
    - Nonthyroidal source of hormone production.

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## DDx Hyperthyroid per RAIU

- **High or normal RAIU:**
  - Graves' dz.
  - Toxic multinodular goiter.
  - Toxic ("hot") nodule.
  - Hashitoxicosis.
  - TSH-secreting tumor (rare).
  - Germ cell tumor (mole, chorioCA, testicular germ cell).
  - Iodine (contrast, amiodarone)—post I.
- **Low RAIU:**
  - Thyroiditis.
    - Subacute granulomatous (de Quervain's—painful).
    - Subacute lymphocytic (painless = "Silent").
    - Amiodarone.
  - Exogenous—iatrogenic, factitious.
  - Struma ovarii.
  - Iodine (contrast, amiodarone)—still ingesting I.

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## Risk Factors For Graves' Dz

- Females : males = 7:1.
- Genetic – FH Graves' or other autoimmune disorders.
- Stressful life events – may lead to immune suppression followed by rebound.
- Smoking (OR = 2).
- Pregnancy/postpartum (30% of young women w/ Graves' had H/O preg w/in 12 months).

ChinEdomol(Div) 2001;55(1):15-9. ChinEdomol(Div) 1995;42(1):303-8. JAMA 1993;269(6):479-82. ArchIntMed 2005;165(14):1606-11. ActaEndocrinol(Copenh) 1987;116(3):213-5

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## The G's of Graves'

- Gender (F)
- Genes (FH)
- Gravidity
- Gravity of life (stress)
- Gaspers (cigarettes)

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## AES Question



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## AES Question 3

Routine acute management of hyperthyroidism includes:

- A. Urgent radioablation.
- B. Use of  $\beta$ -blockers to reduce symptoms.
- C. Use of  $\beta$ -blockers to reduce thyroid hyperfunction.
- D. B + C.
- E. All of the above.

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## Hyperthyroidism: Acute Management

- Beta blockers.
  - Symptomatic relief only—wean when pt improves.
  - **All equally effective.**  $\beta$ -1 selective if relative contraindication.
- Antithyroid drugs (thionamides).
  - **Inhibit formation** of thyroid hormones.
  - Goal: euthyroid within 8 weeks.
  - **Methimazole (MMI)** is the preferred drug.
    - $\downarrow$  side effects, **once daily** dose (usually).
    - 10 – 15 mg daily for **mild-mod**, vs 20 – 40 mg for more severe sx & signs (can **divide bid** to minimize side effects).

ChinEdomol(Div) 49:403-7. ChinEdomol(Div) 1986;63:129. JGIM 1993;70:1216-21. <http://www.ncbi.nlm.nih.gov/pubmed/15441266>

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## Antithyroid Drug Toxicity

- Most toxic rxns occur within 1<sup>st</sup> 3 months.
- **Hepatotoxicity** – rare but can be serious.
  - MMI  $\rightarrow$  cholestatic picture (usu reversible).
  - PTU  $\rightarrow$  **hepatocellular (may be irreversible)**.
    - PTU-related hepatotoxicity may occur days-yrns after starting med (idiosyncratic).
- **Agranulocytosis** – rare, but devastating.
  - Aplastic anemia may occur, and is rarer.
- Questionable value of routine monitoring.

JGIM 2000;16:580-2. JGIM 1995;10:1083-5. Thyroid 2000;10:673-6. AnnIntMed 2007;146(9):637-65. AnnInternMed 2002;137(4):248-54. AnnIntMed 1985;102(1):26-9. ChinEdomol(Div) 1989;66(1):121-30. Thyroid 2008;18(12):1648-6. AnnInternMed 1995;122(12):1214

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## Choice of Antithyroid Drug

- **First choice = MMI.**
- Only use PTU if:
  - 1<sup>st</sup> trimester pregnancy.
  - Life-threatening thyroid storm.
  - Adverse rxn to MMI, esp if not candidate for radioiodine ablation or surgery.
- Note: after 1<sup>st</sup> trimester, potential teratogenic risks of MMI < risk of PTU hepatotoxicity (ATA).

Thyroid 2011;21:1081;JGIM 2009;24:1881-2;Thyroid 2009;19:871-4

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## Antithyroid Drugs: Informed Consent

- **Do informed consent, or don't Rx ATD's.**
  - Risk of **liver** damage – rare but can be serious.
  - Risk of **immune** suppression – very rare, but can be devastating.
  - **Call** right away for any signs of infection, including fever, sore throat, etc; stop med til CBC results.
  - Periodic blood tests, although uncertain benefit and not routinely recommended.

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## Long-term Treatment of Hyperthyroidism

- Antithyroid drugs
- Radioiodine ablation
- Surgery

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## Antithyroid Drugs

- 12-18 months (up to 2 years).
  - Long-term remission rate 20 – 70+%.
  - Initially monitor TSH & FT4/FT3 q 4-6 weeks.
  - In early phase, TSH response is delayed.
  - When TSH rises to normal, follow **TSH** alone.
- Can be used for ≥10 years w/o loss of effect.
- TMNG does **not** go into remission w/ATD's.
  - ATD's may be used either as a bridge to definitive therapy, or as a long-term therapy.

NEJM 2005;352:919-27;JGIM 1999;14:101-6;AnnIntMed 1997;127:616-13;2;En-Endocrinol 2005;13(2):69-70;J Clin EndocrinolMetab 1987;66(3):124-5;Endocr Pract 2011;17:457-50;http://www.upstate.edu

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## Radioiodine Ablation

- Preferred method in US, less popular in Europe & Asia.
- Taken orally.
- Destruction of tissue in 6-18 weeks.
- ATD's in the week before, during, or after radioiodine treatment may reduce cure rate of RAI (PTU may be a worse offender).

J Clin Endocrinol Metab 2002;87(1):1073-7;Thyroid 1991;1:129-35;ClinEndocrinol (Oxf) 2008;68:814-20;http://www.upstate.edu/content/html/radioiodine-in-the-treatment-of-hyperthyroidism?source=search\_result&selectedTab=552571110402;BMJ 2007;334(7622):14

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## Radioiodine Ablation – 2

- Graves' Dz:
  - High-dose RAI curative in up to 90%, with 80% becoming permanently hypothyroid.
  - **May cause or worsen ophthalmopathy.**
- TMNG
  - Destroys primarily hyperfunctioning areas.
  - Some pts will remain euthyroid, though ↑ hypothyroidism w/time.

AnnIntMed 1984;101(4):488-90;NEJM 1994;330(24):1731-6;ClinEndocrinol (Oxf) 2005;62(3):310-5;Clin Endocrinol (Oxf) 2012 Feb;76:297-303;http://www.upstate.edu/content/html/radioiodine-in-the-treatment-of-hyperthyroidism?source=search\_result&selectedTab=552571110402

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## Surgery for Hyperthyroidism

- Subtotal thyroidectomy preferred.
  - 25% ↓ incidence of hypothyroidism vs total.
  - Somewhat ↑ recurrence of hyperthyroidism.
  - Total thyroidectomy may be indicated w/severe disease or large goiter.
- May be preferred if **Graves' ophthalmopathy**.
- Near-total thyroidectomy in TMNG.

Thyroid 2011;23(6):593-601;APP 2005;73:423-430

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## Surgery for Hyperthyroidism – 2

- Large or obstructive goiter.
- Rapid/definitive correction needed.
- Coexisting "cold" (nonfunctioning) nodule – Dx & Tx.
- Coexisting malignancy or hyperparathyroid.
- Pregnant, intol of hyperthyroidism + intol of ATD's.
- ? more cost effective for toxic nodule < 60.

Thyroid 2006;14(1):93-95;http://www.uptodate.com/contents/surgery-in-the-treatment-of-hyperthyroidism-indications-preoperative-preparation-and-postoperative-follow-up/abstract?lang=&rank=1&source=search\_results&search=surgery+for+hyperthyroidism&selectedTitle=5~220&provider=rochester

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## Complications of Thyroidectomy

- Hypoparathyroidism – transient or permanent.
- Recurrent laryngeal nerve injury/vocal cord paralysis – transient or permanent.
- Recurrent hyperthyroidism (~2%).
- Usual surgical risks: bleeding, infection, keloid.

Thyroid 2001;13(2):187-92;World J Surg 2008;32(7):1278-84

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## Case 2

- 76 y.o. man presents with weight loss, fatigue, anorexia.
- PMH: HTN—controlled on meds
- Meds: HCTZ, ASA 81 mg daily
- FH noncontributory
- SH: former smoker, 30 pack-years

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## Case 2 continued

- ROS: no palpitations, no GI sx
- Exam:
  - By your office scale, **30# wt loss** in 6 months.
  - BP 140/82.
  - Pulse 90.
  - No tremor.
  - No goiter.

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## DDx

- Cancer – do you start the big search?
- HIV/AIDS
- Adrenal insufficiency
- Hypercalcemia – malignancy?
- COPD
- Advanced CHF – "cardiac cachexia"
- Depression
- Meds, drugs
- ????????

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## “Apathetic Hyperthyroidism”

- More common in the **elderly** (>70).
- “Apathetic” → no (or few, or overlooked) sx or signs of sympathetic overactivity.
  - Signs of sympathetic hyperactivity were less common in elderly (p<0.001).
  - ↑ DTR’s, sweating, heat intol, tremor, nervousness, polydipsia, ↑ appetite.
- Goiter in 50% of elderly, vs 94% <50 y.o.
- Avg 6 clinical signs in elderly, vs 10.8 in younger pts.

AnnalsMed 1970;72:670; JAmGeriatrSoc 1996;44(1):50-3

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## Apathetic Hyperthyroidism – 2

- Sx that are more common in elderly:
  - **Atrial fib** (35% vs 2%)
  - Anorexia (32% vs 4%)
- 3 signs most highly associated w/hyperthyroidism in elderly:
  - Apathy +/- fatigue (OR=14.8)
  - **Tachycardia** (OR=11.2)
  - **Wt loss** (OR=8.7)
  - These are the only 3 sx in >50% of these pts.

J Am Geriatr Soc 1996;44(1):50-3

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## Hyperthyroidism: When to Refer

- Provider discomfort in managing dz.
- Unable to return to near-normal thyroid function within ~8 weeks.
- Severe sx or signs of thyroid storm → admit.

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## Case 3

- 28 y.o. male presents to your office with fatigue X 6 months.
  - No F/C.
  - Clothes fitting tighter, but doesn't know if wt gain (doesn't have a scale).
  - No CP, but exertional dyspnea and reduced exercise tolerance.
  - + intermittent mild constipation.
  - Endorses nonspecific arthralgias.

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## Case 3 – continued

- PMH neg
- No meds
- NKA
- FH/SH neg
- ROS as above, o/w neg
- Exam:
  - BP 132/98, P 60
  - Goiter?
  - Something funny about his DTR's

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## Lab Results

- CBC WNL
- Chem: Na 134, o/w WNL
- Lipids: TC 248, LDL 164, TG 246, HDL 35
- TSH: **47**

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## Hypothyroidism—Epidemiology

- Prevalence = 4.6% (4.3% subclinical → 93% of all hypothyroidism!).
- Up to 15% of older women (>65).
- 5-8 times more common in women vs men.
  - ICD-10: E03.9.
  - Hashimoto's/other specified: E03.8.

ICM 2002;8(7):489-99; ICM 2004;9(12):493-6; ClinDiagnMed [2015] 3995;A02155-68

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## AES Question



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## AES Question 4

Risk factors for hypothyroidism include all the following EXCEPT:

- A. PMH of thyroid problems.
- B. Turner's syndrome.
- C. HIV/AIDS.
- D. Age under 35.
- E. Rheumatoid arthritis.

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## Risk Factors for Hypothyroidism

- **Previous thyroid problems** (goiter, surgery).
- **Family history** of thyroid disease.
- Other **autoimmune** diseases (Sjögren's, pernicious anemia, DM1, RA, SLE).
- Women w/small body size at birth &/or during childhood.
- **Age** >60 years.
- **Pregnancy** or delivery within past 6 months (esp if prior postpartum thyroiditis).
- Radiation treatment to the thyroid, neck, or chest.
- HIV
- Turner's syndrome.

http://www.endocrine-nidk.nih.gov/edu/hypothyroidism/risks.html; ICM 2006;9(1):493-6; ClinDiagnMed [2013] 37:579-583

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## Symptoms of Hypothyroidism

- Metabolic slowing:
  - **Fatigue**
  - **Cold intolerance**
  - **Wt gain**
  - DOE
  - Cognitive dysfunction
  - **Constipation**
  - Growth failure/delayed puberty in children
- Accumulation of matrix substances:
  - Dry skin (**↓ sweating**)
  - **Edema**
  - Hoarse voice
- Other:
  - **Arthralgias, myalgias**
  - **Depression**
  - **Menorrhagia or oligomenorrhea**
  - Hearing loss

http://www.upToDate.com/contents/Clinical-manifestations-of-hypothyroidism?factbook&language=en&source=research\_result&search=hypothyroidism+symptoms&selectofTitle=1150&provider=moProvider; EndocrRev 1989;10:356-61

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## Signs of Hypothyroidism

- Metabolic slowing:
  - **Bradycardia**
  - Slowed movement & speech
  - Delayed DTR return
- Matrix accumulation:
  - Goiter
  - Coarse skin; cool & pale (↓ blood flow)
  - **Puffy face**, periorbital edema
  - Tongue enlargement
  - Loss of eyebrows (esp lateral 1/3)

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## More Signs of Hypothyroidism

- Diastolic HTN (↑ PVR)
- Pleural/pericardial effusions
- Myxedema coma ≠ pretibial myxedema
- Anemia
- Macrocytosis w/o anemia or deficiency
- High output CHF or angina – in CV pts
- Celiac dz (4-fold incr in hypothyroid pts)
- Carpal tunnel syndrome
- **Thinning hair**

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## Hypothyroid Mnemonic—Mine

- **M**acrocytosis
- **E**dema (incl orbital)
- **T**hyroid Goiter
- **A**nemia
- **B**radycardia
- **O**besity (wt gain)
- **L**ateral eyebrow loss
- **I**rreg menses
- **C**onstipation

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## Lab Abnormalities in Hypothyroidism

- Hyperlipidemia – ↓ lipid clearance → incr LDL &/or TG's.
  - Lipids usually correct w/correction of hypothyroidism.
  - **Consider TSH in pts w/hyperlipidemia.**
- Hyponatremia – ↓ free-H<sub>2</sub>O clearance.
- Transient ↑ Cr (20 – 90% of pts).

ArchGenMed 1999;19(1):79-82. [http://www.uptodate.com/contents/clinical-manifestations-of-hypothyroidism?source=search\\_result&selectedTitle=4&2571210](http://www.uptodate.com/contents/clinical-manifestations-of-hypothyroidism?source=search_result&selectedTitle=4&2571210); MayoClinProc 1993;68(8):880-4; ArchIntMed 1995;155(14):1490-5

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## Causes of Hypothyroidism

- Hashimoto's (chronic autoimmune thyroiditis): **>90%**
- Iatrogenic:
  - Radioiodine therapy
  - Subtotal or total thyroidectomy
  - ATD's
  - Drugs (**amiodarone**, Li, interferon)
- Thyroiditis
- Iodine deficiency (rare in US)/excess
- Thyroid agenesis

[http://www.ncbi.nlm.nih.gov/books/bsf/for\\_fig/book-rendering/part4225](http://www.ncbi.nlm.nih.gov/books/bsf/for_fig/book-rendering/part4225)  
[http://www.uptodate.com/contents/topic-key-words/7938&selectedTitle=27&71210&source=search\\_result](http://www.uptodate.com/contents/topic-key-words/7938&selectedTitle=27&71210&source=search_result)

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## Hashimoto's Autoimmune Thyroiditis

- F:M = 8 – 10:1
- May begin with transient hyperthyroidism – “Hashitoxicosis.”

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## Thyroid Autoantibodies

- Anti-thyroglobulin (anti-Tg).
  - 5-20% of general population.
- Anti-thyroid peroxidase (anti-TPO).
  - 8-27% of general population.

[http://www.uptodate.com/contents/pathogenesis-of-hashimotos-thyroiditis-chronic-autoimmune-thyroiditis?selectedLanguage=en&source=search\\_result&search-url-top&selectedTitle=156&provider=Provider](http://www.uptodate.com/contents/pathogenesis-of-hashimotos-thyroiditis-chronic-autoimmune-thyroiditis?selectedLanguage=en&source=search_result&search-url-top&selectedTitle=156&provider=Provider)

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## Thyroid Autoantibodies – 2

- Hashimoto's:
  - TPO: 90% +
  - Tg: 80-90% +
- Graves':
  - TPO: 50-90% +
  - Tg: 50-70% +
- DM1: 30-40% + for each.
- Relatives of Hashimoto's: 30-50% + for each.

http://www.uptodate.com/contents/pathogenesis-of-hashimotos-thyroiditis-chronic-autoimmune-thyroiditis?source=search\_result&search=thyroiditis&selectedTitle=1155&previous=hashimotos

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## Why Get Antithyroid Ab's?

- Generally unnecessary.
  - If hypothyroid, 90+% Hashimoto's.
  - Most of the rest are thyroiditis or iatrogenic.
  - 2° will still get same treatment.
- May provide prognostic info in pts @ high risk:
  - Such as pregnant women w/thyroid dysfunction – may **predict** later Graves'.
  - May help in dx & prediction of **subclinical** thyroid dz.

Endocr Pract 2012;18:989-1028

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## AES Question



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## AES Question 5

All hypothyroid pts should be given a trial of combined T4/T3 therapy.

- A. True
- B. False
- C. T3, or not T3, that is the question.

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## Treatment of Hypothyroidism

- **Levothyroxine (LT4).**
  - Mean dose is 1.6-1.8 mcg/kg/day (lean body wt more accurate).
    - 112-125 mcg for avg 70 kg pt.
    - Young & healthy: begin w/near target dose.
    - **>50 or CV dz:** start @ 25 – 50 mcg daily.
  - Wide variability.
  - Take on **empty stomach**.
    - Do not take with soy flour (soy formulas).

ECM 2005;9(1):124-7; EndocrPract 1999;5(1):233-8; ECM 2005;9(4):1381-1385-13

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## Goals of Hypothyroidism Treatment

- **Goals of Tx:**
  - Resolution of sx/signs.
  - **Normalize TSH & improve** thyroid [hormones].
  - Avoid overtreatment, esp elderly.

Endocr Pract 2012;18:989-1028; http://www.thyroidmanager.org/faq/faq4/essay-of-thyroid-hormones-and-related-substances/00c-4-serum-tsh-thyroid-stimulating-hormone-thyrotropin-releasing-hormone

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## Goals of Hypothyroidism Treatment - 2

- **Goal = TSH of 0.5 – 2.0 (or 2.5).**
  - No outcome studies to support target level.
  - ATA 2012 said normal range up to 4.12.
  - ATA 2014: target TSH in lower 1/3 of age-specific range may be reasonable, but not universally endorsed.

Endocr Pract 2012;18:989-1026; http://www.thyroidmanager.org/chapter/essay-of-thyroid-hormones-and-related-substances/Wooc-4-sarum-th-thyroid-stimulating-hormonethyrotropin-essay; Thyroid 2014;24(12):1870-1715; JCEM 2002;87:489-499; JCEM 2005;90:5483-5488; JCEM 2005;90:5488-5496

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## Monitoring of LT4 Treatment

- Measure TSH q 4-6 weeks after change in meds.
- **TSH takes 6 weeks to equilibrate** (incl change in endogenous function).
- **TSH once yearly when stable.**

Thyroid 2014;24(12):1870-1715; Endocr Pract 2012;18:989-1026; http://www.thyroidmanager.org/chapter/essay-of-thyroid-hormones-and-related-substances/Wooc-4-sarum-th-thyroid-stimulating-hormonethyrotropin-essay

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## Evidence: Giving T3 Doesn't Help

- Neurocognitive function & psych well-being may not return to normal w/LT4.
- **The vast majority of studies show no advantage to T3 supplementation or partial replacement (12.5/15 + meta-analysis).**
- Risk of hyperthyroidism & long-term effects.

Endocr Pract 2005;10(8):747-53; ClinEndocrinol 2002;57(3):379-85; NEJM 1999;340(8):424-9; JCEM 2003;88(10):4543-50; JCEM 2003;88(10):4551-5; JAMA 2001;285:2952-8; ClinEndocrinol 2004;60:750-7; AnnInternMed 2005;142:42-8; JCEM 2005;90:805-12; JCEM 2005;90:3666-70; JCEM 2006;95(3):389-93; Endocrinol 2005;151:273-8; JCEM 2005;90:846-54; JCEM 2006;95(7):726-9; Endocr Rev 2005;26:895-902; Endocr Rev 2009;30:105-9; http://www.uptodate.com/contents/treatment-of-hypothyroidism?search=neurocognitive\_research\_research&context=off&topic=742571350

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## An Interesting Study

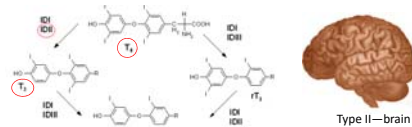
- 697 hypothyroid pts:
  - Validated instruments to assess psych well-being.
  - FT4 & TSH → strong correlation with psych well-being.
  - **No correlation to psych well-being:**
    - FT3
    - rT3, rT3:FT4, FT3:rT3
- ??significance of T3 variation or sl ↓ [T3].

JCEM 2006;91:5389-93; Thyroid 2014;24(12):1870-1715

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## Caveat and Interesting Info

- There may be a **subgroup who responds to T3.**
  - Up to 16% may have a deiodinase gene polymorphism. Some of these pts may feel better w/**appropriate** T3 supplementation.



JCEM 2009;94:1623-9; AnnPhysiol 1998;278:EP15-26; Thyroid 2004;14:271-5; AvonimMed 2016;34:594-6; PLoS One 2013;8:e62015; doi:10.1371/journal.pone.0020202

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## T4:T3 and Supplementation

- Physiologic T4:T3 ratio in humans ~ 10-14:1.
  - Armour Thyroid & Thyrolar have 4:1 ratio of T4:T3.
  - **Trial of ~10:1 ratio of T4:T3 may be reasonable.**
  - T3 (Cytomel) best taken bid (or slow release – unavailable in US). 2<sup>nd</sup> dose midday or afternoon.
  - Avoid overtreating to hyperthyroidism. **MONITOR!**

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## T3 Therapy: How Do You Do It?

- **Reduce LT4 by amount of added T3.**
  - Pt on 125 mcg LT4.
  - 1/10 of dose = 12.5 mcg.
  - Reduce LT4 to 112 mcg and add 12.5 mcg T3.
    - 5 mcg T3: 1.5 am + 1 **lunch/early afternoon.**
  - [If changing **TO** LT4 **FROM** Armour, assume 60 mg Armour ~ 75-100 mcg LT4 (lose T3 “buzz”—rapid action).]

www.update.com/content/treatment-of-hypothyroidism; www.thyroidmanager.org/state/adult-hypothyroidism

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## 2014 ATA: Routine LT3 + LT4

- No consistent evidence of superiority of combo tx over LT4 monotherapy.
  - **Not routinely recommended.**
  - Conflicting reports of benefits.
  - Paucity of long-term outcome data.
- Pts who feel unwell on LT4 alone: insufficient evidence to support **routine** combo tx.

Thyroid 2014;24(12):1670-1711

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## Thyroid & Pregnancy

- Women with thyroid conditions should discuss their condition with their doctor **before** becoming pregnant.
- Opportunity for **preconception counseling** & optimizing maternal & fetal health.
  - Challenging to diagnose
  - **In pregnancy: It is better to be slightly hyper- than slightly hypothyroid.**

http://www.endocrine.mskcc.nih.gov/pubs/hypothyroidism/PdAgoviss

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## AES Question



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## AES Question 6

According to USPSTF and best current evidence, who should be screened for thyroid disorders?

- A. All adults over 60.
- B. All adults over 35.
- C. Women over 50.
- D. People with risk factors
- E. None of the above.

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## Screening for Thyroid Disorders

- American Thyroid Association (ATA): q 5 years, start at 35.
- USPSTF, AAFP (3/15 update): “evidence is insufficient to assess the balance of benefits and harms of screening for thyroid dysfunction in nonpregnant, asymptomatic adults.”
  - No proven outcome advantage to screening.
  - No association w/function, depressive sx, disability in ADLs in an elderly population.
  - Subclinical **hypothyroidism** was assoc'd w/**lower** all-cause/CV mortality, despite higher baseline chol(!).
- Consider targeted screening – risk factors.

http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/thyroid-dysfunction-screening\_AmbinMed\_2004\_14822;128-41;JGIM 2004;19(2):259-9

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## Risk Factors for Thyroid Dz

- Hyper-/hypo-
  - **F**emale gender
  - **A**ge, esp older women > 60
    - 65
  - **P**regnancy/postpartum (be on the lookout for sx)
  - **P**rior thyroid problems
  - **FH**
- Hyper-:
  - Smoking
  - Life stressors (!?)
- Hypo-:
  - **A**utoimmune
  - Turner's
  - Small at birth or in childhood
  - Neck/chest radiation
  - HIV

http://www.uptodate.com/contents/factors-that-cause-hyperthyroidism?source=search\_result&selectedTitle=1~150

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## Unstable Control &/or TSH

- **A**dherence.
- **B**rand/generic changes.
  - ATA & Endocrine Society recommend that pts be maintained on the same brand-name LT4 product.
  - Brand or generic changes: check TSH in 6 weeks, adjust med as needed.
- **C**a<sup>++</sup> or other food interactions.
- **D**rug interactions.
- Other **E**ndocrine (adrenal) or other conditions.

http://www.thyroid.org/professionals/abstract/04\_12\_08\_thyroid.html

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## Drugs That Interfere w/ LT4

- **A**cid reducers (PPI, probably H2, sucralfate)
- **B**ile acid sequestrants (cholestyramine)
- **C**a<sup>++</sup>, **C**arbamazepine
- **D**ilantin, **D**epressants (sertraline, maybe other SSRI's)
- **E**strogen derivatives (incl tamoxifen)
- **F**e
- Check drug interactions when prescribing

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## Practice Recommendations

- Use TSH as the main lab indicator for thyroid disease (SOR A).
- Selective, rather than universal, screening, based on risk factors (SOR B).
- Be aware of, understand, and know signs and symptoms of "apathetic hyperthyroidism" in the elderly.
- Try appropriate combo T4 + T3 therapy (SOR B, C).
- Understand options for treatment of patients with hyperthyroidism, including which patients should be referred to another practitioner, AND what Family Physicians must know and do in order to prescribe antithyroid drugs (SOR B).

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Questions?

## Contact Information

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## References/Suggested Reading

- AACE Hyperthyroidism guideline: *Endocr Pract* 2011;17:457-520.
- *Thyroid* 2014;24(12):1670-1751 – 2014 ATA Guideline on hypothyroidism treatment.
- AACE Hypothyroidism guideline: *Endocr Pract* 2012;18:989-1028.
- [www.thyroidmanager.org](http://www.thyroidmanager.org)

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## Billing & Coding

When services performed in conjunction with:

Office Visit 992xx - \*

\*Time-based selection documentation criteria:

- Face-to-face time
- greater than 50% spent counseling/coordinates care

Additional tests to confirm or monitor:

Laboratory Tests for confirmed diagnosis

84443	Thyroid stimulating hormone (TSH)
84439	T4 Free
84481	Free T3

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## Associated Session

- Hyperthyroidism and Hypothyroidism: PBL

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Interested in More CME on this topic?  
[aafp.org/fmx-endocrine](http://aafp.org/fmx-endocrine)

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## Supplemental Info



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## Effects of Thyroid Hormones

- Gen: body temp regulation, wt maintenance.
- Cellular metabolism: incr insulin-dependent entry of glc into cells, gluconeogenesis, glycogenolysis.
- CV: CO, contractility, lipid metabolism.
- CNS: cognitive function, mental state.
- M/S: muscle tone/strength.
- GI: transit time.
- Renal: free water clearance.
- Repro: menstrual cycles, fertility.
- Skin: hair, skin, nail integrity.
- Pregnancy: neuro development of fetus.

<http://www.fda.gov/CDRHMS/DOCKETS/AC/06/sides/2006-422851-01-02-Pearets%20Clinical.pdf>  
<http://e.hormone.milano.edu/learning/thyroid.html>

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## The Thyroid as “Thermostat”

- A metaphor – most pts understand.
  - When overactive, everything is turned up – feel hot, restless/anxious, hyperactive heart & GI, etc.
  - When underactive, everything is dialed down – slow, cool, fatigue, etc.



Public domain, copyright (c) www.wikipedia.org/wiki/File:Thermostat\_Touch\_Screen\_7\_thermostat.jpg

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## Review of Thyroid Hormones

- T4 = thyroxine:
  - 99.97% **protein bound** (2 ng/dL = free).
  - Produced **exclusively by thyroid**.
  - Half-life ~ 1 week.
  - ~10 X **more prevalent** in serum than T3.
- T3 = triiodothyronine:
  - 99.7% **protein bound** (0.4 ng/dL = free).
  - **80% comes from conversion** of T4 → T3 in peripheral tissues.
  - Half-life ~ 1 day.
  - 3-100 (~10) times **more potent** than T4.

<http://www.thyroidmanager.org/chapter/essay-of-thyroid-hormones-and-related-substances/>

9

AMERICAN ACADEMY OF FAMILY PHYSICIANS

## TSH Upper Limit of Normal

- Most young – middle-aged euthyroid people have a TSH below 2.5 – **3.6**.
- Reducing the upper limit of TSH range to 2.5 will likely label a sizable number of people as “abnormal” (or subclinical hypothyroidism).
  - “...might significantly increase the use of thyroxine therapy for patients in whom there is **no demonstrated therapeutic benefit**.”

ClinChem 2005; Aug;51(8):1480-6; JAMA 2003;290:3195-6

9

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## I Thought Depression Occurred in **HYPOTHYROIDISM!**

- Dysphoria, emotional lability, cognitive dysfunction, & depression are also well-documented in **hyperthyroidism**.

SouthMedJ 2007;100(6):773-4, AnnalsMed 1986;17:205-14

1

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## Graves' Dz vs TMNG

- Graves':
  - Entire gland **diffusely** enlarged.
  - Entire gland making excess thyroid hormone.
- Toxic Multinodular Goiter:
  - Multiple **nodules** on thyroid.
  - Nodules independently produce excess thyroid hormone (autonomously functioning = “hot”).

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## Back to Case 1

- Physical exam shows normal thyroid, no masses or asymmetry.
- Is this Graves' dz, TMNG, or other?
  - Likely Graves':
    - Epidemiology (young woman).
    - No nodules.

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## Laboratory Findings in Hyperthyroidism

- Anemia – normochromic/normocytic.
  - ↑ plasma volume > ↑ RBC mass
- Leukocytosis.
- **Elevated transaminases (aminotransferases).**
- Elevated alkaline phosphatase.
- Low HDL.
- Impaired glc tolerance.

Hepatology 1997;44:1614-8. <http://www.medicines.mcgill.ca/ur/edu/767130-overview>

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## Antibodies in Graves' Disease

- Thyroid **Stimulating** Antibodies (TSAb) = Thyroid **Stimulating** Immunoglobulin (TSI).
  - 1 of 3 types of TSH-receptor antibodies; the others (TSBAb, TBII/TBAb/TRAb) do NOT **stimulate** the thyroid.
  - TSAb/TSI sensitivity 90 – 99%, specificity 99.6% (if measured by sensitive assay).
  - Safe in **pregnancy** – RAIU is **NOT**.

JGIM 1993;8:1027

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## Treatment of Hyperthyroidism

- Acute management: control sx.
  - Beta blockers.
    - ↑ thyroid increases β-receptors in many tissues.
    - β-blockers **reduce sx** quickly.
    - Try β-1 selective if relative contraindication.
    - **All equally effective.**
  - Pregnancy: wean β-blockers as soon as possible – IUGR, hypoglycemia, resp depression, bradycardia.
  - 1 study (1991) → 5-fold ↑ SAb rate.

Endocrinol Rev 1983;4(4):378-88. Acta Obstet Gynecol Scand 1995;74(5):463-5. NEJM 1981;305:1322

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## Acute Management of Hyperthyroidism

- Antithyroid drugs (thionamides).
  - Inhibit formation of thyroid hormones.
  - Goal: euthyroid within 8 weeks.
  - **Methimazole** (MMI) is the preferred drug.
    - ↓ side effects, ↑ duration of action → **once daily** dose (usually).
    - 10 – **15** mg daily for **milder** clinical picture, vs 20 – 40 mg for larger goiter & more severe sx & signs (can divide bid to minimize side effects).

Clin Endocrinology 1997;47:7. Clin Endocrinol (Oxf) 1998;49:127. JGIM 1993;76:1336-21. <http://www.ncbi.nlm.nih.gov/pubmed/10461046>

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## Iodides in Treatment of Hyperthyroidism

- Potassium iodide (SSKI), iodine-KI (Lugol's).
- Inhibit thyroid hormone release.
- Short-term, rapid restoration of euthyroid:
  - **Severe hyperthyroidism/thyroid storm.**
    - More I → more hormone synth → ↑ hyperthyroid.
    - **Wait ≥ 1 hr after MMI** so I<sup>-</sup> not used to synthesize T<sub>4</sub>.
  - Preop – thyroidectomy for Graves'.
  - After radioablation – ? normalizes function faster.
  - Adjunct to MMI in Graves' → FT<sub>4</sub> faster.
- Esophageal or duodenal mucosa injury.

Endocrinology 1985;7:295-7. JAMA 1987;257:2242-6. Clin Endocrinol (Oxf) 2006;68:663-66. JGIM 1988;37:258-9. Clin Endocrinol (Oxf) 2002;56:73-80-92. [http://www.uptodate.com/contents/iodine-in-the-treatment-of-hyperthyroidism?source=search\\_result&selectedTitle=1~150;from=med.2002;68.750.1](http://www.uptodate.com/contents/iodine-in-the-treatment-of-hyperthyroidism?source=search_result&selectedTitle=1~150;from=med.2002;68.750.1)

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## DDx: "I Feel Cold"

- |  |  |
|--|--|
| • General: <ul style="list-style-type: none"><li>– Chronic illness, poor health</li></ul>  | • Endocrine: <ul style="list-style-type: none"><li>– Hypothyroidism.</li><li>– Hypoglycemia.</li><li>– DM nephropathy.</li></ul> |
| • CNS: <ul style="list-style-type: none"><li>– Hypothalamic dysfunction</li><li>– Hypothermia</li><li>– Anorexia nervosa</li></ul> | • CV: <ul style="list-style-type: none"><li>– PAD.</li><li>– Raynaud's.</li></ul>  |
| • Skin: <ul style="list-style-type: none"><li>– Exfoliative dermatitis</li></ul>   | • Blood: <ul style="list-style-type: none"><li>– Anemia.</li></ul>   |

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## Dx of Thyroid Dz in Pregnancy

- **Challenging to diagnose**
- All thyroid hormone levels, incl TSH, change in pregnancy.
- **Free thyroid assays are inaccurate.**
  - **TSH—norms adjusted for pregnancy.**
  - Total T4—multiply ULN & LLN by 1.5.
  - FTI may be more accurate – can use the **regular nonpregnant range.**

http://www.thyroidmanager.org/Chapter4/4.14\_frame.htm; J Clin Endocrinol Biochem 2001;38:329; http://www.thyroidmanager.org/Chapter4/4.14\_frame.htm

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## Risks of Thyroid Dz in Pregnancy

- **Overt** hypothyroidism:
  - Abruption
  - **Preterm** delivery, incl <32 wks
  - **LBW**
  - **Preeclampsia**
  - ↑ C/S rate
  - Perinatal morb/mort
  - Neuropsych & cognitive impairment
  - Postpartum hemorrhage
- **Overt** hyperthyroidism:
  - SAb, stillbirth
  - **Preterm** labor
  - **LBW**
  - **Preeclampsia**
  - CHF

Thyr 2005;35(1):60-71; ObGyn 1993;81(1):349-53; ClinEndo(D) 1995;42(4):353-6; ObGyn 1988;72(1):108-11; Thy 2005;15(4):351-7; ClinEndo(D) 1995;42(3):349-53; NEJM 1995;34(26):549-55; ClinEndo(D) 2000;43(3):360-5

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## Subclinical Thyroid Dz in Pregnancy

- **Thyroid dz sx overlap w/sx of pregnancy.**
- **Subclinical hyper**thyroidism in pregnancy was **NOT** assoc'd w/any adverse pregnancy outcomes.
- **Subclinical hypo**thyroidism in preg **WAS** assoc'd w/adverse outcomes in some studies (low IQ @ 8 y.o., abruptio[n!], 2-fold incr in preterm delivery).

ObstetGynecol 2006;107(2 Pt 1):337-41; NEJM 1999;341(8):549-55; ObstetGynecol 2005;105(2):239-45

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## Subclinical Thyroid Dz in Pregnancy

**In pregnancy: It is better to be slightly hyper- than slightly hypo-thyroid.**

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## What Time of Day to Test TSH?

- Diurnal variation, peak 00:00 – 04:00.
- However, in ambulatory pts, TSH is tested during daytime hrs and results are not/less affected by time of day.
- Do NOT need to hold LT4 to test TSH.
  - TSH secretion responds slowly to changes in T4 status.
  - This is why you wait 6-8 weeks to recheck TSH after med change.

JCEM 1991;72:145-150; Thyroid 2003;13:57-67

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## Thyroid “Set Point”

- Each person has **low variability** in TSH.
  - 0.5 month-to-month variability.
  - Variation in an individual is ~ ½ the variation of the population reference range.
  - TSH chg 0.2 – 1.6 could → chg in thyroid status.
  - ~2/3 of TSH “set point” is **genetically determined.**
- Result in “normal range” may not be normal for that person.
  - Tricky. (Watch for change over time.)

ClinChemLabMed 2005;43:102-5; JCEM 2002; 87:1068-1072; Clin Endocrinol 2008; 68:652-659; JCEM 2004; 89:1181-1187; JCEM 1988;66:588-92; EurEndo 2011;164:781-6

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## TSH: The Future (We Hope)

- TSH normal values may be age-related.
  - Normal values in children ≠ adult normals.
- **Other factors** that may affect TSH:
  - Gender (F>M)
  - Ethnicity (Caucasians>Latinos>African-Americans)
  - Smoking (lowers TSH & may be assoc'd w/less hypothyroidism)

ClinEndocrinol 2009;70:788-791; JClInEndocrinolMetab 2010;95:496-502; JClInEndocrinolMetab 2002;87:489-499

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## Drugs That Affect TSH

- Falsely ↓ TSH:
  - **Glucocorticoids** (≥ 20 mg/day prednisone).
  - **Dopamine**, bromocriptine, levodopa.
    - Dopamine agonists alone do not cause significant central hypothyroidism – can in combo w/non-thyroidal illness (“sick euthyroid syndrome”).
  - Somatostatin analogs (octreotide).
  - Metformin?

BestPrac: Res ClinEndocrinolMetab 2009;23:793-800; Lancet 2001; 357:1013-4; JCEM 1983;57:380-3; WJM 2000;172:102-6; DiabetesCare 2009;32:1589-90; ClinEndocrinol 2012; 2012 Jun 12. doi: 10.1111/j.1365-2265.2012.04468.epub; <http://www.thyroidmanager.org/chapter/assay-of-thyroid-hormones-and-related-substances/>

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## Drugs That Affect TSH – 2

- Falsely ↑ TSH (usu <10):
  - Dopamine antagonists (**neuroleptics**, **metoclopramide**).
  - **Amphetamine**
  - Theophylline
  - Iodinated contrast

BestPrac: Res ClinEndocrinolMetab 2009;23:793-800; Lancet 2001; 357:1013-4; JCEM 1983;57:380-3; WJM 2000;172:102-6; DiabetesCare 2009;32:1589-90; <http://www.thyroidmanager.org/chapter/assay-of-thyroid-hormones-and-related-substances/>

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## Drugs That Affect Free T4

- Falsely ↓ FT4:
  - **Androgens** (anabolic steroids)
  - Niacin
  - **Phenytoin**
  - **Carbamazepine**
  - **Phenobarbital**

EndocrinolMetabClinNamer 2001;30:265-89; BestPracResClinEndoMetab 2009;23:753-67; PedEndoRev 2003;1:251-6; ClinChem 2000;46:1395-1400; WJM 2000;172:102-6; [www.thyroidmanager.com](http://www.thyroidmanager.com)

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## Drugs That Affect Free T4 – 2

- Falsely ↑ FT4:
  - **Estrogen**
  - Heroin
  - **Methadone**
  - **Amiodarone**
  - Heparin, esp IV
  - **Phenytoin**
  - High-dose **salicylates**
  - **Furosemide** (IV >80 mg/day)
  - Propranolol, **β-blockers**
  - Iodinated contrast

EndocrinolMetabClinNamer 2001;30:265-89; BestPracResClinEndoMetab 2009;23:753-67; PedEndoRev 2003;1:251-6; ClinChem 2000;46:1395-1400; QJM 2001;94:471-3; WJM 2000;172:102-6; ClinEndocrinol 1987;26:423-31; JCEM 1987;65:1259-64; [www.thyroidmanager.com](http://www.thyroidmanager.com)

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## Secondary Hypothyroidism

- Low TSH & low (or low-normal) Free T4
  - **May have normal or slightly high TSH** – **inappropriate** for low level of FT4 (tricky—FT4 reliability).
    - **84% normal TSH.**
    - 8 – 25% mildly elevated (5-10).
  - Normal TSH in these pts may be due to TSH w/↓ biologic activity but normal immunoreactivity to test.

Pituitary 2008;11:181-6; EurEndocrinol 2004 Jan;150:1-6; JCEM 2000;85:3631-5; EndocrinolMetabClinNorthAm 2000;29:399-415; <http://www.update.com/content/central-hypothyroidism>

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## Secondary Hypothyroidism – 2

- Rare –  $\leq 1\%$  of hypothyroidism.
- Causes:
  - **Brain** lesion (tumor, cyst, abscess).
  - Pituitary hemorrhage or infarction.
  - Iatrogenic – surgery, radiation.
  - Infiltrative – sarcoidosis, TB, other.

Pituitary 2008;11:181-6; EurJEndocrinol 2004 Jan;150:1-6; JCI 2000;85:3631-5; <http://www.uptodate.com/content/central-hypothyroidism>

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## When to Suspect 2° Hypothyroidism

- Known **hypothalamic or pituitary** disease.
  - Traumatic brain injury.
  - Sheehan's syndrome.
  - SAH.
  - Prior surgery or radiation.
  - Young woman w/amenorrhea.
- Mass lesion in the pituitary.
- Symptoms and signs of hypothyroidism are associated with **other hormonal deficiencies**.

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## 2° Hypothyroidism

- 26 cases of hypopituitarism/56,000 tests & population of 471,000  $\rightarrow$  0.00047% of tests & 0.000055% of population.
- BUT missed hypopit is problematic.
  - Litigation.
  - Missed dz, morbidity, burden of suffering.
- Big expense to **routinely** do both tests.
- Is it worth it to abandon “TSH-first” strategy, and get TSH + FT4 on all? Probably not at present. Stay tuned....

Lancet 2001;357:1013-4; ClinEndocrinol 2003;56:20-1

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## Low(-ish) FT4 + SI High TSH

- Get anti-TPO
  - +  $\rightarrow$  autoimmune thyroiditis (Hashimoto's)  $\rightarrow$  1°.
- Get pituitary hormones (FSH, LH) +/- E2 or T.
  - Low FSH/LH, esp in postmenopausal woman,  $\rightarrow$  pituitary dz.
  - Low T + low or NI LH in men  $\rightarrow$  pituitary.
  - Prolactin not reliable – can be  $\uparrow$  in either.

<http://www.uptodate.com/contents/central-hypothyroidism>

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## Unexpectedly High LT4 Requirement

- Also consider:
  - Celiac dz.
  - Atrophic gastritis.
  - *H. pylori* gastritis.

<http://www.thyroid.org/thyroid-guidelines/hypothyroidism2014/>; Thyroid 2014 Oct; 271 (suppl 4 of pt 1): S10-S16; JCI 2012;97:4419-22; AnnMed 2012;135:278-82

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## Take-Home Points

- Thyroid dz is common.
- Diagnosis of thyroid disorders.
- “Apathetic hyperthyroidism” of elderly.
- Risk factors for thyroid dz.
- Evaluation and management of hypo- & hyperthyroidism.
- Trial of T3 in some.
- Women & thyroid—preconception counseling.

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