

Hyperthyroidism

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Thyrotoxicosis Symptoms

- Weight loss, despite increased appetite
- Sweating, heat intolerance
- Tachycardia, atrial fibrillation
- Frequent loose stools
- Emotional lability, restlessness, tremor
- Weakness, fatigue, dyspnea on exertion
- Graves' ophthalmopathy

Definition of Thyrotoxicosis

- A low or undetectable TSH in the setting of clinical hyperthyroidism
 - ✓ May be present with a normal Free T4 and T3
 - ✓ Rarely can be mediated by TSH: normal or elevated TSH in the setting of elevated FreeT4 and/or T3

Cardiac Effects of thyrotoxicosis

- Tachycardia, widened pulse pressure and elevated systolic blood pressure
- Atrial fibrillation
 - ✓ 8% of all patients develop this
 - ✓ 15% of those 70-79 develop in first 30 days
- Heart Failure
 - ✓ Occurs in 6% of thyrotoxic patients
 - ✓ Felt to be rate-related cardiomyopathy

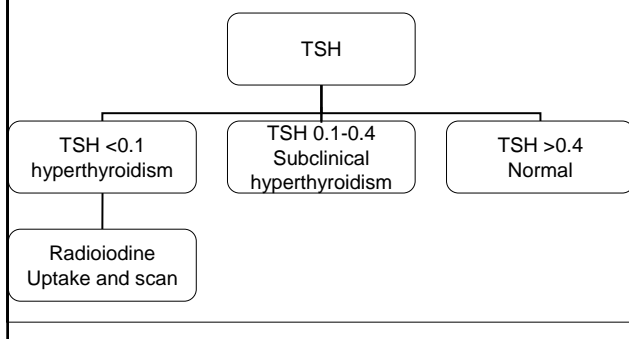
Physical Exam Findings

- Tachycardia, systolic HTN
- Pressured speech, being “fidgety”
- Exophthalmos, lid lag, scleral show
- Goiter, thyroid nodule or tender thyroid
 - ✓ Bruit over goiter pathognomonic for Graves’
- Warm, sweaty skin that may be “smooth”
- Fine tremor, brisk reflexes

Critical diagnostic test: I^{131} Uptake and Scan

- | | |
|--|---|
| <ul style="list-style-type: none"> • Low iodine uptake <ul style="list-style-type: none"> ✓ Thyroiditis ✓ Exogenous ✓ Ectopic ✓ Iodine-induced ✓ amiodarone | <ul style="list-style-type: none"> • High iodine uptake <ul style="list-style-type: none"> ✓ Graves’ disease ✓ Toxic MNG ✓ Toxic adenoma ✓ “hashitoxicosis” ✓ TSH-mediated |
|--|---|

Suspect thyrotoxicosis:

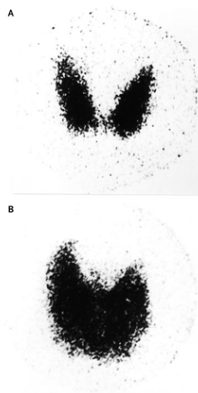


Graves’ Disease

- Autoimmune hyperthyroidism
- Caused by antibodies that activate the TSH receptor
 - ✓ TSH receptor Ab’s and Thyroid Stimulating Immunoglobulin
- “Hashimoto’s” antibodies usually also present: Anti thyroid peroxidase Abs

Graves' Disease

- Peak incidence 30-50yo
- Strong familial predisposition
- Female:male 9:1
- 15-25% remission rate with medical management
 - ✓ Usually in patients with mild disease on presentation



Radioiodine uptake and scan In Graves' disease:

- Uptake is high usually >50%
- Scan shows diffuse, symmetric uptake

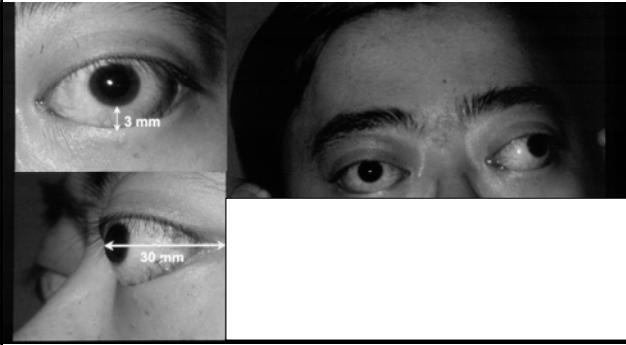
Brent GA, NEJM 2008 Jun 12;358(24):2594-605.

Graves' disease
Diffuse Goiter

- Right lobe>left
- Firm gland



Graves' Disease Ophthalmopathy Exophthalmos (Proptosis)



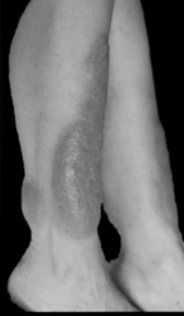
Toxic Adenoma and Toxic MNG

- Focal hyperplasia of thyroid follicular cells with functional capacity which is independent of TSH regulation
- More common in those >50yo
- Localized, somatic activating mutation of the TSH receptor gene
- Rarely if ever spontaneously remits
- Can be associated with isolated T3 toxicosis

Exophthalmos (Proptosis)

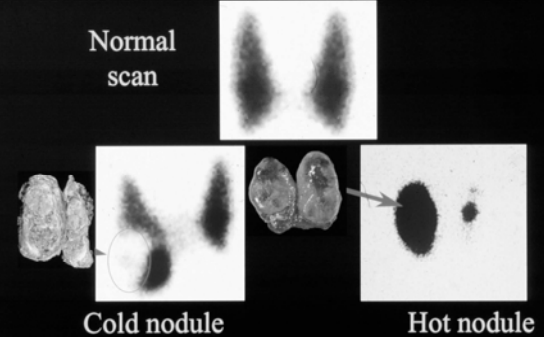


Graves' Disease Pretibial Myxedema

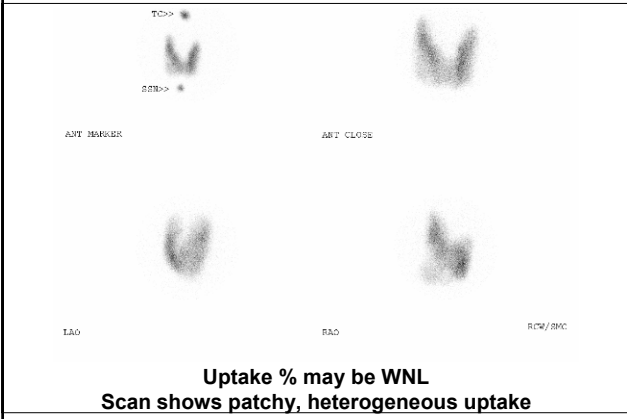


Thyroid Radionuclide Scans

^{123}I or $^{99\text{m}}\text{Tc}$



Radioiodine Scan of Toxic Multinodular Goiter



Antithyroid Medications, cont

- PTU – comes in 50mg tablets
 - ✓ Start at 100mg or 150mg TID
 - ✓ Non-compliance with TID dosing frequent
- Methimazole – 5mg and 10mg tablets
 - ✓ Start at 20-30mg qd x 5d then can frequently decrease to 10mg per day
- If they've been on these meds for 12mo and still hyper, the thyrotoxicosis is NOT going away – move to definitive therapy

Treatment: Medications

- Beta blockade for symptomatic relief of palpitations and cardio-protection
- Thionamides: PTU and Methimazole
 - ✓ PTU: more inconvenient TID dosing
 - ✓ Methimazole: Once daily
 - ✓ 5% develop pruritic rash
 - ✓ With longer exposure of higher doses, agranulocytosis and elevated LFTs

Treatment: I¹³¹

- In Graves disease, goal should be total ablation of thyroid gland
 - ✓ Typical doses of 10-22mCi
- TMNG, can try to ablate hyperfunctional nodule(s) and leave remaining normal tissue intact
- Takes 6 weeks to 6 months for ablation
- Very safe: used since 1950's with no increased incidence cancer or leukemia

Radiation Safety

- 3 foot (arm's length) distance x 3 days
 - ✓ Should avoid small children completely
- Avoid exposure to body fluids for 7 days
- Avoid pregnancy for 6-12 months
- Actual radiation dose/exposure is very small: similar to flying in a plane from Columbus to San Francisco and back!

Thyroid Surgery for Definitive Treatment of Hyperthyroidism



¹³¹I Therapy: follow-up

- Draw labs in 4 weeks: FreeT4
 - ✓ Every 4 weeks
- Begin Synthroid once FT4 is in the lower part of the normal range
- Synthroid dosing: 1.6mcg/kg



Thyroid Surgery

- Not first choice in most thyrotoxic pts
- Risk of surgical complications
 - ✓ Hypoparathyroidism
 - ✓ Recurrent laryngeal nerve injury
- Patient must be euthyroid prior to surgery



Thyroid Surgery

- Treatment of Choice in Select individuals:
 - ✓ Severe hyperthyroidism that failed I¹³¹
 - ✓ Moderate to severe orbitopathy
 - Could be made worse by radioactive iodine
 - ✓ Suspicious “cold” nodule in the setting of hyperthyroidism

Subacute thyroiditis, continued

- Will not respond to Antithyroid medications or I¹³¹
- Beta blockade for symptomatic relief
- Radioiodine uptake/scan shows very low percentage uptake - <5%
- Typical three phase response: Hyperthyroidism, then hypo, then recovery
- 10% of patients go on to develop overt hypothyroidism

Subacute Thyroiditis

- Release of preformed hormone
- Frequently begins in setting of adjacent inflammation
 - ✓ URI or other viral illness
- Self limited – typically lasts 6-12 weeks
- May have thyroid tenderness

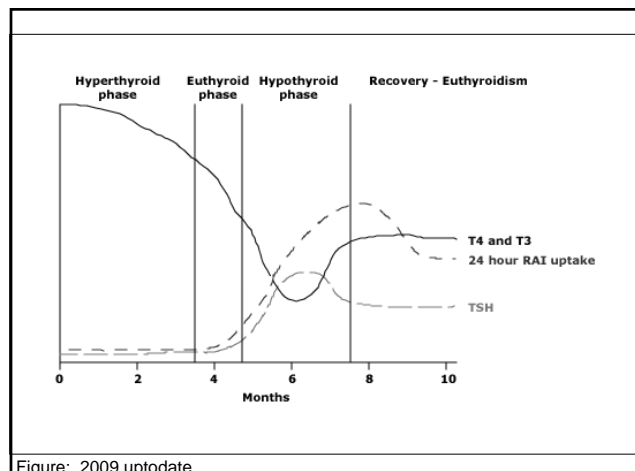


Figure: 2009 update

Amiodarone-induced thyrotoxicosis

- Amiodarone is 33% iodine
- Hypothyroidism is the more common result
- 2% of patients develop thyrotoxicosis
 - ✓ Dumping of stored hormone: thyroiditis
 - Lasts 2-6 months
 - Treat with beta blockade, steroids
 - ✓ Excess iodine load in Graves' like picture
 - Usually do see a goiter, family history
 - May respond to methimazole

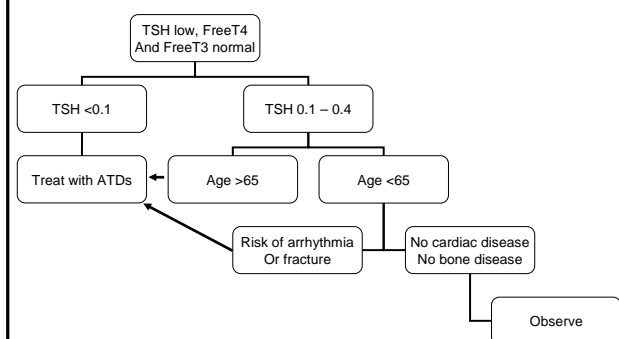
Subclinical Hyperthyroidism

- Suppressed TSH with normal FreeT4 and FreeT3
- Etiology similar to overt hyperthyroidism
 - ✓ More likely to be TMNG than Graves, however
- 40% remit within one year of diagnosis; rarely does this progress to thyrotoxicosis

Amiodarone-induced thyrotoxicosis

- Cannot use radioiodine scan for diagnosis
- Cannot use I¹³¹ for treatment
- Thyroidectomy may be necessary
 - ✓ Not always the best surgical risk patients, though
- Endocrine consult definitely helpful!

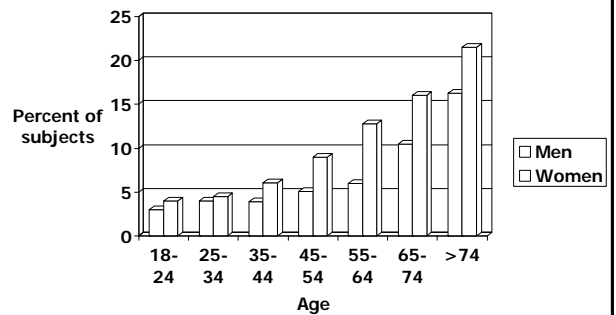
Subclinical Hyperthyroidism



Hypothyroidism

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Elevated TSH levels



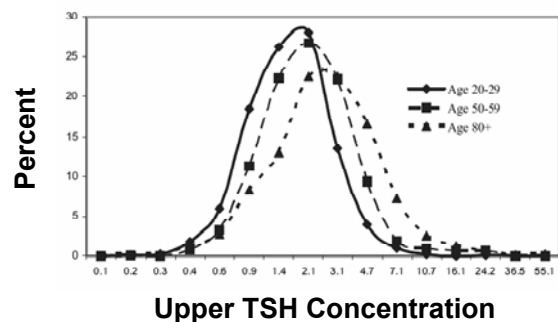
ArchInternMed 2000;160:526-534

National Health and Nutrition Examination Surveys (NHANES III)

- Survey of 13K people with no known thyroid disease
 - ✓ 4.6% hypothyroid
 - 4.3% subclinical hypothyroidism
 - 0.3% overt hypothyroidism
 - ✓ 11% had elevated TPO Ab
 - ✓ 10% had elevated Tg Ab

J Clin Endocrinol Metab 83: 3401-3406, 1996

TSH distribution by age in US



J Clin Endocrinol Metab, December 2007, 92(12):4575-4582

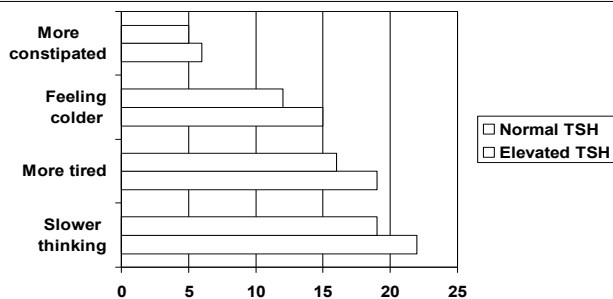
Clinical Symptoms and Signs

- | | |
|---|---|
| <ul style="list-style-type: none"> • Fatigue • Constipation • Impaired memory • Depression • Muscle weakness • Menstrual disturbance • Infertility • Cold intolerance | <ul style="list-style-type: none"> • Hoarseness • Goiter • Periorbital edema • Weight gain • Nerve entrapment syndromes • Bradycardia • Dry skin |
|---|---|

Associated Conditions

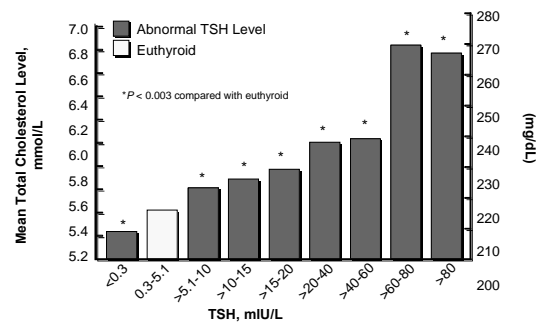
- Laboratory test abnormalities
 - ✓ Hypercholesterolemia
 - ✓ Hyponatremia
 - ✓ Hyperprolactinemia
 - ✓ Hyperhomocysteinemia
 - ✓ Anemia
 - ✓ CPK elevation

Percentage of patients with hypothyroid symptoms



Ann Int Med 2000; 160: 526-534

Consequences of Hypothyroidism ↑ Cholesterol When Mild & Overt



Canaris GJ, et al. Arch Intern Med. 2000;160:526-534.

Radiological Abnormalities



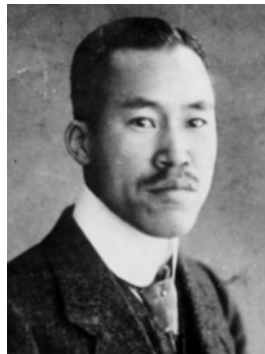
- ✓ Pericardial effusion
- ✓ Pleural effusion
- ✓ Pituitary enlargement

Medications affecting thyroid function

- | | |
|--|--|
| <ul style="list-style-type: none"> • Amiodarone • Lithium • Interferon α, Interleukin 2 | <ul style="list-style-type: none"> • Cholestyramine • Ferrous Sulfate • Omeprazole, lansoprazole • Calcium carbonate |
| <ul style="list-style-type: none"> • Dopamine, dobutamine • Glucocorticoids | <ul style="list-style-type: none"> • Phenobarbital • Rifampin • Phenytoin • Carbamazepine |
| <ul style="list-style-type: none"> • Estrogen • Tamoxifen • Methadone | |

Causes of Hypothyroidism

- Hashimoto's thyroiditis
- Post-surgical
- Radiation exposure
- Radioactive iodine
- Drugs
- Central hypothyroidism
- Iodine deficiency/excess



Hashimoto Hakaru

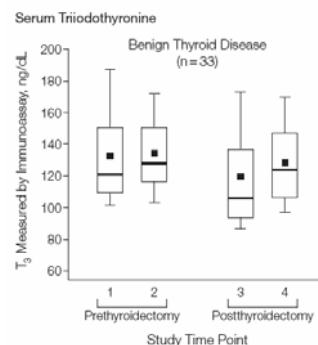
Treatment

- T4 replacement
 - ✓ 1.6-1.8 mcg/kg (ideal body weight)
 - ✓ Elderly, CAD – 12.5 to 25mcg/day
- Check TFTs in 6-8 weeks
- Re-assess at 6 months
- IV dose is 75-80% of PO

Pediatric Patients

- 1-3 years old 4-6 mcg/kg
- 3-10 years old 3-5 mcg/kg
- 10-16 years old 2-4mcg/kg
- Once started, probably best to continue therapy until growth and pubertal development are complete

T3 levels pre- and post-operatively

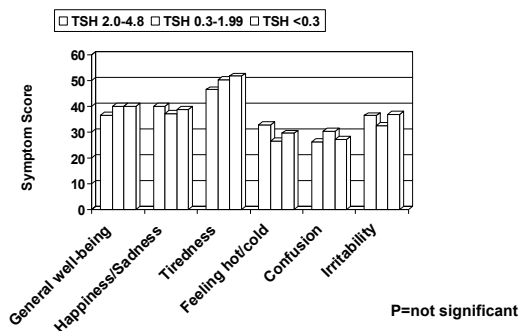


JAMA, February 20, 2008—Vol 299, No. 7

T3 Therapy

- Anecdotal reports of patients feeling better with it
- Serum half life 12 hours
- Target organs have deiodinases to convert T₄ to T₃
- Adds another drug to the medication regimen

Symptom scores by serum TSH level



J Clin Endocrinol Metab, July 2006, 91(7):2024-2029

Screening

- **AACE and AAFP – periodic screening of elderly women**
- **ACP – women >50 years**
- **ATA – women over age of 35 should be checked every five years**
- **USPSTF – does not recommend screening adults or children**
- **“Aggressive case finding in those >60y and others at high risk for thyroid dysfunction”**