Thyroid Disease

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ENDOCRINOLOGY

APRIL 5, 2022

Case

- 38 yo man c/o fatigue, cold intolerance, depression, constipation and weight gain.

- What laboratory test should you order to screen for his likely condition?
  - Free T4 (thyroxine)
  - Total T3 (triiodothyronine)
  - Reverse T3
  - Thyroid-stimulating hormone
  - Thyroid stimulating immunoglobulin

Case

- 38 yo man morbidly obese, c/o fatigue, cold intolerance, depression, constipation and weight gain.

- What laboratory test should you order to screen for his likely condition?
  - Free T4 (thyroxine)
  - Total T3 (triiodothyronine)
  - Reverse T3
  - **Thyroid-stimulating hormone**
  - Thyroid stimulating immunoglobulin

Case

- 38 yo man morbidly obese, c/o fatigue, cold intolerance, depression, constipation and weight gain.

- What laboratory test should you order to screen for his likely condition?
  - Free T4 (thyroxine)
  - Total T3 (triiodothyronine)
  - Reverse T3
  - **Thyroid-stimulating hormone**
  - Thyroid stimulating immunoglobulin

2/2/2018: TSH 1.79

Brief Physiology Review

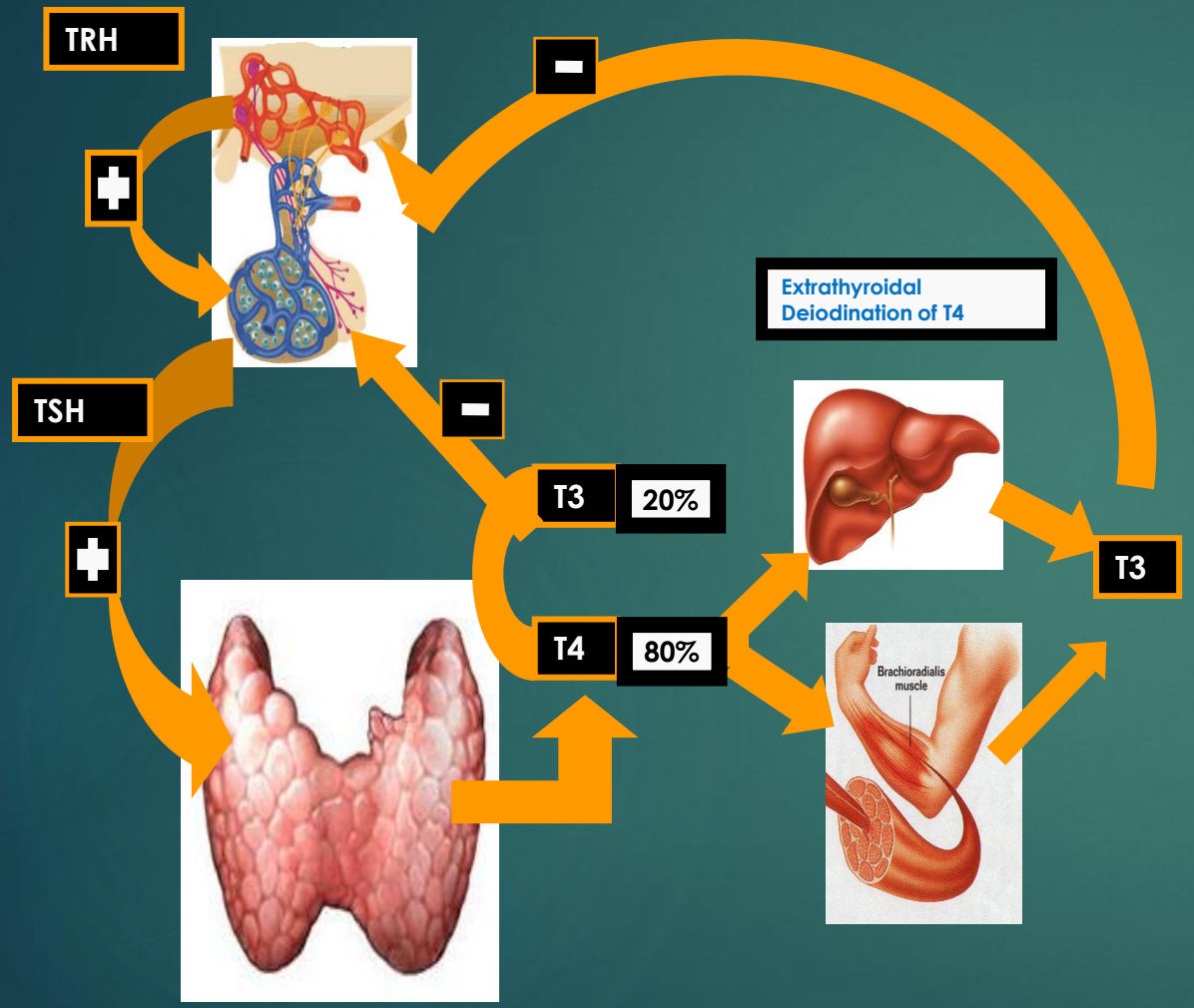
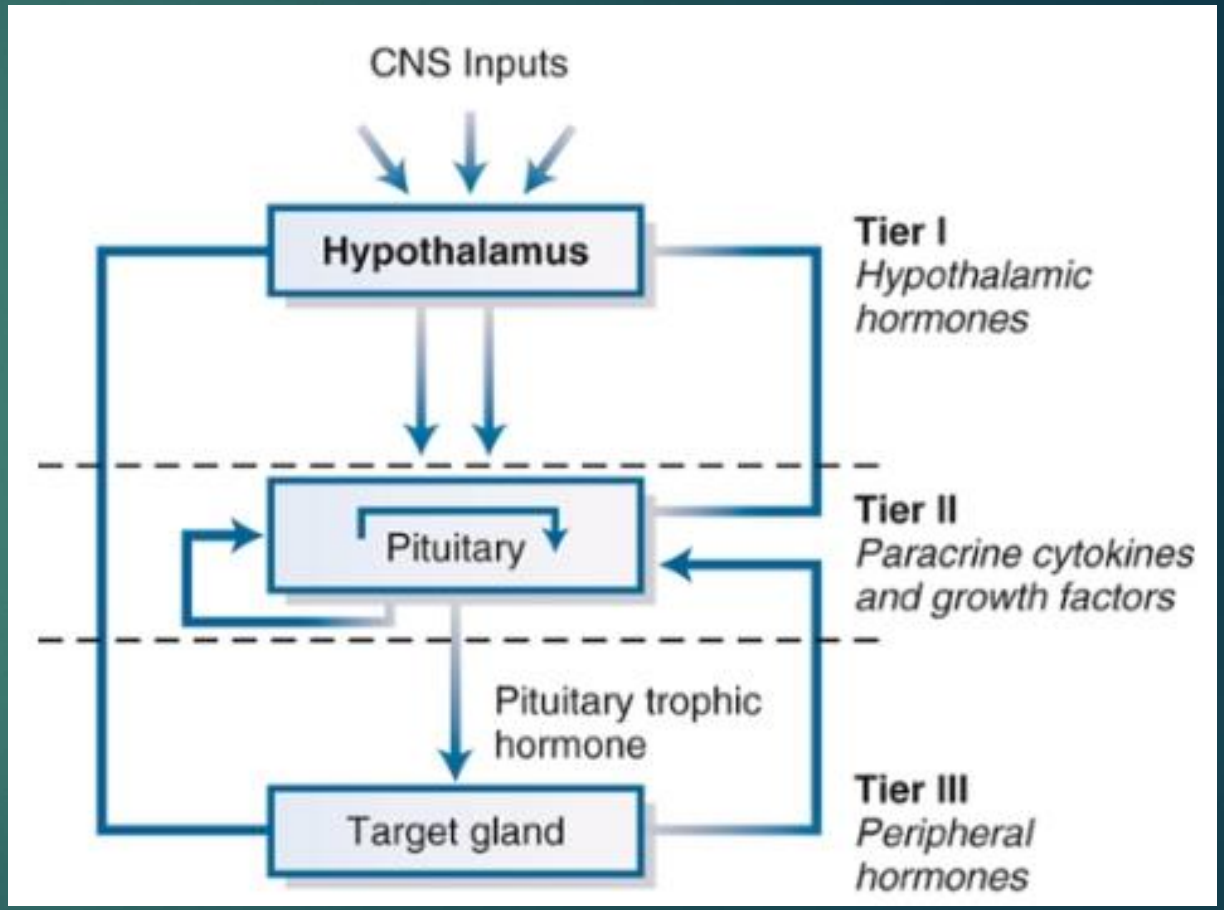


Figure 8-3. Williams Textbook of Endocrinology.



TSH First

- A normal serum TSH value in ambulatory patients without associated disease or pituitary dysfunction has a **high negative predictive value** in ruling out both primary hypothyroidism and hyperthyroidism
- Free T4 may only be estimated if TSH is abnormal
- ”TSH first” strategy of thyroid function testing has important limitations

Who should be tested for thyroid dysfunction?

- Clinical manifestations of hyperthyroidism or hypothyroidism

Major symptoms and signs of hypothyroidism

Mechanism	Symptoms	Signs
Slowing of metabolic processes	Fatigue and weakness Cold intolerance Dyspnea on exertion Weight gain Cognitive dysfunction Mental retardation (infantile onset) Constipation Growth failure	Slow movement and slow speech Delayed relaxation of tendon reflexes Bradycardia
Accumulation of matrix substances	Dry skin Hoarseness Edema	Coarse skin Puffy facies and loss of eyebrows Periorbital edema Enlargement of the tongue
Other	Decreased hearing Myalgia and paresthesia Depression Menorrhagia Arthralgia Pubertal delay	Diastolic hypertension Pleural and pericardial effusions Ascites Galactorrhea

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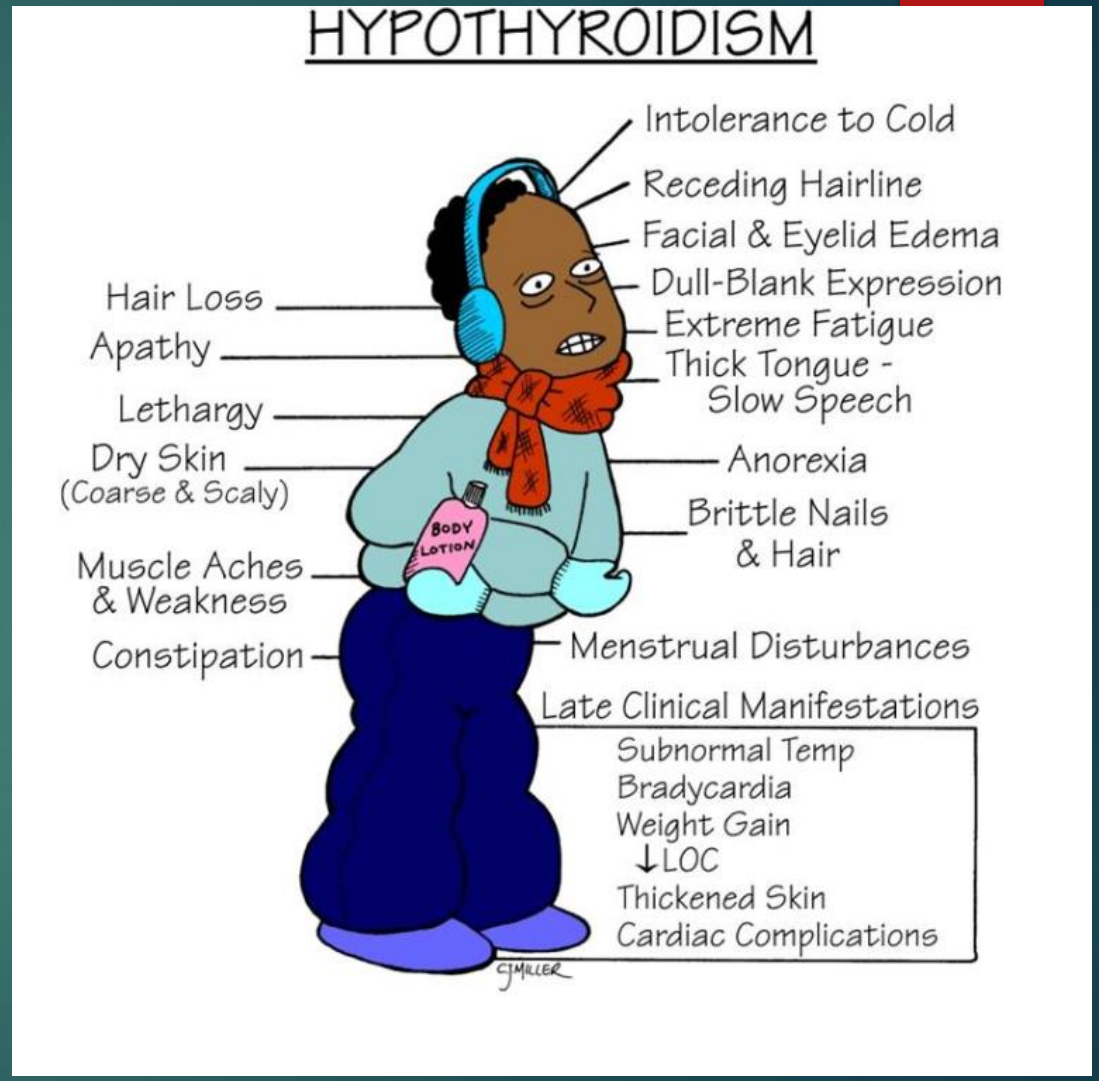

Groups with an Increased Likelihood of Thyroid Dysfunction

Previous thyroid disease or surgery

Goiter

Associated autoimmune disease

Diabetes mellitus, type 1

Celiac disease

Scleroderma

Irradiation of head and neck

Radical laryngeal/pharyngeal surgery

Recovery from Cushing's syndrome

Gout ?

Environmental irradiation ?

Thalassemia major (24)

Primary pulmonary hypertension ?

Polycystic ovarian syndrome

Endometriosis

Drug therapy

Amiodarone

Lithium

Thalidomide

Chemotherapy for sarcoma

Stavudine,-other potent retroviral agents

Tyrosine kinase inhibitors:
Sunitinib, Imatinib, Motesanib, Sorafenib

Sjögren syndrome

Morbid obesity ?

Breast cancer

Hepatitis C (pre-treatment)

Down's syndrome

Turner's syndrome

Biological agents

Interferon alpha

Ribavirin

Interferon beta

Interleukin-2

Therapeutic use of antibodies

Growth hormone treatment

Pituitary or cerebral irradiation

Head trauma

Very low birth weight premature infants

Case

- 28 yo woman c/o fatigue, cold intolerance, depression, constipation and weight gain. She had miscarriage last year. Mother and sister have hypothyroidism
- Labs last month showed TSH 4.1 (normal 0.45-4.5)
- What laboratory test should you?
  - Free T4 (thyroxine)
  - Total T3 (triiodothyronine)
  - TPO
  - Thyroid-stimulating hormone
  - Thyroid stimulating immunoglobulin

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- Detailed history and physical exam are important
  - Puberty, periods, pregnancy and delivery, breast feeding
  - Goiter, skin hypopigmentation, DTR, nails

- OTC supplement
  - ”thyroid supplement” and “Adrenal supplement”
- Meds
- Impending or early pregnancy
- Radiation exposure
- FHx

Case

- 38 yo man c/o fatigue, cold intolerance, depression, constipation and weight gain.
- He has gynecomastia, nipple sensitivity, decreased facial hair, low libido & headache
- PE: gynecomastia, loss of peripheral vision.
- Outside labs showed TSH 1.79
- What laboratory test(s) should you order?
  - Free T4 (thyroxine)
  - Prolactin
  - Cortisol
  - TPO
  - Morning Testosterone

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2/2/2018:

PRL	**26128**
TSH	**1.79**
FT4	**0.5**
FSH	**2.4**
LH	**1.4 L**
Testo	**13**

Case

- Pituitary MRI 2018
  Large lobulated mass sellar and supresellar **4.8x3.5x5.7 cm**

- MRI pituitary in March2019 showed **no mass**

TSH alone is not enough!

- **Pituitary disease**
- **Glucocorticoids and dopaminergic agents** have a potent effect to suppress TSH secretion
- TSH is subnormal in **starvation or caloric deprivation, acute illness, or opioid use**
- Transient increases during **recovery from critical illness**

Case

- 28 yo man c/o fatigue, cold intolerance, depression, constipation and weight gain. Mother and sister have hypothyroidism
- Labs last month showed TSH 5.1 (normal 0.45-4.5)

- What laboratory test(s) should you?
  - Free T4
  - TPO Antibodies
  - Repeat TSH with ref' FT4 in 6-8 weeks from last month
  - Start treatment and repeat TSH in 6-8 weeks

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Case

- 28 yo woman c/o irregular light menses, anxiety, and no wt changes
- OBGYN rec' endocrine w/u.
- Labs last month showed TSH 0.2 (normal 0.45-4.5)
- What laboratory test should you?
  - Free T4 (thyroxine) and Free T3 (triiodothyronine)
  - TPO and Thyroglobulin Antibodies.
  - Repeat Thyroid-stimulating hormone in 1 month
  - Thyroid stimulating immunoglobulin

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  - TPO and Thyroglobulin Antibodies.
  - Repeat Thyroid-stimulating hormone with ref' FT4
  - Thyroid stimulating immunoglobulin

Subclinical Thyroid

- The following five criteria define endogenous subclinical thyroid dysfunction:
  - TSH increased above, or decreased below designated limits
  - Normal free T4 concentration (and free T3 for hyperthyroidism)
  - The abnormality is not due to medication
  - There is no concurrent critical illness or pituitary dysfunction.
  - A sustained abnormality is demonstrated over 3-6 months

f/u on Pituitary Macroadenoma Case

- AUG2019, Pt called asking to review labs done at the PCP office.
  - he did not get surgery but taking Cabergoline
- PCP told the pt he is taking too much thyroid medication and would like to decrease his dose.
- Pt is concerned this is the reason for his anxiety.

- TSH: 0.01 0.45-4.5
  Free T4: 1.24 0.8-1.77
  Free T3: 2.6 2.0-4.4

- **Does he have subclinical hyperthyroidism?**

Monitoring Dose

- Primary Hypothyroidism
  - Monitor TSH levels every 6 weeks after dose adjustment
  - Goal TSH within normal limits
- Central Hypothyroidism
  - Goal Free T4 levels in mid-upper normal range
- Always ask about compliance with medication before dose changes

Case

- 30 yo woman has T1DM and hypothyroidism called the office after having +ve pregnancy test at home.
- She is on insulin pump and CGM. Last A1c 6.2%
- Levothyroxine 50 mcg daily – last TSH 1.8

- What is her TSH target now?

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TSH target in pregnant 0.5-2

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- How to adjust her thyroid medication?
  - 1. Repeat TSH now and in 6 weeks
  - 2. Repeat Ft4 only since TSH is not reliable in pregnancy
  - 3. Double her dose now and triple in the 3/3
  - 4. Increase thyroid dose by 30% now

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  4. Increase thyroid dose by 30% now

TSH 7.3 when she was 3 weeks

Case

- 40 yo woman c/o irregular menses and tremors.
- Pt has neck swelling, but no pain. HR: 103
- Thyroid Glands: diffusely enlarged X3 times, RT >Lt, no nodules, no bruit. fine tremors present. No orbitopathy

- Given his most likely diagnosis what will his thyroid labs look like?

1. TSH elevated, Free T4 Low
2. TSH elevated, Free T4 elevated
3. TSH low, Free T4 Elevated
4. TSH and Free T4 normal
5. I didn't check his thyroid labs because he doesn't have a thyroid condition.

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2. TSH elevated, Free T4 elevated
3. **TSH low, Free T4 Elevated**
4. TSH and Free T4 normal
5. I didn't check his thyroid labs because he doesn't have a thyroid condition.

TSH 0.012
FT4 6.81

“Suppressed” TSH

- Terminology for abnormal TSH values has also become inconsistent
- The term “suppressed” should be avoided in describing subnormal-detectable values
- Undetectable (<0.03 mU/l) and a subnormal-detectable range 0.05-0.4 mU/l
  - Different diagnostic and prognostic significance
  - Probability of progression to overt thyroid dysfunction

Hyperthyroidism/Thyrotoxicosis

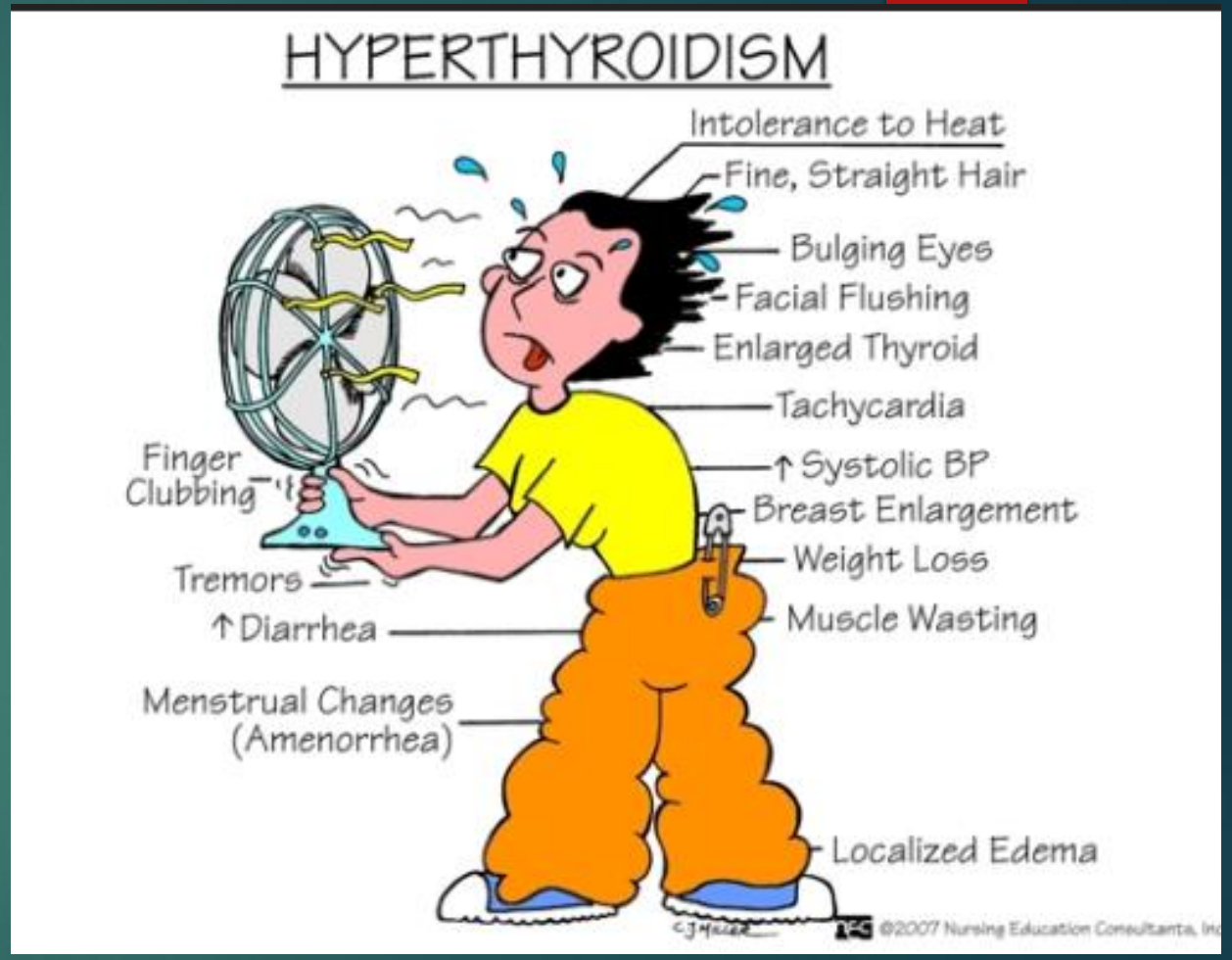
- Excess thyroid hormone levels

Clinical Signs

- Goiter - Pemberton sign
- Bruit in thyroid gland (Graves Disease)
- Tremor
- Tachycardia (Atrial fibrillation)
- Moist skin
- Hair loss
- Exophthalmos (Graves disease)
- Lid Lag (Stare)
- Non-pitting Edema (Graves disease)
- Hyperreflexia
- Acropachy

Clinical Symptoms

- Anxiety
- Palpitations
- Tremor
- Heat intolerance
- Sweating
- Weight Loss
- Loose bowel movements
- Lower extremity edema
- Menstrual irregularities (lighter period)
- Elderly patient may experience depression-like symptoms



nclexies.files.wordpress.com

Thyrotoxicosis: Causes

- Hyperthyroidism (Primary)
  - Graves' Disease
  - Solitary Toxic Nodule
  - Toxic Multinodular Goiter -**Plummer disease of thyroid**
  - Subacute Thyroiditis (Painful)
  - Silent and post-partum Thyroiditis
  - Inflammatory processes
    - Medications, eg, Amiodarone, Lithium
    - Radiation
- Exogenous hormone ingestion

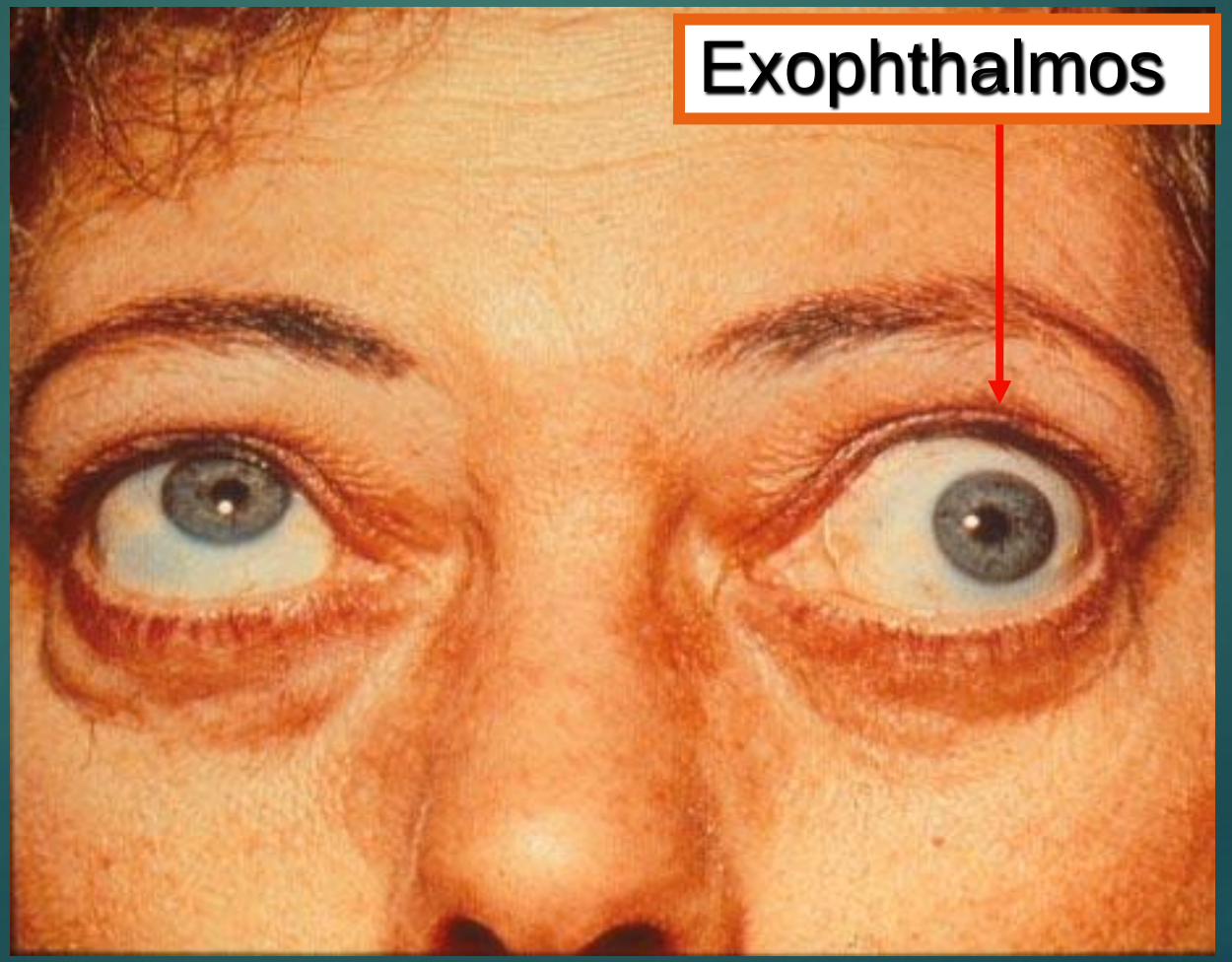
- Secondary
  - TSH Secreting Pituitary Adenoma

Graves' Physical Exam Findings:

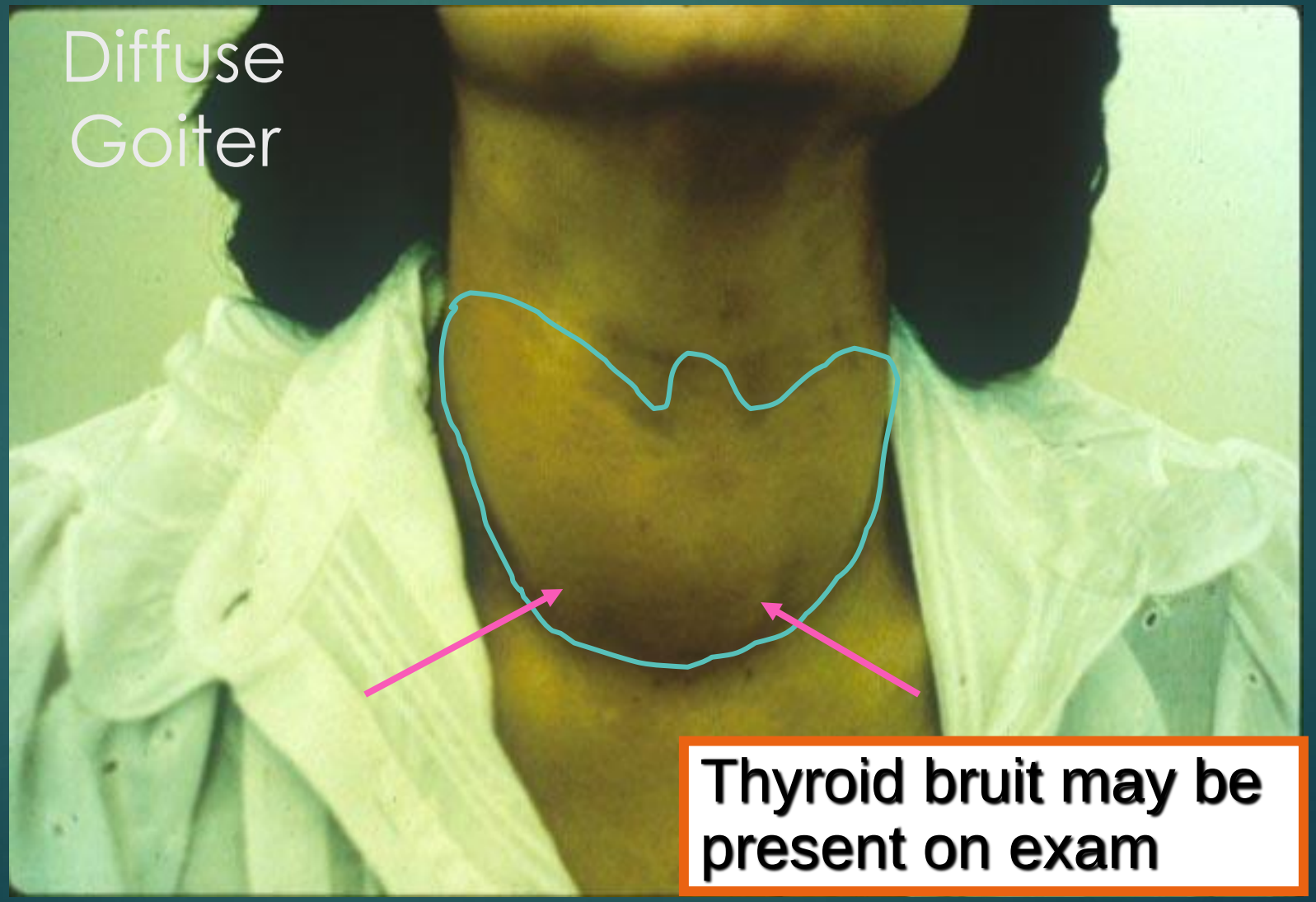
- Exophthalmos

Graves' Physical Exam Findings:

- Infiltrative Ophthalmopathy



Graves' Physical Exam Findings:



Graves' Physical Exam Findings:

Pre-Tibial Myxedema

What shall I order?

- TSH—Low to undetectable
- Free T4—Normal to High
- Free T3—Normal to High
- Thyrotropin Receptor Antibodies
  - TRAB, TSI, TBI
- Radioiodine Uptake and Scan
- Thyroid Ultrasound
  - Useful if nodules present
  - Also looking at blood flow to thyroid gland

Test	Graves Disease	MNG	Toxic Adenoma	Thyroiditis
TSH				
Free T4				
Free T3				
RAI Uptake				
TRAbs				

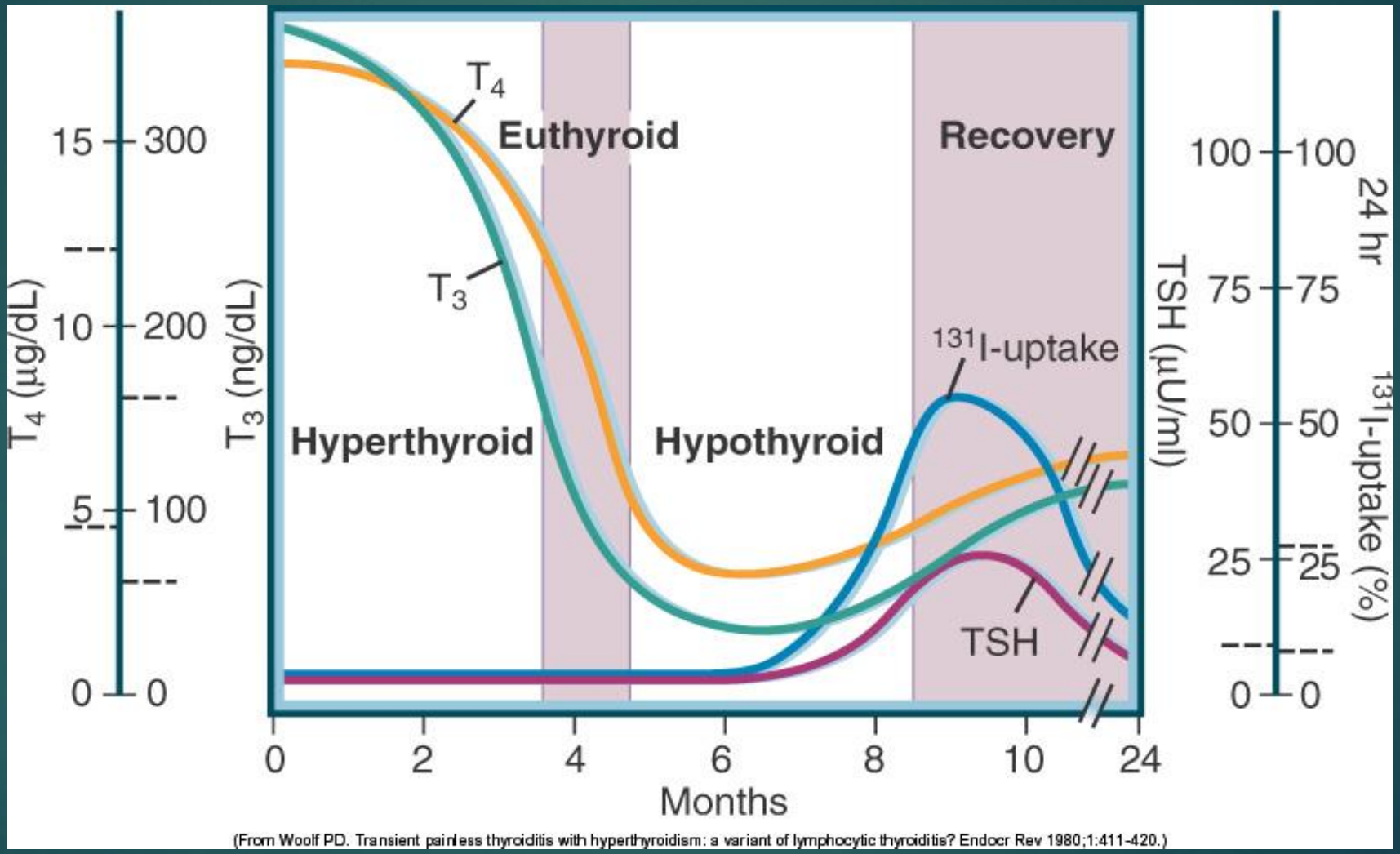
Test	Graves Disease	MNG	Toxic Adenoma	Thyroiditis
TSH	LOW			
Free T4	HIGH			
Free T3	HIGH			
RAI Uptake	Diffuse Increased Uptake			
TRAbs	++			

Test	Graves Disease	MNG	Toxic Adenoma	Thyroiditis
TSH	LOW	LOW		
Free T4	HIGH	HIGH		
Free T3	HIGH	Normal/HIGH		
RAI Uptake	Diffuse Increased Uptake	Patchy increased uptake		
TRAbs	++	--		

Test	Graves Disease	MNG	Toxic Adenoma	Thyroiditis
TSH	LOW	LOW	LOW	
Free T4	HIGH	HIGH	HIGH	
Free T3	HIGH	Normal/HIGH	Normal/HIGH	
RAI Uptake	Diffuse Increased Uptake	Patchy increased uptake	Single Focus with suppressed rest of gland	
TRAbs	++	--	--	

Test	Graves Disease	MNG	Toxic Adenoma	Thyroiditis
TSH	LOW	LOW	LOW	Low/Normal/High
Free T4	HIGH	HIGH	HIGH	Low/Normal/High
Free T3	HIGH	Normal/HIGH	Normal/HIGH	Low/Normal/High
RAI Uptake	Diffuse Increased Uptake	Patchy increased uptake	Single Focus with suppressed rest of gland	Decreased
TRAbs	++	--	--	-- (possibly + TPO)

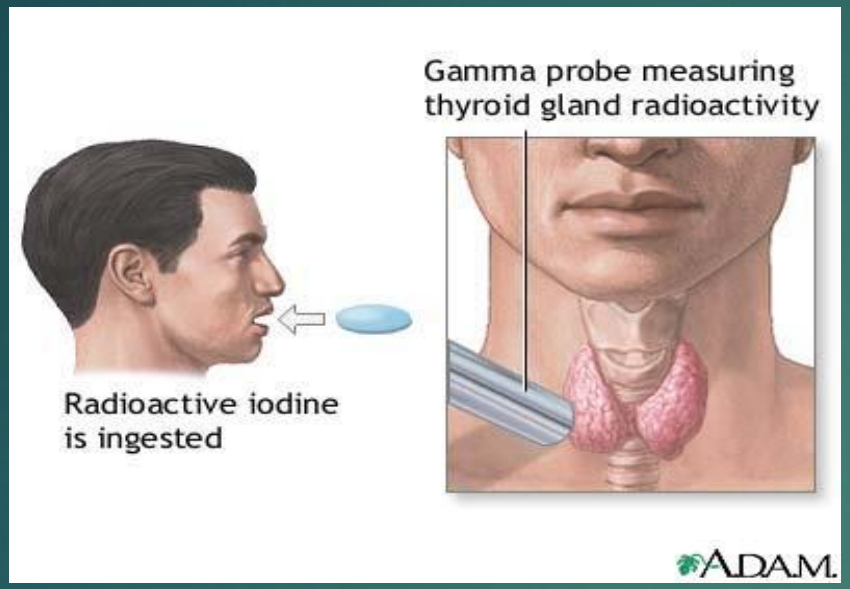
Silent Thyroiditis: Course

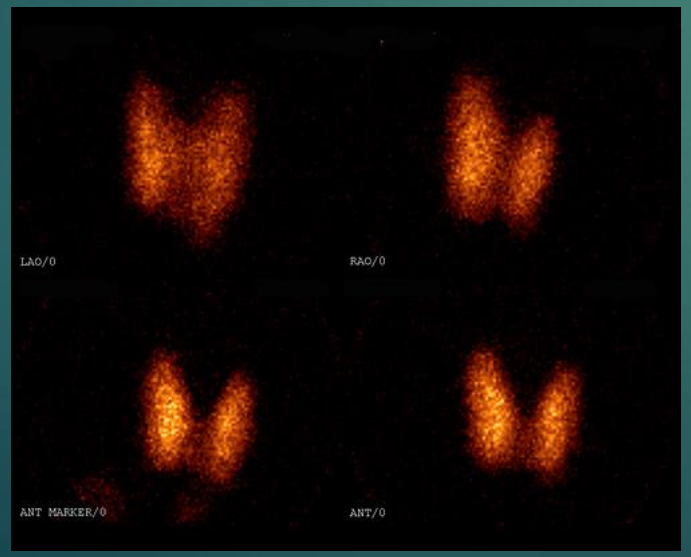


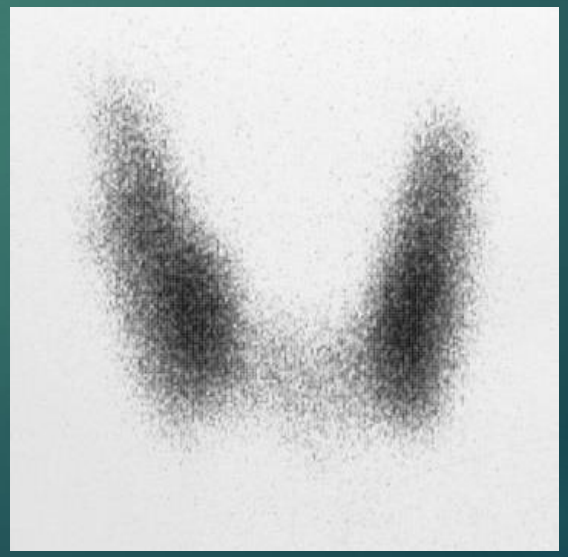
(From Woolf PD. Transient painless thyroiditis with hyperthyroidism: a variant of lymphocytic thyroiditis? Endocr Rev 1980;1:411-420.)

Williams Textbook of Endocrinology, Fig 11-16, 2008

Thyroid uptake and scan

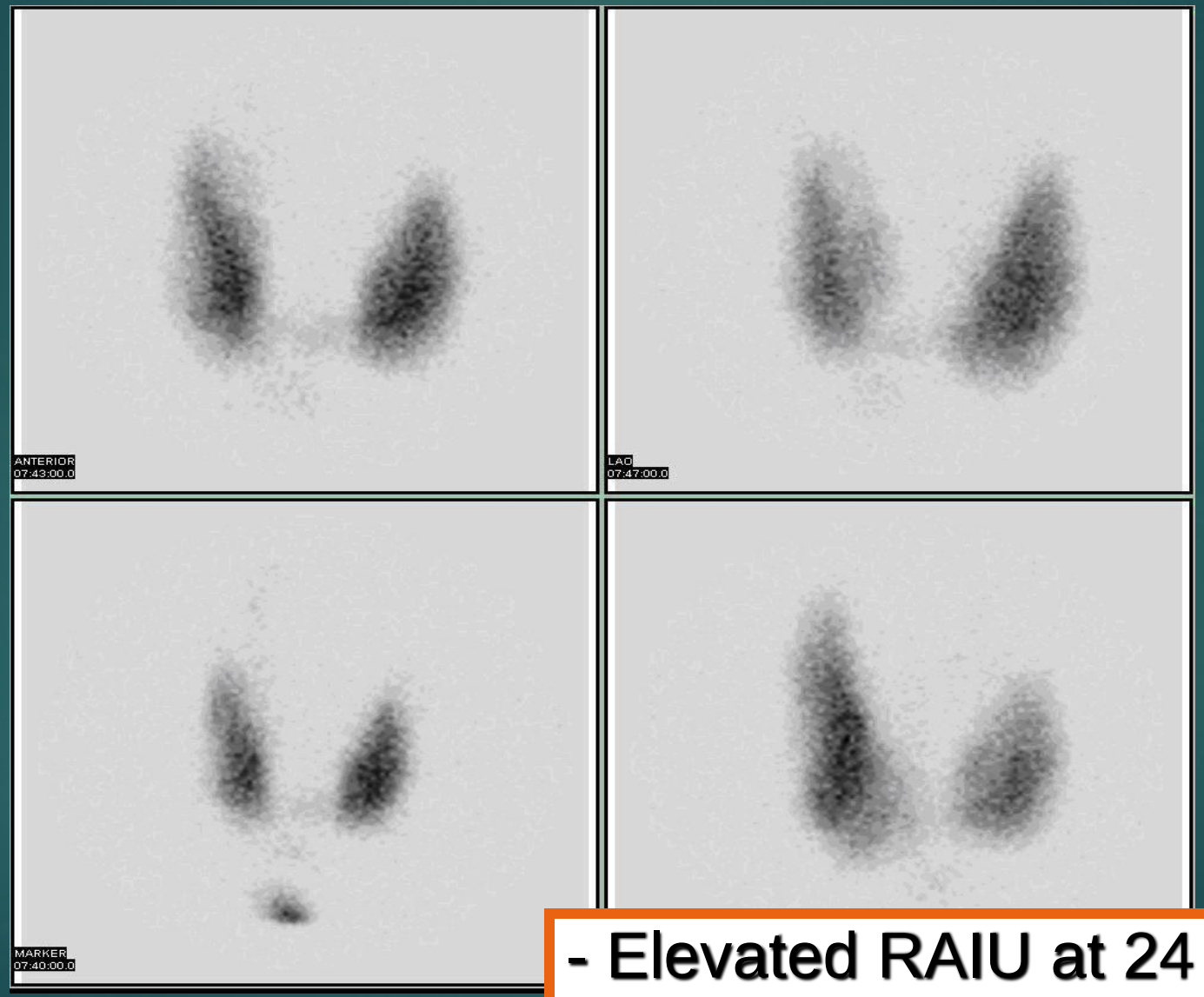






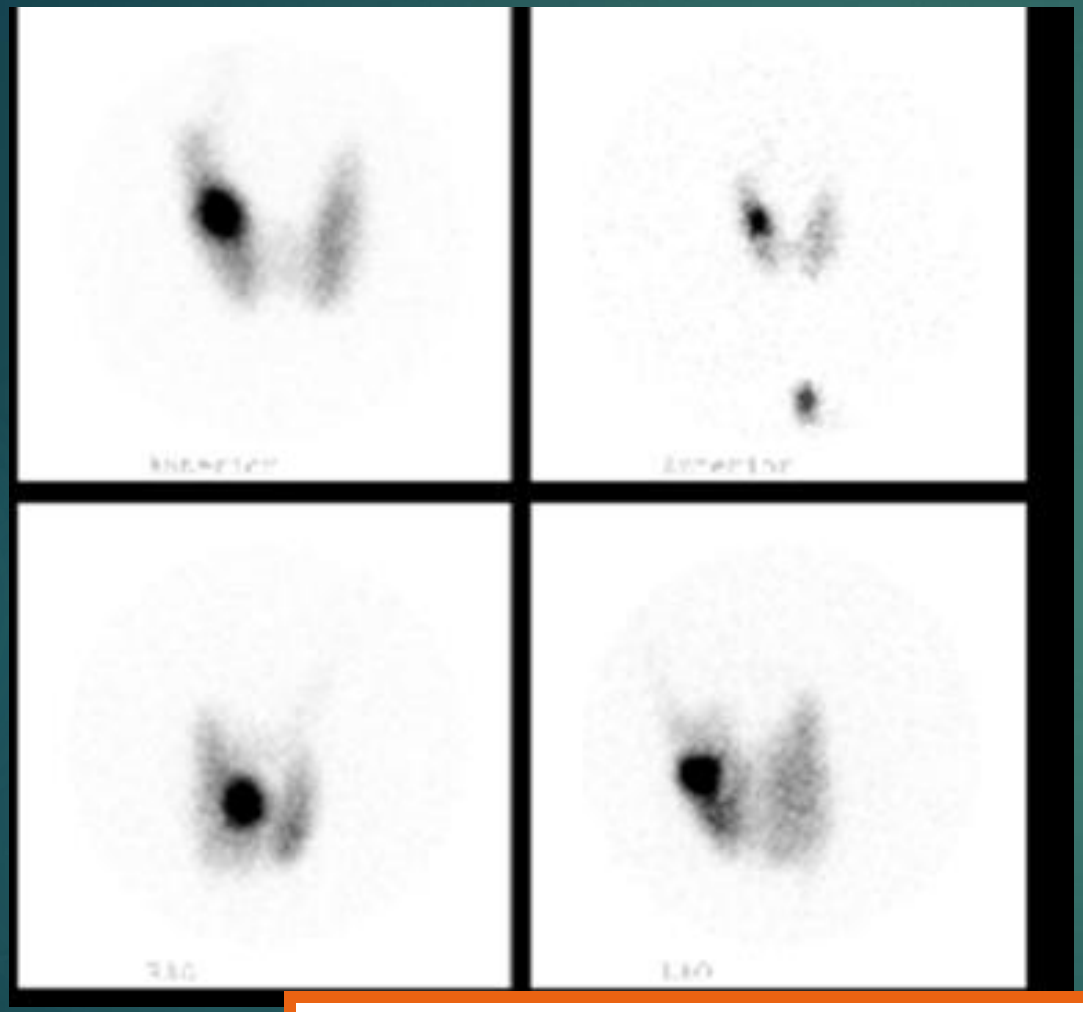
Images from Google.com

What is the diagnosis?



- Elevated RAIU at 24 hours
- Diffuse uptake on scan

What is this diagnosis?



- Focal area of uptake on scan (left panel) corresponding to nodule on ultrasound (right)

Diagnosis?

- Low RAIU at 24 hours
- None or limited uptake on scan

Hyperthyroid Treatment Options

- Medical Treatment
- RAI ablation (I-131)
- Surgical Resection

Hyperthyroid Treatment Options

- Medical Treatment
  - Beta Blockers: Propranolol, Metoprolol, Atenolol
  - Thionamides: Methimazole, Propylthiouracil (PTU)
    - Adverse reactions: hepatic toxicity, agranulocytosis, rash
  - Monitor TSH and T4
  - Goal FT4/TSH within normal limits

Hyperthyroid Treatment Options

- **RAI ablation (I-131)**
  - Takes up to 6 months to normalize
  - Often hypothyroidism occurs afterwards requiring Levothyroxine
  - Use caution in exophthalmos
  - Contraindicated in pregnancy or breast feeding

Hyperthyroid Treatment Options

- Surgical Resection
  - Immediate
  - Requires Levothyroxine

Thank You!!

Questions?

References

- Uptodate articles
  - Diagnosis of hyperthyroidism
  - Overview of the clinical manifestations of hyperthyroidism in adults
  - Diagnosis of and screening for hypothyroidism in nonpregnant adults
  - Treatment of primary hypothyroidism in adults
  - Clinical Manifestations of hypothyroidism
- Williams Textbook of Endocrinology 13th edition