Before discussing thyroid diseases, let's review some **physiology** and **tests** which will help with decision making.

Physiology

TRH is secreted by the hypothalamus. It stimulates the anterior pituitary to make **TSH**. TSH stimulates the thyroid to make **T4/T3** in a 10:1 ratio. T3 is **more potent** than T4; T4 is converted into T3 in the periphery to exert its effects. Most of the T4 is **inactive**, bound to **Thyroglobulin Binding Protein**. Only 0.1% is free and active. **Free T4** is tightly regulated and **doesn't change** in the absence of thyroid disease. **Total T4** changes with alterations in **protein** (pregnancy, OCPs, cirrhosis, nephrosis). The effect of T4/T3 is to ↑ metabolism (**catabolic** and **thermogenic**).

Tests

Screen people with a history of thyroid disease and any **woman over the age of 50**. The best screen is the **TSH**. If it's: low = hyperthyroidism, high = hypothyroidism, normal = euthyroid.

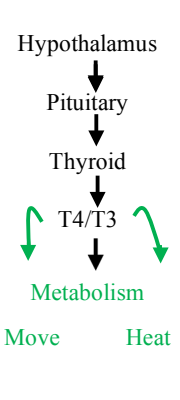
Looking at **Free T4** is useful in confirming an atypical screening TSH because there's a disease associated with every TSH+T4 combination. However, a **normal TSH means Euthyroid** (highly sensitive). Do NOT get a Free T4 if TSH is normal; instead, ignore the Free T4 if TSH is normal. Sick people can get what's called **sick euthyroid syndrome** (they're sick, T4 is wacky but TSH is normal), but there's no need do anything.

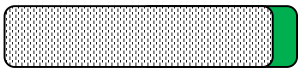
Free T3 is pretty much useless unless you suspect hyperthyroid despite a normal T4.

Look at the chart to the right. What it says is, "the only diseases that really matter are High TSH + Low T4 and Low TSH + High T4." That's **primary hypothyroidism** and **primary hyperthyroidism**. If there's a primary hypothyroidism, simply give synthroid.

When a **hyperthyroid** patient is encountered a **RAIU scan** can help with a diagnosis. Radiolabeled Iodine is picked up by active thyroid tissue which lights up = "**hot**" while inactive tissue does not = "**cold.**" Finally, there are **antibodies** that when present in some diseases are **specific** (but they're **not sensitive)**. While helpful, they're academic rather than confirmatory.

Confirmation is made by **FNA Biopsy**. More on Biopsying and RAIUs in the thyroid nodule section.





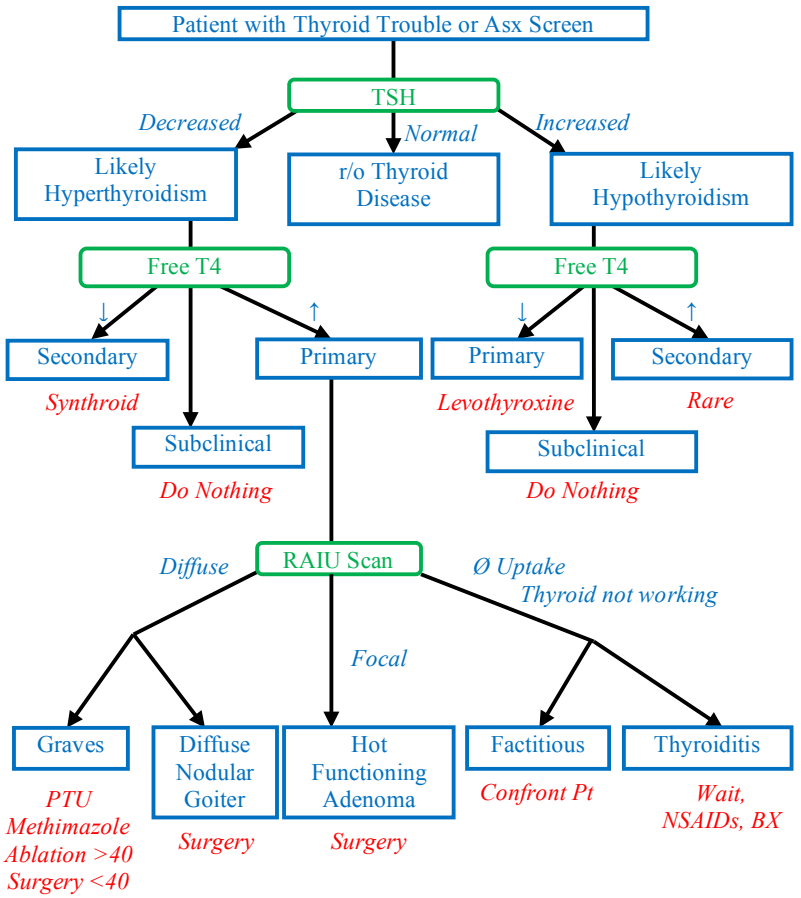
Thyroid Binding Globulin Bound T4 (inactive)

Estrogen: Pregnancy ↑Protein, ↑Total T4, Nrml Free T4

Cirrhosis: Nephrosis ↓Protein, ↓Total T4, Nrml Free T4

Tests

TSH	Best Screening Test. ↑ Hypothyroid, ↓ Hyperthyroid Normal = Euthyroid. Some states can fool you, so…
Free T4	Confirms TSH findings
Free T3	Only if ↓ TSH and normal or ↓ T4
RAIU	Evaluate a 1° Hyperthyroidism. Differentiates between causes of hyperthyroid. May not be necessary with a good story



Hypothyroidism

Introduction

Hypothyroidism is a product of ↓metabolism secondary to ↓T4. This causes the patient to slow down. A variety of things slow: heart (**bradycardia**), mind (**dementia**), reflexes (↓ **DTRs**), bowel function (**constipation**), and metabolism (**weight gain**). Hypothyroidism is easier than hyperthyroidism because regardless of how they got there, there's only one treatment - **Levothyroxine**. Screen with **TSH** (it'll be elevated). Confirm with **T4** (it'll be low) and replace as needed. Don't do any **biopsies** or **RAIU scans** as they are extraneous.

Iatrogenic

The **most common** cause of hypothyroidism is **iatrogenic**. We treat hyperthyroidism and cancer with ablation or surgery, leaving the patient without a thyroid. This is why close follow up is necessary with these patients. Eventually, the circulating T4 diminishes and the patient becomes hypothyroid. When the patient's TSH begins to rise, exogenous **T4** must be substituted with **Levothyroxine**.

Hashimoto's

The **most common disease** that causes hypothyroidism is Hashimoto's. It's caused by a **lymphocytic infiltrate** secondary to antibodies (**Antithyroid Peroxidase** and **antithyroglobulin 90% Specific**). The only way to definitively diagnose is with a biopsy, but because Hashimoto's is **irreversible** and the patient presents with hypothyroidism, just treat the hypothyroid. The natural course of the disease is a period of transient hyperthyroidism followed by transient hypothyroidism.

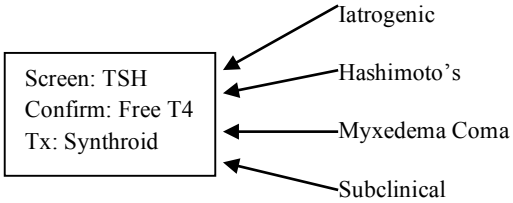
Myxedema Coma

If the hypothyroid gets really bad, or there's a precipitating event, everything shuts down. Like thyroid storm this is a **medical emergency.** This time it's characterized by **hypothermia**, **hypotension**, and **coma**. Initiate supportive care (**IVF**, **Warming Blankets**) and give **high-dose T4**. Because peripheral conversion is impaired, also give straight up **T3** if **T4 fails** or symptoms are severe from the start.

Subclinical

If the ↑ **TSH** + **Normal T4/T3**, the patient needs to be followed. If **Ab** ⊕ they'll eventually progress to hypothyroid. If **Ab** ⊖ they might get better. There's no consensus on when to start treatment, but generally make the patient happy by **treating when symptoms start** and treat everyone with **overt hypothyroidism** (**TSH>10**).

Hypothyroid	Myxedema coma
Bradycardia	Hypothermia
Dementia	Hypotension
↓DTRs	Altered Mental Status
Constipation	
Brittle Hair/Nail	



Ø Complicated Nonsense. Be able to spot it, give Levothyroxine as needed. That's it.

Hyperthyroidism

Thyroid Storm
- Fever
- Delirium
- Hypotension

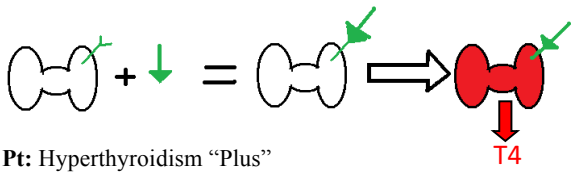
Hyperthyroidism
- Heat Intolerance
- Diarrhea
- Sweating
- Palpitations
- Weight Loss
- Afib

Introduction

Hyperthyroidism is caused by too much T4. It can come either from **overproduction** as in Graves, **exogenous intake** (factitious or struma ovarii), or ↑**release** as in Thyroiditis. The symptoms are ↑ **metabolism** (heat intolerance, diarrhea, sweating, palpitations, tachycardia, Afib, and Weight Loss). Determining a definitive diagnosis may require a **biopsy,** but it's usually not necessary.

1) Graves

An **autoimmune disease** caused by **thyroid stimulating antibodies** that mimic TSH and cause proliferation of cells as well as ↑ production of T4. This causes a **diffuse homogeneous** enlargement of the thyroid. It's the most common cause of hyperthyroidism. Beyond the usual hyperthyroid condition there can also be **pretibial myxedema** and **ophthalmopathy** (**proptosis** and **exophthalmos**) - both unique to Graves. It's essentially a clinical diagnosis, but thyroid labs will show: ↓ **TSH**, ↑ **T4**, and a **Diffuse RAIU**. **Antibodies** (80% Sp, Ø Se) can be checked, but the focus should be on treatment. Control their **symptoms** with **propranolol**. To help them out of a hyperthyroid state use **PTU** (safe in **p**regnancy) or **Methimazole**. Be careful not to start these drugs if awaiting RAIU or ablation. These patients require definitive therapy: **Radioactive Iodine Ablation** or **Surgery** (usually if pregnant, 2nd trimester surgery). Since this will make them hypothyroid follow up and start **synthroid** when hypothyroid. Finally, the **ophthalmopathy** may worsen despite treatment; treat it with **steroids** or **radiation**.



Pt: Hyperthyroidism "Plus"
- Pretibial Myxedema = Swelling of the Feet
- Ophthalmopathy = Proptosis + Exophthalmos

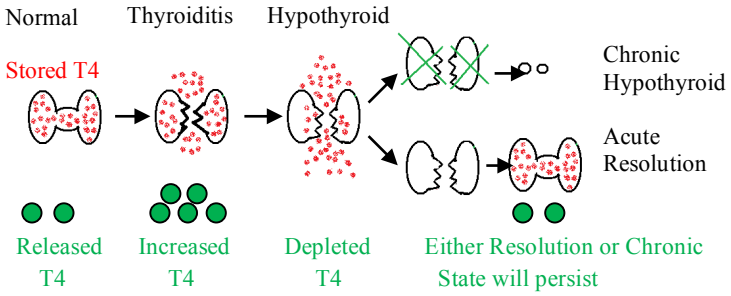
Dx: ↓ TSH, ↑ T4, Diffuse RAIU ↑, ⊕ Anti-Thyroid Ab

Tx: Acute: Propranolol to control adrenergic symptoms
PTU or Methimazole to quell hyperthyroid state
Chronic: Radioablation with radioactive iodine
Surgery if Pregnant

F/u: Synthroid when hypothyroid, after treatment
Steroids/Radiation for Ophthalmopathy, if worsens

2) Thyroiditis

In an inflammatory process, even **destructive ones**, the first step is to break open the cells and **release stored T4**. This causes a **transient hyperthyroidism**. If the insult is acute (**infection/trauma**) or subacute (**subacute thyroiditis**) the thyroid will recover - sometimes with a period of hypothyroidism. Rarely does this require intervention. If chronic (Hashimoto's), destruction wins = persistent hypothyroidism. Because TSH/T4 looks like Graves, differentiate with **RAIU** (cold inactive thyroid) and **ESR/CRP** (elevated in Hashimoto's only).

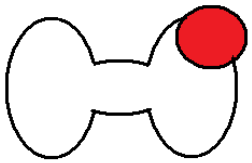


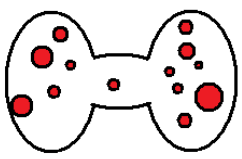
Thyroiditis

Acute: trauma, infection, drugs	Supportive	Resolution
Subacute: Silent = Lymphocytic, ⊕ TPO	Antibodies	Resolution
Painful = Viral Granulomas	Supportive	
Chronic: Hashimoto's	NSAIDs Steroids	Resolution Hypothyroid

3) Toxic Multinodular Goiter or Adenoma

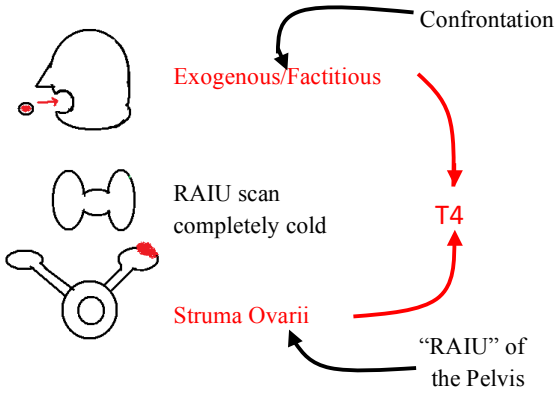
For whatever reason, **autonomous nodules** referred to as "**hot**" produce T4 without an off switch. Rarely cancer (see workup for thyroid nodules), nodules can usually be seen on **RAIU** or felt on an **exam**. Because the rest of the thyroid senses too much T4 it shuts off, so only the toxic nodules light up. "Toxic" means "Makes T4."


Toxic Adenoma


Toxic Multinodular Goiter

4) Factitious and 5) Struma Ovarii

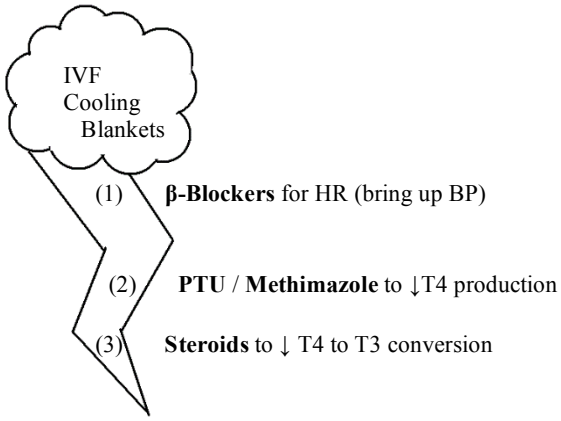
If someone that's normal to begin with gets levothyroxine the thyroid will **shut off** (↓ **TSH Ø RAIU**). Still, the T4 will remain high. The only way this can happen is if she's taking it **exogenously** (as in **Synthroid** to lose weight or we dosed a hypothyroid patient with too much of it) or if there's a **tumor somewhere** other than the thyroid (usually a dermoid cyst/teratoma of the ovary). Use the **Sestamibi scan** of the ovaries to r/o tumor then confront her about her factitious disorder. These two are together because 1 - the RAIU is normal and 2 - on the test both will be woman.

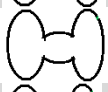


6) Thyroid Storm

When the hyperthyroidism gets out of control it's a life threatening **emergency**. It's a clinical diagnosis - defined by someone with hyperthyroidism plus **alarm symptoms** = **fever, delirium**, and **hypotension**. They have such heat intolerance that they burn up and such tachycardia that there's hypotension. After making the diagnosis start immediate supportive therapy with **IVF** and **cooling blankets**. To treat, start **Propranolol** (β-Blockers) to slow the heart down and get the BP back up. Give **PTU or Methimazole** to reduce the production of new thyroid hormone. Finally, **steroids** will reduce the T4 to T3 conversion.

In storm, **Iodide** can be given. The thyroid can **either** pick up Iodide or make Thyroid Hormone; it preferentially picks up Iodide. For a temporizing measure, use Iodide to ↓ T4. If not fixed that Iodide will be used to make T4 (**Iodide Escape**). That'll make the patient worse. A single storm is indication for definitive therapy (removing the thyroid altogether).



Disease	*Path*	*Patient*	*TSH*	*T4*	*RAIU*	*Diagnosis*	*Treatment*
Graves	Autoimmune stimulating antibodies	Hyperthyroid +ophthalmopathy +Pretibial Myxedema	↓	↑		**Anti-TSH-R Antibody**	Propranolol PTU/Methimazole Radioactive Ablation Surgery
Thyroiditis Painless Subacute Lymphocytic +TPO Painful Subacute Granuloma Viral Chronic Lymphocytic		Either painful or painless transient hyperthyroidism that may persist	↓	↑	N/A	Bx for Infiltrate **Anti-Peroxidase Antibody** (TPO)	NSAIDs Wait **Synthroid** if Hypothyroid
Toxic Goiter	Autonomous Nodules Secrete T4	Hyperthyroid with palpable nodules	↓	↑		Bx if suspicious for cancer	
Factitious	Exogenous T4, Oral	Hyperthyroid, often in a woman	↓	↑		Confrontation	Stop taking exogenous T4
Struma Ovarii	Ovarian tissue Dermoid Cyst produces T4	Hyperthyroid, always in a woman	↓	↑		"RAIU" of the Ovaries, **Sestamibi Scan**	Remove the Cyst
Thyroid Storm	Super mega ultra hypothyroidism	Hyperthyroid ⊕ CHF ⊕ AMS ⊕ Fever	↓↓	↑↑	Any , no one diagnostic	Diagnosis Ø Needed Just Treat, and treat fast	IVF, Cooling Blankets, Steroids, Propranolol, PTU, Iodide