# Hyperthyroidism in Primary Care

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# Disclosures

I. None relevant to today's topic (or thyroid disease)

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| **SPEAKERS BUREAU/ HONORARIA:** | **Diabetes/Obesity:** CPD Network Association, Eli Lilly, Novo Nordisk, Dexcom, Abbott (FreeStyle Libre) |
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| **OTHER:** | Assistant Professor in Medicine (Dalhousie) |

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CPD = Continuing Professional Development

# Objectives

*Patient Oriented

I. Explain the most common **causes** of hyperthyroidism in adults and an *approach to initial **workup**
II. Understand some **nuances** and possible **pitfalls** in thyroid function interpretation and investigation
III. Outline the **initial treatment** of patients with common forms of hyperthyroidism
IV. List the criteria for involving **endocrinology** (and what to include in the referral)




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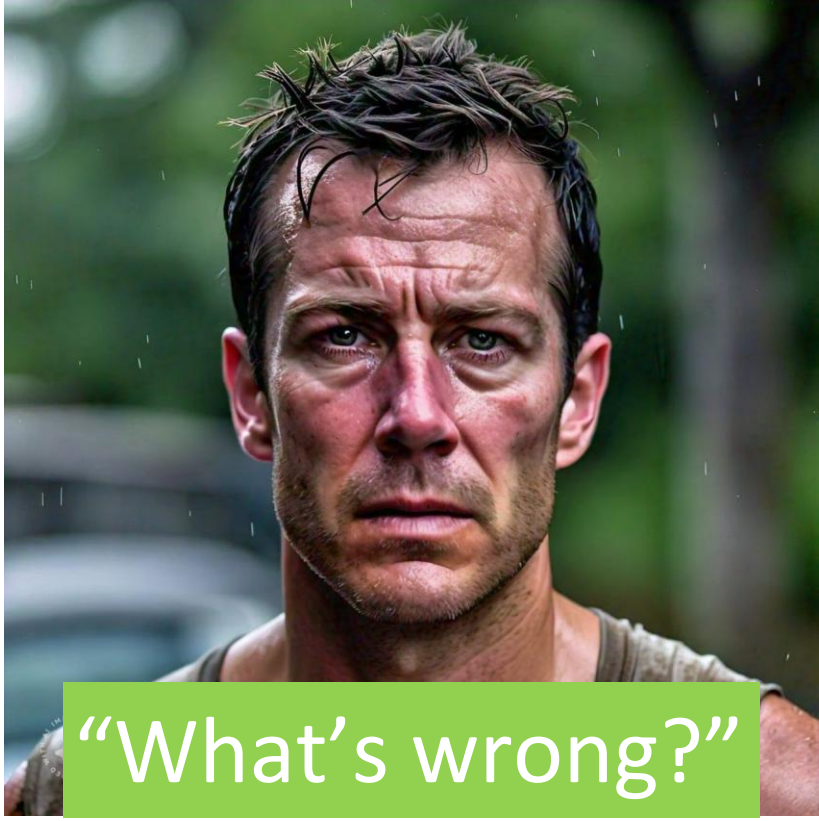
“I think there is something wrong with my thyroid”

# Case: DQ 38M




- New diagnosis of hyperthyroidism
- 2 weeks of anterior neck pain, swelling following upper respiratory tract infection
- 1 week of palpitations, tremor, diaphoresis, anxiety
- Past Medical History: nil
- Medications: *biotin supplements (for "hair health")
- Exam: tremor, tachycardia, ?L-sided nodule
- TSH undetectable ↓, fT4 32.2 ↑, CRP 110 ↑

Next steps?



Generated image by Meta AI, 2024

TSH = thyroid-stimulating hormone; fT4 = free thyroxine; CRP = C reactive protein

# “Why do I feel unwell?”

# Case 2: GD 73M

"Why do I feel unwell?"

- New diagnosis of atrial fibrillation and heart failure
  - Also found to have hyperthyroidism
- 2 week history of palpitations
- Past Medical History: reflux, allergies, gout
- Medications: rabeprazole, cetirizine, allopurinol (no biotin)
- Exam: tachycardia, heart failure, normal thyroid
- TSH undetectable ↓, fT4 28.4↑

Next steps?



Generated image by Meta AI, 2024

TSH = thyroid-stimulating hormone; fT4 = free thyroxine

# “Why is my thyroid high?”

# Case 3: TA 43F

"Why is thyroid high?"

- Recurrent hyperthyroidism
- 6 weeks palpitations and weight loss after upper respiratory tract infection
- Past Medical History: ?hyperthyroidism in India
- Medications: carbimazole x few months ~1year ago, no biotin
- Exam: palpable R nodule
- TSH undetectable ↓, fT4 17.9, fT3 7.4↑

"T3-toxicosis"

Next steps?



Generated image by Meta AI, 2024

TSH = thyroid-stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine

# I. Hyperthyroidism:

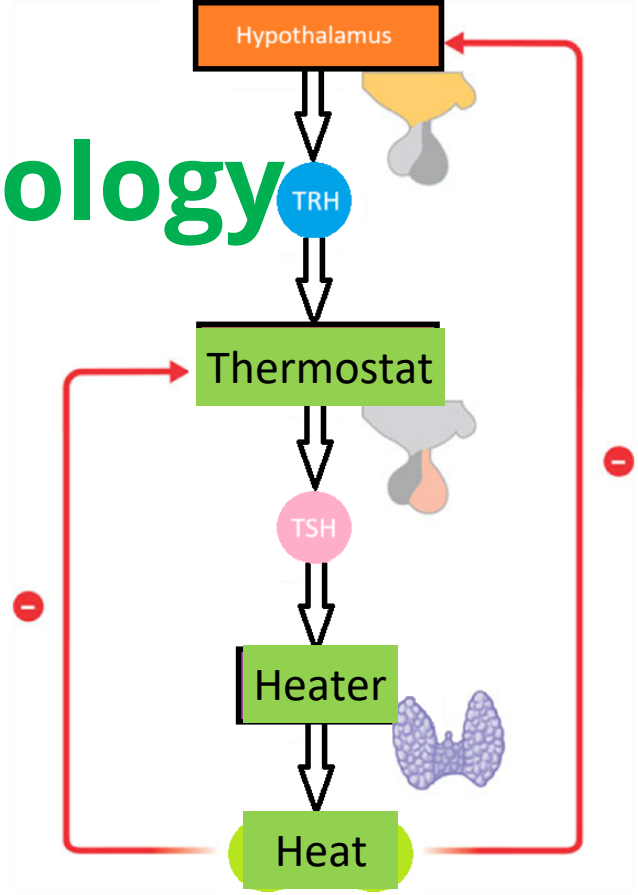
Terminology: technical clarification

- Thyrotoxicosis: clinical condition of excess thyroid hormone in serum
- Hyperthyroidism: overproduction of thyroid hormone from overactive gland
  (Practically, I use these terms interchangeably)
  - Subclinical: ↓ TSH, normal fT4/fT3
  - Overt: ↓ TSH, ↑ fT4/fT3



[2]Ross et al. 2016; [3]Ross et al. 2025
TSH = thyroid-stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine

# I. Hyperthyroidism: Etiology




1. Overproduction of thyroid hormones (T4 and T3)
   - Excessive stimulation by trophic factors
   - Constitutive activation (autonomy)
2. Release of stored thyroid hormones
3. [Extrathyroidal source of thyroid hormones]

"Why is my thyroid high?"



[2]Ross et al. 2016; [3]Ross et al. 2025

TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine

# I. Hyperthyroidism: DDx

## Excess synthesis vs. release?

| Increased RAIU[a] | Decreased RAIU |
|---|---|
| TSH-induced hyperthyroidism | Inflammatory thyroid disease |
| TSH-secreting tumors | Subacute thyroiditis |
| Selective pituitary resistance to $T_4$ | Painless thyroiditis |
| Thyroid stimulators other than TSH | Ectopic thyroid tissue |
| TSAb (Graves' disease) | Struma ovarii |
| hCG (trophoblastic diseases) | Metastatic follicular carcinoma |
| Thyroid autonomy | Exogenous sources of thyroid hormone |
| Toxic adenoma | Medications containing thyroid hormone or iodine |
| Multinodular goiter | Food sources containing thyroid gland |

[a]The RAIU may be decreased if the patient has been recently exposed to excess iodine.

| THYROTOXICOSIS: MAJOR CAUSES |
|---|
| **EXCESS SYNTHESIS (HYPERTHYROIDISM)** |
| **Autoimmune:** **Graves' disease**, **Hashimoto's** |
| **Autonomous thyroid tissue:** **Toxic adenoma**, **Toxic multinodular goitre** |
| **TSH-mediated:** TSH-producing adenoma (TSHoma), Non-neoplastic TSH-mediated |
| **hCG-mediated:** Hyperemesis gravidarum, Trophoblastic disease (choriocarcinoma, molar) |
| **EXCESS RELEASE (PREFORMED)** |
| **Thyroiditis:** Subacute granulomatous [de Quervain's], Painless (silent, lymphocytic – postpartum), Medications (**amiodarone**, **lithium**, **immune checkpoint inhibitor**), Radiation, Palpation |
| **Congenital:** Thyroid agenesis/dysgenesis, Defects in hormone synthesis |
| **EXCESS EXOGENOUS** |
| **Thyroid Replacement:** T4, T3 |
| **Iatrogenic:** TSH suppression (e.g. cancer) |
| **Factitious Hyperthyroidism** |
| **ECTOPIC** |
| **Struma ovarii:** Ovarian teratoma |
| **Metastatic Thyroid Cancer:** Follicular Carcinoma |
| *Adapted from [1]AAFP, [2]ATA, [3]Ross et al. 2025 |



[1]Kravets 2016

TSH = thyroid-stimulating hormone; T4 = (levo)thyroxine; T3 = liothyronine

hCG= human chorionic gonadotropin; RAIU = radioactive iodine uptake; TSAb = thyroid-stimulating antibody

# I. AAFP Approach

## The "Big Three":

1. Thyroiditis
2. Graves' disease
3. Toxic nodule(s)

Others:

- Medications
- hCG
- TSH
- Ectopic

**Table 1. Etiology and Pathogenesis of Hyperthyroidism**

| *Etiology* | *Mechanism* |
|---|---|
| **Most common causes** | |
| Graves disease | Autoimmune process in which antibodies stimulate the TSH receptor leading to overproduction of thyroid hormones |
| Painless or transient (silent) thyroiditis | Autoimmune destruction of thyroid tissue leading to a release of preformed thyroid hormones |
| Toxic adenoma (Plummer disease) | Somatic mutation in TSH receptor or Gs alpha gene in a thyroid nodule |
| Toxic multinodular goiter | Expansion of clonogenic cells with an activating TSH receptor mutation |
| **Less common causes** | |
| Drug-induced thyroiditis | Overproduction of thyroid hormones (amiodarone-induced thyrotoxicosis type 1) or release of preformed thyroid hormones (amiodarone-induced thyrotoxicosis type 2, interferon alfa, interleukin-2, or lithium) |
| Hyperemesis gravidarum | High level of β-hCG stimulates TSH receptors |
| Postpartum thyroiditis | Variant of painless thyroiditis with the same mechanism, occurring after delivery |
| Subacute granulomatous (de Quervain) thyroiditis | Painful inflammation of the thyroid gland caused by viral infection, often with fever, triggering a release of preformed thyroid hormones |
| **Rare causes** | |
| Factitious thyrotoxicosis | Surreptitious ingestion of thyroid hormones |
| Metastatic follicular thyroid cancer | Metastasis of functional follicular thyroid cancer |
| Struma ovarii | Ectopic thyroid tissue in ovarian dermoid tumor produces thyroid hormones |
| Trophoblastic tumor or a germ cell tumor | Tumor produces β-hCG, which stimulates thyroid TSH receptors |
| TSH-secreting pituitary adenoma | Tumor secreting large quantities of TSH, and not responding to thyroxine and triiodothyronine feedback |

*β-hCG = beta human chorionic gonadotropin; TSH = thyroid-stimulating hormone.*



[1]Kravets 2016
AAFP = American Academy of Family Physicians

“Could this be caused by my medications?”

# Interfering Agents

"What about my meds?"

| DRUGS AND THYROID FUNCTION | |
|---|---|
| **HYPOTHYROIDISM** | |
| **Inhibition of Hormone Synthesis or Release** | Thiomanides, **Lithium**, Perchlorate, Aminoglutethimide, Kelp, **Iodine** (Amiodarone, Contrast, Iodide [SSKI], Expectorants, Betadine douches, Topical antiseptics), Thalidomide |
| **Decrease T4 Absorption** | Calcium, Iron, Cholestyramine, Colestipol, Colesevelam, Chromium, Aluminum hydroxide, Sucralfate, Raloxifene, Proton pump inhibitors, Sevelamer, Sertraline, Lanthanum carbonate |
| **Immune Dysregulation** | Interferon alfa, Interleukin-2, Immunotherapy (**checkpoint inhibitors**) |
| **TSH Suppression** | Dopamine, Bexarotene (increased T4 clearance) |
| **Destruction** | Immunotherapy (**checkpoint inhibitors**), Tyrosine kinases inhibitors |
| **Type 3 Deiodination** | Tyrosine kinases inhibitors |
| **ABNORMAL THYROID FUNCTION TESTS** | |
| **Low TBG** | Androgens, Danazol, **Glucocorticoids**, Niacin, L-asparaginase |
| **Decreased T4 Binding** | Salicylates, Salsalate, Furosemide, Heparin, Non-steroidal anti-inflammatory drugs |
| **Increase T4 Clearance** | Phenytoin, Carbamazepine, Rifampin, Phenobarbital, Ritonavir, Imatinib |
| **TSH Suppression** | Dopamine, **Glucocorticoids**, Octreotide |
| **Impaired T4 to T3 Conversion** | **Amiodarone**, Propylthiouracil, Contrast/Iiopanoic acid, **Glucocorticoids**, Propranolol, Nadolol |
| *Adapted from [2]ATA, [1]AAFP, [4]Ross et al. 2025 | |

*Pearl: review medication changes

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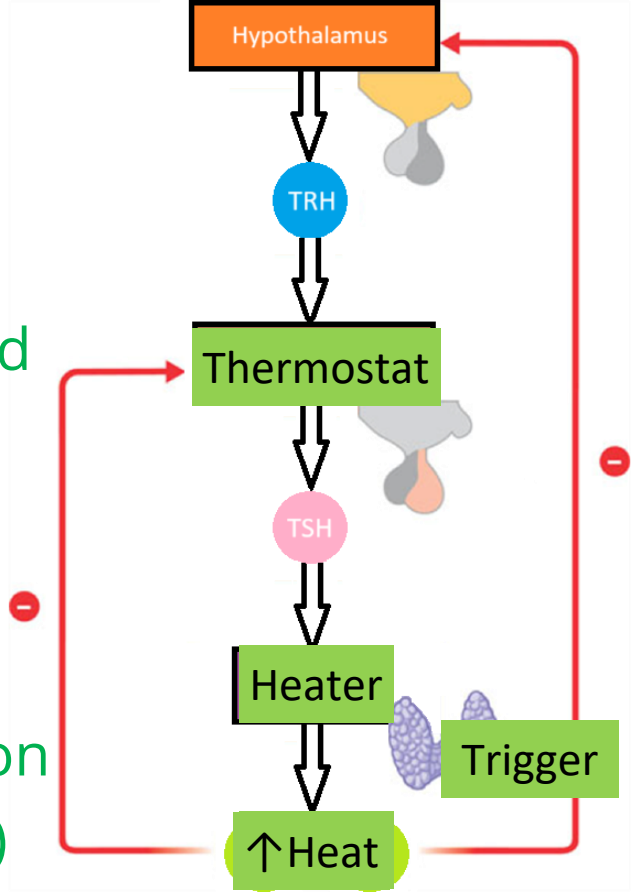
[2]Ross et al. 2016; [1]Kravets 2016

TSH = thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine; TBG: thyroxine binding globulin

PPIs = proton pump inhibitors; SSKI = saturated solution of potassium iodide

# 1. Thyroiditis

"What's wrong?"




- Thyroid "irritated", releasing stored thyroid hormones (T4 > T3), then absence of new hormone synthesis ("stunned")
  - Many triggers: viral, postpartum, neck palpation, radiation, medications, iodine supplements (*lion's mane, ashwanganda*)
- Can follow upper respiratory or GI infection
- Phasic: thyrotoxic, hypothyroid, (recovery)
  - This makes the diagnosis
  - Hashimoto's: most common cause of primary hypothyroidism
- TPO antibody is often positive, CRP elevated
- Uptake and scan: no uptake (decreased from normal)
  - Rarely needed



TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine
GI = gastrointestinal; TPO = thyroid peroxidase; CRP = C reactive protein

# 1. Thyroiditis

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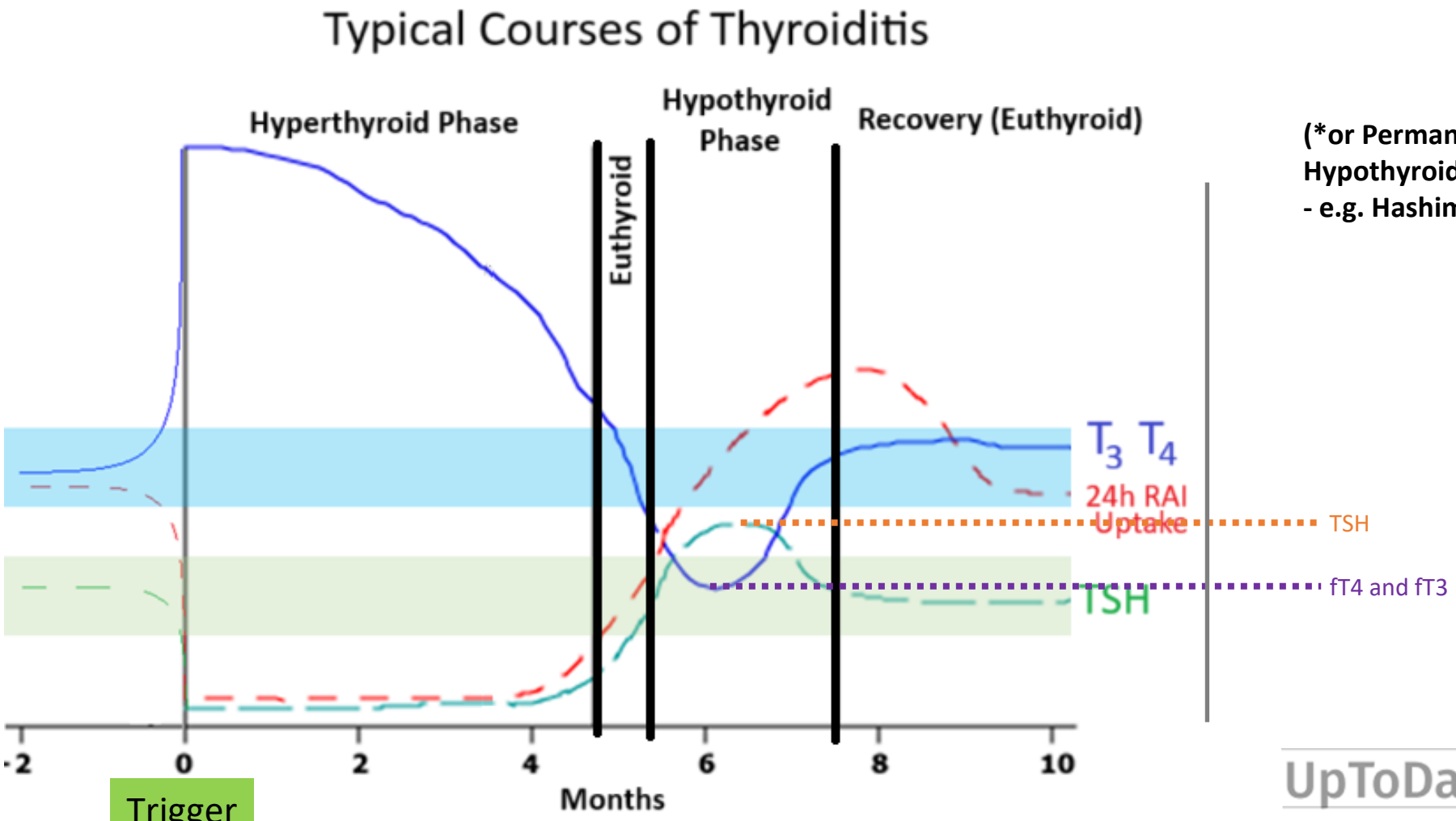
| THYROIDITIS: MAJOR CAUSES |
|---|
| **PAINFUL (TENDER)** |
| **Subacute:** Granulomatous, Suppurative (de Quervain's), Nonsuppurative |
| **Infectious:** Acute or Chronic |
| **Iatrogenic:** Radiation, Palpation/Trauma |
| **PAINLESS** |
| **Painless:** Silent, Lymphocytic (Spontaneous, Subacute) |
| **Drugs:** Lithium, Amiodarone (type 2), Immunotherapy (checkpoint inhibitors), Tyrosine kinase inhibitors, Interferon alpha, Interleukin 2 |
| **Chronic lymphocytic:** **Hashimoto's**, Postpartum |
| **Fibrous:** Reidel's, IG4-related, invasive |
| *Adapted from [5]Ross et al. 2025 |

*Pearl: acute pain usually means thyroiditis



IG4 = immunoglobulin G4

# 1. Thyroiditis




**(*or Permanent Hypothyroidism) - e.g. Hashimoto's**

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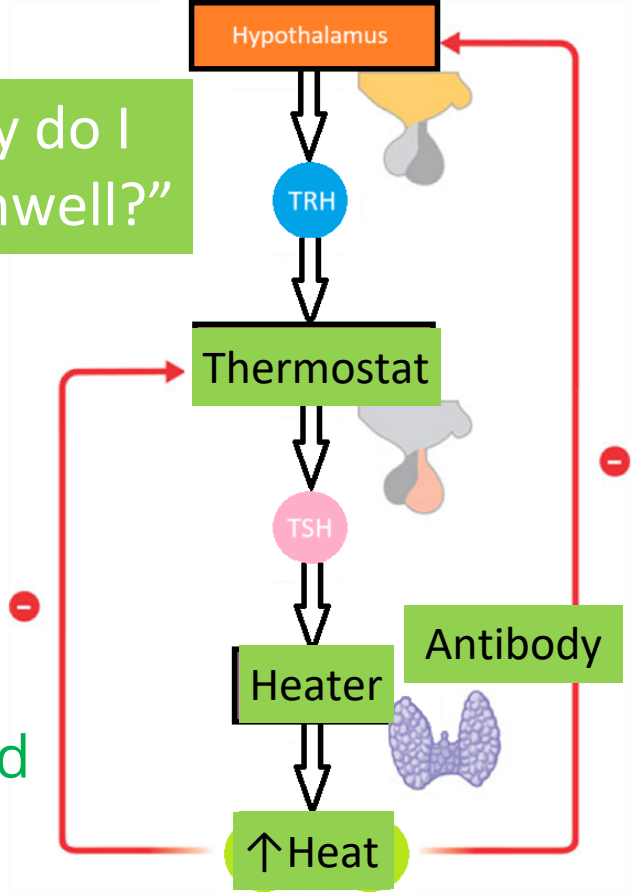
Adapted from [5]Ross et al. 2025
TSH = thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine; RAI = radioactive iodine

# 2. Graves' Disease

"Why do I feel unwell?"



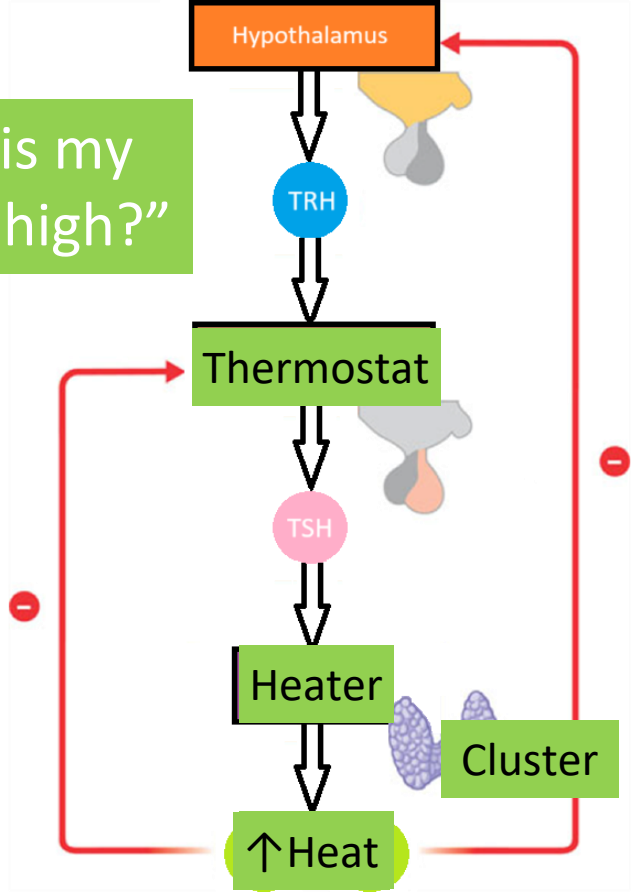

- Autoantibody triggers inappropriate increased synthesis of new thyroid hormone (T3 > T4)
- Autoimmune: antibodies are usually positive
  - This makes the diagnosis
- Shorter subclinical hyperthyroidism period progresses to overt hyperthyroidism
- Ocular manifestations
- 30% of cases go into permanent remission after 12-18 months of antithyroid therapy
- Uptake and scan: diffuse, homogenous, increased uptake with no hot/cold nodules
  - (I only order this when antibodies are negative)



TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine

# 3. Toxic Nodule(s)

"Why is my thyroid high?"




- Groups of thyroid cells becomes autonomous, inappropriately increasing new thyroid hormone synthesis (T3 > T4)
- Antibodies are usually negative
- Longer subclinical hyperthyroidism progresses to overt (10% progress each year)
- Uptake and scan: concentrated uptake in one (or more) "hot" nodules with background suppression of remaining thyroid tissue (*not in pregnancy)
  - This makes the diagnosis



TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine

# I. Hyperthyroidism: Approach

1. Symptoms?
   - Palpitations, tremor, diaphoresis, heat intolerance, diarrhea, polyphagia, unintentional weight loss, worsened anxiety, irritability/decreased concentration, congestive heart failure, weakness, oligo/amenorrhea
   - Ocular manifestations: proptosis, chemosis, blepharitis, diplopia
2. Offending agents?
   - Biotin, iodine, medications (levothyroxine, liothyronine, steroids, lithium, amiodarone, checkpoint inhibitors, cytokines, tyrosine kinase inhibitors)
3. Repeat testing in 6-8 weeks (after minimizing interference from 2.)
   - Thyroid function studies: TSH, fT4, fT3
   - Antibodies: TPO, thyroid receptor antibodies (or thyroid-stimulating immunoglobulin)
   - CBC, CRP, ALT, bilirubin, hCG (females of child-bearing age)
4. Imaging
   - Uptake (quantity) and scan (quality): probably best to leave for Endocrinology



TSH = thyroid-stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine; TPO = thyroid peroxidase; CBC = complete blood count; CRP = C reactive protein; ALT = alanine aminotransferase; hCG = human chorionic gonadotropin

# I. Symptoms

Pathognomonic for Graves' disease:

- Orbitopathy (esp. with smoking)
  - Exophthalmos
  - Periorbital edema
- Pretibial myxedema
- Thyroid acropachy

Graves' Diagnosis:

1. Symmetrically enlarged thyroid +
2. New onset orbitopathy +
3. Moderate to severe hyperthyroidism

**Table 2. Signs and Symptoms of Hyperthyroidism**

**Adrenergic**

Palpitations, tachycardia, anxiety, tremor, jitteriness, diaphoresis, heat intolerance, stare, lid lag, hyperdefecation (not diarrhea)

**Cardiovascular**

Tachycardia, irregular pulse (in atrial fibrillation), dyspnea, orthopnea and peripheral edema (in heart failure)

**Cutaneous**

Onycholysis (Plummer nails), patchy or generalized hyperpigmentation (especially of the face and neck)

Symptoms pathognomonic for Graves disease: pretibial myxedema (thyroid dermopathy) and thyroid acropachy (clubbing of fingers and toes accompanied by soft-tissue swelling of the hands and feet)

Patchy vitiligo can also be observed in Graves disease

**Hypermetabolism**

Weight loss in spite of increased appetite, fever (in thyroid storm)

**Neuromuscular**

Brisk peripheral reflexes with accelerated relaxation phase and weakness of proximal muscles

**Neuropsychiatric**

Anxiety, rapid and pressured speech, insomnia, psychosis (if hyperthyroidism is severe)

**Ocular**

Increased lacrimation, incomplete closure of the eyes when sleeping reported by the patient's partner, photophobia, increased eye sensitivity to wind or smoke, grittiness or sensation of a foreign body or sand in the eyes

Symptoms pathognomonic for Graves disease: exophthalmos, periorbital edema, diplopia, blurred vision, reduced color perception



[1]Kravets 2016; [2]Ross et al 2016

# Hyperthyroidism: Approach

**Symptoms?**
- Palpitations or tremor?
- Neck pain or swelling?

**Repeat labs**
- 6-8 weeks
- No biotin x 7 days
- Offending agent?

**Abnormal exam?**
- Goitre
- Nodule

**Persistent, overt hyperthyroidism**

***Subclinical hyperthyroidism**

Beta blockade if palpitations or heart rate >90

NSAIDS (+/- GCs)

fT4, fT3
**TRAB**, TPO
CBC, ALT, bilirubin, CRP
(**hCG**)

Thyroid ultrasound

***Pearl: treat symptoms, then order further tests**



NSAIDs = nonsteroidal anti-inflammatory drugs; GCs = glucocorticoids
fT4 = free thyroxine; fT3 = free triiodothyronine; TRAB = thyroid receptor antibody; TPO = thyroid peroxidase;
CBC = complete blood count; CRP = C reactive protein; ALT = alanine aminotransferase; hCG = human chorionic gonadotropin

# II. Nuances of Investigations

A. Biotin
B. Subclinical hyperthyroidism
C. Steady-state
D. Pregnancy
E. T4 vs. T3; free vs. total
F. Thyroid antibodies
G. In-patients
H. Ultrasound



T4 = free thyroxine; T3 = triiodothyronine

“Does it matter if I take biotin? Can’t hurt, right?”

# A. Biotin


Benefits of using
Biotin capsules
Improve skin health
Makes your hair thicker and longer
Brittle nails
Prevent hair fall
Treat Dandruff


BIOTIN
XOVAK
~pharma~
100% Plant-Based Vegetarian
Made from
Organic
10000 mcg Per Veg. Capsule
100% Vegan
Organic Herbs
Natural Vitamins
100% Vegetarian
100% Plant Based Formula
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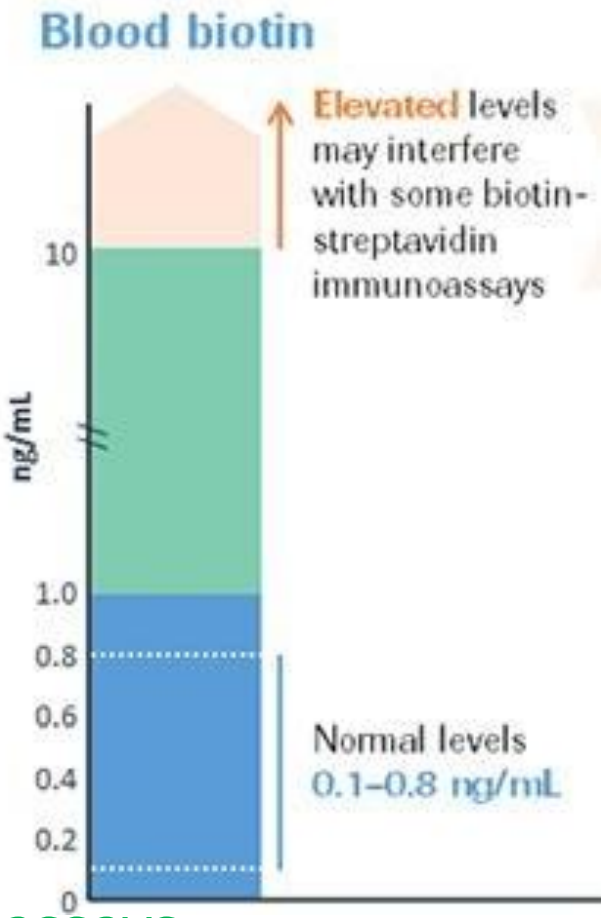
# A. Biotin

"Does it matter if I take biotin?"




- Vitamin B7 (water-soluble)
  - Many names: vitamin H, coenzyme R, factor S, factor W, vitamin Ba, protective factor X
- Biotin-streptavidin is one of nature's strongest non-covalent interactions
  - In vitro diagnostic tests take advantage of by immobilizing biotinylated capture antibodies
- Up to 85% of common immunochemistry analyzers used biotin-streptavidin immunoassays
- Immunoassay manufacturers and FDA have issued safety warnings about biotin interference
  - Reported levels of 1.0-1200ng/mL



[7]Pazirandehm & Burns 2021; [8]Rodrigo et al 2022; [9]Haddad, Giacherio, & Barkan 2019

# A. Biotin

Immunoassay refresher: 2 methods of analyte detection

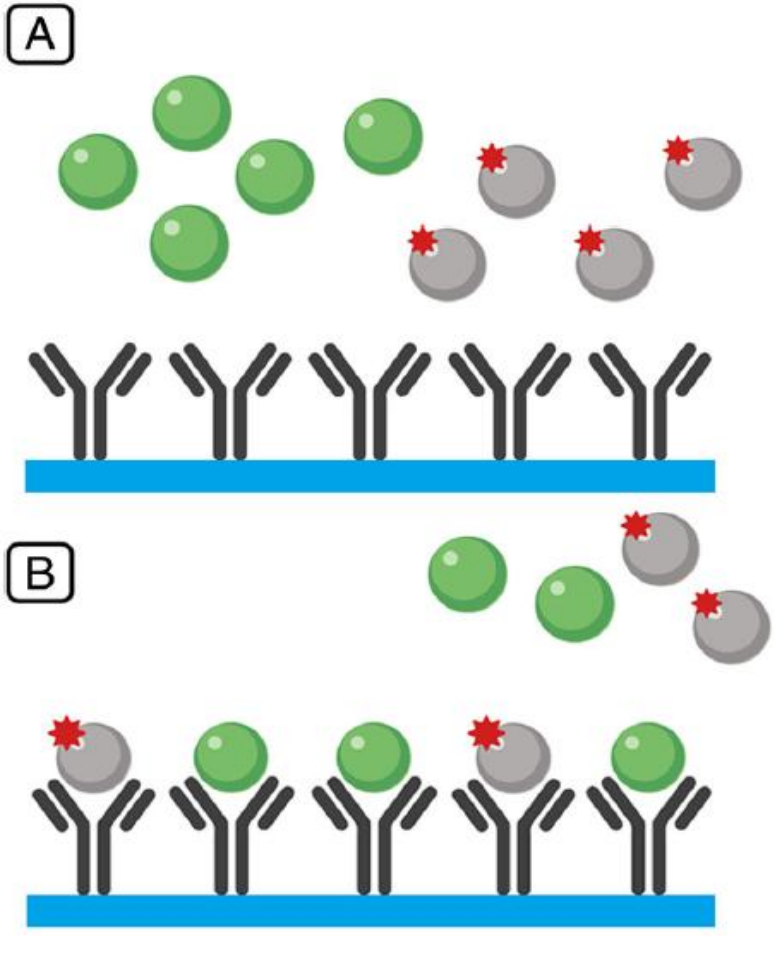
A. Competitive assay
   - Patient's analyte and known quantity of labelled analyte compete for specific antibodies
   - After wash off, signal of bound labelled analyte measured: $[Patient's\ analyte] \propto {}^{1}/_{signal}$

B. Non-competitive assay (sandwich)
   - Patient's analyte binds to fixed capture antibody, then labelled antibody binds to the fixed antibody complex
   - After wash off, signal of labelled antibody complexes measured: $[Patient's\ analyte] \propto signal$



[7]Pazirandehm & Burns 2021; [8]Rodrigo et al. 2022; [9]Haddad, Giacherio, & Barkan 2019; [10]Bowen et al. 2019

# Competitive Assay

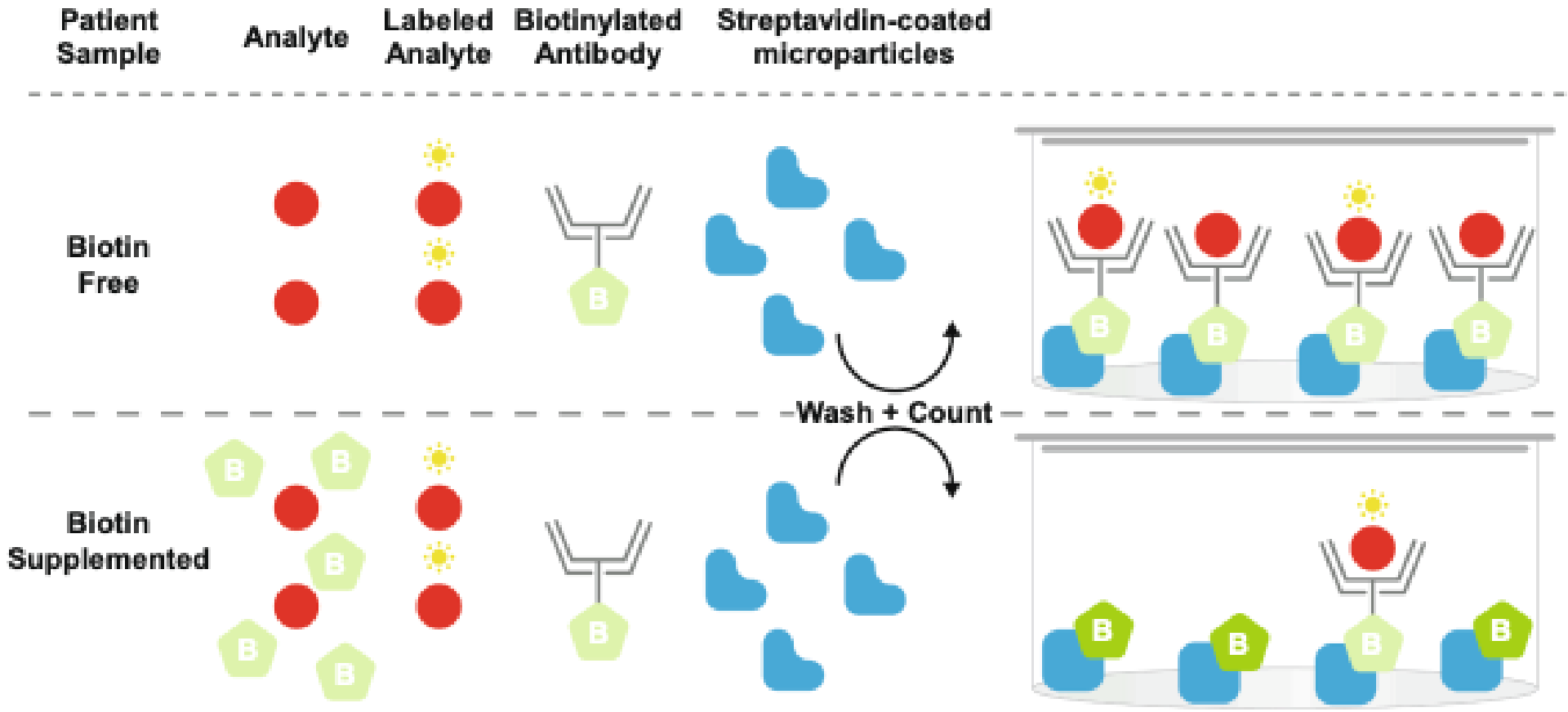



$$[Patient's\ analyte] \propto {}^{1}/_{signal}$$



[7]Pazirandehm & Burns 2021; [8]Rodrigo et al. 2022; [9]Haddad, Giacherio, & Barkan 2019; [10]Bowen et al. 2019

# A. Competitive assay $[Patient's\ analyte] \propto {}^{1}/_{signal}$

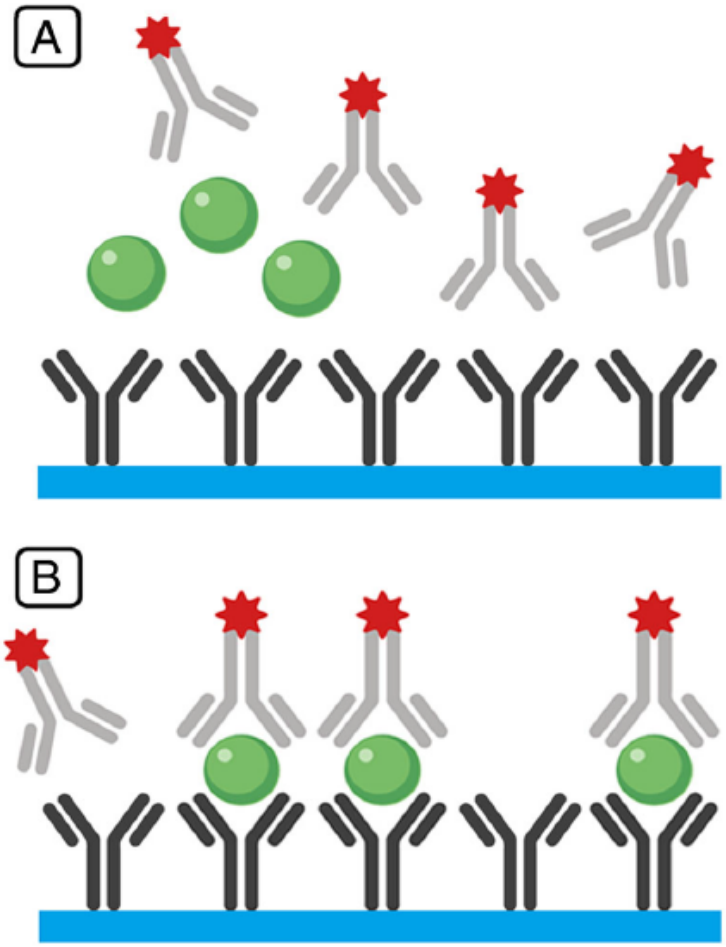



Biotin falsely decreases measured signal (falsely high result)



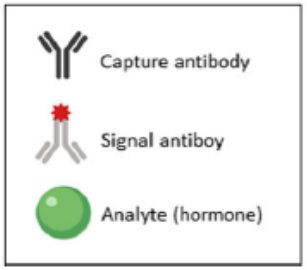
[7]Pazirandehm & Burns 2021; [8]Rodrigo et al. 2022; [9]Haddad, Giacherio, & Barkan 2019; [10]Bowen et al. 2019

# Non-competitive Assay




Sandwich

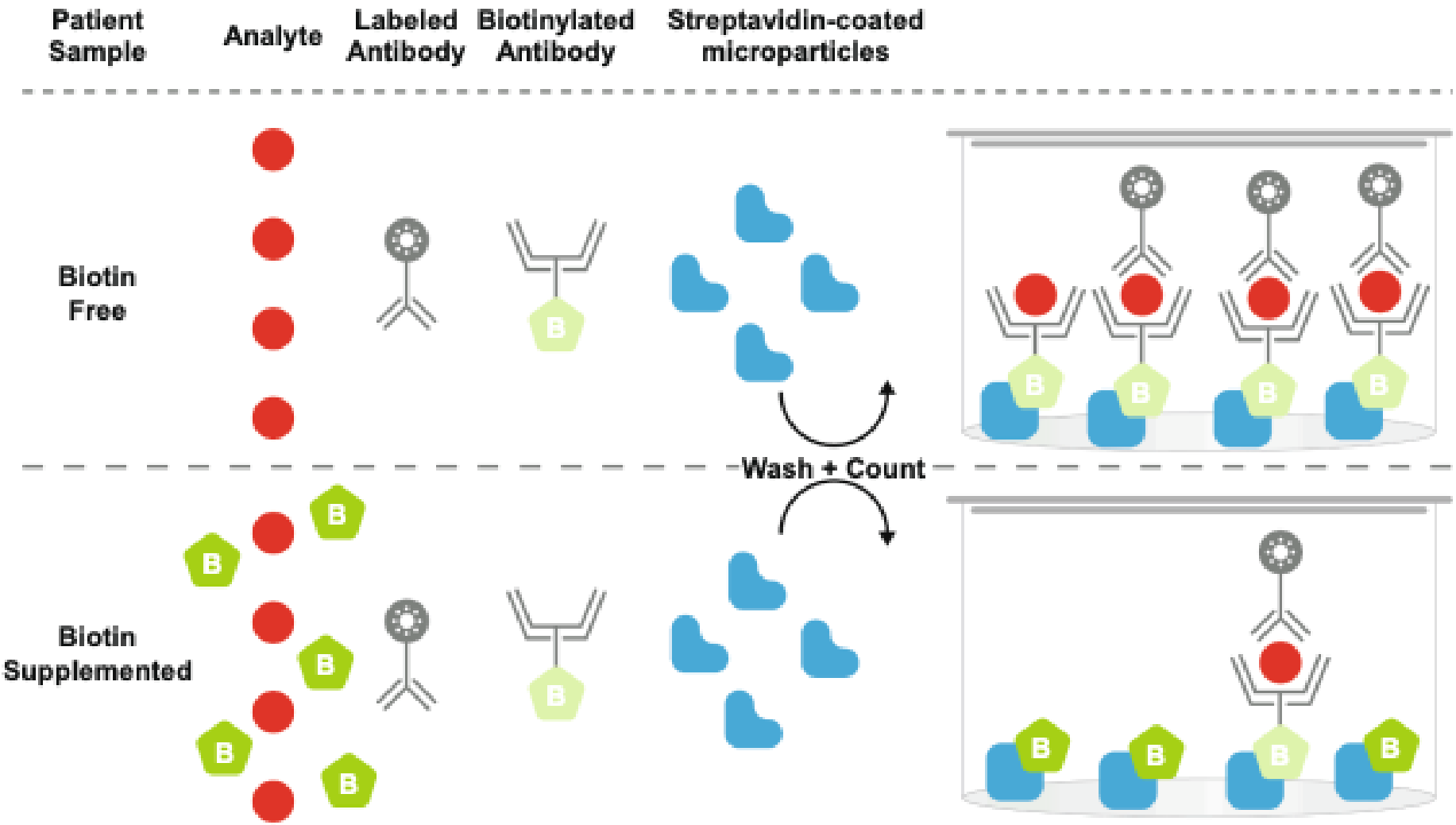
$$[Patient's\ analyte] \propto signal$$






[7]Pazirandehm & Burns 2021; [8]Rodrigo et al. 2022; [9]Haddad, Giacherio, & Barkan 2019; [10]Bowen et al. 2019

# B. Non-competitive assay $[Patient's\ analyte] \propto signal$




Biotin falsely decreases measured signal (falsely low result)



[7]Pazirandehm & Burns 2021; [8]Rodrigo et al. 2022; [9]Haddad, Giacherio, & Barkan 2019; [10]Bowen et al. 2019

# A. Biotin

↓TSH + ↕fT4/fT3 = 1º hyperthyroidism

- Falsely <u>low</u> immunometric assays (e.g. TSH) ↓
- Falsely <u>high</u> competitive-binding assays (e.g. fT4, fT3, TRAB, TPO) ↑

*Hormones*

| Test | Potential impact |
|---|---|
| Parathyroid Hormone (LAB108) | False decrease |
| Follicle Stimulating Hormone (LAB86) | |
| Luteinizing Hormone (LAB88) | |
| Adrenocorticotropic Hormone (LAB511) | |
| Prolactin (LAB531) | |
| Growth Hormone (LAB525) | |
| Insulin (LAB7389) | |
| C-Peptide (LAB521) | |
| Insulin-Like Growth Factor 1 (LAB8787) | |
| Anti-Mullerian Hormone (LAB7364) | |
| Cortisol (LAB61) | False increase |
| Estradiol (LAB523) | |
| Testosterone (LAB124) | |
| Progesterone (LAB529) | |
| Dehydroepiandrosterone Sulfate (LAB524) | |

*Nutritional Markers*

| Test | Potential impact |
|---|---|
| Ferritin (LAB68) | False decrease |
| Vitamin D, 25-Hydroxy (LAB535) | False increase |
| Vitamin B12 (LAB67) | |
| Vitamin B12, Reflexive (LAB882) | |
| Folate (LAB69) | |

*Other Proteins*

| Test | Potential impact |
|---|---|
| Immunoglobulin E (LAB74) | False decrease |
| Myoglobin (LAB105) | |
| Sex Hormone Binding Globulin (LAB4945) | |

*Pregnancy-Related Markers*

| Test | Potential impact |
|---|---|
| Pregnancy Screen, Qualitative (LAB1166) | False decrease |
| HCG – Pregnancy (LAB1148) | |
| HCG – Tumor Marker or Pregnancy (LAB142) | |



fT4 = free thyroxine; fT3 = free triiodothyronine; TRAB = thyroid receptor antibody; TPO = thyroid peroxidase

# A. Biotin

Assays at The Moncton Hospital lab should not be susceptible to biotin interference

## Multivitamin

30-60
mcg/day

No recommended daily intake (RDI) exists, as deficiencies are rare

## Hair & nail supplement

5,000-10,000
mcg/day

More than 125 times the suggested intake

## Experimental therapeutic regimen

>10,000
mcg/day

Doctor-directed for specific patient populations

**1** **ASK** your patients to report everything they are taking, including prescription and OTC medicines, vitamins and supplements, prior to a blood draw.

**2** **UNDERSTAND** that many patients are not aware that they are taking high dose biotin because it is packaged as a supplement for hair, skin and nail beauty.

**3** **INFORM** your patients about how to prepare for blood work. If they take high dose biotin, they will need to **wait** before a blood draw.

*Pearl: when in doubt, hold biotin for 7 days

“Can my thyroid levels change as I get older?”

# B. Subclinical Hyperthyroidism

- Persistently ↓ TSH, normal free T4 and T3
  - Inverse logarithmic relationship
  - TSH more sensitive: better screening test
- Can be caused by any etiology discussed above
  - Steroids/lithium cause this (moreso than overt)
- Age matters:

"Can thyroid change with age?"

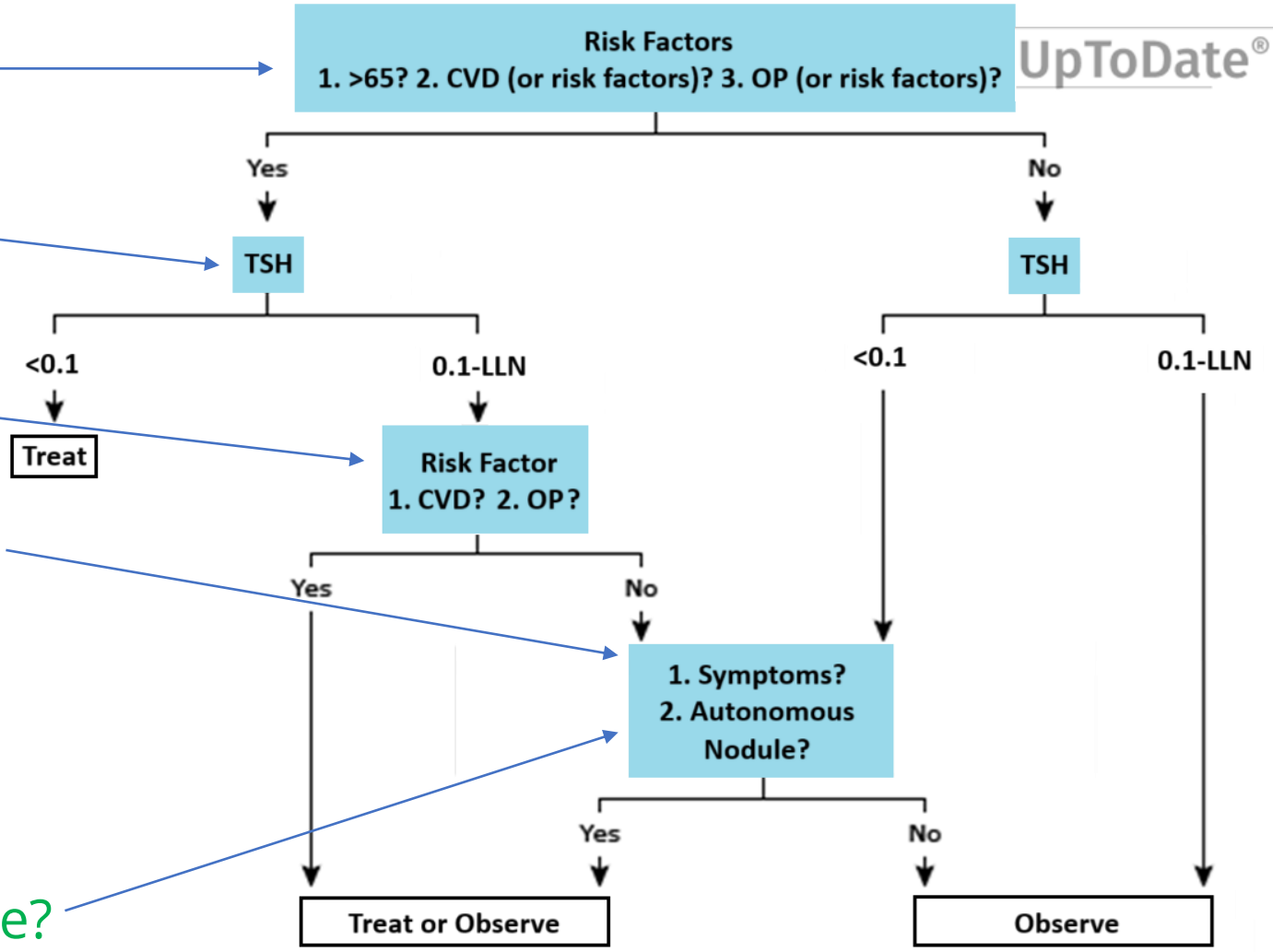
  - Younger patients more tolerant
  - Older patients (>65y) at increased risk
    - Bone: osteopenia, osteoporosis, fragility fracture
    - Embolic: ?myocardial infarction, atrial fibrillation (transient ischemic attack/stroke)



TSH = thyroid stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine

# B. Subclinical Hyperthyroidism

1. Age?
2. TSH?
3. CVD?
   OP?
4. Symptoms?
   - Palpitations
   - Tremor
   - Heat intolerance
   - Insomnia
5. Toxic Nodule?



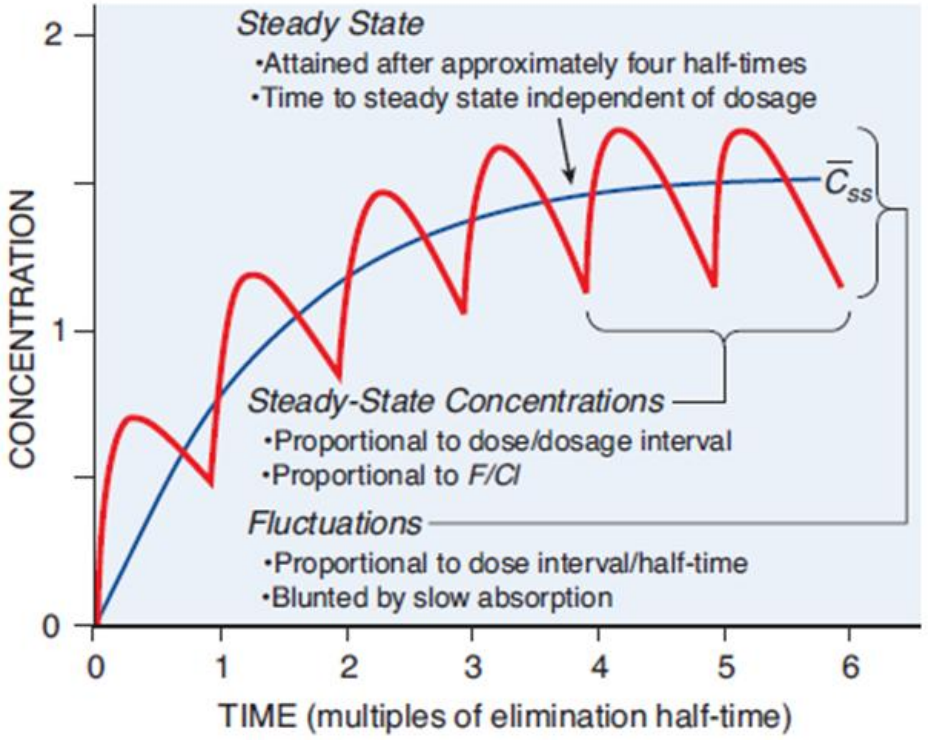



Adapted from [5]Ross et al. 2024
TSH = thyroid stimulating hormone; CVD = cardiovascular disease; OP = osteoporosis; LLN = lower limit normal

“Can we recheck my thyroid next week?”

# C. Steady State

- Changes in thyroid function tests take time
- Repeating <6 weeks not recommended
- Exception: write "exception" on req
  - Pregnancy: every 4 weeks
  - New atrial fibrillation




"Can we recheck next week?"



[1]Kravets 2016; [2]Ross et al. 2016

# D. Pregnancy

- TSH range of normal is assay specific
  - Based off young, non-pregnant adults
- If reference range not provided, use the ATA trimester standard:
  - 1st trimester: 0.1-2.5
  - 2nd trimester: 0.2-3.0
  - 3rd trimester: 0.3-3.0

***Pearl: pregnancy targets are different**

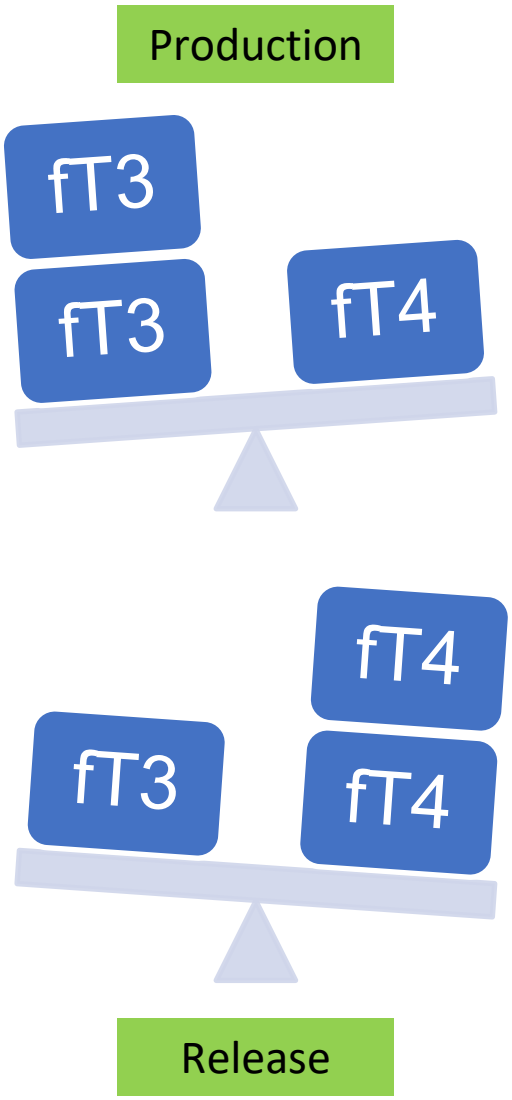


[1]Kravets 2016; [2]Ross et al 2016
TSH = thyroid-stimulating hormone; ATA = American Thyroid Association

# “What is my total T4?”

# E. Free T4 vs. Free T3

- Lab will automatically run these if TSH abnormal (reflexive)
- Thyroid makes T4:T3 14:1
  - T3 predominance: increased production seen in Graves'/toxic nodule(s) ["hyperthyroidism"]
  - T4 predominance: increased release in thyroiditis (any cause)
- Total T4 or total T3: do not order

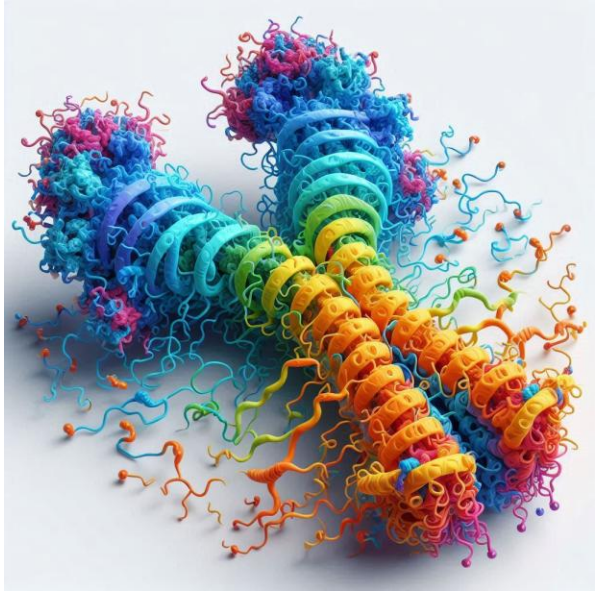





[2]Ross et al. 2016
TSH = thyroid stimulating hormone; T4 = thyroxine; T3 = triiodothyronine

“Is this because of my immune system?”

# F. Thyroid Antibodies



- Thyroid receptor antibodies (TRAB): TSH binding inhibition immunoglobulin (TBII)
  - >4: highly sensitive for Graves' disease
  - Cheaper: preferred by lab
- Thyroid stimulating immunoglobulin (TSI):
  - Highly sensitive for Graves' disease
  - More expensive (can require special approval)
- Thyroid peroxidase (TPO): less helpful
  - Marker of potential autoimmune thyroid dysfunction (once per patient lifetime)
    - Elevated in Graves' disease (not specific)
    - Elevated in Hashimoto's disease/thyroiditis
    - Elevated in normal thyroid (annual TSH screening)

"Is this my immune system?"



Image created by Microsoft Copilot, 2025
[2]Ross et al. 2016; [1]Kravets 2016; [3]Ross et al. 2025
TSH = thyroid stimulating hormone; N = normal

# F. Other tests

- Anti-thyroglobulin antibodies: do not order
  - Role in thyroid cancer treatment monitoring
- Thyroglobulin: do not order
  - Measure of functioning thyroid
  - Role in thyroid cancer treatment monitoring

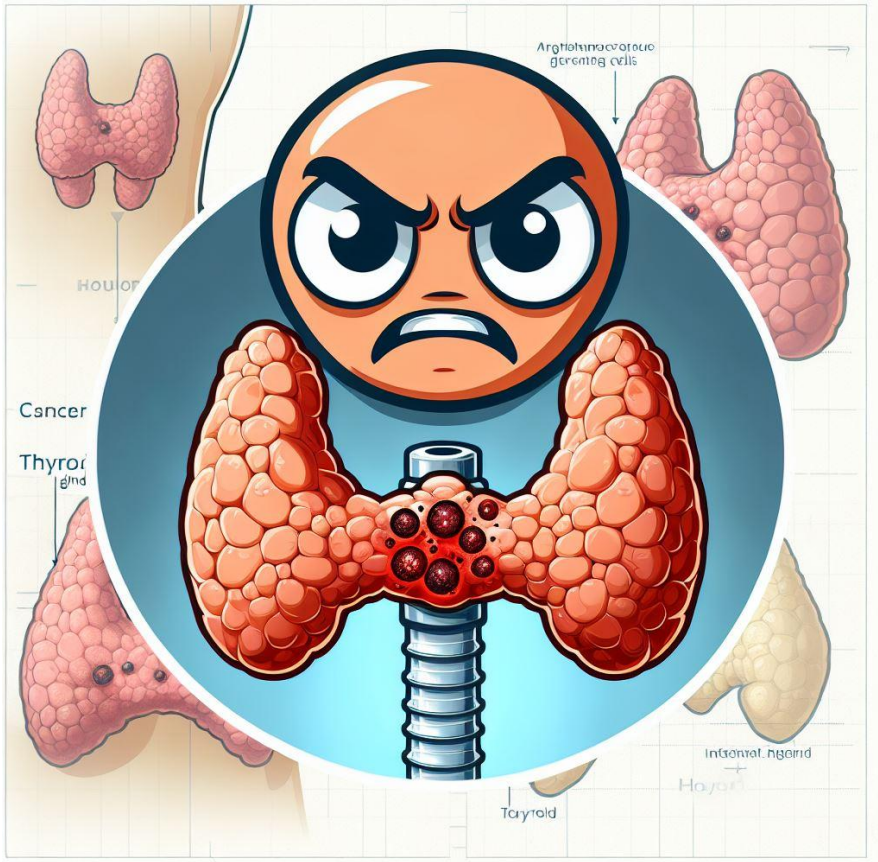
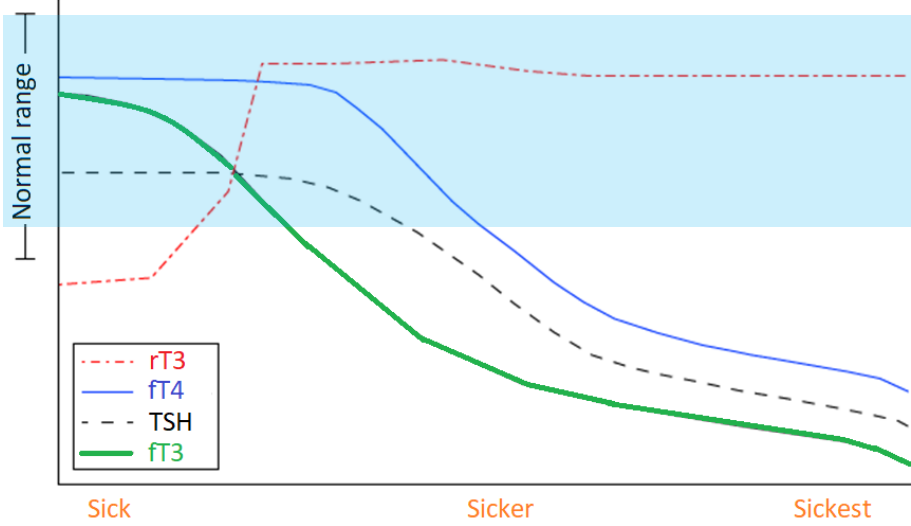





Image created by Microsoft Copilot, 2024

# G. In-patients




- Sick euthyroid syndrome
  - Best to repeat in 6-8 weeks as an outpatient
- Checkpoint inhibitors: hyper- or hypothyroidism
  - Oncology: protocol for monitoring
- Thyroid storm: rare complication
  - Diagnosis: Burch-Wartofsky Score

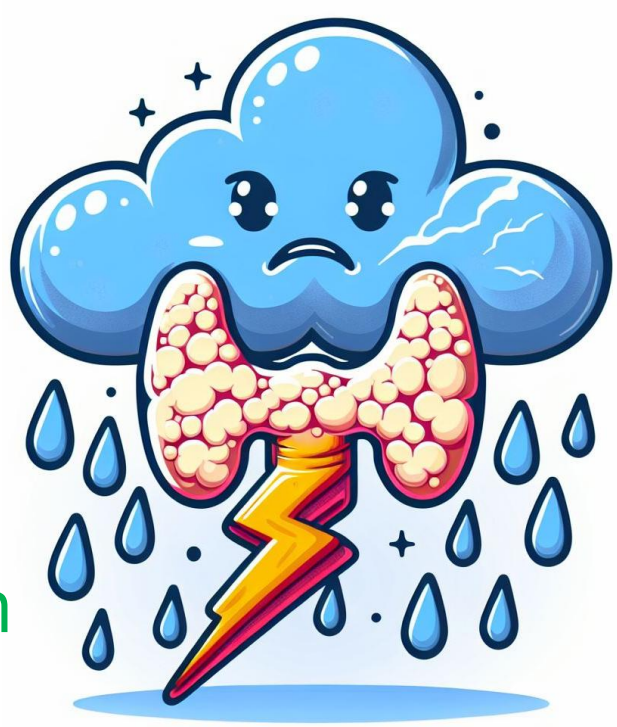




Image created by Microsoft Copilot, 2024

[2]Ross et al. 2016; adapted from [3]Ross et al. 2025

# G. In-patients

Iodine (CT contrast):

- Wolff-Chaikoff: protective
  - Excess iodine exposure reduces thyroid synthesis
- Jod-Basedow: abnormal
  - Abnormal thyroid cells “escape” and use excess iodine to increase thyroid synthesis (hyperthyroidism)

[Recent iodine exposure makes thyroid uptake/scan less reliable and radioactive iodine therapy less effective.]

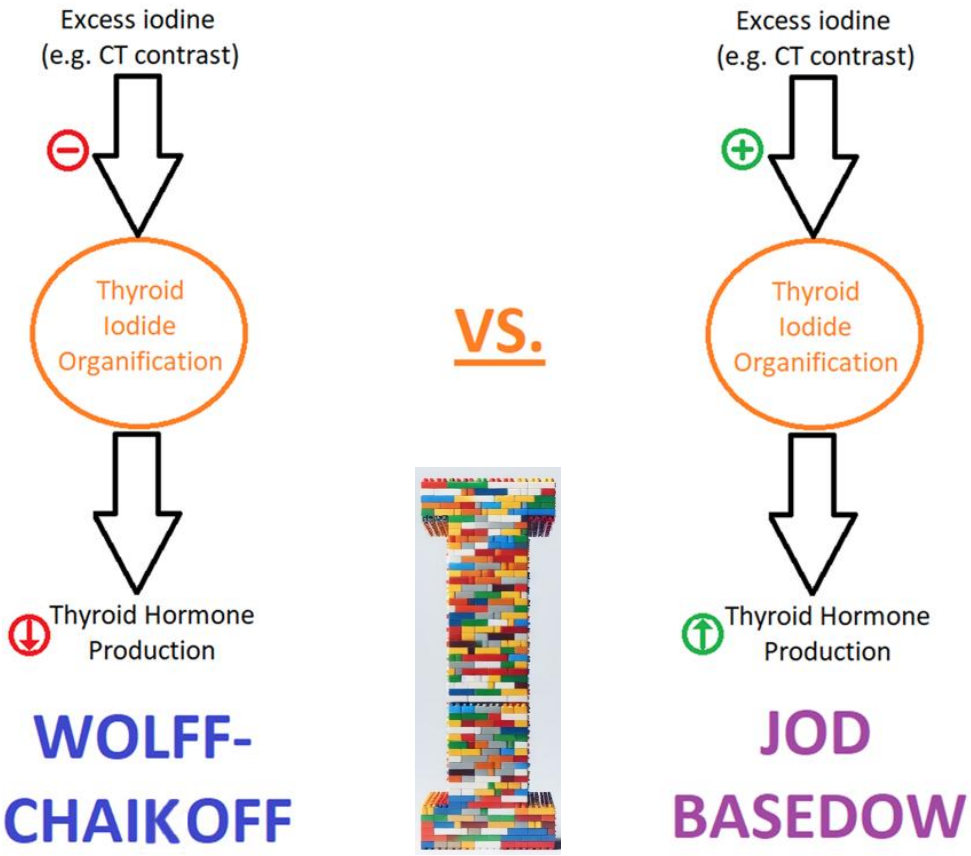
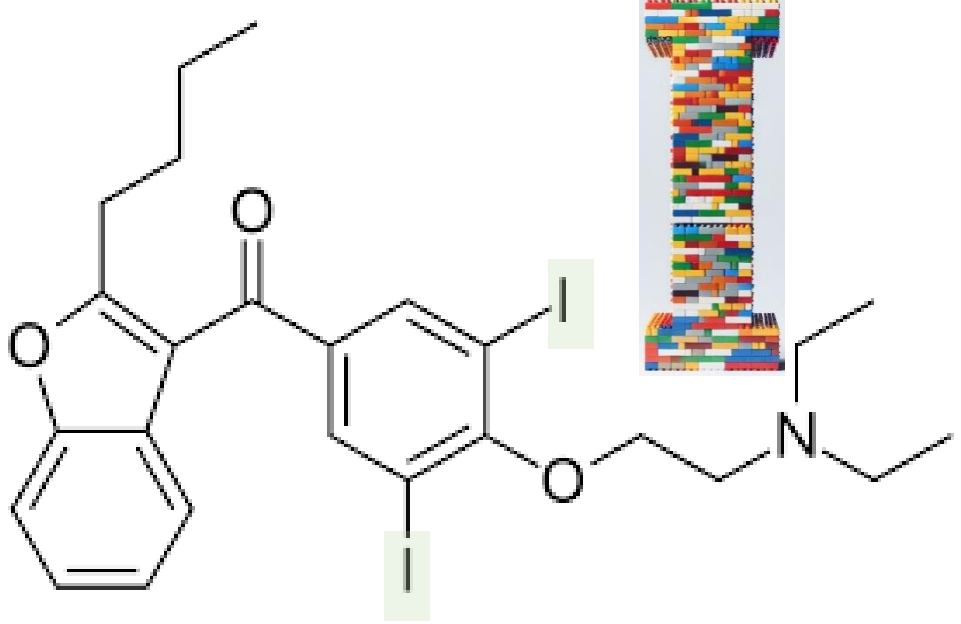





Image created by Microsoft Copilot, 2024

[1]Ross et al. 2016

# G. In-patients




Iodine (amiodarone): long half-life (baseline testing recommended)

- Hypothyroidism
- Hyperthyroidism: amiodarone-induced thyrotoxicosis
  - Type 1: pre-existing goitre or latent Graves' disease
  - Type 2: destructive thyroiditis

"Do I have to stop amiodarone?"



Image created by Microsoft Copilot, 2024

[1]Ross et al. 2016; [3]Ross et al. 2025

# “Can I have a thyroid ultrasound?”

# H. Ultrasound

- Order only if abnormal exam

- Helpful for investigating:
  - Goitre
  - Nodules

- NOT helpful for hypothyroidism/hyperthyroidism
  - Need special training to accurately collect and interpret results within this context

"Can I have a thyroid ultrasound?"



Image created by Microsoft Copilot, 2024

# Choosing Wisely – Canada

- Don’t routinely order a thyroid ultrasound in patients with abnormal thyroid function tests unless there is a palpable abnormality of the thyroid gland.
- Don’t routinely test for Anti-Thyroid Peroxidase Antibodies (anti-TPO).

*Pearl: let patient presentation guide testing



[11]https://choosingwiselycanada.org/; [1]Kravets 2016

# III. Hyperthyroidism: Treatment

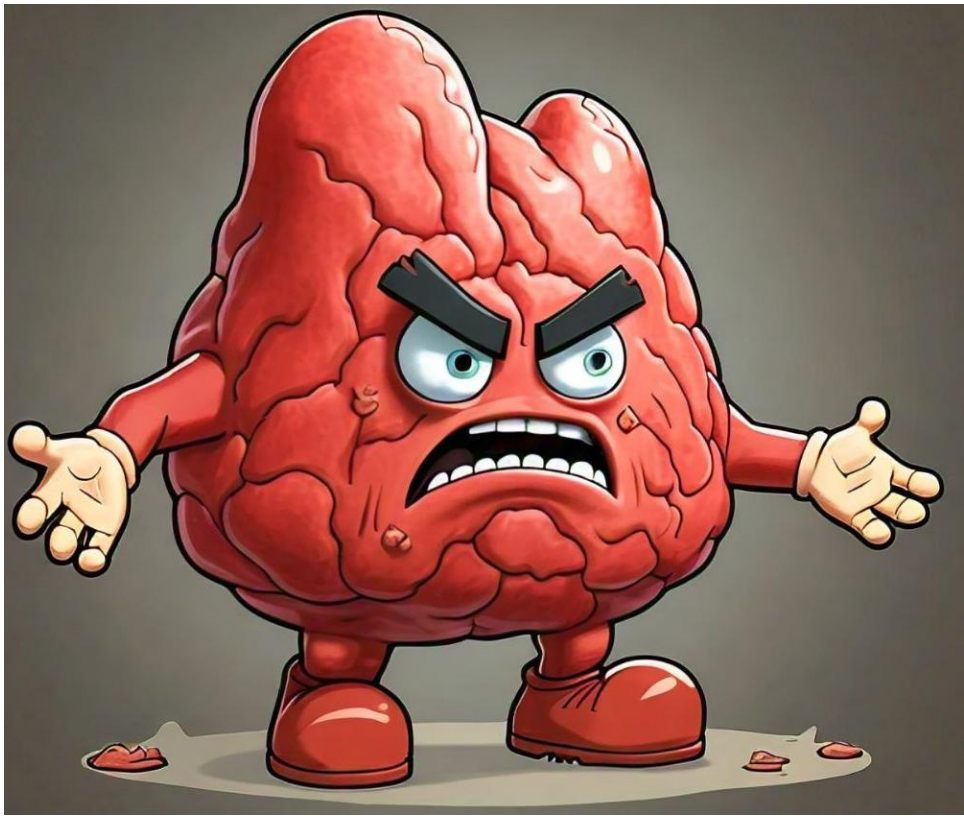
- Age
  - >65
- Symptoms
  - Palpitations, tremor, diaphoresis, heat intolerance, diarrhea, polyphagia, unintentional weight loss, worsened anxiety, irritability/decreased concentration, congestive heart failure, weakness, oligo/amenorrhea
- Severity
  - Overt hyperthyroidism (fT4 or fT3 >1.5 ULN)
  - Moderately correlates with symptoms



[2]Ross et al 2016
fT4 = free thyroxine; fT3 = free triiodothyronine; ULN = upper limit normal

# III. Thyroiditis Therapy

- Symptoms: beta blockade
  - Propranolol vs. other
- Subacute: pain
  - NSAIDs (naproxen 250-500 mg twice daily)
  - GCs (prednisone 20-40mg)



- Rarely require antithyroid medication



Generated image by Meta AI, 2024

[6]Burman et al. 2025.

NSAIDs = nonsteroidal anti-inflammatory drugs; GCs = glucocorticoids

## Table 5. Pharmacologic Treatment of Hyperthyroidism

| *First-line agents* | *Dosage* | *Adverse effects* | *Comments* | *Cost** |
|---|---|---|---|---|
| **Beta blockers** | | | | |
| Atenolol | 25 to 100 mg orally once per day | Exacerbation of congestive heart failure | Selective beta$_1$ blocker; safer than propranolol in asthma or chronic obstructive pulmonary disease; once-daily dosing improves compliance | $5 |
| Propranolol | Immediate release: 10 to 40 mg orally every eight hours<br>Extended release: 80 to 160 mg orally once per day | Exacerbation of congestive heart failure or asthma | Decreases $T_4$ to $T_3$ conversion; nonselective beta blocker | $20 to $84 for immediate release<br>$76 to $152 for extended release |
| **Antithyroid medications** | | | | |
| Methimazole (Tapazole) | 5 to 120 mg orally per day (can be given in divided doses) | Dose-related agranulocytosis | Contraindicated in the first trimester of pregnancy | $20 to $100 ($45 to $900) |
| Propylthiouracil | 50 to 300 mg orally every eight hours | Agranulocytosis not related to dose; liver dysfunction; rash, including ANCA-associated vasculitis | Drug of choice in the first trimester of pregnancy; carries a higher risk of liver failure than methimazole | $60 to $400 |
| **Ancillary agents** | | | | |
| Glucocorticoids | Prednisone: 20 to 40 mg orally per day for up to four weeks<br>Hydrocortisone: 100 mg intravenously every eight hours with subsequent taper | Hyperglycemia in patients with diabetes mellitus, otherwise few short-term adverse effects | Used in severe hyperthyroidism or thyroid storm to reduce $T_4$ to $T_3$ conversion; also used in severe subacute thyroiditis | Prednisone: $20<br>Hydrocortisone: NA |
| Nonsteroidal anti-inflammatory drugs | Depends on the specific agent | Nephrotoxicity; gastrointestinal bleeding | Treats pain in subacute thyroiditis | — |

*ANCA = antineutrophil cytoplasmic autoantibodies; NA = not applicable; $T_3$ = triiodothyronine; $T_4$ = thyroxine.*

[1]Kravets 2016

# III. Graves'/Adenoma Therapy

- Symptoms: beta blockade (for 3-4 weeks)
  - Propranolol (preferred in pregnancy) vs. other
- Antithyroid medications:
  - (*Propylthiouracil: preferred during 1st trimester)
  - Methimazole: preferred during all other times
    - Overt hyperthyroidism: 10mg PO twice daily
  - Rare side effects:
    - Rash (Stephen-Johnson syndrome or vasculitis)
    - Jaundice (liver dysfunction): ALT, bilirubin
    - Fever/severe odynophagia (agranulocytosis): neutrophils
- Radioactive iodine ablation (esp. adenoma)



[1]Ross et al. 2016; [1]Kravets 2016

# III. Pregnancy Therapy

- Pregnancy improves autoimmune conditions (e.g. Graves' disease)
- Postpartum flare is common
  - As is postpartum thyroiditis
- Antithyroid medications have been linked to inutero malformations
  - T1: PTU is safer than methimazole
- Pregnant body needs more thyroid hormones (i.e. lower TSH)
  - Treatment target: T4 and T3 around ULN



[1]ATA 2016; [2]Ross et al. 2016
T1 = first trimester; PTU = propylthiouracil; TSH = thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine

# Hyperthyroidism: Approach

**Symptoms?**
- Palpitations or tremor?
- Neck pain or swelling?

Beta blockade if palpitations or heart rate >90

NSAIDS (+/- GCs)

**Repeat labs**
- 6-8 weeks
- No biotin x 7 days
- Offending agent?

fT4, fT3
**TRAB**, TPO
CBC, ALT, bilirubin, CRP
(**hCG**)

**Abnormal exam?**
- Goitre
- Nodule

Thyroid ultrasound

**Persistent, overt hyperthyroidism**

*Subclinical hyperthyroidism (5mg PO once daily)

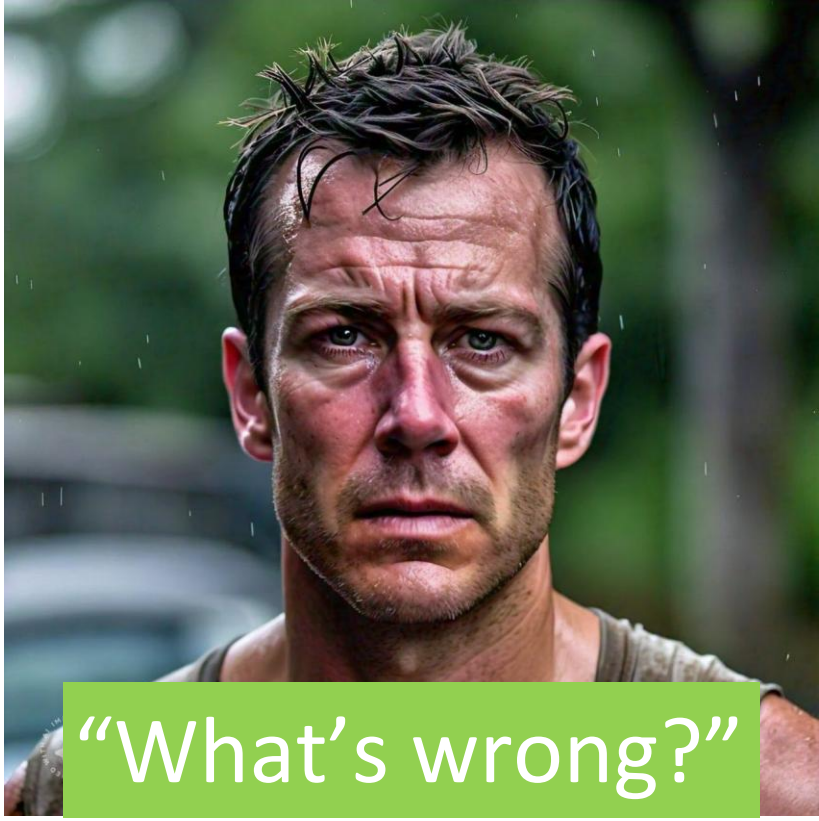
Methimazole 10mg PO twice daily x 2 weeks, then 10mg PO thereafter



NSAIDs = nonsteroidal anti-inflammatory drugs; GCs = glucocorticoids
fT4 = free thyroxine; fT3 = free triiodothyronine; TRAB = thyroid receptor antibody; TPO = thyroid peroxidase;
CBC = complete blood count; CRP = C reactive protein; ALT = alanine aminotransferase; hCG = human chorionic gonadotropin

# Back to our patients…

# Case: DQ 38M




- New diagnosis of hyperthyroidism
- 2 weeks of anterior neck pain, swelling following upper respiratory tract infection
- 1 week of palpitations, tremor, diaphoresis, anxiety
- Past Medical History: nil
- Medications: *biotin supplements (for "hair health")
- Exam: tremor, tachycardia, ?L-sided nodule
- TSH undetectable ↓, fT4 32.2 ↑, CRP 110 ↑

Next steps?



Generated image by Meta AI, 2024

TSH = thyroid-stimulating hormone; fT4 = free thyroxine; CRP = C reactive protein

# Case: DQ 38M

- Symptomatic (tremor/palpitations): propranolol
  - Neck pain and swelling: naproxen, prednisone
- In 6-8 weeks, repeat labs (after holding biotin for 7 days)
  - TSH, fT4, fT3, antibodies (thyroid receptor antibody AND anti-TPO), CBC, ALT, bilirubin
- Abnormal exam: order thyroid ultrasound

- Most likely: subacute thyroiditis (de Quervain's)

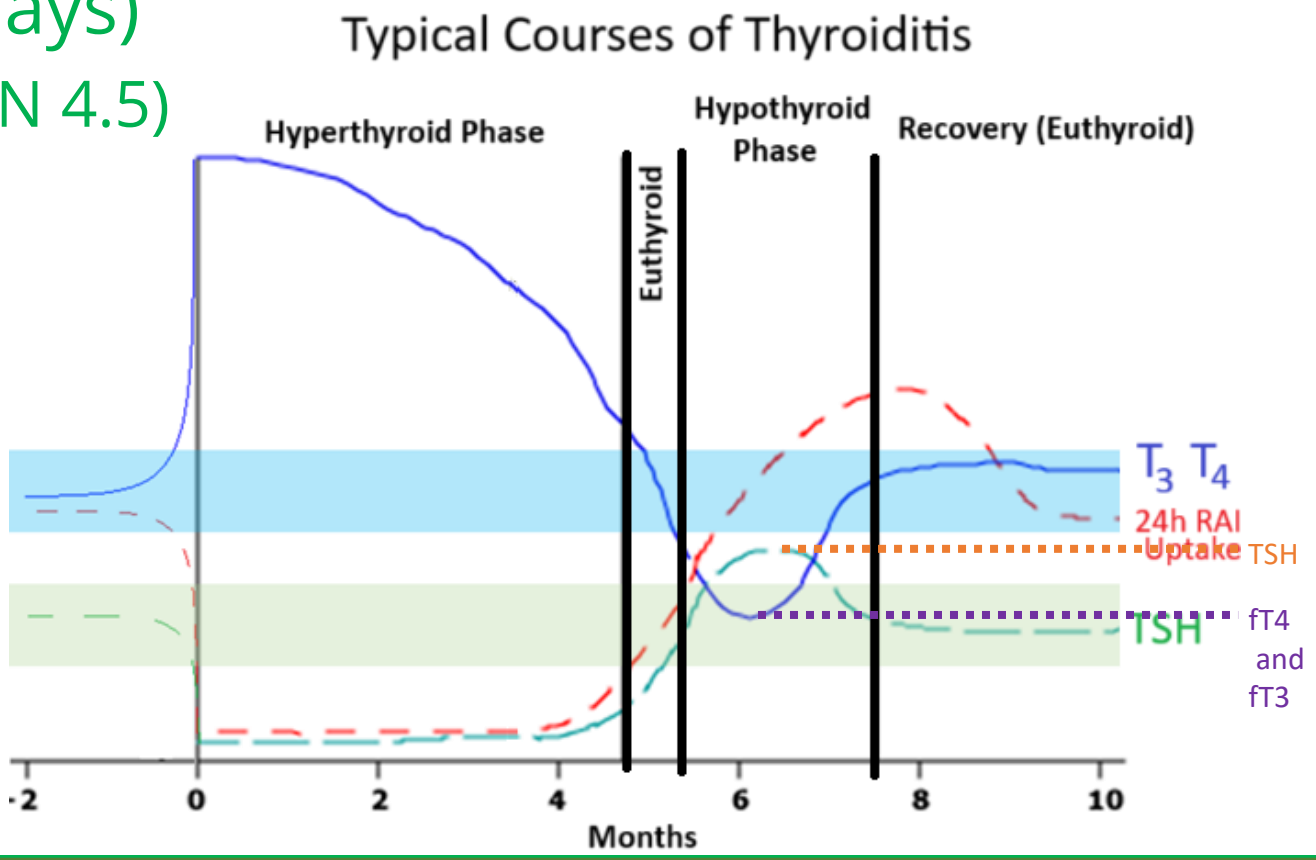


Generated image by Meta AI, 2024

TSH = thyroid-stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine; TPO = thyroid peroxidase; CBC = complete blood count; ALT = alanine aminotransferase;

# Case 1: DQ 38M

- Repeat labs in 2months' (after holding biotin for 7 days)
  - TSH 9.9 (ULN 4.5)
  - fT4 11.5
  - CRP 0.4
  - TRAB <1.3
  - TPO < 3
  - Neut 2.1



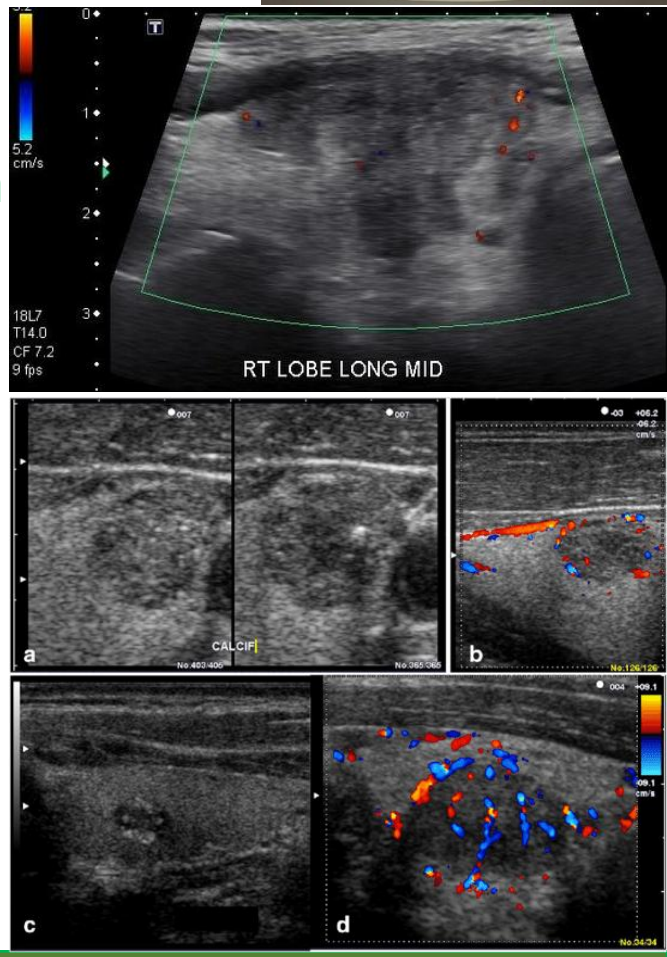

Generated image by Meta AI, 2024 Adapted from [5]Ross et al. 2025



TSH = thyroid-stimulating hormone; T4 = free thyroxine; T3 = free triiodothyronine; TRAB = thyroid receptor antibody; RAI = radioactive iodine; TPO = thyroid peroxidase; CRP = C reactive protein; ULN = upper limit of normal

# Case: DQ 38M

- Thyroid ultrasound:
  - There is a large 1.8 x 2.0 x 3.4 centimetre rounded well circumscribed lesion within the left lobe of the thyroid gland. This is solid and hypoechoic relative to background parenchyma. Lesion is wider than tall with no calcifications.
  - Diffuse heterogeneity of the background thyroid parenchyma with large lobular masses within both lobes of the thyroid gland. Given the provided history of fevers in the degree of heterogeneity/ size of bilateral nodules, findings are favoured on the basis of subacute De Quervain Thyroiditis.



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# ACR TI-RADS

| COMPOSITION (Choose 1) | |
|---|---|
| Cystic or almost completely cystic | 0 points |
| Spongiform | 0 points |
| Mixed cystic and solid | 1 point |
| Solid or almost completely solid | 2 points |

| ECHOGENICITY (Choose 1) | |
|---|---|
| Anechoic | 0 points |
| Hyperechoic or isoechoic | 1 point |
| Hypoechoic | 2 points |
| Very hypoechoic | 3 points |

| SHAPE (Choose 1) | |
|---|---|
| Wider-than-tall | 0 points |
| Taller-than-wide | 3 points |

| MARGIN (Choose 1) | |
|---|---|
| Smooth | 0 points |
| Ill-defined | 0 points |
| Lobulated or irregular | 2 points |
| Extra-thyroidal extension | 3 points |

| ECHOGENIC FOCI (Choose All That Apply) | |
|---|---|
| None or large comet-tail artifacts | 0 points |
| Macrocalcifications | 1 point |
| Peripheral (rim) calcifications | 2 points |
| Punctate echogenic foci | 3 points |

**Add Points From All Categories to Determine TI-RADS Level**

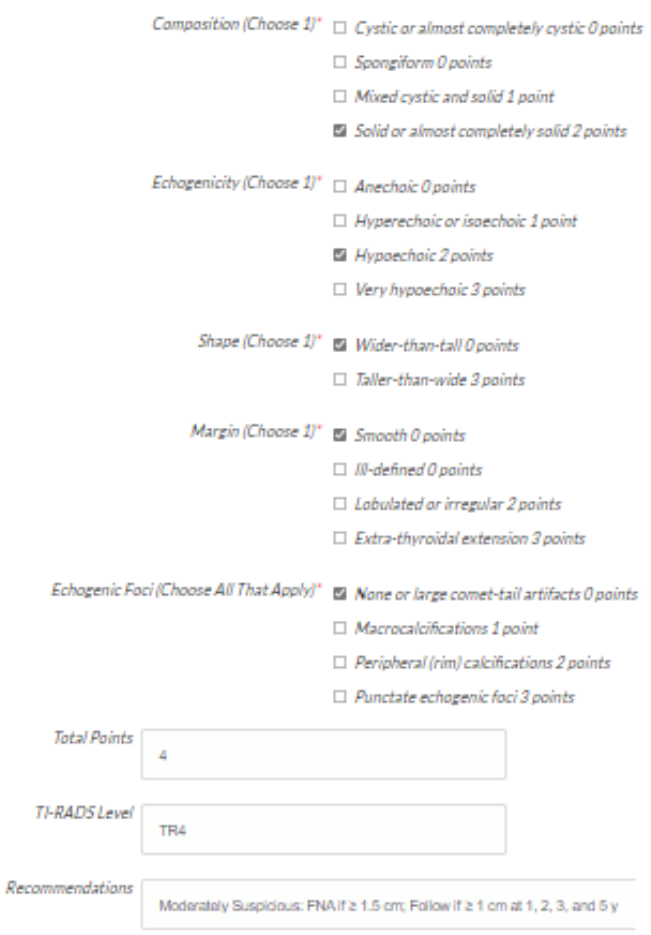
| 0 Points | 2 Points | 3 Points | 4 to 6 Points | 7 Points or More |
|---|---|---|---|---|
| **TR1** | **TR2** | **TR3** | **TR4** | **TR5** |
| **Benign** | **Not Suspicious** | **Mildly Suspicious** | **Moderately Suspicious** | **Highly Suspicious** |
| No FNA | No FNA | FNA if ≥ 2.5 cm<br>Follow if ≥ 1.5 cm | FNA if ≥ 1.5 cm<br>Follow if ≥ 1 cm | FNA if ≥ 1 cm<br>Follow if ≥ 0.5 cm* |

| COMPOSITION | ECHOGENICITY | SHAPE | MARGIN | ECHOGENIC FOCI |
|---|---|---|---|---|
| *Spongiform:* Composed predominantly (>50%) of small cystic spaces. Do not add further points for other categories.<br>*Mixed cystic and solid:* Assign points for predominant solid component.<br>Assign 2 points if composition cannot be determined because of calcification. | *Anechoic:* Applies to cystic or almost completely cystic nodules.<br>*Hyperechoic/isoechoic/hypoechoic:* Compared to adjacent parenchyma.<br>*Very hypoechoic:* More hypoechoic than strap muscles.<br>Assign 1 point if echogenicity cannot be determined. | *Taller-than-wide:* Should be assessed on a transverse image with measurements parallel to sound beam for height and perpendicular to sound beam for width.<br>This can usually be assessed by visual inspection. | *Lobulated:* Protrusions into adjacent tissue.<br>*Irregular:* Jagged, spiculated, or sharp angles.<br>*Extrathyroidal extension:* Obvious invasion = malignancy.<br>Assign 0 points if margin cannot be determined. | *Large comet-tail artifacts:* V-shaped, >1 mm, in cystic components.<br>*Macrocalcifications:* Cause acoustic shadowing.<br>*Peripheral:* Complete or incomplete along margin.<br>*Punctate echogenic foci:* May have small comet-tail artifacts. |

**Refer to discussion of papillary microcarcinomas for 5-9 mm TR5 nodules.*

# Case: DQ 38M

- Thyroid ultrasound:
  - There is a large 1.8 x 2.0 x 3.4 centimetre rounded well circumscribed lesion within the left lobe of the thyroid gland. This is solid and hypoechoic relative to back-ground parenchyma. Lesion is wider than tall with no calcifications.
  - Diffuse heterogeneity of the background thyroid parenchyma with large lobular masses within both lobes of the thyroid gland. Given the provided history of fevers in the degree of heterogeneity/size of bilateral nodules, findings are favoured on the basis of subacute De Quervain Thyroiditis.
- TIRADS 4: FNA if >1.5cm



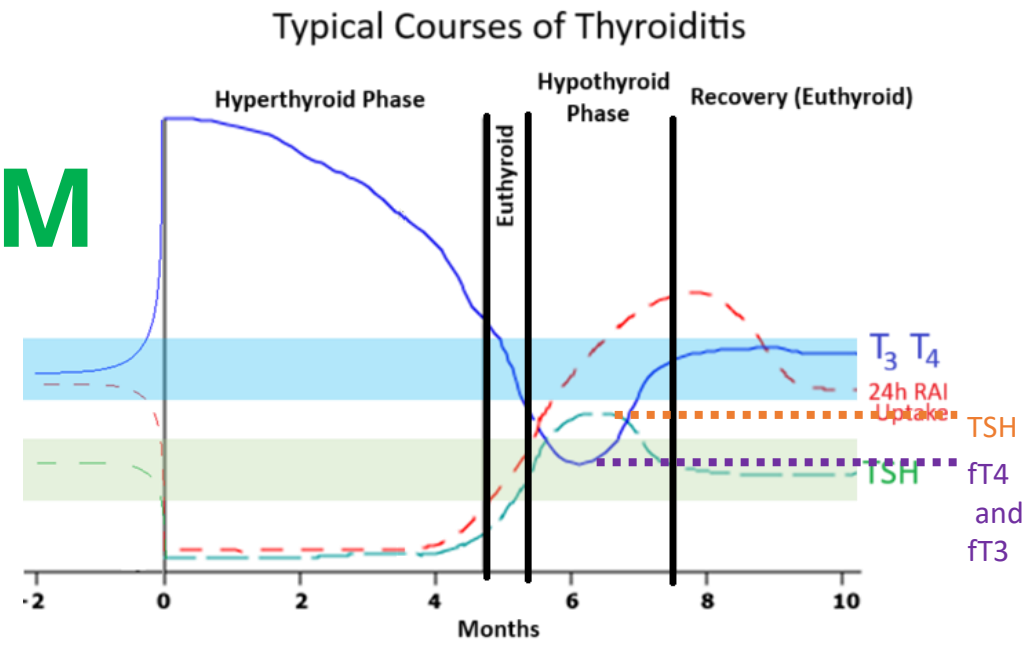



Generated image by Meta AI, 2024

TIRADS = Thyroid Imaging Reporting and Data System; FNA = fine needle aspiration

https://tiradscalculator.com/

# Case 1: DQ 38M




1. Thyroiditis:
   - Course: self-limiting thyrotoxicosis

   A. Biochemical euthyroidism possible
   B. Transient hypothyroidism common
   C. Permanent hypothyroidism common
      - e.g. Hashimoto's thyroiditis

*Pearl: thyroiditis may not require treatment



Adapted from [5]Ross et al. 2025
TSH = thyroid-stimulating hormone; T4 = free thyroxine; T3 = free triiodothyronine; RAI = radioactive iodine

# Case 2: GD 73M

"Why do I feel unwell?"

- New diagnosis of atrial fibrillation and heart failure
  - Also found to have hyperthyroidism
- 2 week history of palpitations
- Past Medical History: reflux, allergies, gout
- Medications: rabeprazole, cetirizine, allopurinol (no biotin)
- Exam: tachycardia, heart failure, normal thyroid
- TSH undetectable ↓, fT4 28.4↑

Next steps?



Generated image by Meta AI, 2024

TSH = thyroid-stimulating hormone; fT4 = free thyroxine;

# Case 2: GD 73M

- Symptomatic (tremor/palpitations):
  - Calcium channel blocker (acute, decompensated heart failure)
- Normal thyroid: no ultrasound
- Further labs (done right away given atrial fibrillation)
  - fT3 (“exception”), antibodies (thyroid receptor antibody AND anti-TPO), CBC, ALT, bilirubin, CRP

- fT3 15.7 ↑ (ULN 6), TRAB 32 ↑, TPO 24 ↑, CRP 9.6 ↑
  - T3 predominance: fT4 28.4 ↑ (ULN 19)

- Most likely: Graves’ disease (remission in ~30-40%)
  - Started methimazole 10mg PO daily

Image created by Microsoft Copilot, 2025

ULN = upper limit of normal



TSH = thyroid-stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine; TRAB = thyroid receptor antibody; TPO = thyroid peroxidase; CBC = complete blood count; ALT = alanine aminotransferase; CRP = C reactive protein

# Case 3: TA 43F

"Why is thyroid high?"

- Recurrent hyperthyroidism
- 6 weeks palpitations and weight loss after upper respiratory tract infection
- Past Medical History: ?hyperthyroidism in India
- Medications: carbimazole x few months ~1year ago, no biotin
- Exam: palpable R nodule

"T3-toxicosis"

- TSH undetectable ↓, fT4 17.9, fT3 7.4↑

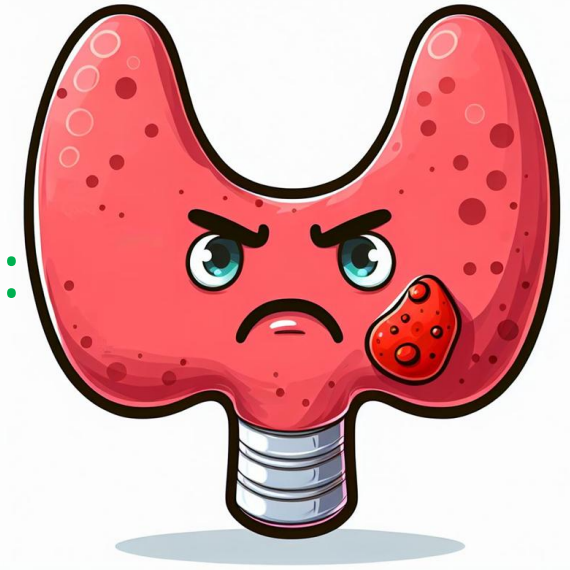
Next steps?



Generated image by Meta AI, 2024

TSH = thyroid-stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine

# Case 3: TA 43F



- Symptomatic (tremor/palpitations):
  - Metoprolol PO twice daily x 6 weeks
- Given previous history, start methimazole 5mg PO
  - *hCG <2.3 (add on to labs)
- In 6-8 weeks, repeat labs:
  - TSH, fT4/fT3 (“exception”), antibodies (thyroid receptor antibody AND anti-TPO), CBC, ALT, bilirubin, CRP
- Abnormal exam: order thyroid ultrasound

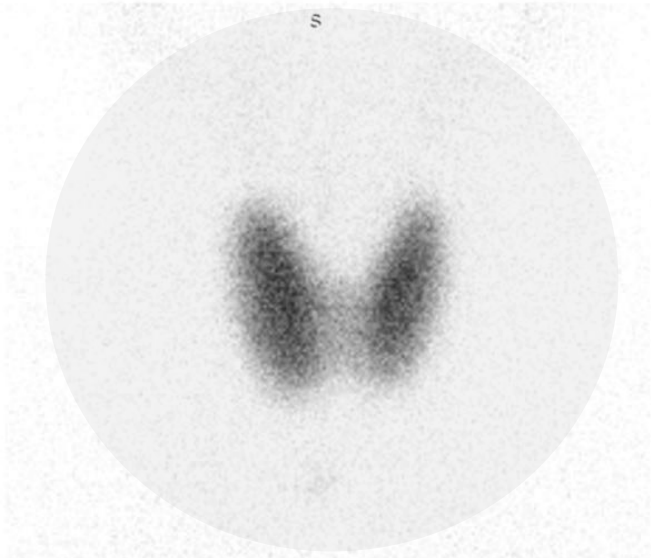


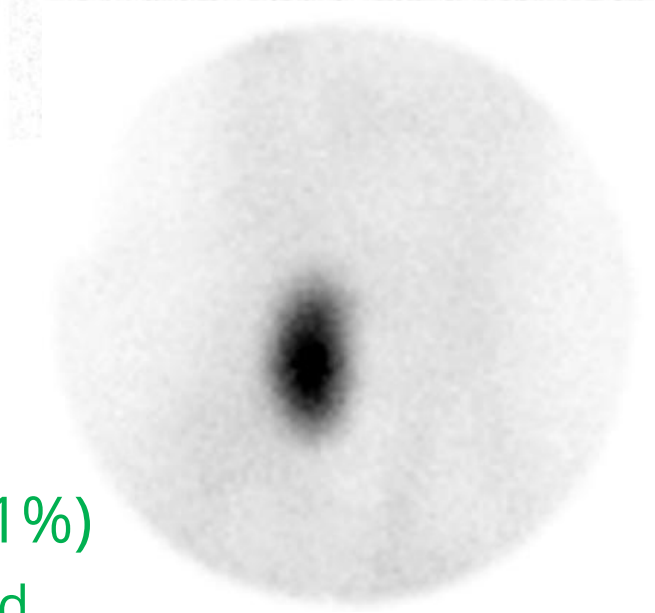
Image created by Microsoft Copilot, 2025

TSH = thyroid stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine; TPO = thyroid peroxidase; CBC = complete blood count; CRP = C reactive protein; ALT = alanine aminotransferase; hCG = human chorionic gonadotropin

# Case 3: TA 43F

- Repeat labs (methimazole 5mg):
  - TSH 0.38 ↓
  - fT4 11.0
  - fT3 4.4
  - TRAB 1.67
  - TPO <3.0
  - HCG <2.3
- Thyroid uptake and scan
  - Given negative antibodies





- Most likely: toxic nodule (remission <1%)
  - Radioactive iodine ablation recommended



TSH = thyroid stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine; TRAB = thyroid receptor antibody; TPO = thyroid peroxidase; hCG = human chorionic gonadotropin

# IV. When to Call Endocrinology

- Thyroid storm
- Overt hyperthyroidism lasting >3 months
- Pregnancy (esp. overt hyperthyroidism)
- Amiodarone
- Checkpoint inhibitor
- Rare causes

- When something does not make sense…

"I want to see a specialist"

# IV. Endo Referral Checklist

- ❑ Clear clinical question
- ❑ Symptoms of hyperthyroidism
- ❑ Supplements containing biotin, iodine
- ❑ Updated medication list, including drug allergies, medications tried for this issue
- ❑ Repeat 6-8 weeks later (7 days no biotin):

  TSH, free T4, free T3, antibodies (thyroid receptor antibody AND anti-TPO),
  CBC, ALT, bilirubin, CRP, hCG (if female)
- ❑ Thyroid ultrasound (only if abnormal exam)



TSH = thyroid stimulating hormone; fT4 = free thyroxine; fT3 = free triiodothyronine; TPO = thyroid peroxidase; CBC = complete blood count; CRP = C reactive protein; ALT = alanine aminotransferase; hCG = human chorionic gonadotropin

# Take Away Points

- Keep the differential for hyperthyroidism simple
  - Basic workup reveals most causes
- Be mindful of common nuances of thyroid testing
  - Try to eliminate interferences before repeating
- Initial hyperthyroid treatment is symptomatic
- Refer hyperthyroidism to Endocrinolgy when:
  - Long-term treatment required
  - Pregnancy or medication-induced
  - Rarer causes
  - When something does not make sense…

# Questions?
# Thoughts?

# Resources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AAFP = American Academy of Family Physicians; ATA = American Thyroid Association

# Resources: Biotin/Other


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11. Choosing Wisely Canada https://choosingwiselycanada.org/