THYROID DISEASE AND TESTING

Jack L. Snitzer, D.O., FACOI, FACE, CCD
MAPA MEETING
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JACK L. SNITZER, D.O.
410-572-8848

JACK.SNITZER@PENINSULA.ORG
NO CONFLICTS OF INTEREST
THYROID

- Goiter
- Hyperthyroidism (overt and “subclinical”)
- Hypothyroidism (overt and “subclinical”)
- Nodules
- Cancer
- Blood Tests
- Radiologic tests
- Medications
Frequency of thyroid issues

- Autoimmune thyroid disease (Hashimoto’s and Graves’) is about 7 times more common in women than men
- 1 out of every 10-20 women will develop hypo- or hyperthyroidism
- Goiter: up to one of every 10-20 people
- Nodule(s): up to one of every 10-20 people
PALPATION

• Low anterior neck

• I prefer palpating from in front of the patient, so I can see simultaneously see what and where I am palpating. I use one hand and then the other hand.

• Many people palpate from behind.
PALPATION

• From the from, use thumbs and/or fingers. Might need to use each hand (I often feel with my right fingers and thumb [standing on the patient’s right] and confirm using my left fingers and thumb [standing on the patient’s left side])
PALPATION

• Neck in neutral position usually, so the neck muscles don’t tense up (you might end up feeling the muscles more than the thyroid)
• So, don’t over-extend the neck.
• Don’t have the neck flexed with the chin down (the thyroid might then drop too low, below the sternum)
PALPATION

• Large neck muscles might confuse the patient and practitioner and might make the neck look larger. Might have to move the neck muscles out of the way with your fingers (palpate medial to the neck muscles [sternocleidomastoid])
PALPATION

• A fat pad over the sternal notch/upper sternum often looks like a goiter, but is soft and anterior to the thyroid on palpation.
PALPATION

• Is the thyroid (or nodule) soft, or firm, or hard? Is it mobile or fixed?
• Is the thyroid or the nodule tender to palpation?
• Is there a hum over the thyroid, which would suggest large blood flow (such as in hyperthyroidism due to Graves’ disease)?
Midline neck structures; note thyroid gland in anterior aspect of neck.

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Lower neck, thumbs and/or other fingers
Neck neutral. Goiter.
Neck extended
SCREENING

No consistent recommendations. Some organizations recommend routine screening (TSH) at 65 years of age; some at 50 years of age; Some organizations do not recommend routine screening.

Some organizations recommend pre-pregnancy screening, some do not.

See: US Preventive Services Task Force
SCREENING

• USPSTF: no data on screening benefits. No data on benefits of treating subclinical hypothyroidism

This is a population oriented approach.
SCREENING

• AMERICAN THYROID ASSOCIATION
Screen all adults who are not pregnant starting at 35 years old and every 5 years.
SCREENING

- AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS (AACE)

Routine TSH in older patients, with emphasis on women with non-specific symptoms. This approach is slanted toward the occasional significant benefits when mildly symptomatic individuals are treated.
SCREENING

- All newborns are screened with a TSH and free T4
SCREENING

• I would recommend screening relatives of individuals with hypo or hyperthyroidism with a TSH every few years, particularly female relatives. Check earlier if symptoms.

• TSH for any child with developmental issues or behavioral/performance change
THYROID testing

• TESTS:
  1. TSH
  2. Free T4
  3. Thyroid peroxidase antibody (TPO)
  4. Free T3
  5. Scan
  6. 24 hour uptake
  7. Ultrasound
  8. (T4, T3, T3-uptake, T7 or FTI)
  9. Thyroglobulin level and antibody
THYROID testing

• Most thyroid hormone (T4 and T3) is bound to protein in the blood, mostly to thyroid-binding globulin (TBG).

• Only free T4 and free T3 are active.

• The thyroid makes about 95% T4 and 5% T3. Each cell in the body then converts T4 into T3. T3 has the main effects in the body (each cell and affecting the TSH).
THYROID testing-TSH

• TSH
  - Most sensitive test for hypothyroidism.
  - Most sensitive test for hyperthyroidism.
  - Generally best screening test.
  - Not useful in patients with central hypothyroidism or for following patients with hyperthyroidism after the TSH is suppressed until the pituitary thyrotrophs recover from being suppressed and can make TSH again (which can take 3-4+ months).
THYROID testing-free T4

- Free T4
  - to confirm hyperthyroidism and degree of hyperthyroidism.
  - to confirm primary hypothyroidism (generally not needed unless you suspect central hypothyroidism).
  - to diagnosis and follow central hypothyroidism (TSH is not accurate in central hypothyroidism).
  - to follow treatment (with levothyroxine or with anti-thyroid drugs) until pituitary thyrotrophs can make TSH again in someone with hyperthyroidism or who is over-treated with levothyroxine to the point that the TSH is suppressed (until the pituitary thyrotrophs have recovered and can make TSH again)
  - to follow a patient when the TSH is undetectably low or is suspected to be undetectably low (patient with suspected pituitary tumor or pituitary insufficiency or hyperthyroidism or on too much levothyroxine)
THYROID testing - TPO

- THYROID PEROXIDASE ANTIBODY (TPO)
  - to confirm Hashimoto’s thyroiditis as cause of hypothyroidism (although negative TPO doesn’t rule out Hashimoto’s).
  - to determine the likelihood of a goiter or high risk patient becoming hypothyroid.
  - to prognosticate the likelihood of Graves’ disease remitting spontaneously.
  - to help interpret the results of thyroid nodule biopsy.
THYROID testing-free T3

- Free T3
  - to determine if patient has a disorder converting T4 to T3 (unusual). TSH is very sensitive to free T3 (except in the very rare condition of complete insensitivity to thyroid hormone).
  - to determine adequate replacement in patients with central hypothyroidism along with free T4.
  - to follow Graves’ disease along with free T4 (Graves’ often makes a disproportionately high amount of T3)
THYROID testing-
total T4 and T3

- These tests are generally not used anymore, but are still on the thyroid panels.
1. T4; T3; T3-uptake; T7 (FTI)
   - T4 and T3 are total hormone levels. Often not accurate.
   - Basically archaic tests.
2. T3-uptake: measures amount of thyroid-binding globulin. Used to correct total T4 to get FTI (T7). FTI (T7) is an estimate of free T4.
THYROID testing-thyroglobulin

• NOTE: thyroglobulin antibody and thyroglobulin levels are generally not useful, except in thyroid cancer follow-up after thyroidectomy. They have some utility in evaluation of thyroid inflammatory disorders and are being studied for other uses.

• Thyroglobulin is different than thyroid-binding globulin
THYROID testing-scans

- **SCAN**
  - to determine the functional status of the thyroid or nodule.
  - to differentiate hot, warm, cold, and cool nodules.
  - If cold or cool areas: biopsy if palpable nodule or get ultrasound to see if cold area corresponds to a discrete nodule.

NOTE: scans do not diagnose hypo- or hyperthyroidism. Scans of hypothyroid patients are generally very messy and usually not helpful. Technetium scans may occasionally misclassify nodules.
THYROID testing- scans

Many small thyroid nodules are below the resolution of a scan
THYROID testing-uptakes

• 24 HOUR UPTAKE
  -to determine ability to take up iodine. Mostly useful for calculation of dosage of radioactive iodine for treatment of hyperthyroidism.

• Note: Low uptake in a biochemically hyperthyroid patient: transient thyroiditis, iodine-induced hyperthyroidism, surreptitious use of thyroxine.
THYROID-ultrasound

- ULTRASOUND
  -to determine architecture of thyroid.
  -to follow size of nodules.
  -to confirm a cold/cool area found on a thyroid scan as being an actual nodule.
  -to assist biopsy of non-palpable nodules (and palpable nodules)
THYROID

• Notes:
  - In euthyroid women taking OCP’s and pregnant women:

  elevated total T4 is expected and meaningless, but Free T4 and TSH are not affected
HYPOTHYROIDISM: types

- Hypothyroidism
  1. Hashimoto’s thyroiditis (often has positive thyroid peroxidase antibody: TPO)
  2. Post-surgical
  3. Post-ablative (after RAI)
  4. Transient thyroiditis (silent, subacute, post-partum, etc.). Hypothyroidism occurs after the hyperthyroid phase.
HYPOTHYROIDISM: types

• 5. External Radiation: (Chernobyl, Three Mile Island, XRT to the neck for cancer treatment or for treatment of tonsils, thymus gland or acne; possibly radium rod treatment for tonsils);

  Radiation can affect the thyroid decades later and increases the risk for benign and malignant head and neck tumors.
HYPOTHYROIDISM: types

6. Central (low TSH and low Free T4).
7. Iodine-induced (excess iodine: Wolff-Chaikoff effect)
8. Iodine deficiency
9. Meds: amiodarone (due to iodine overload); interferon (due to autoimmune activation); lithium (due to dysregulation of thyroxine production/secretion), etc.
10. Congenital
HYPOTHYROIDISM: types

11. “Sub-clinical” hypothyroidism. Mildly elevated TSH with normal free T4. This is a very common scenario.


13. Endocrine disruptors.
HYPOTHYROIDISM

Dx: TSH elevated;

(Doesn’t matter if the free T4 is normal)
   (In central hypothyroidism, which is rare except for patients with panhypopituitarism, TSH is low and free T4 is low; OR free T4 is low and TSH inappropriately normal.)
HASHIMOTO’S

Hashimoto’s (most common cause of hypothyroidism). It is autoimmune: TPO (thyroid peroxidase antibodies) often positive (at least in the early stages before the thyroid is fully destroyed); the immune system destroys the thyroid over a period of time. Might or might not fully destroy the thyroid.

Note: negative TPO antibody test doesn’t necessarily mean it isn’t Hashimoto’s, but should consider other causes of hypothyroidism. Note: the thyroid is often normal in size, but can be small or large.
SURGICAL HYPOTHYROIDISM

• Might be partial or complete resection. Dose depends on how much functional thyroid is remaining.
• Occasionally the thyroid can grow back.
POST-ABLATIVE HYPOTHYROIDISM

• After RAI (radioactive iodine) treatment of hyperthyroidism. The goal is development of hypothyroidism. If a good dose is given, should become hypothyroid about 2 months after RAI given. When develops hypothyroidism, start full replacement dose of levothyroxine.
TRANSIENT THYROIDITIS

• Can be silent; or painful (subacute).
• Can be viral or autoimmune.
• Generally the patient is hyperthyroid for 2 months, then hypothyroid for two months, then euthyroid.
• Occasionally the patient stays hypothyroid permanently, especially if TPO is positive.
EXTERNAL RADIATION

• Can cause hypothyroidism or head and neck tumors (benign or malignant) years or decades later.

• Prophylactic iodine given if nuclear accident occurs.
CENTRAL HYPOTHYROIDISM

• TSH is not useful, since the pituitary cannot make TSH.
• Free T4 will be low and TSH will be inappropriately normal or low.
• Follow the Free T4 level (not the TSH). Would ideally like to see the free T4 mid-normal to top-normal.
• Have a knowledge about what a replacement dose of levothyroxine is for the patient’s weight.
IODINE DEFICIENCY

• Can cause hypothyroidism by lack of substrate to form thyroid hormone.
• More likely in a third world country, but might be pockets of iodine deficiency in the USA.
• Spot urine iodine if needed.
IODINE EXCESS

• Wolff-Chaikoff effect.

Excess iodine can cause hypothyroidism, hyperthyroidism or have no effect on thyroid function.
MEDICATION INDUCED HYPOTHYROIDISM

• amiodarone (due to iodine overload);
• interferon (due to autoimmune activation);
• lithium (due to dysregulation of thyroxine production/secretion), etc.
• Others
Lack of development or function of the thyroid in utero
ENDOCRINE DISRUPTORS

- Chemicals/Toxins that interfere with thyroid function/thyroid hormone production.

Evolving field of endocrinology.
HYPOTHYROIDISM-symptoms

Symptoms:
Cold, constipated (decreased frequency of bowel movements), slow heart rate, fatigue, weakness, myalgias, variable weight gain or inability to loss weight, edema, bloating, hair thinning, dry skin, irregular menses, etc.
NOTE: no need to get scan or ultrasound unless concerned about a palpable nodule, rapid growth, or compressive symptoms, in which case an ultrasound might be ordered.

Patients with Hashimoto’s often have messy looking thyroids due to the destructive process.

Scan cannot be done if on thyroxine and generally not warranted to stop thyroxine for 4-6 weeks to get a scan (order ultrasound if you think you feel a nodule).
HYPOTHYROIDISM-treatment

Levothyroxine (Synthroid, Levoxyl, generic, or Tirosint).

Debate: generic versus Brand.

If using generic, would prefer that the generic company is the same each refill. If not, check TSH 2 months after change.

DOSES of Synthroid and Levoxyl and generic levothyroxine available:

25; 50; 75; 88; 100; 112; 125; 137; 150; 175; 200; 300 mcg
TIROSINT

• This is a gel cap formulation of levothyroxine. It contains no dyes or gluten.

• Doses (mcg): 13, 25, 50, 75, 88, 100, 112, 125, 137, 150.
TIMING OF THYROXINE DOSE

• Take levothyroxine ideally 1-2 hours apart from calcium and iron pills (which can bind thyroxine) and antacids (which change the pH and therefore the absorption).

• Proton pump inhibitors can cause decreased absorption of thyroxine (regardless of time of administration) by changing the pH.

• Coffee, fiber, meals, etc.
HYPOTHYROIDISM-treatment

Approximate Full replacement dose:
weight (kg) x 1.7 = mcg levothyroxine

The dose is affected by GI absorption of thyroxine. Most individuals absorb about 75% of the oral dose of Synthroid, Levoxyl or generic thyroxine. Possibly higher absorption of Tirosint.

Remember that we often diagnose hypothyroidism before the thyroid is completely destroyed, therefore the patient will need a lower than full replacement dose initially which will likely need to be increased over time.
If cardiac disease suspected or if over (?) 50+ years old, start low dose (25-50 mcg daily).

May need to start full or near full replacement dose in patients with significant hypothyroidism if safe to do so.

Generally need to start full dose when the patient becomes hypothyroid following radioiodine ablation.
HYPOTHYROIDISM-treatment

Titrate dose progressively in one direction, slowly increasing as needed and repeating a TSH every 2-3 months (no sooner than every 6 weeks generally).

If stable on a lower than expected replacement dose of thyroxine, check TSH once or twice yearly.

Generally no reason to make large changes in the thyroxine dose unless patient is significantly hypothyroid and can tolerate large changes.

Thyroxine has a high therapeutic index: small changes affect the TSH significantly.
Levothyroxine dose

Things that affect thyroxine dose by altering thyroid binding globulin (TBG) level:

- estrogen, OCP’s
  cause increased TBG which causes increased binding to T4 and increased dose of T4 to maintain a stable Free T4 level

- testosterone, malnutrition:
  cause decreased TBG
OTHER THYROID SUPPLEMENTS

- Kelp or Seaweed: should be avoided since they have unpredictable amounts of iodine; usually have no effect on the thyroid (in thyroid replete areas of the world), but can cause hyperthyroidism or even hypothyroidism. They also certainly won’t help someone who doesn’t have a thyroid (RAI ablation, surgery, thyroid destruction due to Hashimoto’s)
CYTOMEL (T3)

• It is T3 (Liothyronine)
  Unfortunately, it is rapid-acting and short-acting, so it has a “burst effect”, which is a stimulant effect shortly after taking it. This stimulant effect can overly stimulate the heart and other organs, which in ill or sensitive patients, can be problematic.
  The stimulant effect can treat depression (psychiatrists use it for severely depressed patients refractory to anti-depressants) as “induction therapy”.
  Also, the stimulant effect can give people more energy briefly, which leads to the mistaken assumption that the thyroid is the main cause of their fatigue since they might felt better after getting T3.
T3

• We think that people need about 50-75 mcg daily T3 (which is partially produced in the thyroid and the rest is converted from T4 by each cell in the body).
They are working on a long-acting form of T3.

T3 might be needed in the rare patient who can’t convert T4 into T3.

Note: when giving T3, the T3 actually takes away the body’s self-regulating ability of turning T4 into T3, since T3 is the strong end-product that the cells use.
CYTOMEL

- Its effect is often mis-represented in online forums due to people misconstruing its stimulant effect, which makes them feel stimulated, as representing a thyroid effect ("It must be my thyroid because Cytomel made me feel better").
T3

• I caution my patients with T3 preparations (and other things) not to assume that since you feel better on it, it must mean that you were lacking it in the first place.

For instance: I have more energy when I have caffeine, but this doesn’t mean that my body was lacking caffeine in the first place.
OTHER THYROID SUPPLEMENTS

• Armour (T4 and T3).
• NatureThroid (T4 and T3). Euthroid.

These are combinations of T4 and T3. They are from animal thyroids. They actually contain a higher ratio of T3 to T4 than is found in humans. Therefore, the stimulant or “burst effect” of T3 is present, and in a greater amount than in humans.
SUBCLINICAL HYPOTHYROIDISM

• High TSH (but under 15 or so).
• Normal free T4.
• Under the age of 65, treatment might be recommended.
• Over the age of 65, observation might be more reasonable.
**SUBCLINICAL HYPOTHYROIDISM**

- Treatment benefited people 40-70 years old.
- Older than 70 years old, treatment might have increased cardiovascular events.
- Treating subclinical hypothyroidism decreased the rate of ischemic heart disease in patients age 40-70 by 39%. All cause mortality was decreased by 64% in a review of medical records of United Kingdom (4,735 patients in 2001 followed for 8 years).
Thyroid in pregnancy

- Check TSH pre-conception in thyroid patients.
- Check TSH pre-conception in normal women?
  - Keep TSH in low normal range if possible (0.5-2.5).
  - Check TSH every 2-3 months in thyroid patients if stable.
  - Check TSH every 4-6 weeks if making adjustments.
  - Thyroxine dose might increase during pregnancy due to: 1. increased estrogen causing increased thyroid binding globulin; 2. Increased weight.
Post-Partum thyroiditis

• Up to 25% of all women develop this within the first 6 months after delivery.

• Initially hyperthyroid, then hypothyroid then euthyroid.

• If TPO +, may become permanently hypothyroid.
HYPERTHYROIDISM causes

- GRAVES’ (most common in younger people; might have bulging eyes: proptosis, orbitopathy)
- Meds (Amiodarone).
- Kelp/Seaweed.
- NODULE(S).
- Transient thyroiditis/Post-partum thyroiditis.
AMIODARONE

- AMIODARONE induced hyperthyroidism:
  - Usually low uptake, so RAI not effective.
  - Might be fairly refractory to therapy with anti-thyroid drugs.
  - The iodine may redistribute for many months after discontinuation of amiodarone, so the hyperthyroidism might persist for months to over one year.
HYPERTHYROIDISM treatment

• RAI, with a goal of causing permanent hypothyroidism; if a reasonable dose is given, hypothyroidism occurs 2 months later
• Methimazole (watch LFT’s); might slowly affect the liver
• PTU 1st trimester pregnancy only. Watch for acute liver injury
HYPERTHYROIDISM treatment (cont’d)

- Surgery: generally last resort
- Observation
- (Treatment of thyroid storm is in auxiliary slides)
GOITER

1. Check TSH.

2. Check thyroid peroxidase (TPO) antibody once.
   If Positive: check TSH about yearly.
   If Negative, TSH every 1-3 years.

3. If compressive symptoms (dysphagia, stridor, hoarseness): trial of thyroxine suppression (levothyroxine 25-50 mcg usually a reasonable starting dose for suppression) to keep the TSH between about 0.1 and 0.5. Consider surgery.
GOITER

- Generally no need to check ultrasound or scan unless question of a nodule to palpation or compressive symptoms (ultrasound).
- If hyperthyroid, might get scan and 24 hour uptake, if planning to treat with RAI-131.
- Palpate thyroid at least yearly.
GOITER

• Compressive symptoms could include:
  Stridor, DOE, Hoarseness, Dysphagia
  (especially solid food)
NODULES

• Probably more common in patients with hypothyroidism due to Hashimoto’s, likely due to the destructive process causing a “lump-bumpy gland”. Therefore, try not to order ultrasounds on patients with Hashimoto’s unless you think you feel a nodule.
NODULES

- Ultrasound to follow size of nodules.
- Scan: generally not needed to determine if cold/cool nodules are present. Cold nodules are higher risk of being cancer, but still only 10-20% risk.
- Hot nodules: lower risk of being cancer but only really in a hyperthyroid patient if the nodule suppresses the remainder of the gland.
- There are discordant nodules (hot on Tc scans but cold on iodine scans)
NODULES

• If history of radiation to neck (external XRT, radium rods), ultrasound regularly and biopsy new nodules $>0.5$-1 cm.
NODULES

• Most studies suggest Hashimoto’s slightly increases the risk of a nodule being thyroid cancer.
NODULES: biopsy

Generally nodules >1 cm are more likely to be considered for biopsy.

Some data suggest if a nodule has no concerning features and there are no concerns in the patient’s history, then 2 cm or larger might be the cutoff for biopsy.
NODULES: biopsy

There are no definitive ultrasound criteria to suggest higher or lower risk of a nodule being malignant.

Suspicious features:
- microcalcifications
- solid
- size > 2 cm
NODULES: biopsy

Ultrasound features that might be more concerning:
Hypoechoic
Taller than wide
Irregular margins
Intranodular vascularity
Suspicious lymph nodes
NODULES

- Increased concern if:
  - Irregular borders
  - Over 4 cm
  - Hypoechoic
  - Taller than wide
  - Rapid growth
  - Hypervascular
  - Cold on scan
NODULES

1. Hot nodules are less likely to be cancer, but not always. It is more reassuring if the hot nodule is suppressing the remainder of the thyroid and the patient is hyperthyroid.

2. Cysts are not 100% of the time benign.
3. Multiplicity of nodules does not guarantee benign disease.
4. Each nodule has its own risk.
**NODULES: TI-RAD**

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Suspicious US features: solid marked hypoechochogenicity, hypoechochogenicity microlobulated or irregular margins microcalcifications taller than wide shape

*Kwak Radiology 2011:260:892*
COMMON MISTAKES

- Changing the thyroid dose too much or too rapidly based on TFT results
- Not realizing that the TSH takes a few months to be useful after being suppressed
- Forgetting the TSH isn’t useful in hypopituitary patients
- Ordering scans or ultrasounds for mild, smooth asymptomatic goiters
- Mistaking overlying muscle for a goiter
ADJUSTING THE DOSE

• If the blood test is borderline normal, determine if the dose should be adjusted based on knowledge of what a usual dose is and based on patient preference. Might often give the patient a choice whether to change the dose a little if that option exists.
THYROID SYMPTOMS

• Remember: patients (and providers) tend to seek out and accept information that supports their pre-existing philosophy.
• So if they go online, they will understand and quote information that seems to make sense to them in this framework.
COMMON MISTAKES

• Ordering a total T4 or total T3
• Not checking a TSH, etc. after changing doses; TSH should be checked in about 2 months after any change of dose. (Free T4 also if the TSH is suppressed.)
• Not watching an ALT in patients on anti-thyroid drugs
• Diagnosing hyper- or hypo-thyroidism based on a scan alone without TFT’s
COMMON MISTAKES

• Assuming all patients with a high TSH have to be treated and have permanent hypothyroidism (they might have transient thyroiditis or random fluctuation of TSH)

• Placing too much emphasis on each exact TSH level; there are random fluctuations throughout the day and levels might vary even in well treated patients; and absorption of thyroxine might vary minimally periodically unpredictably

• Assuming all individuals with a high-normal TSH are better off with a higher does of levothyroxine to achieve a low-normal TSH
COMMON MISTAKES

• Suppressing a goiter or a nodule with too much thyroxine. If suppression is used at all, the TSH should be between 0.1 and 0.5 ideally for suppression.

• Being too aggressive with titrating the thyroxine dose in medically sick individuals

• Assuming that the patient’s weight, energy, etc. are exclusively controlled by the thyroid and that even a top normal TSH indicates the thyroid is the main and only cause of all the patient’s symptoms or problems

• Not looking for other diseases to explain a patient’s symptoms
COMMON MISTAKES

• Propagating a prior incorrect diagnosis of permanent hypothyroidism (Hashimoto’s thyroiditis) in a patient who might have actually been started on thyroxine due to transient thyroiditis or based on symptoms and patient expectations

• Checking TSH too often if stable or if adjusting treatment

• Checking a TSH too infrequently if still adjusting dose or if patient is on a less than full replacement dose based on weight
COMMON MISTAKES

Saying to a patient after a blood test that the thyroid is high or low (?do you mean the TSH blood test or thyroid function? Since the TSH blood test goes in the opposite direction to the thyroid function).
COMMON MISTAKES

• Treating someone based on an initially mildly elevated TSH (under 15 or so). Should consider repeating the TSH in 1 month or so (along with TPO) and decide whether to treat. This way, won’t be unnecessarily treating transient or “subclinical” hypothyroidism.
THYROID

TSH testing ideally should be obtained in the morning before taking the dose of thyroxine. Not of critical importance in most cases.

TSH ranges are being re-evaluated.
THYROID CASE #1

31 year old with TSH 7.4 and normal free T4
THYROID CASE #1

- Possible early hypothyroidism (Hashimoto’s thyroiditis) vs. transient thyroiditis vs. euthyroid sick vs. lab error/fluctuation/normal for patient.
- Rule out transient, post-partum, or subacute thyroiditis
  - tender neck
  - sed rate elevated but during the hyperthyroid stage
  - recent URI
  - post-partum state
  - positive or negative TPO
THYROID CASE # 1

• Since TSH is under 15 or so would generally get confirmatory testing before treating.
THYROID CASE #1

• Check TSH in 1-2 months along with TPO.
  *If positive, start 25-50 mcg levothyroxine daily.
  *If TSH normal but TPO positive, might either treat and check TSH 2 months to check on dose, or observe and repeat TSH in 4 months.
  *If TSH is still elevated, but TPO is negative, might either treat and repeat TSH 2 months to check on the dose, or observe and repeat TSH 4 months
THYROID CASE  #2

31 year old with TSH 49 and normal free T4
THYROID CASE  #2

Same discussion as case #1, but more likely to be permanent Hashimoto’s with the TSH so high.

Would likely treat with levothyroxine 25-50 mcg daily right away.

Clinical point: free T4 might still be normal even with a significantly elevated TSH
THYROID CASE #3

81 year old with TSH 7.4 and low free T4
THYROID CASE #3

- Check TPO
- low TSH and low free T4 classic for permanent hypothyroidism (Hashimoto’s)
  (but still could be transient thyroiditis)

If TPO positive:
  Consider 25 – 50 mcg levothyroxine and check TSH in 2-3 months and titrate slowly

If TPO negative: check TSH in 1-2 months and treat if still high (or just treat if symptomatic)
THYROID CASE #3

• Need to make sure (less commonly) not central hypothyroidism and the elevated TSH is actually not as elevated as it should be due to pituitary insufficiency. Does she have any symptoms that might suggest further work-up for pituitary insufficiency, such as flu-like symptoms?
THYROID CASE #4

31 year old with a goiter. TSH normal. Total T4 high.
THYROID CASE #4

Check TPO.
Since TSH is normal, patient probably euthyroid.
Total T4 is high as expected since this patient is on an OCP. (free T4, which is not necessary since the TSH was normal, would be normal)

(These cases do not represent pituitary tumors making TSH, which is very rare)
THYROID CASE #5

Low TSH (0.1 and on repeat <0.005) and low Free T4 at 0.3.
THYROID CASE #5

Central hypothyroidism.
Order MRI of pituitary with and without contrast and check pituitary function.
Other possibilities include euthyroid sick syndrome; or acute recovery stage from hyperthyroidism or acute post-ablative hypothyroidism (pituitary thyrotrophs are still suppressed during which time the pituitary can not yet make TSH).
THYROID CASE #6

25 year old female (70 kg) post-partum after delivering a healthy baby 6 months ago. She is tired and can’t lose the last 5 pounds of her pregnant weight. TSH: 20. Free T4 normal.
THYROID CASE #6

This could be post-partum thyroiditis in the later (hypothyroid stage). The hyperthyroid stage resolved before this.

Treatment:

1. Check TPO now. If positive, likely to have developed permanent hypothyroidism due to Hashimoto’s (either spontaneously after pregnancy or following post-partum thyroiditis). Could consider treating with levothyroxine 25-50 mcg daily.

2. Observe and check TPO and TSH in 1 month and decide if treatment needed. If TSH still high and no better, especially if TPO is positive, could treat with levothyroxine 25-50 mcg daily.
THYROID CASE #7

• 55 year old female with TSH low at 0.20 on levothyroxine 50 mcg daily. Has been on this dose for 15 years without ever having to change doses. Started thyroid hormone then due to fatigue and “borderline TFT’s”.

• Her weight is 80 kg.

Therefore, calculated expected full replacement dose of levothyroxine would be about 137 mcg daily if she had no functioning thyroid tissue.
THYROID CASE #7

1. Does she truly have and did she ever have hypothyroidism? Might have been started on thyroxine for suppression of a goiter or nodules, or might have had mildly abnormal TFT’s (Total T4 or TSH, etc.), or might have had transient thyroiditis at diagnosis, or might have been treated based on symptoms.

2. She is on a much lower than anticipated replacement dose and has not needed any increases. So this makes me question a diagnosis of Hashimoto’s.
THYROID CASE #7

- Check TPO. If negative, very likely doesn’t have Hashimoto’s, and could either decrease or stop the levothyroxine and check a TSH in 6 weeks.

- If TPO is positive, probably continue the levothyroxine and check TSH 1-2 times yearly if stable.
THYROID CASE # 8

- 72 year old male with hypothyroidism for 14 years. Dose has slowly increased. Currently taking 200 mcg daily.
- Has stable coronary artery disease s/p stents a couple years ago.
- Wt: 70 kg.
- TSH: <0.005. Free T4 is high at 2.2.
THYROID CASE # 8

• On too much levothyroxine, which is even more important given the history of heart disease.
• Based on weight, a usual replacement dose of levothyroxine would be about 112-125 mcg daily.
THYROID CASE # 8

• Rec: decrease the dose of thyroxine from 200 mcg daily to 125 mcg daily and check TSH and free T4 in 6-8 weeks.

• This is one of the few times I would decrease the dose more aggressively. He has CAD and Free T4 is high.
THYROID CASE # 8

- Remember, the next TSH might not be accurate since it might take 3-4+ months for the pituitary thyrotrophs to recover and make TSH again. Therefore, have to ballpark the correctness of the dose based on free T4 level and knowledge of what a usual replacement dose should be.
THYROID CASE #9

50 year old with hypothyroidism for 5 years. She is 70 kg. On levothyroxine 75 mcg daily. TSH has been normal on this. No TSH is 5.2. Feels well.
THYROID CASE #9

• OPTIONS:

• Increase the dose to 88 mcg daily.

• Continue the current dose and repeat TSH in 2-3 months.
• What if her TSH was top normal at 4.5?
• What if she had been feeling tired and cold.

• Then options remain increase the dose to 88 mcg daily or repeat the TSH, based on her clinical individual situation.
AUXILIARY SLIDES

- MYXEDEMA and THYROID STORM
MYXEDEMA

• SEVERE HYPOTHYROIDISM LEADING TO DECREASED MENTAL STATUS, HYPOTHERMIA, AND OTHER SYMPTOMS RELATED TO SLOWING OF FUNCTION OF MULTIPLE ORGANS
MYXEDEMA

• Usually not in a coma at presentation
• High mortality rate 30-40%
MYXEDEMA: CLUES TO DIAGNOSIS

• Thyroidectomy scar
• History of I-131 treatment
MYXEDEMA

• Usually the culmination of long-standing hypothyroidism or can be precipitated by an acute event (infection, myocardial infarction, cold exposure, sedatives, especially opioids)
MYXEDEMA: FINDINGS

- Hypotension
- Bradycardia
- Hypothermia
- Hyponatremia (due to impaired free water excretion due to inappropriate anti-diuretic hormone or impaired renal function)
- Hypoglycemia (due to hypothyroidism or adrenal insufficiency)
MYXEDEMA: FINDINGS

- Hypoventilation
- Puffy hands, face, enlarged tongue (deposition of mucin: myxedema)
- Pericardial effusion
- Note: might not be able to mount a febrile response to acute infection
MYXEDEMA

• Most cases are in patients with primary hypothyroidism.
MYXEDEMA: TFT’s

- High TSH and low free T4

- Note: if the TSH is low or normal and the free T4 is low, then need to consider a hypothalamic or pituitary cause (central hypothyroidism)
MYXEDEMA: Consider adrenal insufficiency

- Give hydrocortisone 100 mg IV every 8 hours before treating with thyroxine

If a patient is hypoadrenal, thyroxine can exacerbate this and precipitate acute adrenal crisis if given before glucocorticoid is given

Try to draw a cortisol level before the hydrocortisone is given; if the level eventually returns over 20 mcg/dL, then the hydrocortisone might be able to be stopped
MYXEDEMA: TREATMENT

- T4 (levothyroxine)
  (The risk of atrial arrhythmia and MI need to be weighed against the mortality of myxedema coma)

- ?T3: debatable whether to give T3. T3 is quicker acting and T4 to T3 conversion is decreased in these patients
MYXEDEMA: TREATMENT

- T4: IV (not po due to decreased GI absorption)

200-400 mcg IV then 1.6 mcg/kg/day then change to po when doing better
MYXEDEMA: TREATMENT

• T3 (if given)

5-20 mcg then 2.5-10 mcg every 8 hours
MYXEDEMA: TREATMENT

• Passive warming (not active warming, which could cause vasodilation)
THYROID STORM
DEFINITION

• LIFE-THREATENING CONDITION CHARACTERIZED BY SEVERE CLINICAL MANIFESTATIONS OF THYROTOXICOSIS
THYROID STORM CAUSES

- Surgery (operating on a non-prepped hyperthyroid gland, or non-thyroidal surgery)
- Trauma
- Infection
- Acute iodine load
- Parturition
THYROID STORM

• Can occur in patients with Graves’ disease, multinodular goiter, or solitary nodule
THYROID STORM

- Free T4 and free T3 levels probably higher in thyroid storm than in thyrotoxicosis, but the degree of elevation is not a criterion for diagnosis
THYROID STORM

SYMPTOMS

• Exaggeration of usual hyperthyroid symptoms.
• Tachycardia
• Congestive heart failure
• Hypotension from cardiovascular collapse
• Fever 104-106 degrees
• Agitation, anxiety, delirium, psychosis, stupor, coma
• Nausea, vomiting, diarrhea, abdominal pain, hepatic failure
THYROID STORM EXAM

- Might have goiter
- Might have ophthalmopathy
- Tremor
- Warm, moist skin
LAB TESTS

• Classic TFT’s: Low or suppressed TSH, high free T4; high free T3
• High calcium
• Hyperglycemia
• Elevated liver tests
• Elevated or low WBC’s
RADIOLOGIC TESTS

- Uptake and scan not needed
- Ultrasound generally not needed unless concerning nodule(s) felt
TREATMENT

• Don’t delay treatment for radiologic tests
• ICU: there is a 30-40% mortality rate
• Generally similar treatment as hyperthyroidism but increased doses and increased frequency of dosing
• Might need fluids or diuretics
• Note: these patients have increased metabolism of drugs
TREATMENT

• Avoid aspirin, which can cause increased T4 and T3 levels by interfering with protein binding
• Beta-blockers: propranolol 60-80 mg po every 4-6 hours titrated to heart rate; or 0.5-1 mg IV over 10 minutes then 1-2 mg over 10 minutes every few hours
TREATMENT

• Thionamides: to block new thyroid hormone synthesis

Methimazole 20 mg po every 4-6 hours.
PTU (propylthiouracil) 200 mg every 4 hours.

Can be given via NG tube or rectally if needed
THIONAMIDES

• PTU can decrease the conversion of T4 to T3 and is also faster acting, so might be better choice initially.

• However, PTU can have more liver toxicity so don’t want to use it in the long run
IODINE

- To block release of thyroid hormone. Give for 5-7 days. Can start 1 hour or longer after thionamide given.
- Large dose of iodine inhibit organification of iodine in the thyroid (Wolff-Chaikoff effect). This effect can wear off after several days, so if surgery is anticipated, should be done within 8-10 days of starting iodine.
IODINE

- SSKI: (38 mg iodine per drop)
  Five drops every 6 hours

- Lugol’s: (8 mg iodine per drop)
  10 drops every 8 hours
GLUCOCORTICOIDS

- Hydrocortisone 100 mg IV every 8 hours
  or
- Dexamethasone 1-2 mg IV every 6 hours

Glucocorticoids decrease T4 to T3 conversion and decrease any underlying inflammation
SURGERY

- Thyroidectomy after thyroid is prepped as mentioned

- Plasmaphoresis has been reported to temporize a patient for surgery but used only in refractory cases

- If pregnant, might need thyroidectomy, ideally in the 2nd trimester