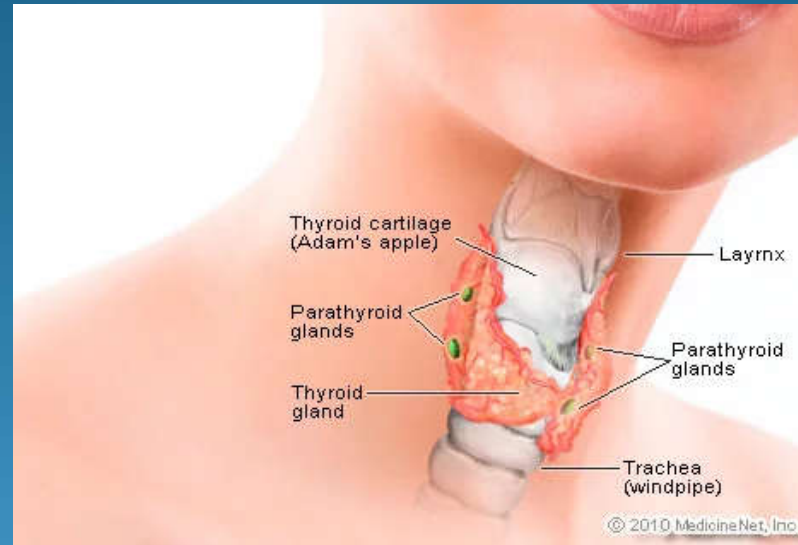


Thyroid Disease

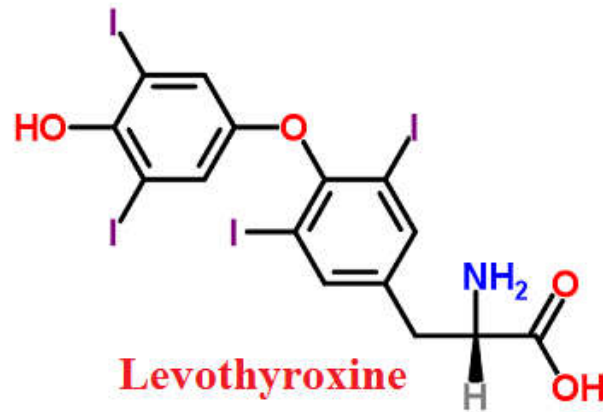


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Topics:

- Thyroid hormone replacement therapy
- Screening for thyroid disease
- Thyroid nodule evaluation
- The euthyroid “weak and tired” patient
- Thyroid testing in hospitalized patients
- Thyroid disease and pregnancy
- Follow up of patients with thyroid cancer

Thyroid Hormone Replacement Therapy



Molecular formula: C₁₅H₁₁I₄NO₄

Average mass: 776.870 Da

Chemical name: O-(4-Hydroxy-3,5-diiodophenyl)-
3,5-diiodo-L-tyrosine

Case #1: The “I’m ‘Natural’ and I’m Happy” Patient



The patient is a 42 year old Caucasian female who just moved to the area and is establishing care with you.

She has a history of hypothyroidism due to Hashimoto's thyroiditis, but is otherwise in good health. She attributes her good health to being a Vegan. She exercises vigorously an hour daily, and enjoying natural herbs and supplements.

She is on Armour desiccated thyroid extract, 60 mg once daily, with a recent TSH of 2.1.

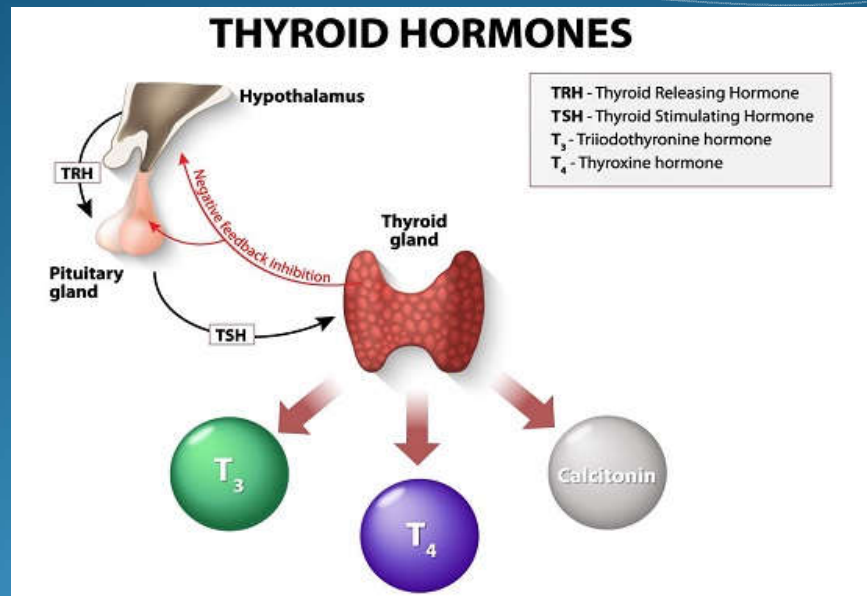
On physical examination she is a fit and trim woman who looks younger than her stated age. She asks you for a refill of her Armour thyroid extract.

What should you do with this patient?

1. Stop the Armour thyroid extract and change her to a T₄ preparation, as desiccated thyroid is an outdated product and can cause the patient harm.
2. Leave her on Armour, as she is feeling well and has had no complications from using the medication.
3. Stop the Armour thyroid and start tri-iodothyronine (T₃), as it is the active thyroid hormone.



Thyroid hormone



The thyroid gland produces both T₄ and T₃

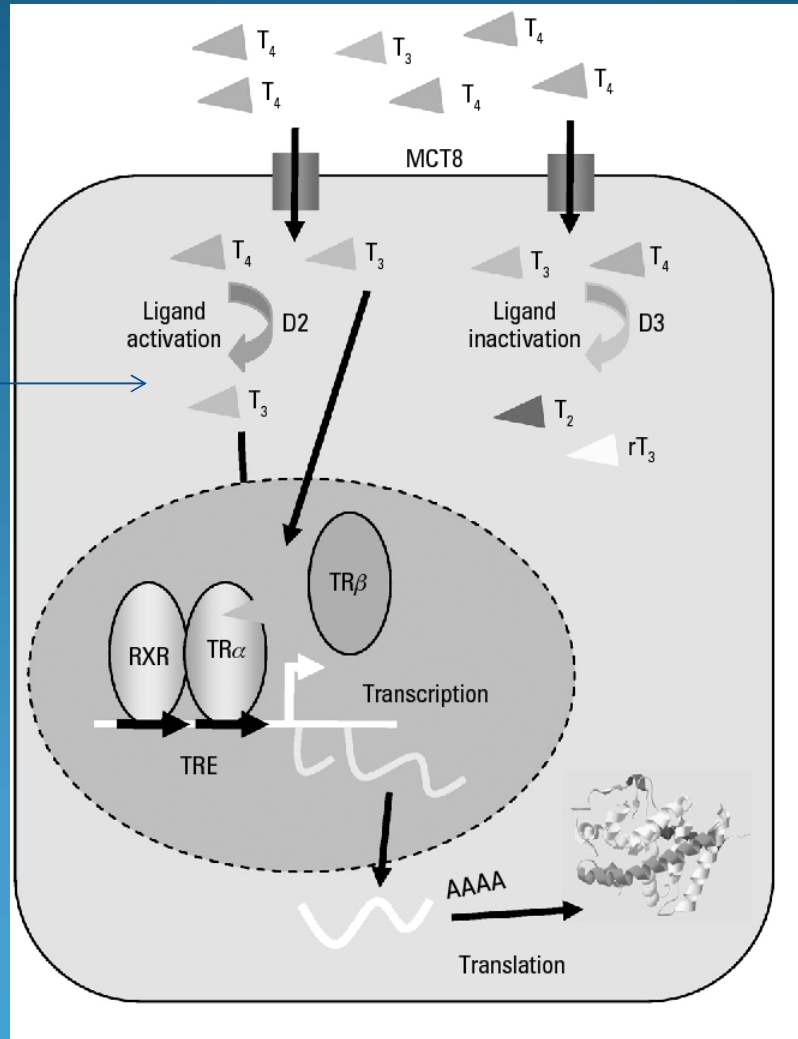
80% is T₄. T₄ is an inactive pro-hormone

20% is T₃, which is the active thyroid hormone

Why does the thyroid gland produce primarily T₄?

Mechanism of Action

5' deiodinase



Levothyroxine “T₄”

Common T₄ replacements: Synthoid, Unithroid, Levoxyl,

- most individuals feel well on T₄ preparations
- choose the least expensive brand name
- generic levothyroxine, although least expensive, is less desirable due to brand variability in absorption

Triiodothyronine “T₃”

- There is no place for T₃ by itself in the treatment of hypothyroidism
- T₃ is rapidly absorbed, with a rapid high peak, and a duration of action of 6 hours

Desiccated Thyroid Extract (Armour, Nature-throid)



- Desiccated thyroid extract is not FDA approved (it's use and manufacture was grandfathered in due to being in production before 1938 when the FDA was founded).
- However, it is required by the FDA to meet consistency and potency standards
- It is safe to use in young, healthy individuals
- Caution should be used or its use avoided in patients with known **CAD** or other serious cardiac disease, and the **elderly** (due to their cardiac status being unknown and the greater risk for arrhythmias).
- It is dosed differently than levothyroxine preparations: 90% of patients need either 30 mg or 60 mg to maintain a euthyroid state.

Causes of hypothyroidism

1. Hashimoto's thyroiditis – most common in Western societies. Thyroid peroxidase antibody.
2. Iodine deficiency – more frequent in third world countries
3. Surgical removal of the thyroid gland
4. Radioactive iodine ablation of the thyroid for hyperthyroidism
5. Medications – amiodarone, excessive iodine intake (fad diets), chronic heavy narcotic use (suppresses TSH release), chronic glucocorticoid use, others.

Screening For Thyroid Disease

The infographic features a central illustration of a woman with short orange hair, wearing a green dress and black heels. She is standing with her hands on her hips. Lines connect various symptoms listed on either side to her body, such as her hair, eyes, thyroid area, and weight.

Hypothyroidism	Hyperthyroidism
<ul style="list-style-type: none"> • Hair loss • Inability to think clearly • Goiter (enlarged thyroid) • Reduced heart rate • Strong fatigue • Sensitivity to cold • Dry skin • Weight gain • Puffiness • Memory problems • Constipation • Irregular menstrual periods • Severe PMS • Depression, mood swings • Joint, muscle pain • High cholesterol 	<ul style="list-style-type: none"> • Hair loss • Bulging eyes • Goiter (enlarged thyroid) • Heart palpitations • Tremors • Heat intolerance • Sleep disturbances • Weight loss • Shortness of breath • Diarrhoea • Increased appetite • Irregular menstrual periods • Muscle weakness • Sweating • Anxiety, nervousness • Depression, mood swings

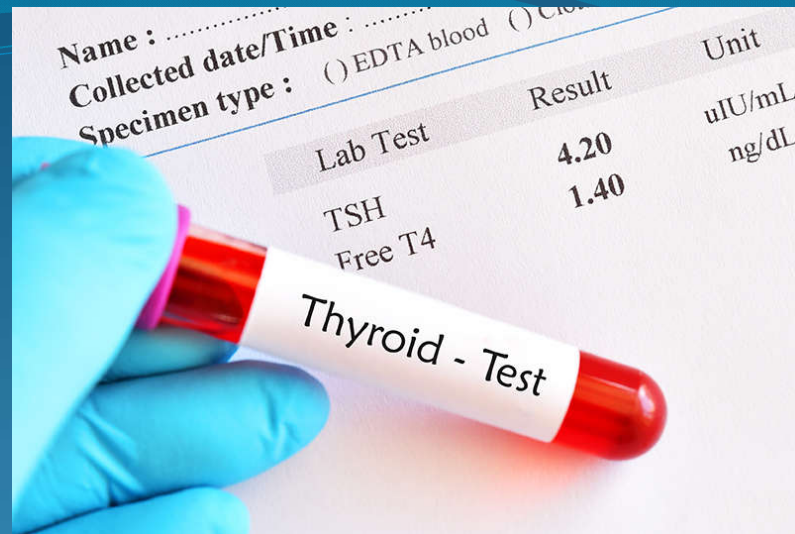
Case #2: “Let’s Spend Money!”



This patient is a 32 year old Caucasian female who sees you with multiple complaints.

She feels chronically fatigued, and has been slowly gaining weight despite exercising 30 minutes daily. She's noted dry skin and brittle hair. Her menstrual cycles are monthly but more irregular. She has become somewhat depressed, with occasional crying spells.

She's happily married, and works full time as a bank teller. She has no prior medical problems, but does have a strong family history of hypothyroidism in her mother, grandmother, and a sister.



What tests would you order to screen her for hypothyroidism?

1. TSH, Free T₄
2. TSH, Free T₄, Free T₃
3. TSH, T₃RU, Total T₄, Total T₃
4. TSH, Free T₄, thyroid peroxidase antibody titer
5. TSH



- Prior to the early 1980's, TSH assay was relatively insensitive
- Total T₄, Total T₃, T₃RU useful for screening then
- Now, TSH assay is a 3rd generation super sensitive assay

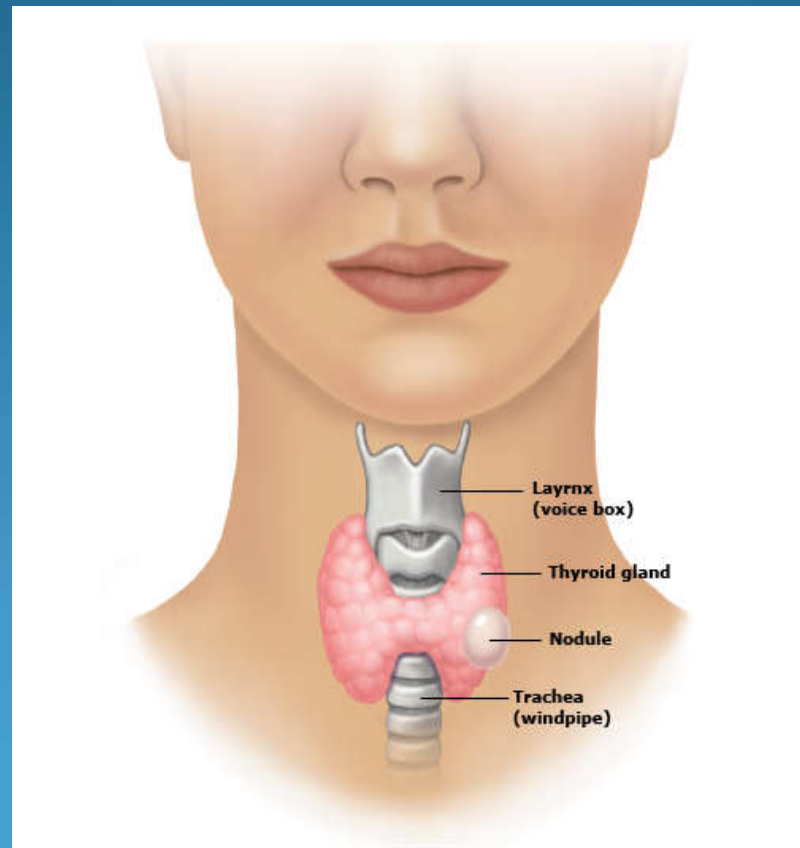
- TSH only is needed as a screening test for thyroid disease, and for long term follow up of hypothyroid patients on thyroid hormone replacement.

- T₄ and T₃ levels are needed in patients on anti-thyroid medication, patients s/p ¹³¹I ablation, and patients with secondary hypothyroidism (i.e. pituitary failure).
- T₃ resin uptake is an antiquated test rarely needed today.

The thyroid peroxidase antibody titer is positive...now what?

- Positive antibody titers in a euthyroid patient causes no known symptoms by itself
- A euthyroid woman with positive antibodies and a normal TSH, but >2.5 $\mu\text{u/L}$, is more than four times as likely to develop hypothyroidism in 13 years than if her TSH is <2.5 $\mu\text{u/L}$.
- Reassure a euthyroid patient with a positive thyroid peroxidase that the antibodies have no known effect except on thyroid tissue.
- Monitor a TSH at least twice yearly in euthyroid patients with positive antibodies to monitor for development of hypothyroidism. You do not need to send these patients to an endocrinologist.

Thyroid Nodule Evaluation



**Case #3:
“I’ve Found A Thyroid
Nodule, and I’d Really Like
To Spend More Money!”**

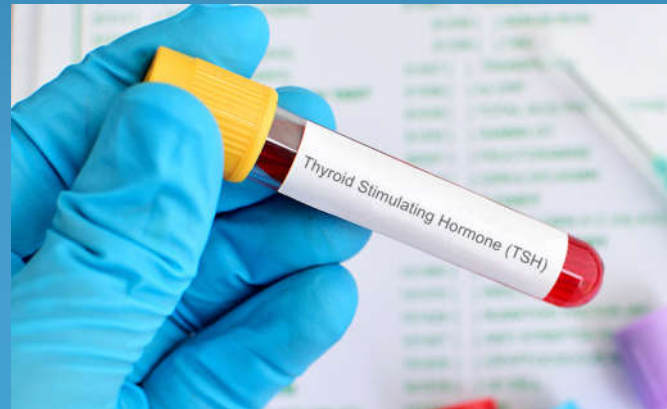
A 48-year-old woman is evaluated for a thyroid nodule discovered incidentally during screening ultrasonography for carotid atherosclerosis at a church health fair.

She has no history of radiation exposure and no family history of thyroid cancer. Her physical exam is normal, and the thyroid nodule cannot be palpated. Her TSH is normal at 1.6 mU/ml.

Ultrasonography shows an isolated 1.5 cm solid nodule in the mid-right thyroid lobe. There is no increased blood flow and no calcifications seen within the nodule.

There is an endocrinologist available in your area.
What tests would you order before you send the patient for an endocrine consult?

1. TSH, Free T₄ and a repeat thyroid ultrasound
2. TSH, Free T₄, and iodine thyroid scan
3. TSH, Free T₄, Free T₃, thyroid scan and MRI of pituitary
4. TSH

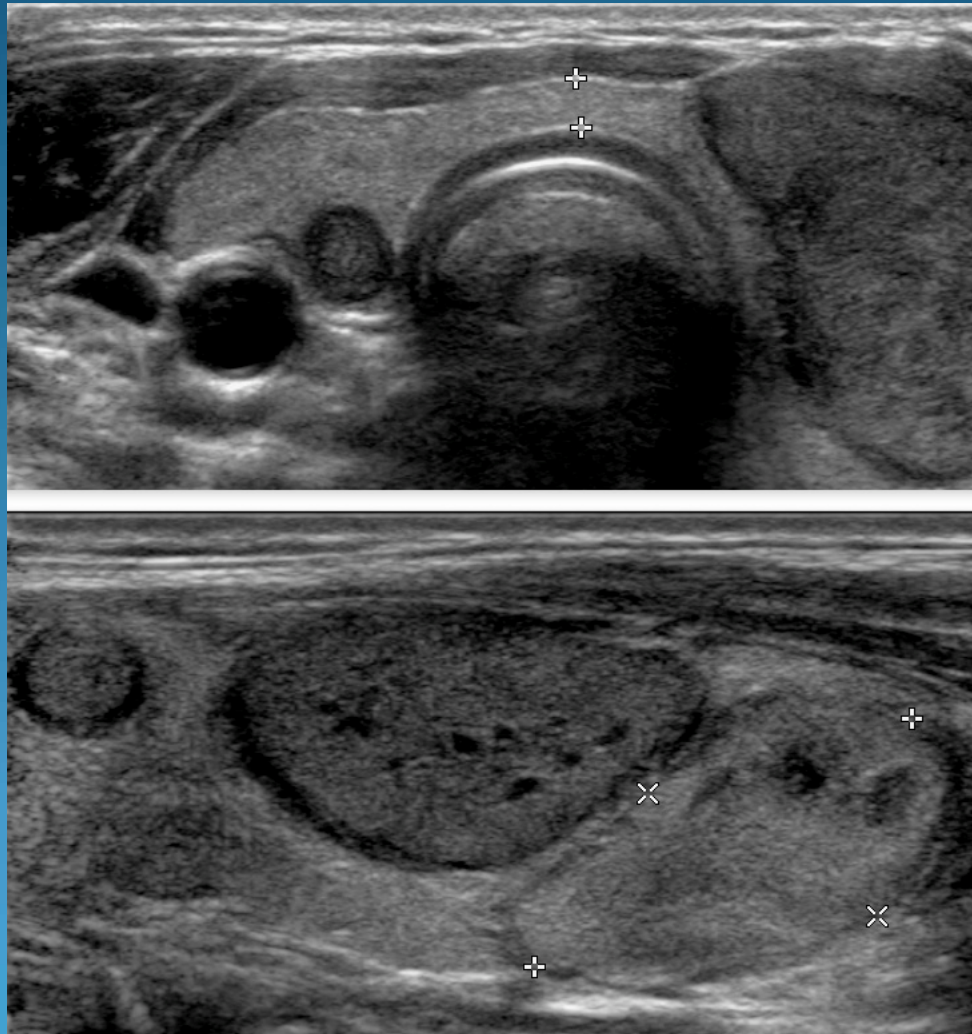


- The risk for malignancy in a thyroid nodule is up to 15%.
- The risk for malignancy for nodules in a multinodular thyroid gland is identical to that of an isolated thyroid nodule.
- If the patient is euthyroid (i.e. normal TSH) , any nodule greater than 1cm in size should be considered for biopsy.
- Thyroid iodine scanning has no place in the evaluation of a euthyroid patient with a thyroid nodule or a multinodular thyroid gland.



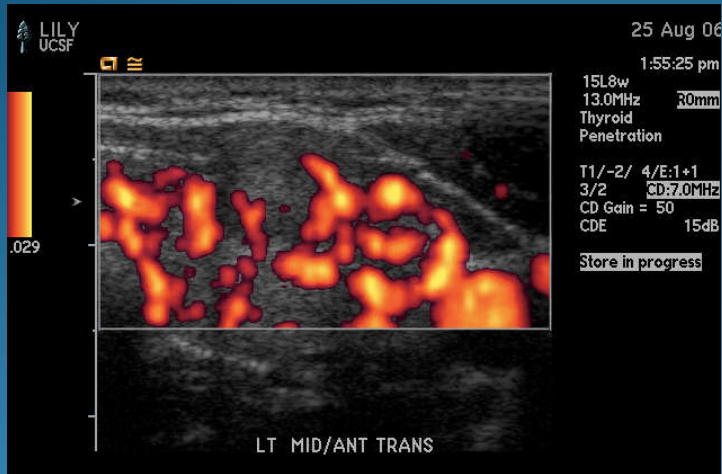
- Thyroid ultrasound is crucial in the evaluation of a nodular thyroid gland, but if the patient is to be referred to an endocrinologist, they will do the study.
- Suspicious ultrasound characteristics include speckled calcifications, increased blood flow, a nodule taller than wide and irregular borders
- Recommendation for the primary care MD: If you identify a thyroid nodule, or a multinodular thyroid gland, obtain a TSH and refer to endocrinology. No other evaluation is needed on your part

Multinodular thyroid gland

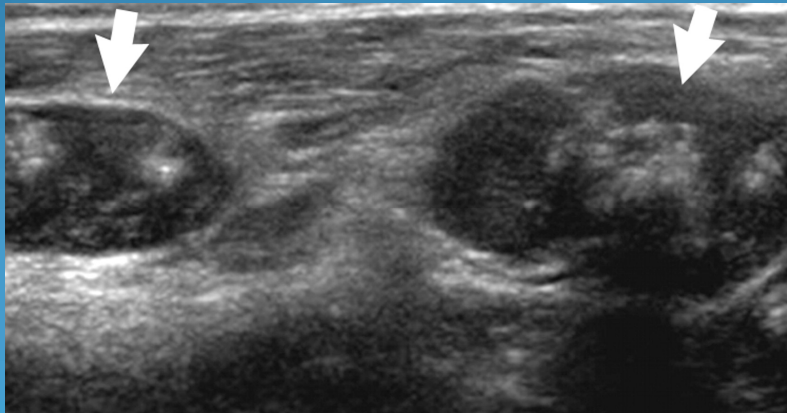




Ultrasound findings worrisome for malignancy



Increased blood flow



Thyroid calcifications



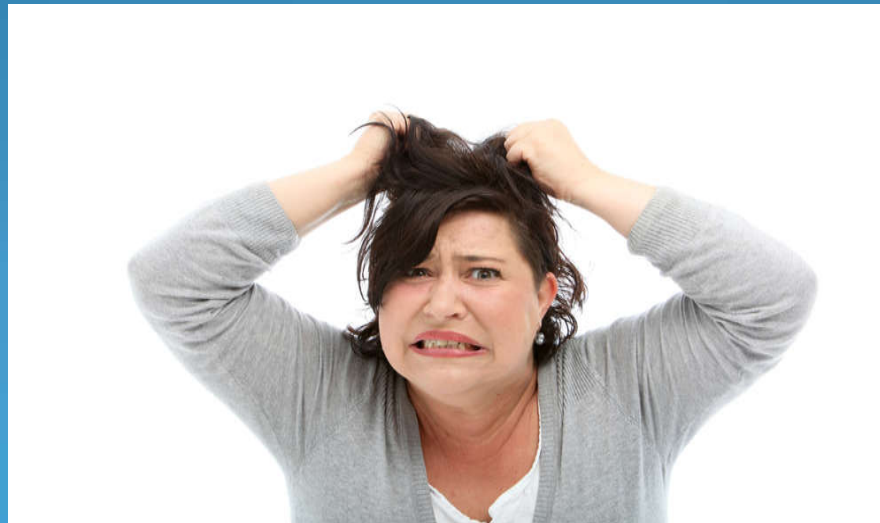
Taller than wide
Thyroid nodule:
Papillary thyroid
carcinoma

Afirma Assay

(Veracyte, Inc.)

- Approximately 15-30% of nodules sampled by FNA are indeterminate, or “follicular lesions of undetermined significance” (FLUS)
- Previously these patients were sent for thyroid surgery, though most of these nodules prove to be benign
- The Afirma assay screens an indeterminate biopsy for 167 genetic markers for thyroid cancer
- 60 – 70% of thyroid cancers harbor at least one genetic mutation
- This assay has a sensitivity of greater than 90% and a negative predictive value of greater than 95%, when combined with cytological review, for detecting thyroid cancer in an indeterminate nodule

The Euthyroid “Weak and Tired” patient....All my problems are related to my thyroid.....



Case #4:

“My Thyroid Tests Are Normal, But I Still Feel Terrible. Doctor, You Are My Last Hope!”

A 45 year old female is seen by you because of profound chronic fatigue.

She was previously diagnosed as having Chronic Fatigue Syndrome, and extensive evaluation by three other well respected primary care physicians has failed to reveal any other pathology. However, over the years she's been started on prednisone for possible Sarcoidosis, dyazide for fluid retention, plaquenil for symptoms of rheumatoid arthritis and lupus, tenormin for anxiety, estrogen replacement therapy, and a variety of other medications for non-specific symptoms.

Her screening TSH has repeatedly been between 1 and 2.5. She's not satisfied with her diagnosis of Chronic Fatigue Syndrome, and has researched her symptoms on-line. She's convinced that she has "Wilson's Syndrome," and has been encouraged by fellow readers of a Wilson's Syndrome blog to start on thyroid hormone replacement.

“Wilson’s Syndrome”

- Coined in 1990 by E. Denis Wilson, M.D. of Longwood Florida
- Patients are euthyroid, but can have virtually “every symptom known to man.”
- Diagnosed by an average body temperature of less than 98.6F.
- He claimed the disease could be treated by a specially formulated compounded sustained release form of T₃.

In 1991, a 50-year-old woman died after T₃ prescribed by Wilson caused tachycardia which led to a fatal myocardial infarction.

Wilson lost a malpractice lawsuit brought against him by the woman's daughter, was fined \$10,000 by the Florida State Board of Medicine, had his license suspended, and was ordered to undergo psychological testing.

Although he no longer practices medicine, he still promotes the syndrome, now known as "Wilson's Temperature Syndrome," and still recommends the use of T₃ for its therapy.

In 1999, the American Thyroid Association concluded:

- There is no scientific evidence that supports the existence of “Wilson’s Syndrome.”
- The diagnostic criteria for “Wilson’s Syndrome” are imprecise –many persons normally have body temperatures less than 98.6F, especially in morning hours.
- There is no scientific evidence that T₃ is better than placebo for management of nonspecific symptoms in individuals with normal thyroid hormone concentrations.

Thyroid Testing in Hospitalized Patients

**Case #5:
Abnormal thyroid tests in
a seriously ill hospitalized
patient**

A 77 year old nursing home resident has been hospitalized for one week because of E.coli urosepsis.

She initially required two days of i.v. dopamine with i.v. fluids to support her blood pressure. Her vital signs and white blood cell count has slowly improved on i.v. antibiotic therapy and supportive i.v. fluids.

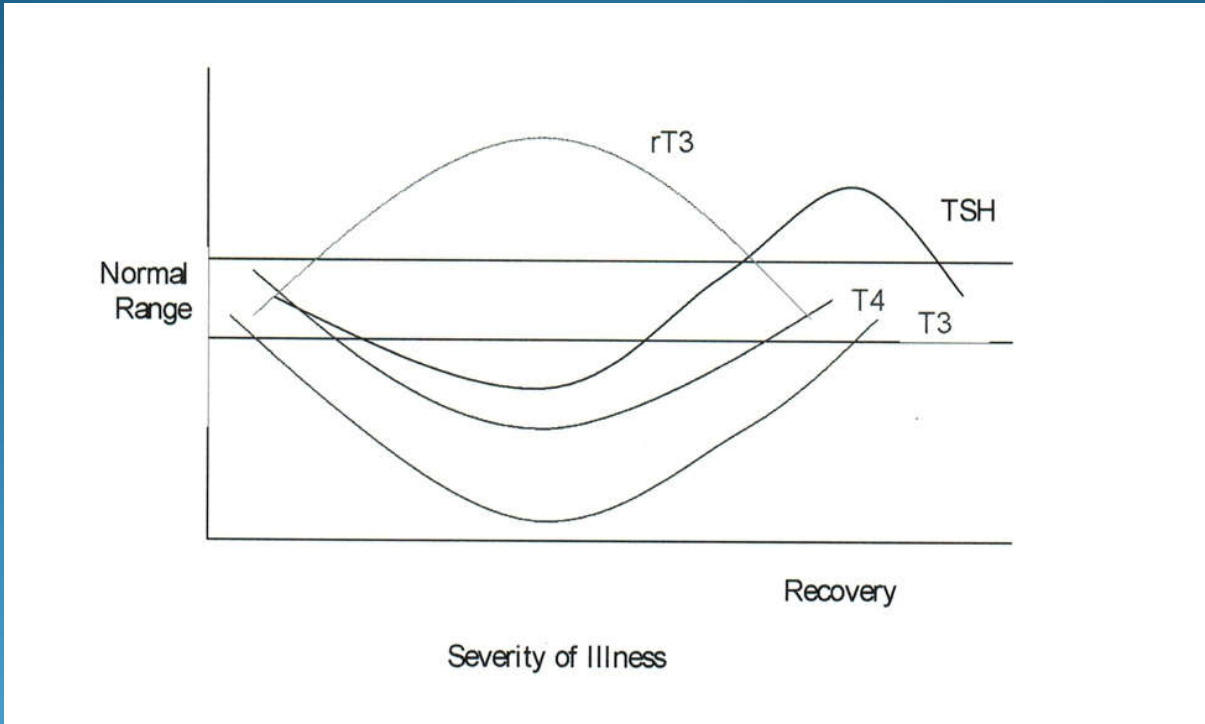
She has no history of hypothyroidism. Because of continued lethargy and confusion, thyroid function tests are obtained. Her TSH is mildly low at .8 mU/L, and her total T₄ is mildly low at 3.8 mg/dl.



What additional tests would you order for this patient?

1. Repeat TSH, free T₄, free T₃
2. A reverse T₃ and a thyroid ultrasound
3. Iodine thyroid scan
4. Pituitary MRI
5. Do nothing; reassess her thyroid tests 3 weeks after discharge

Euthyroid Sick Syndrome



Euthyroid Sick Syndrome

- euthyroid sick syndrome prevents excessive tissue catabolism during serious illness
- it is distinguished from hyperthyroidism by a low TSH and a low T₃ (hyperthyroid patients have a low TSH and an elevated T₃)
- It is distinguished from central hypothyroidism by an elevated reverse T₃ (in central hypothyroidism the reverse T₃ is usually low – due to low T₄ levels)

Drugs that affect thyroid hormone levels



- Dopamine** - inhibits TSH release. Results in secondary reversible hypothyroidism
- Dobutamine** - mild suppression of TSH release
- Glucocorticoids** - inhibit TSH release from the pituitary; also inhibits T₄ to T₃ conversion peripherally
- Amiodarone** - can cause hypothyroidism (high iodine content saturating a normal gland) or hyperthyroidism (high iodine content feeding an unrecognized toxic multinodular thyroid, or causing thyroiditis in a otherwise normal gland)

Thyroid Disease and Pregnancy

Hypothyroidism

Increased need for thyroid hormone replacement during pregnancy, and especially by the 3rd trimester

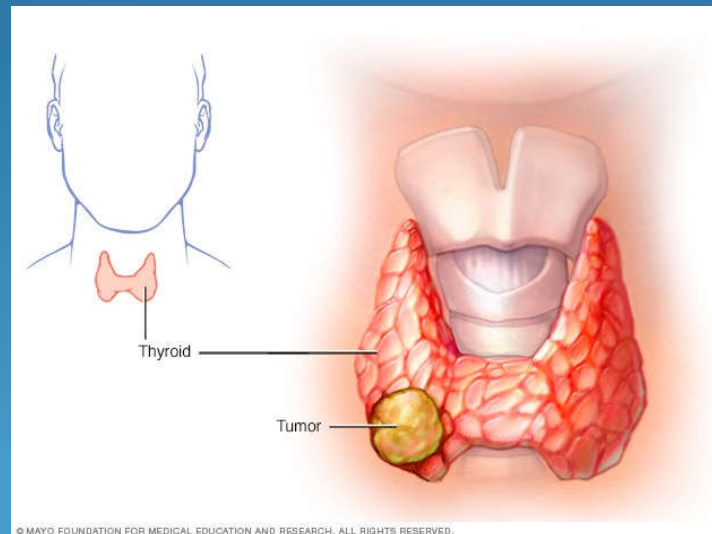
Hypothyroid pregnant patients – as soon as diagnosed, add two additional doses of their thyroid hormone each week (“double up” on two days of the week)

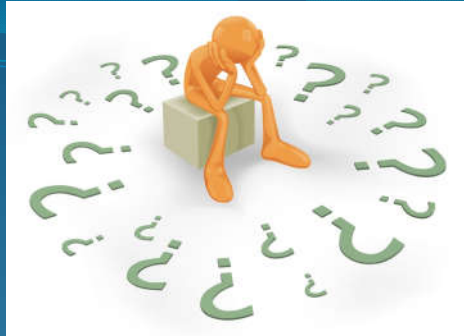
Due to greater volume of distribution of thyroid hormone

Hyperthyroidism

- Radioactive iodine scanning/iodine uptake is absolutely contra-indicated due to potential fetal thyroid damage from radioactive iodine
- Use PTU in first trimester (rare risk for aplasia cutis with methimazole during organogenesis), then methimazole
- Safe to breast feed with mother on either PTU or methimazole. These drugs are excreted in breast milk, but only in small
- amounts and don't appear to affect development

Follow Up of Patients With Thyroid Cancer





- If no endocrinologist available in your area, then the minimum testing necessary every 6 months is a **TSH** and **thyroglobulin**. It is important to always do a thyroglobulin, as this is the blood marker for persistent or recurrent thyroid cancer. Patients with positive anti-thyroglobulin antibodies must have a thyroglobulin RIA assay.
- Neck ultrasound to look for abnormal lymphadenopathy sometimes indicated also.
- For most patients, follow up is life-long. For some patients at low risk for recurrence, follow up can be ended after 10 years.
- Best to leave follow up to an endocrinologist

Questions?