



Brigham and Women's Hospital

Founding Member, Mass General Brigham

Thyroid Disease

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- Clinical focus: Thyroidology
- Research focus: Clinical data modeling

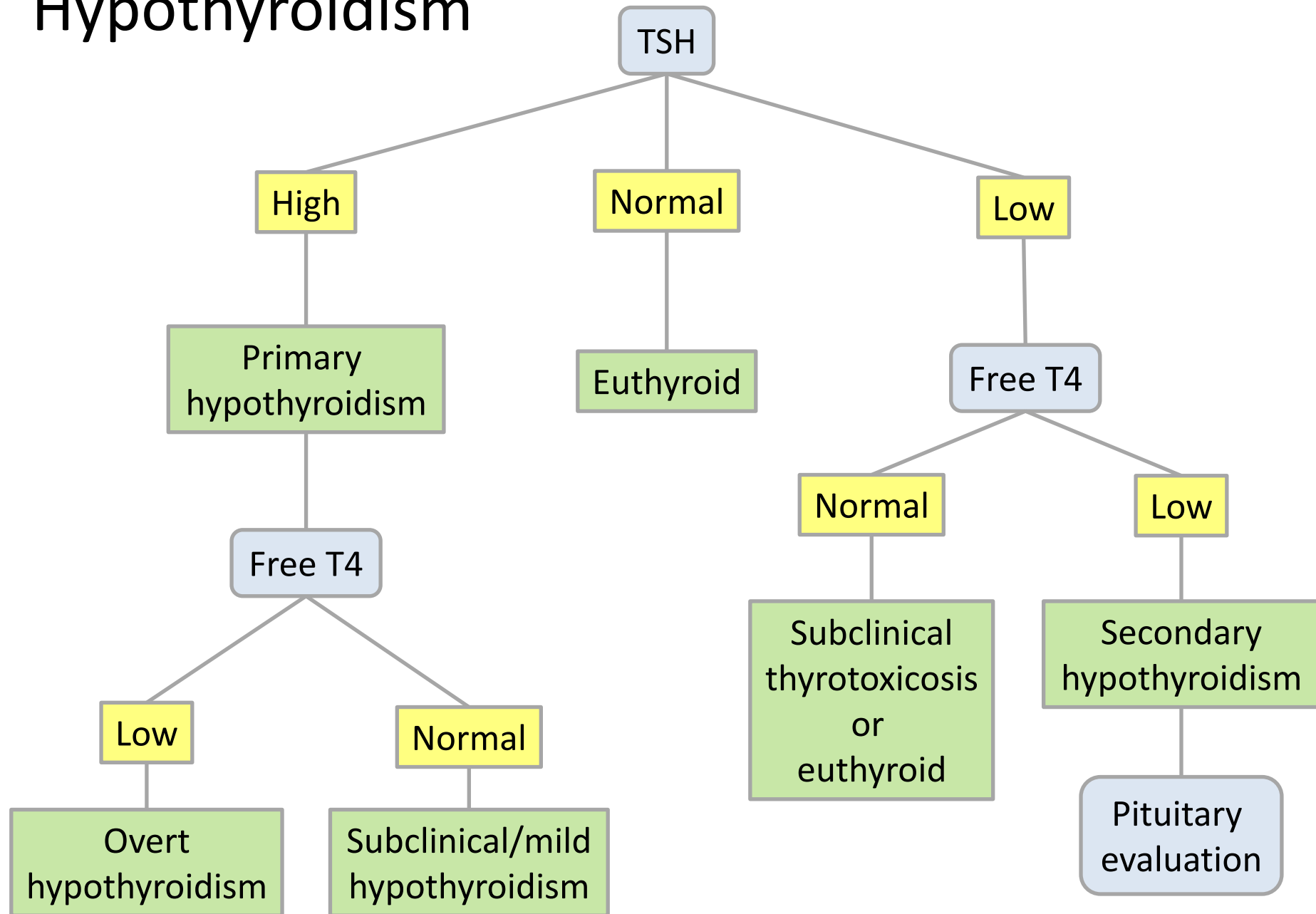
Disclosures

- Sanofi: Consulting

Learning Objectives

- Diagnosis and treatment
 - Hypothyroidism
 - Hyperthyroidism
- Essential concepts
 - Non-thyroidal illness
 - Thyroiditis
 - Thyroid nodules

Hypothyroidism



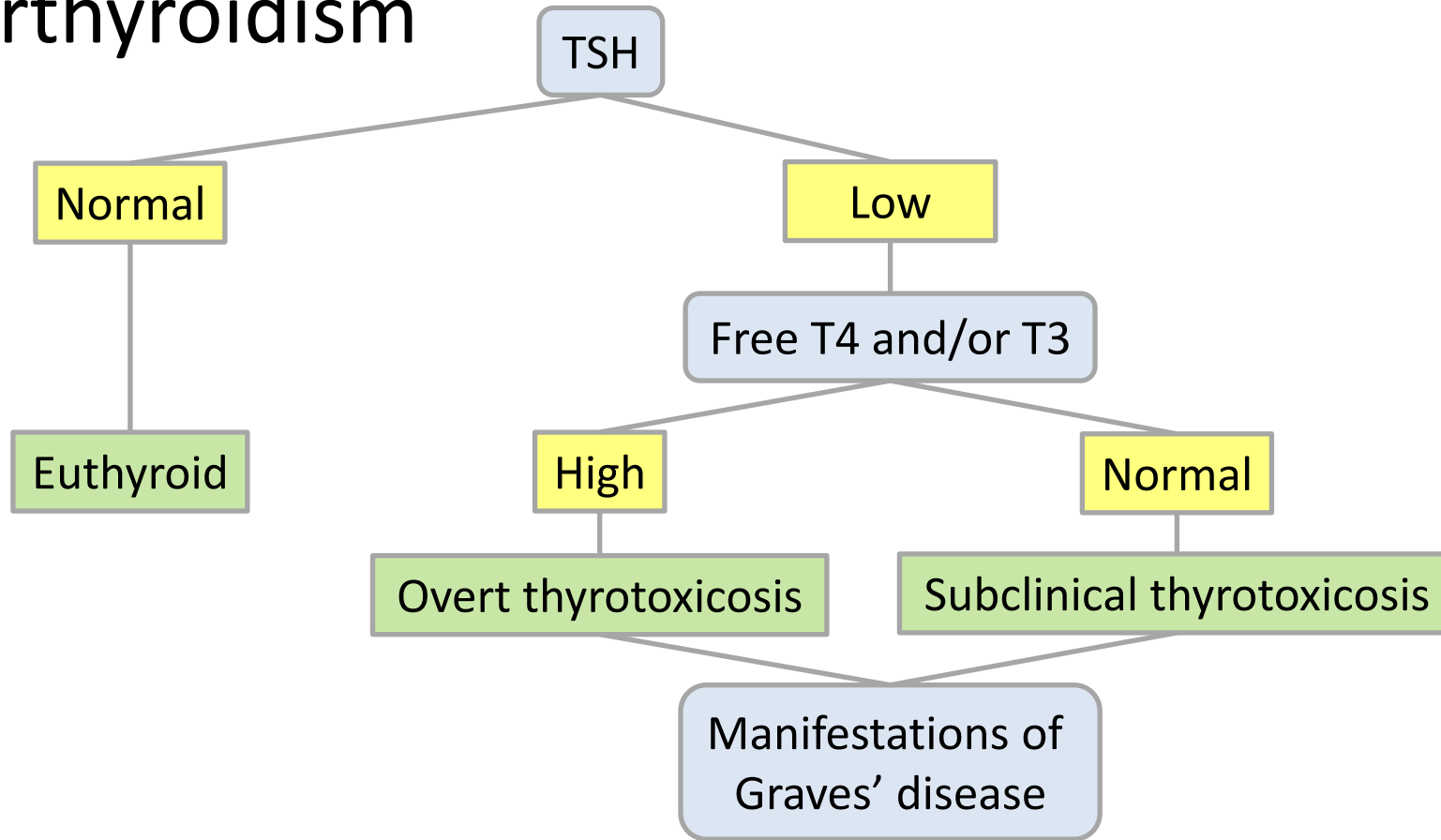
Hypothyroidism: Treatment

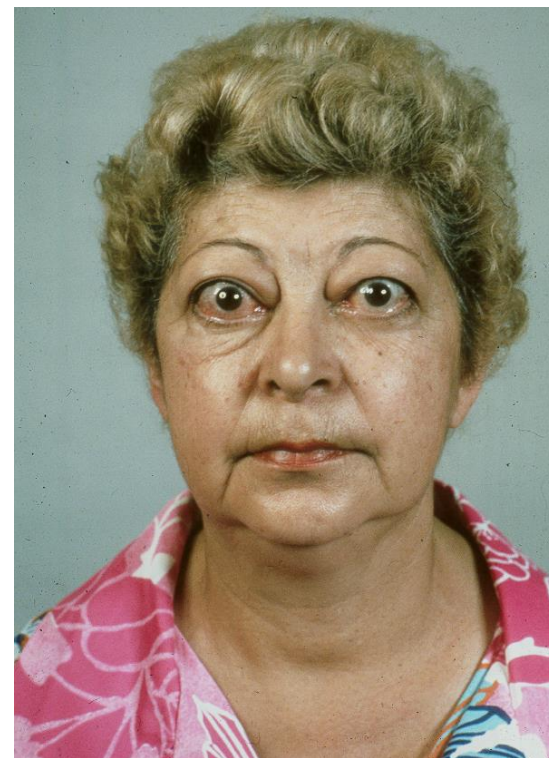
- Levothyroxine (Synthroid[®], Levoxyl[®], Unithroid[®], Levotheroid[®], Tirosint[®], Thyquidity[™]) 25-300 mcg
- Taken once daily
- Starting dose
 - Healthy young adults 0.8 mcg/lb daily
 - Age $\geq$ 65 25-50 mcg daily
 - Cardiac ischemia 12.5-25 mcg daily
- Reduce daily dose by 25% when administered IV
- Check a TSH level 6 weeks after starting or adjusting a dose

Hypothyroidism: Treatment

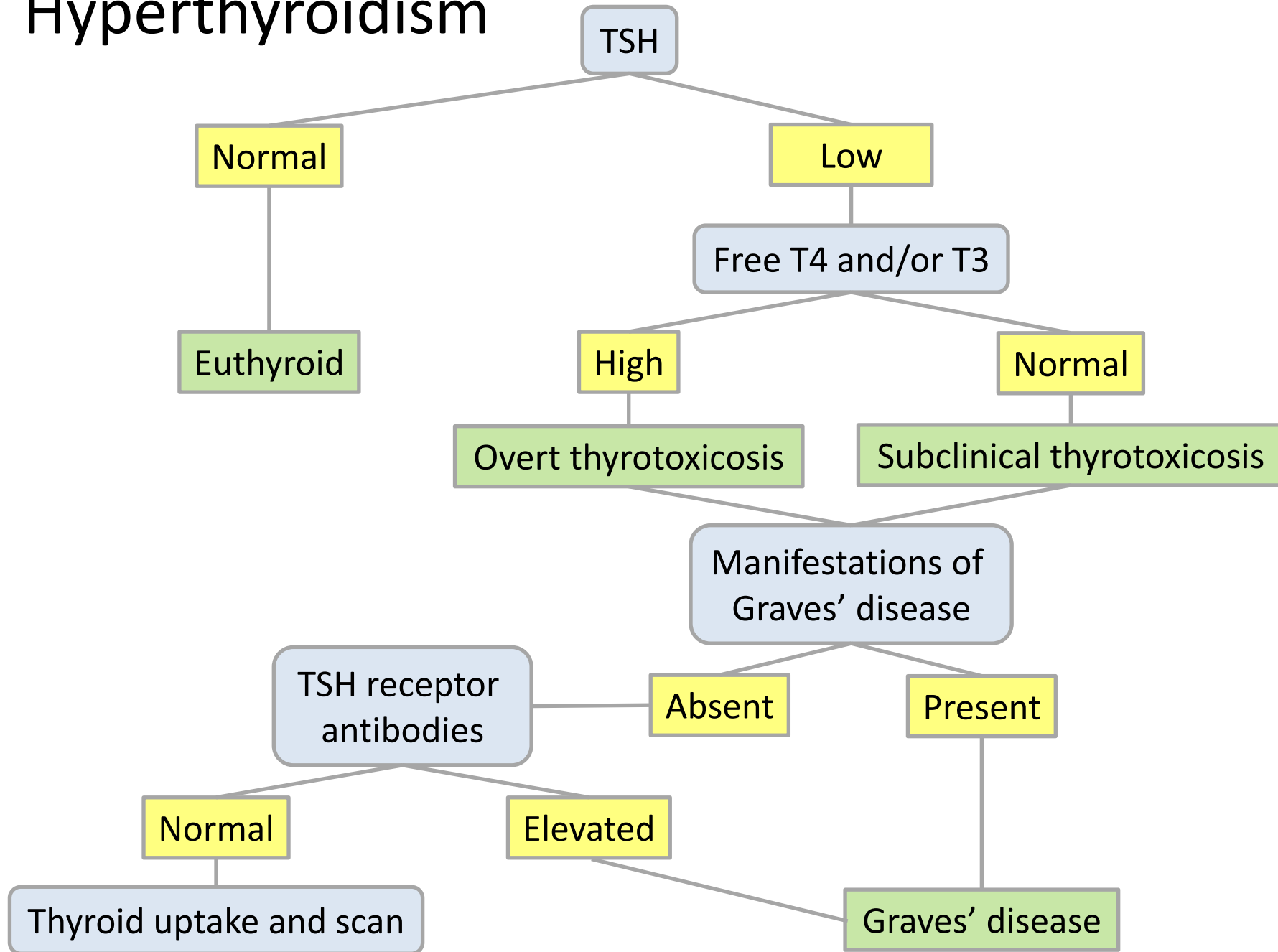
- Subclinical (mild) hypothyroidism
 - Indications for treatment are controversial, especially in the elderly
 - Usually treated if TSH > 10 -15 mIU/L
- Pregnancy
 - Doses often need to be increased during early stages of pregnancy
 - Try to maintain TSH levels between 0.5-2.5 mIU/L during the first trimester
- Secondary hypothyroidism
 - TSH levels are not informative
 - Adjust dose to maintain normal free T4 levels

Hyperthyroidism





Hyperthyroidism



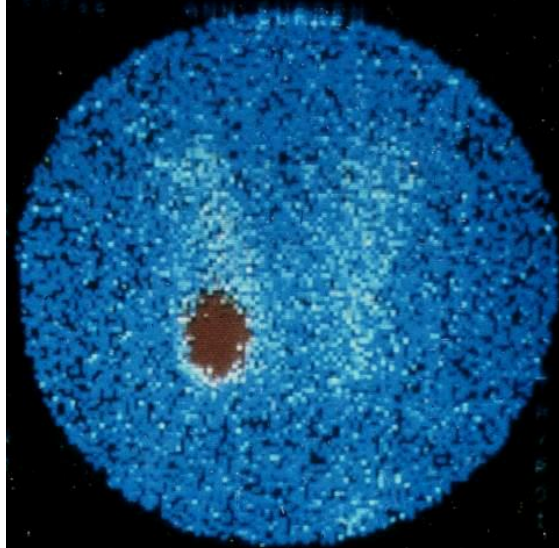
Thyroid Uptake and Scan

- High uptake = Hyperthyroidism
- Low uptake = Thyroiditis (or iodine exposure)
- Patterns

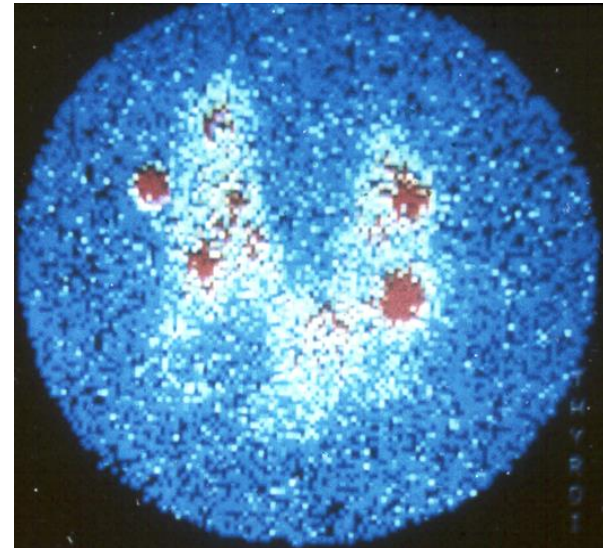
Graves' disease



Toxic adenoma



Toxic multinodular goiter



Hyperthyroidism: Management

- Beta blockers
 - Atenolol: 25-50 mg daily
 - Propranolol LA: 60-80 mg daily
- Antithyroid drugs
- Radioactive iodine
 - Can't be given while pregnant or breastfeeding
- Thyroid surgery
 - When a patient who is allergic to antithyroid drugs can't be treated or refuses to be treated with radioactive iodine
 - When substernal extension causes significant compressive symptoms
- Radiofrequency ablation
 - May be used to treat autonomously functioning nodules

Antithyroid Drugs

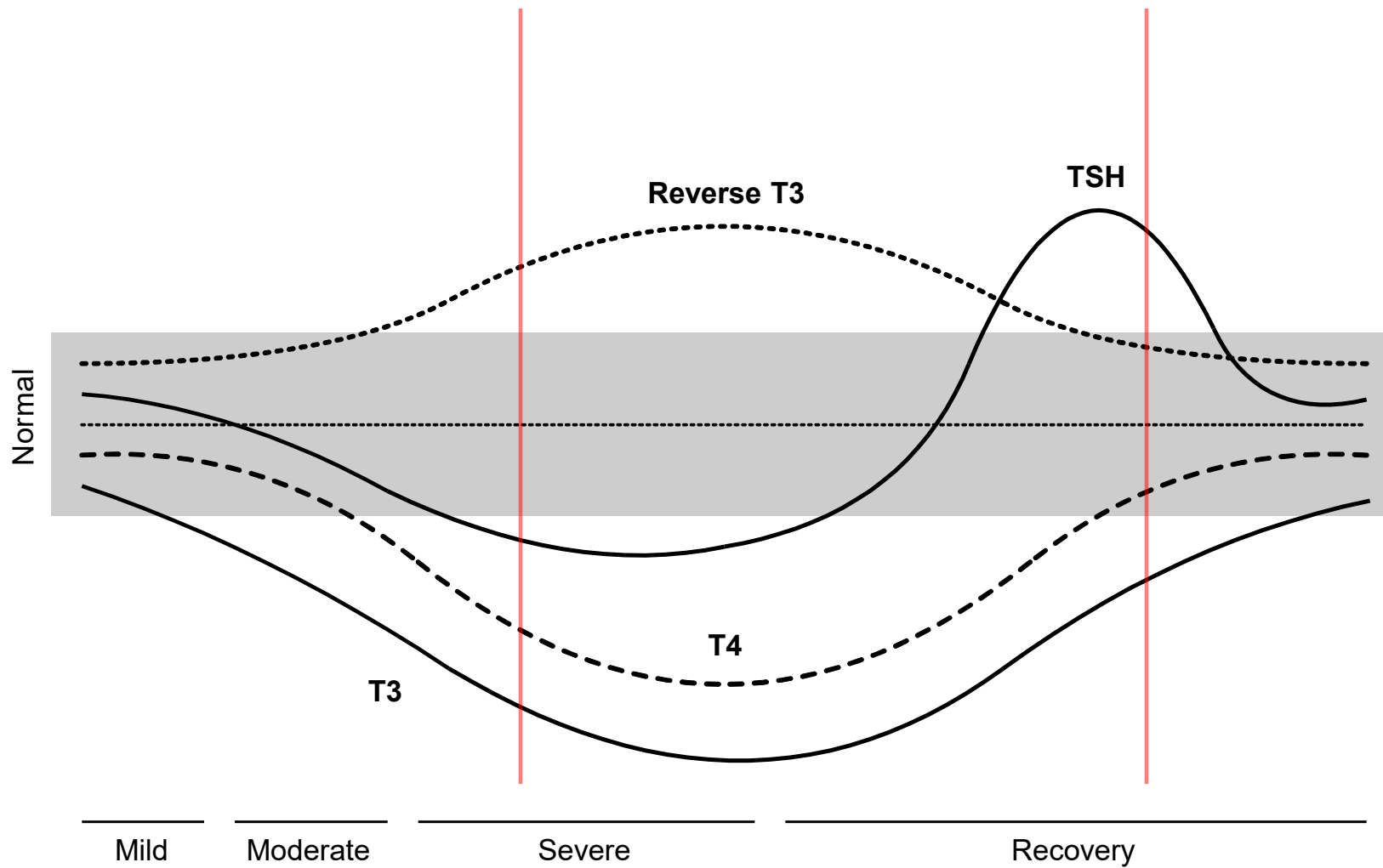
- Methimazole
 - Agent of choice in most cases
 - Can be taken once daily
 - Started at a dose of 5-40 mg daily
 - Recheck thyroid hormone levels 3-4 weeks after starting or changing a dose
 - Adverse effects
 - Common: pruritis, rash
 - Rare: agranulocytosis, hepatotoxicity, vasculitis

Antithyroid Drugs

- When to use propylthiouracil
 - Prior to conception and during the first trimester of pregnancy
 - Methimazole has been associated with birth defects
 - Consider switching to methimazole during the second trimester
 - In cases of thyroid storm
 - Acts to block peripheral conversion of T4 to T3
 - When a patient who is allergic to methimazole declines radioactive iodine treatment or surgery

Non-Thyroidal Illness

- “Euthyroid sick syndrome”
- Transient changes in hypothalamic-pituitary function, thyroid hormone secretion, and deiodinase activity that occur in the setting of acute physiologic stress
- Combinations of changes may suggest underlying thyrotoxicosis and/or hypothyroidism



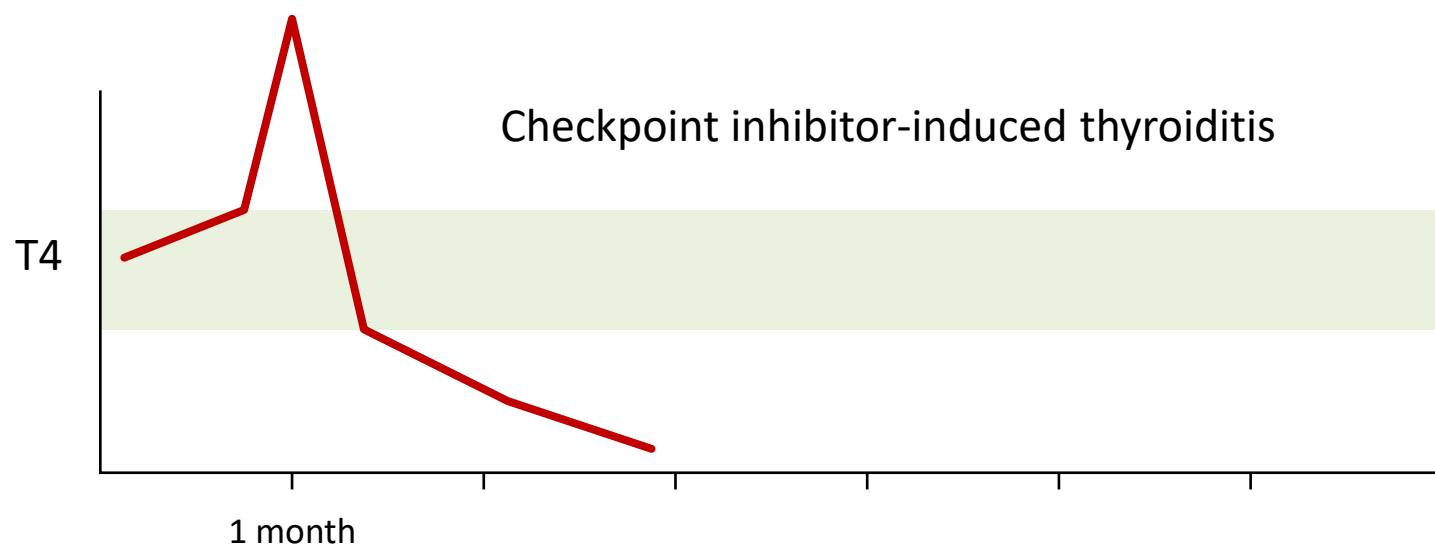
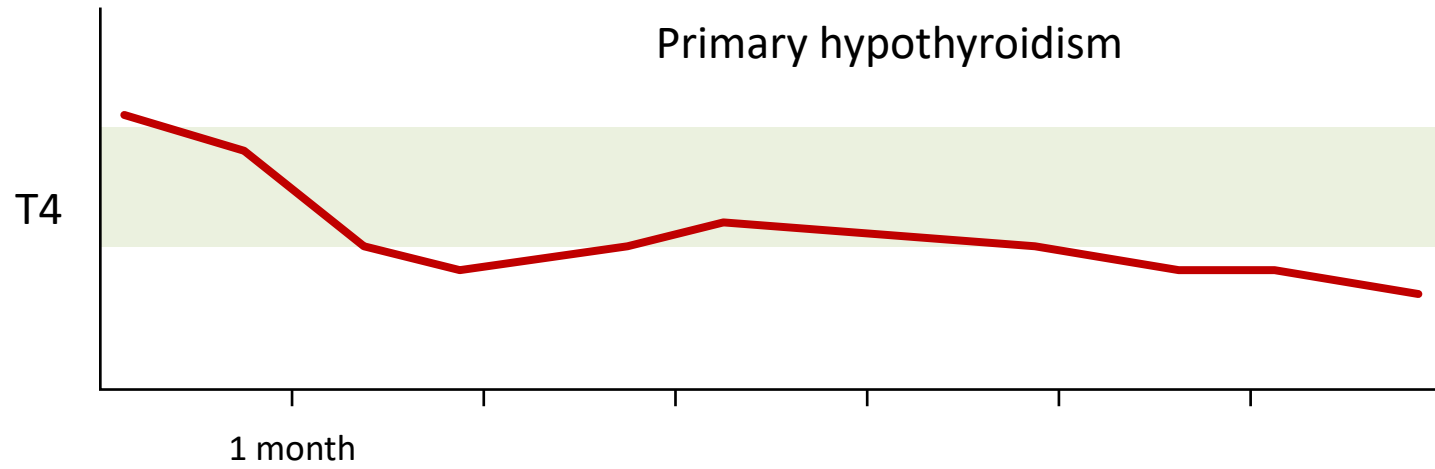
Thyroiditis

	Thyroid pain	ESR/CRP	Thyroid uptake
Subacute thyroiditis	Present	Elevated	Low
Autoimmune thyroiditis	Absent	Normal	Low

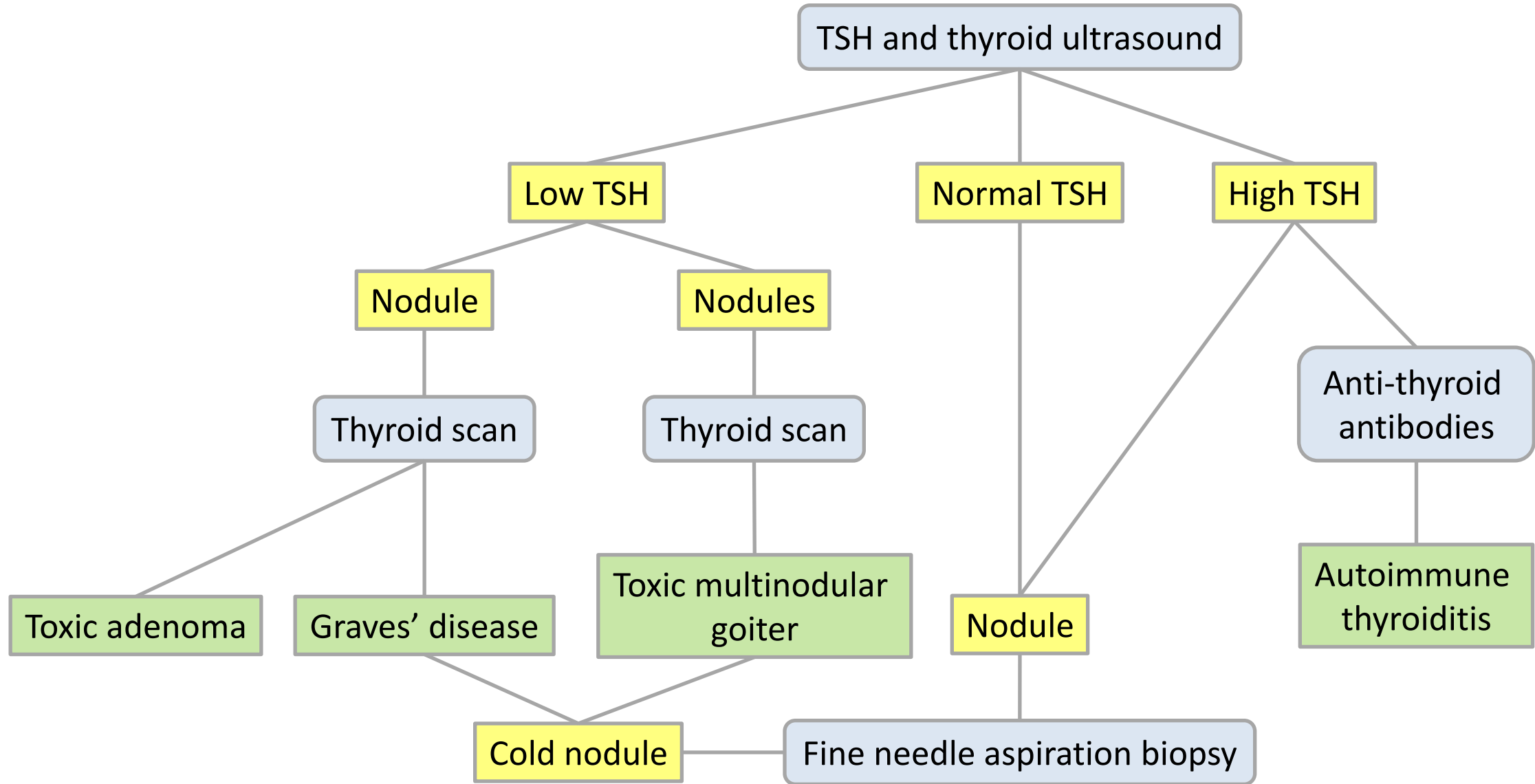
- Thyroid pain can be treated with high dose ibuprofen, naproxen, aspirin, celecoxib, or prednisone 20-40 mg daily
- Beta blockers attenuate thyrotoxic symptoms
- Treatment with levothyroxine during hypothyroid phases may alleviate fatigue and lethargy

Checkpoint Inhibitors

- Immunologic enhancement can trigger new-onset autoimmune thyroiditis
- May present with severe thyrotoxicosis followed by rapid progression to overt hypothyroidism
- Need to monitor TSH and free T4 levels every 4-6 weeks after starting treatment and every 2-3 weeks after diagnosis



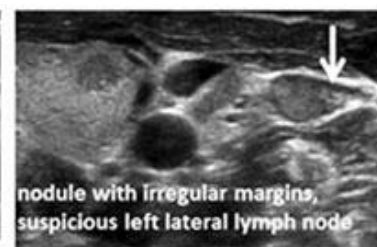
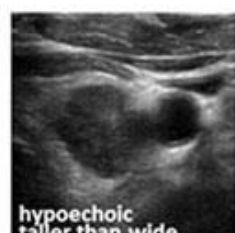
Thyroid Nodules



Thyroid Nodules: ATA FNA Criteria

- ≥ 1.0 cm
 - Hypoechoic nodules
 - Nodules with suspicious features
- ≥ 1.5 cm
 - Isoechoic nodules
 - Hyperechoic nodules
- ≥ 2.0 cm
 - Spongiform nodules

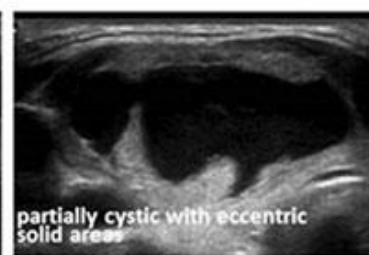
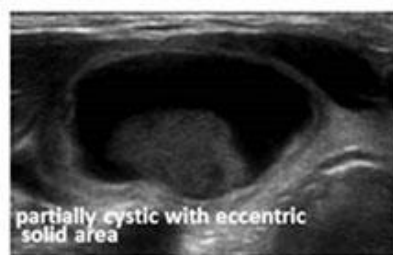
High
Suspicion
>70-90%



Intermediate
Suspicion
10-20%



Low
Suspicion
5-10%



Very low
Suspicion
<3%

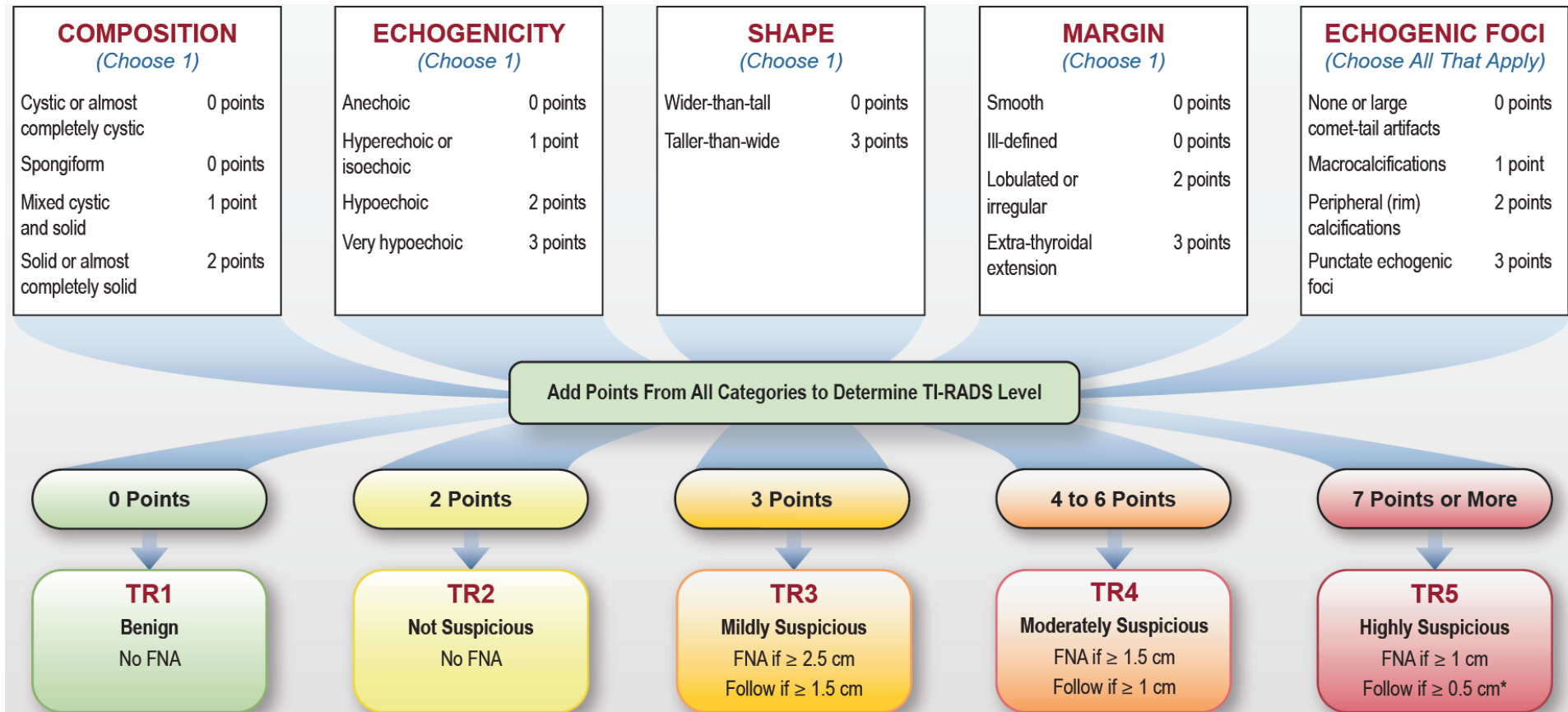


Benign
<1%



Risk of malignancy

ACR Thyroid Imaging Reporting and Data System (TI-RADS)



Thyroid Nodules: TI-RADS FNA Thresholds

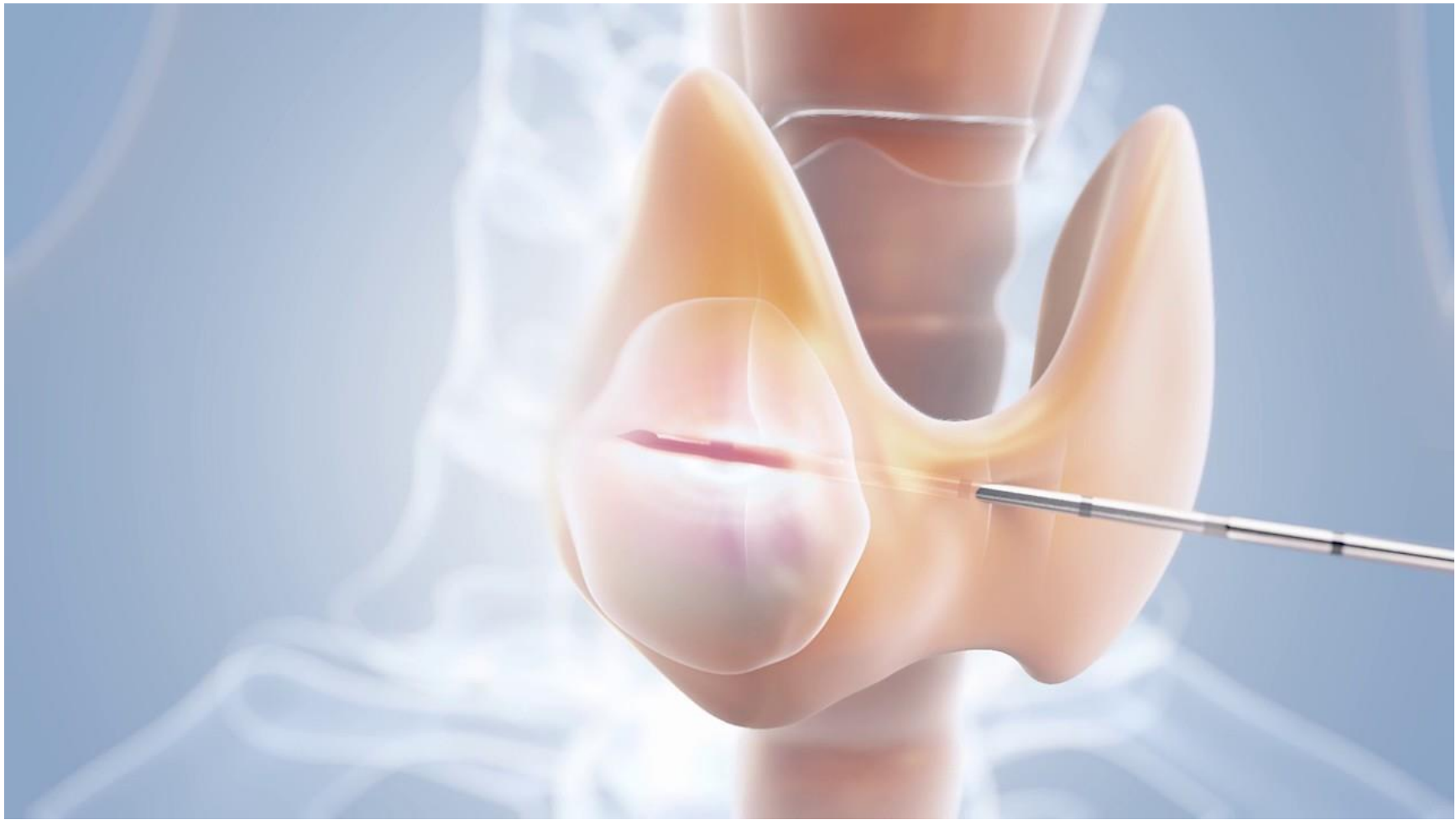
- TI-RADS 1 or 2: Not required
- TI-RADS 3: ≥ 2.5 cm
- TI-RADS 4: ≥ 1.5 cm
- TI-RADS 5: ≥ 1.0 cm
- Previously biopsied benign thyroid nodules that have enlarged do not need to be re-sampled*

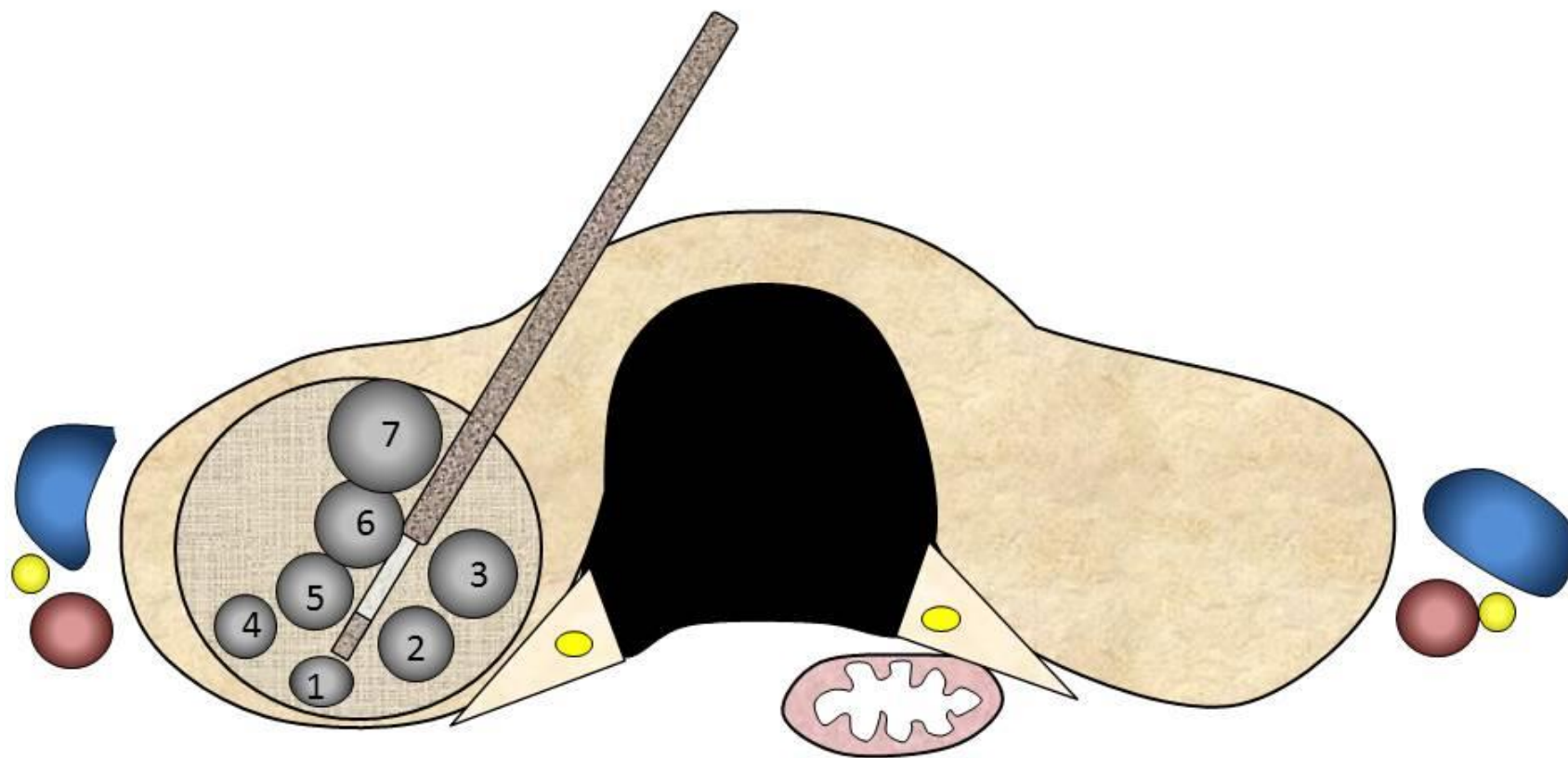
Bethesda System for Reporting Thyroid Cytopathology

		Malignant
II	Benign	0 - 3%
III	Atypia of undetermined significance	10 - 30%
IV	Suspicious for a follicular neoplasm	25 - 40%
V	Suspicious for malignancy	50 - 75%
VI	Malignant	97 - 99%

Thyroid Nodules: Management

- Benign
 - Monitor with serial imaging
 - Radiofrequency ablation if enlargement causes compressive symptoms
- Atypia of undetermined significance
 - Repeat biopsy +/- genetic profiling (Afirma[®], ThyroSeq[®] ThyGeNEXT[®] + ThyraMIR[®])
- Suspicious for a follicular neoplasm
 - Repeat biopsy +/- genetic profiling
- Suspicious for malignancy
 - Hemithyroidectomy or total thyroidectomy
- Malignant
 - Hemithyroidectomy or total thyroidectomy





Question 1

A 55-year-old female is noted to be tachycardic during a routine physical exam. Lab tests show TSH 0.02 mIU/L with follow up lab tests showing free T4 2.3 ng/dL and T3 289 ng/dL. She denies any anterior neck discomfort, weight loss, palpitations, anxiety, tremor, heat intolerance, or insomnia. Physical exam reveals a slightly enlarged thyroid without any nodularity and no evident proptosis, periorbital swelling, or ocular injection.

Question 1

What should you do next?

- A. Check anti-thyroid peroxidase and anti-thyroglobulin antibodies
- B. Check TSH receptor stimulating and binding antibodies
- C. Check a thyroid uptake and scan
- D. Check an ESR
- E. Start methimazole at a dose of 10 mg daily

Question 2

A 61-year-old female with metastatic melanoma is starting on treatment with an immunotherapy regimen incorporating nivolumab and ipilimumab. Her TSH level checked a year ago was 1.5 mIU/l.

Question 2

Which lab tests should be followed to monitor her thyroid function during treatment?

- A. TSH levels checked at 4-6 week intervals
- B. Free T4 and T3 levels checked at 4-6 week intervals
- C. TSH and free T4 levels checked at 4-6 week intervals
- D. TSH and free T4 levels checked at 2-3 month intervals
- E. Anti-thyroid peroxidase antibody levels checked at 2-3 month intervals

MOC Reflective Statement

- The TSH level is the most sensitive index of thyroid function
- Treatment of subclinical thyroid disease may be optional in most cases
- TSH receptor antibodies can be reliably used to diagnose Graves' disease
- Checkpoint inhibitors can trigger rapidly progressive autoimmune thyroiditis and hypothyroidism
- Ultrasound findings and TI-RADS scoring should be used to determine which thyroid nodules need to be biopsied
- Radiofrequency ablation is emerging as a non-surgical approach to management of enlarging benign thyroid nodules

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