



**Brigham and Women's Hospital**

Founding Member, Mass General Brigham

# Thyroid Disease

Matthew Kim, MD

Clinical Director

Division of Endocrinology, Diabetes and  
Hypertension

Brigham and Women's Hospital

Assistant Professor

Harvard Medical School



## Matthew Kim, MD



Washington University School of Medicine  
Medicine Residency @ UPENN/HUP  
Endocrinology Fellowship @ Johns Hopkins  
Medical Informatics Fellowship @ NLM  
Assistant Professor of Medicine @ HMS  
Clinical Director, Endocrinology @ DFCI/BWH

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

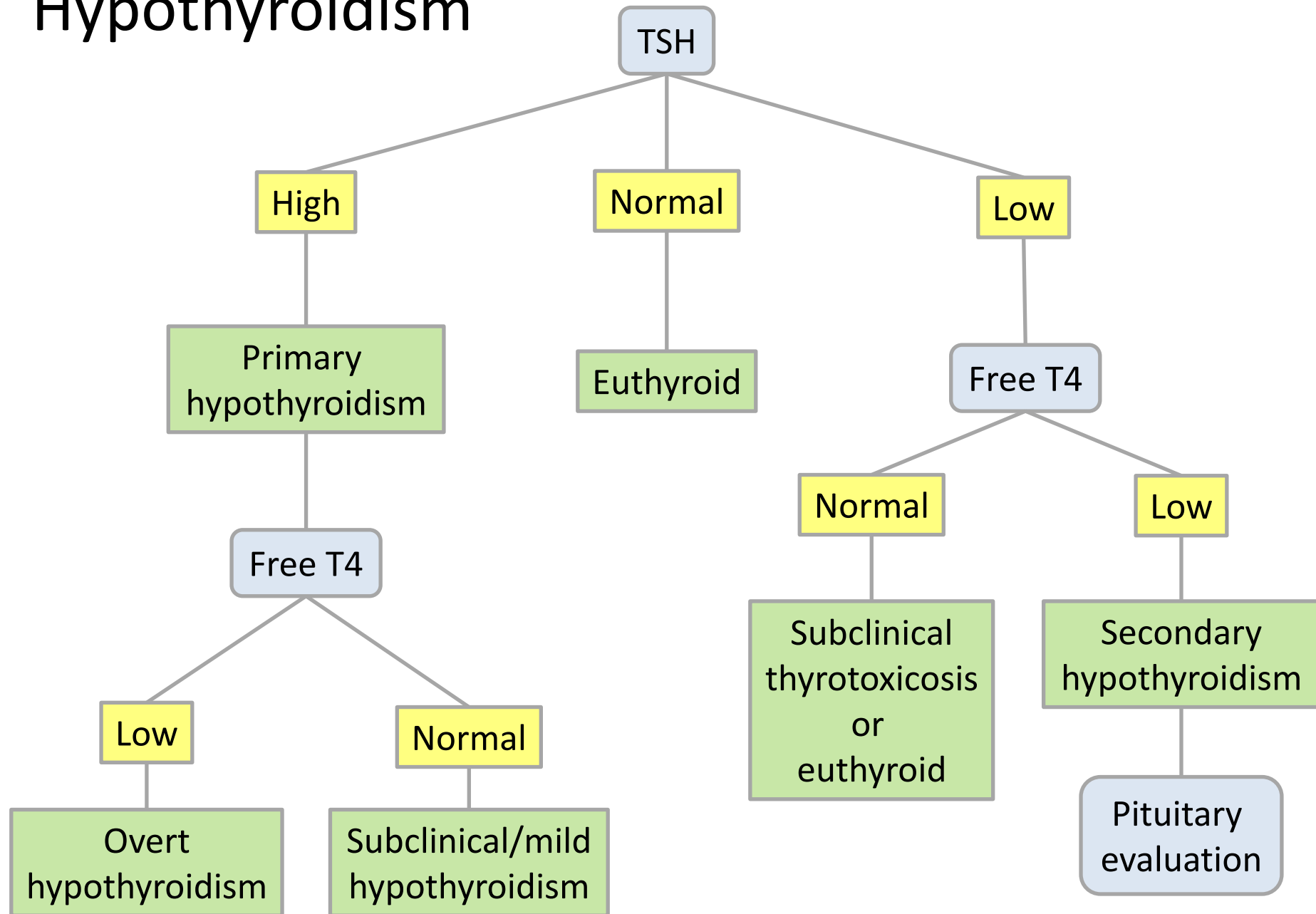
# Disclosures

- Sanofi: Consulting

# Learning Objectives

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

# Hypothyroidism



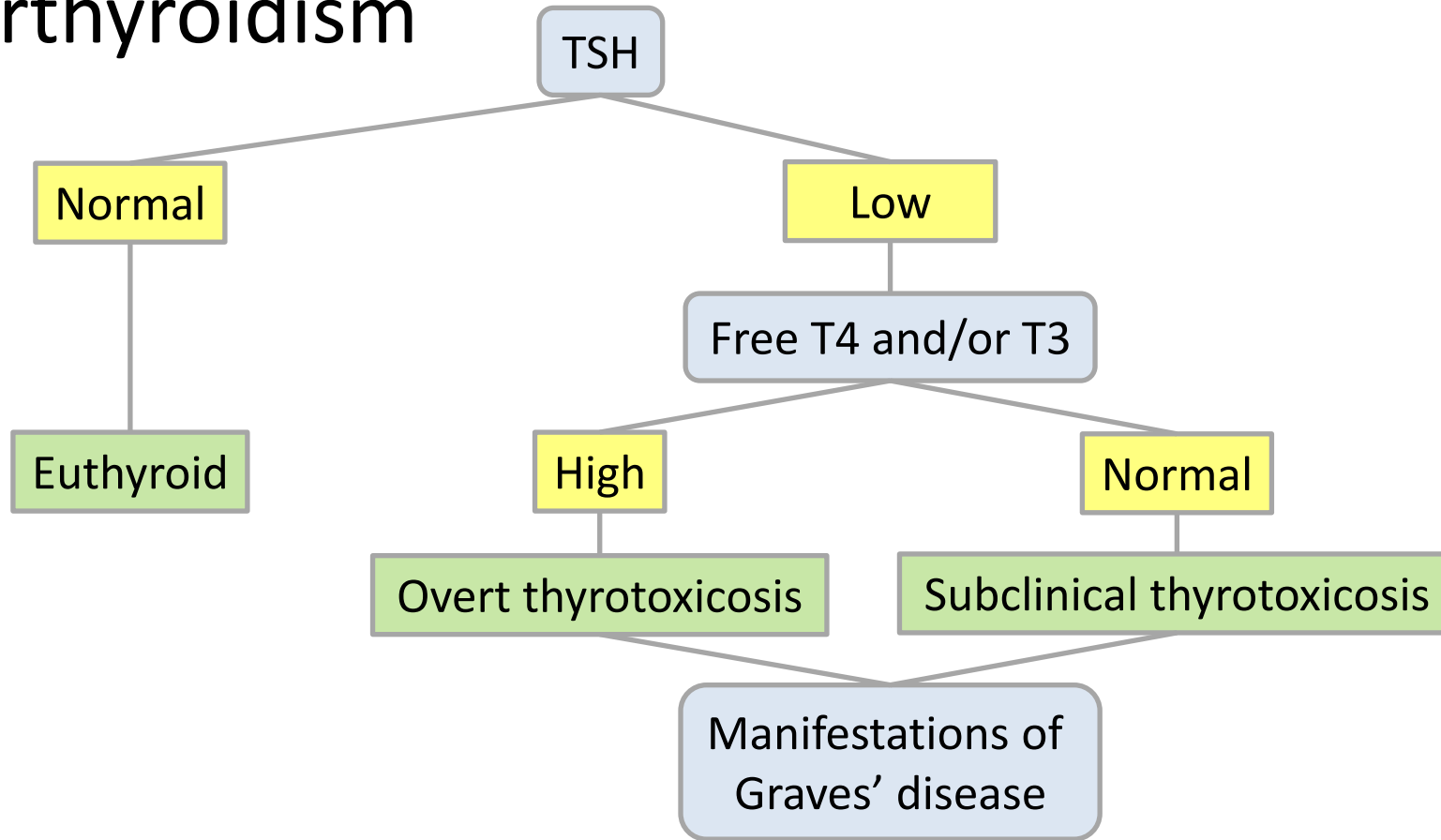
# Hypothyroidism: Treatment

- Levothyroxine (Synthroid<sup>®</sup>, Levoxyl<sup>®</sup>, Unithroid<sup>®</sup>, Levotheroid<sup>®</sup>, Tirosint<sup>®</sup>, Thyquidity<sup>™</sup>) 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

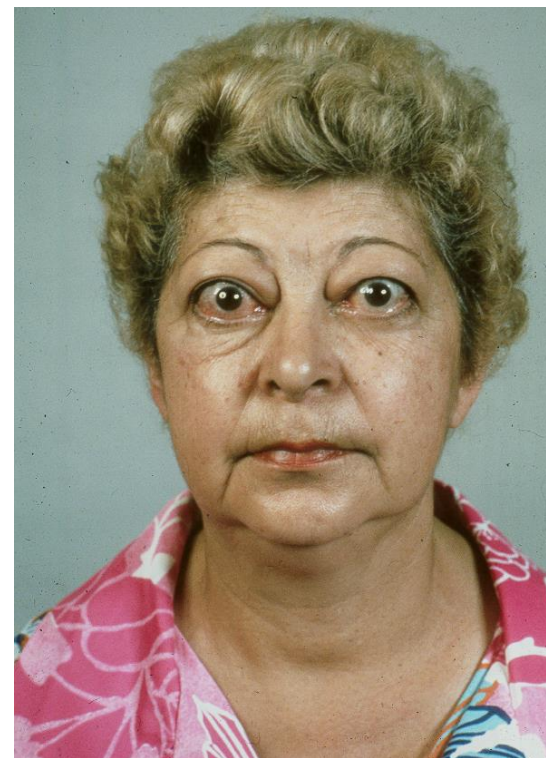
# Hypothyroidism: Treatment

- 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

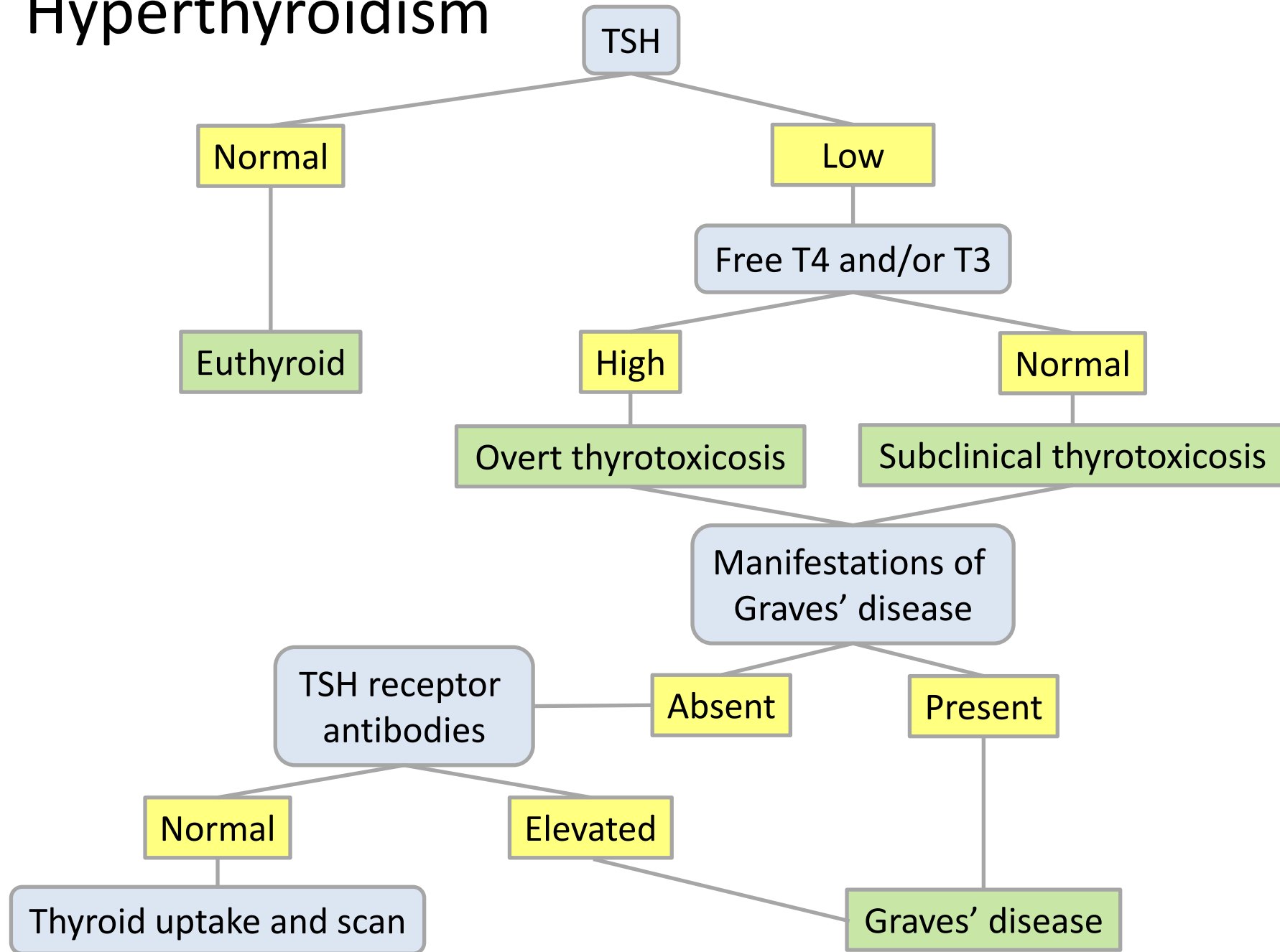
# Hyperthyroidism







# Hyperthyroidism



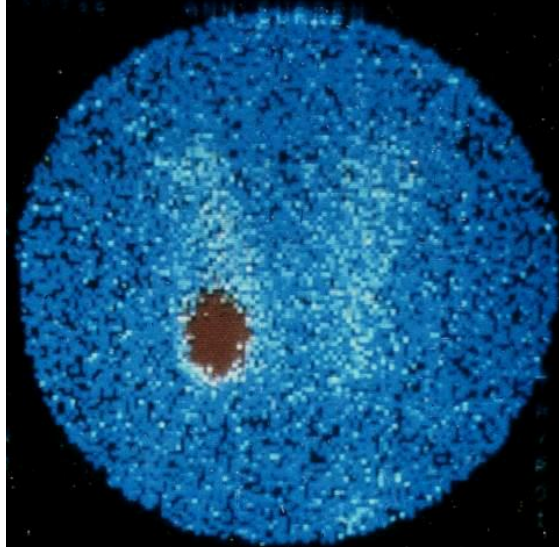
# Thyroid Uptake and Scan

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

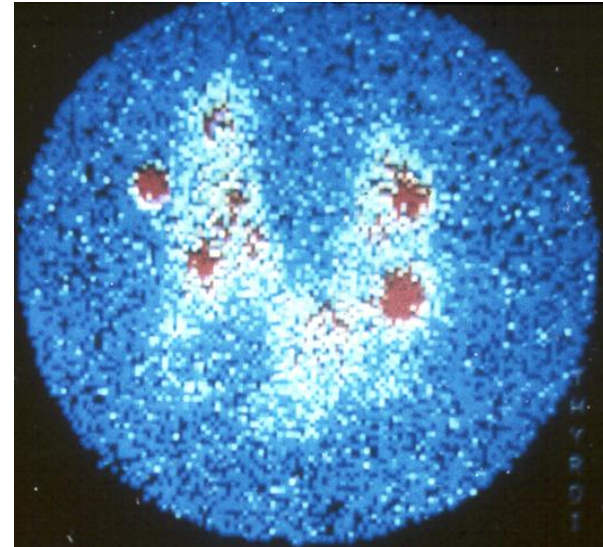
Graves' disease



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

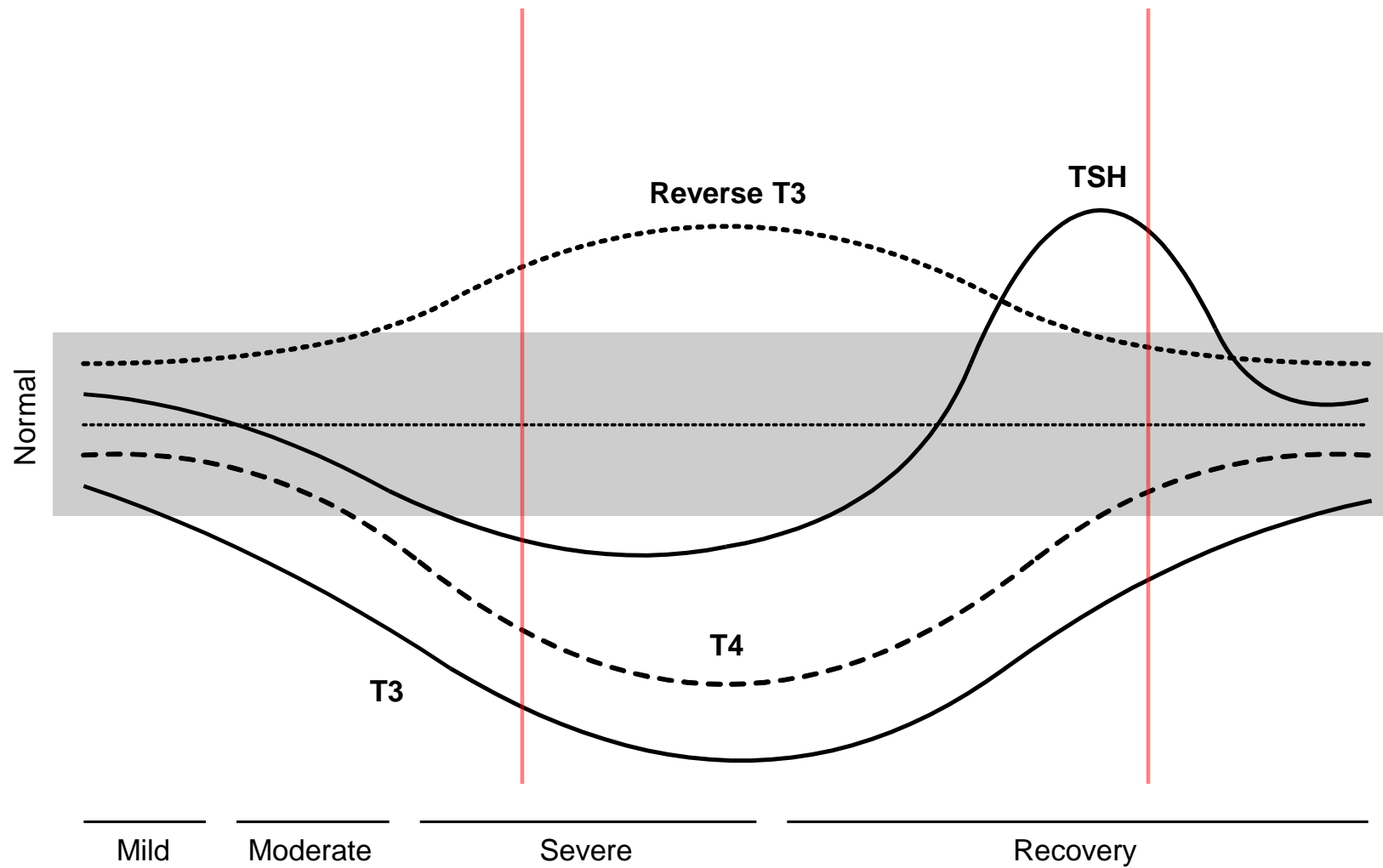
# Antithyroid Drugs

- 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







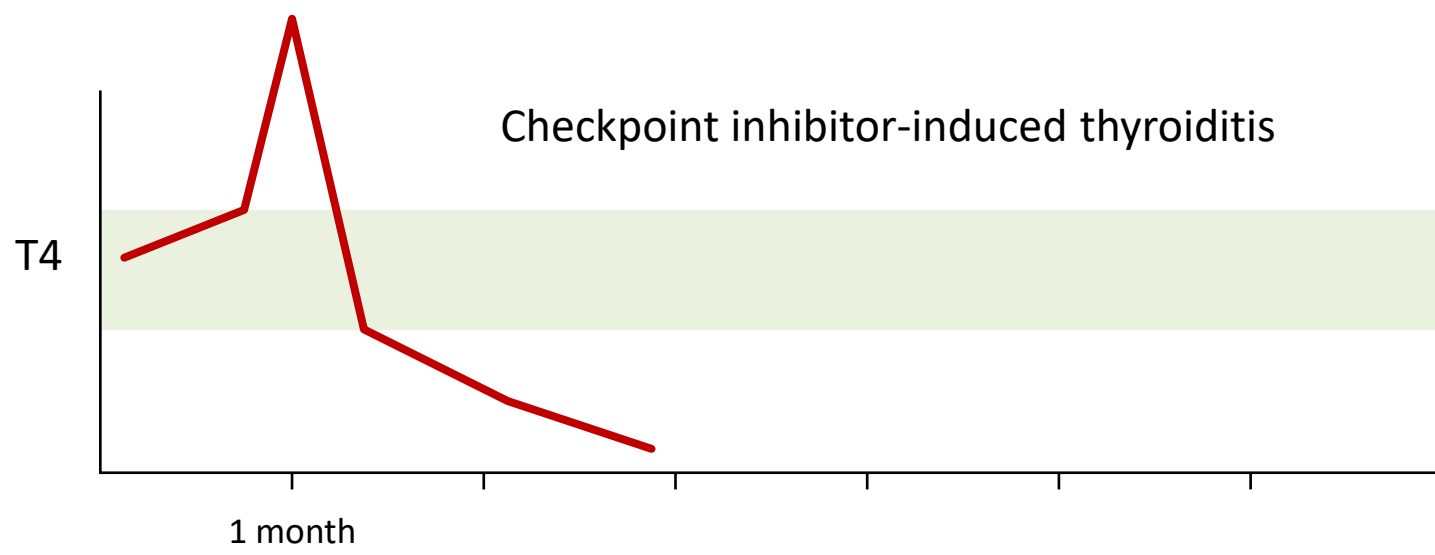
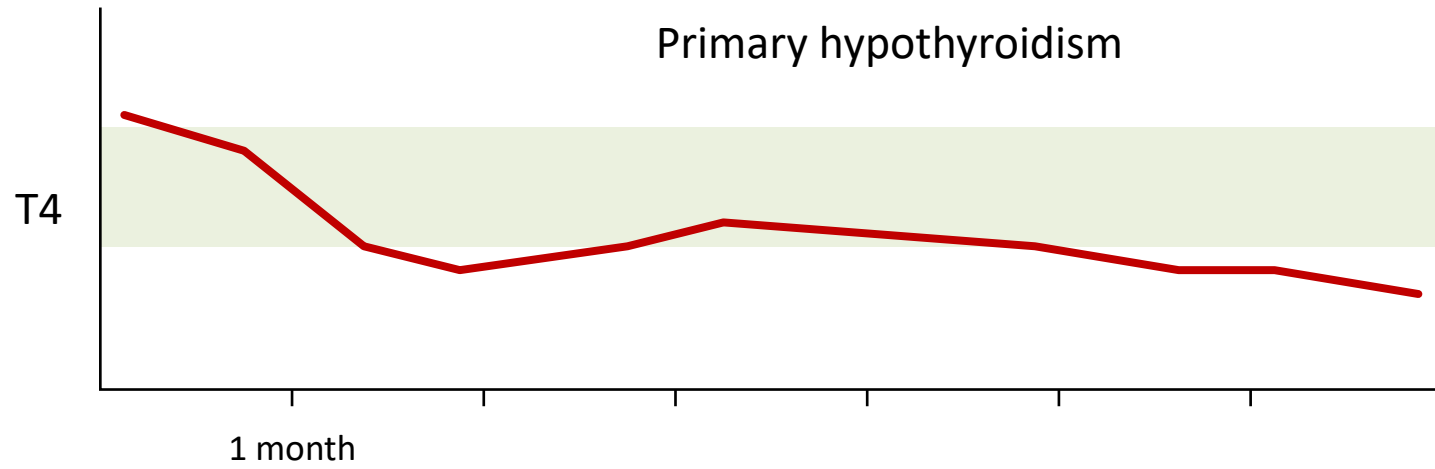
# Thyroiditis

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

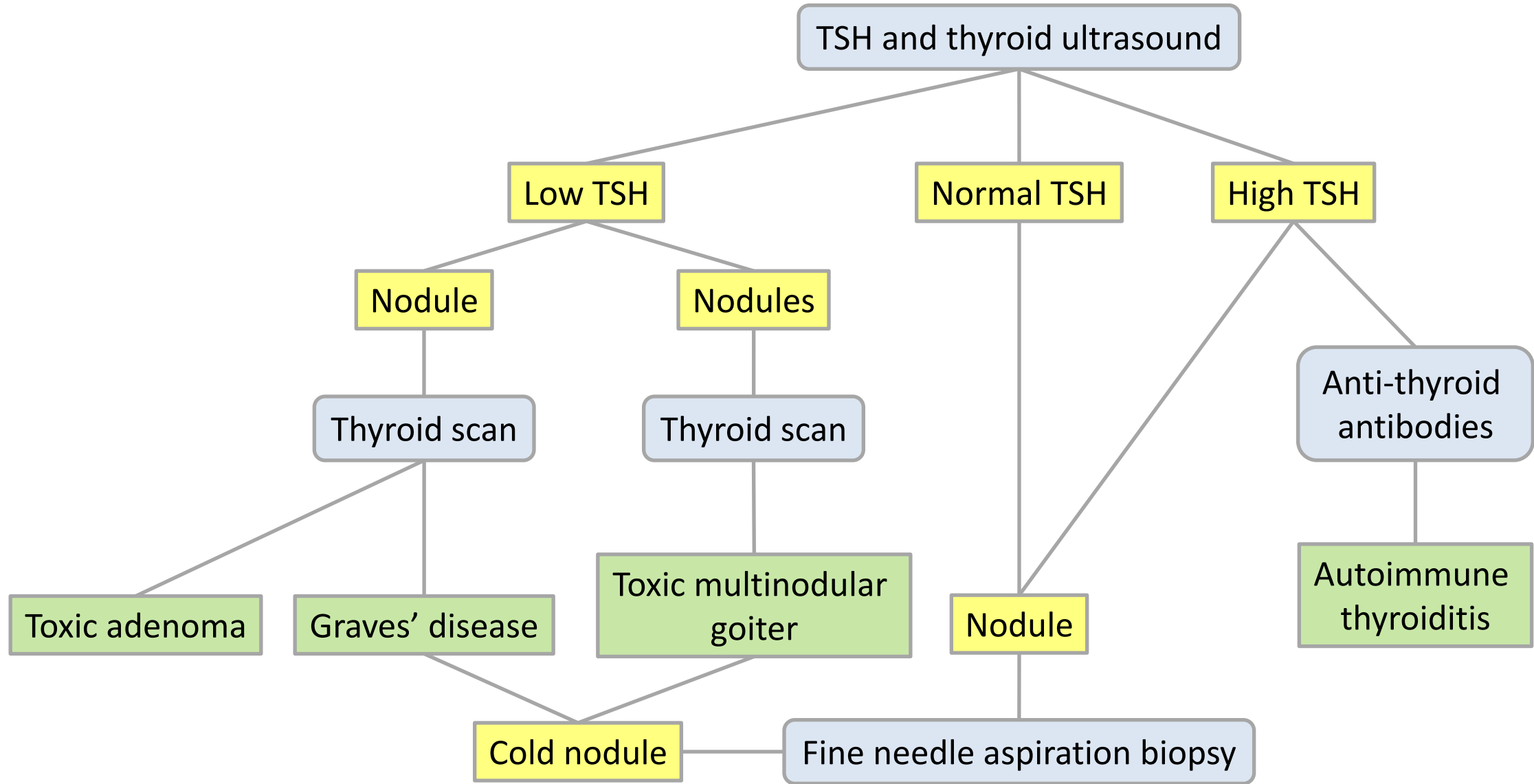
- Thyroid pain can be treated with high dose ibuprofen, naproxen, aspirin, celecoxib, or prednisone 20-40 mg daily
- Beta blockers attenuate thyrotoxic symptoms
- Treatment with levothyroxine during hypothyroid phases may alleviate fatigue and lethargy

# 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



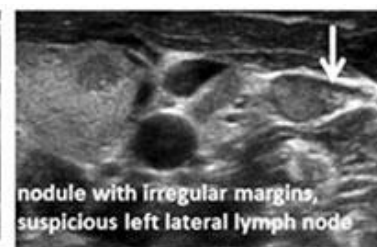
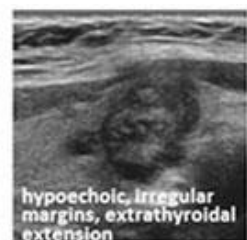
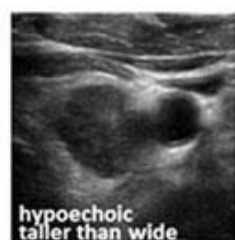
# Thyroid Nodules



# Thyroid Nodules: ATA FNA Criteria

- $\geq 1.0$  cm
  - Hypoechoic nodules
  - Nodules with suspicious features
- $\geq 1.5$  cm
  - Isoechoic nodules
  - Hyperechoic nodules
- $\geq 2.0$  cm
  - Spongiform nodules

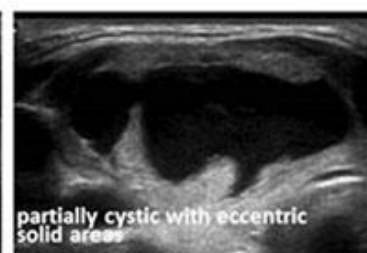
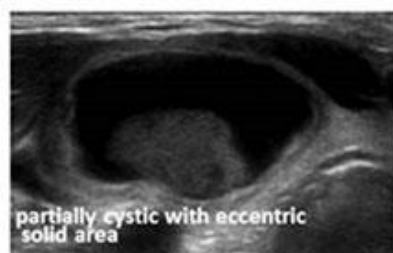
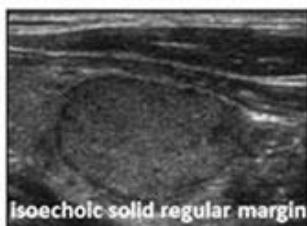
High  
Suspicion  
>70-90%



Intermediate  
Suspicion  
10-20%



Low  
Suspicion  
5-10%



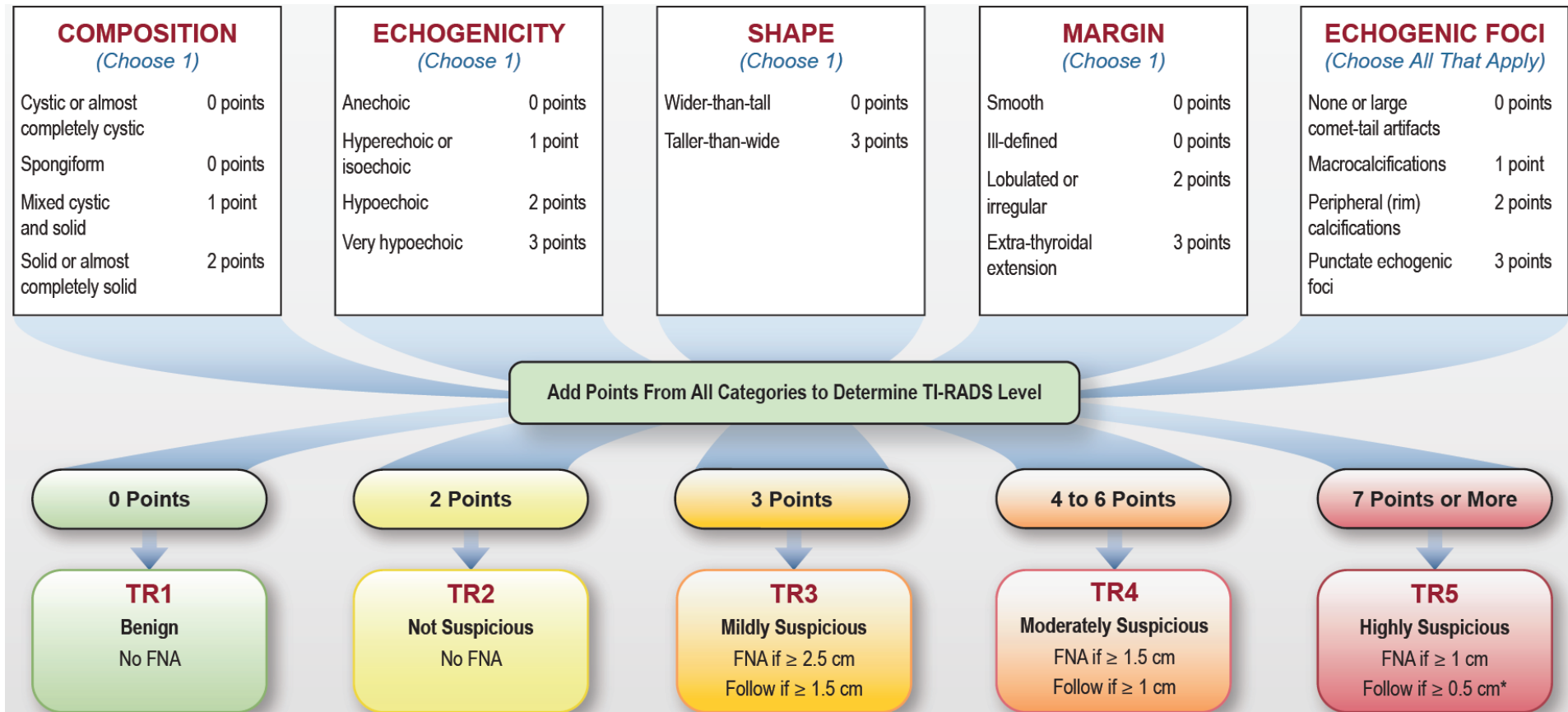
Very low  
Suspicion  
<3%



Benign  
<1%



# 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:  $\geq 2.5$  cm
- TI-RADS 4:  $\geq 1.5$  cm
- TI-RADS 5:  $\geq 1.0$  cm
- Previously biopsied benign thyroid nodules that have enlarged do not need to be re-sampled\*

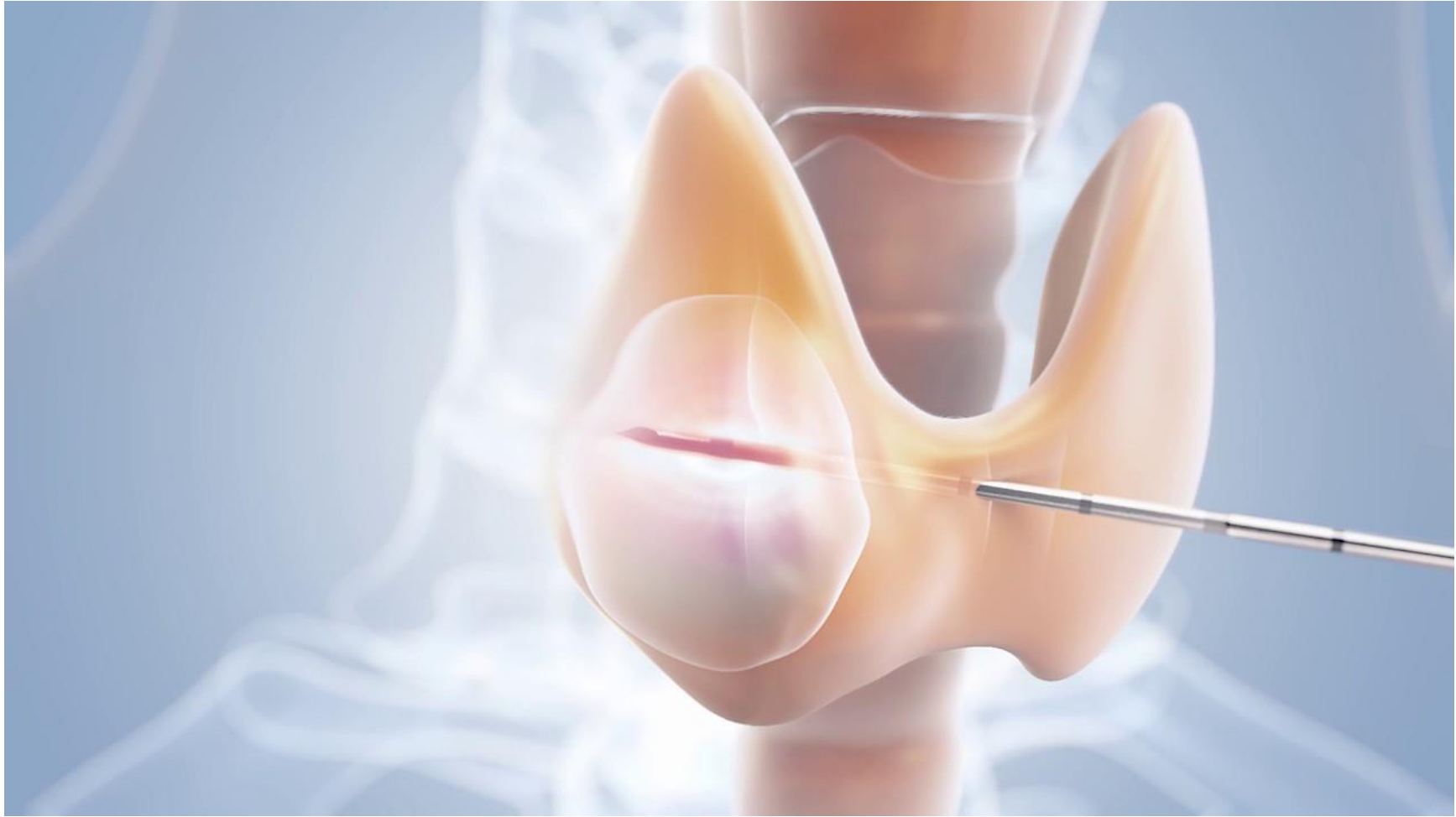


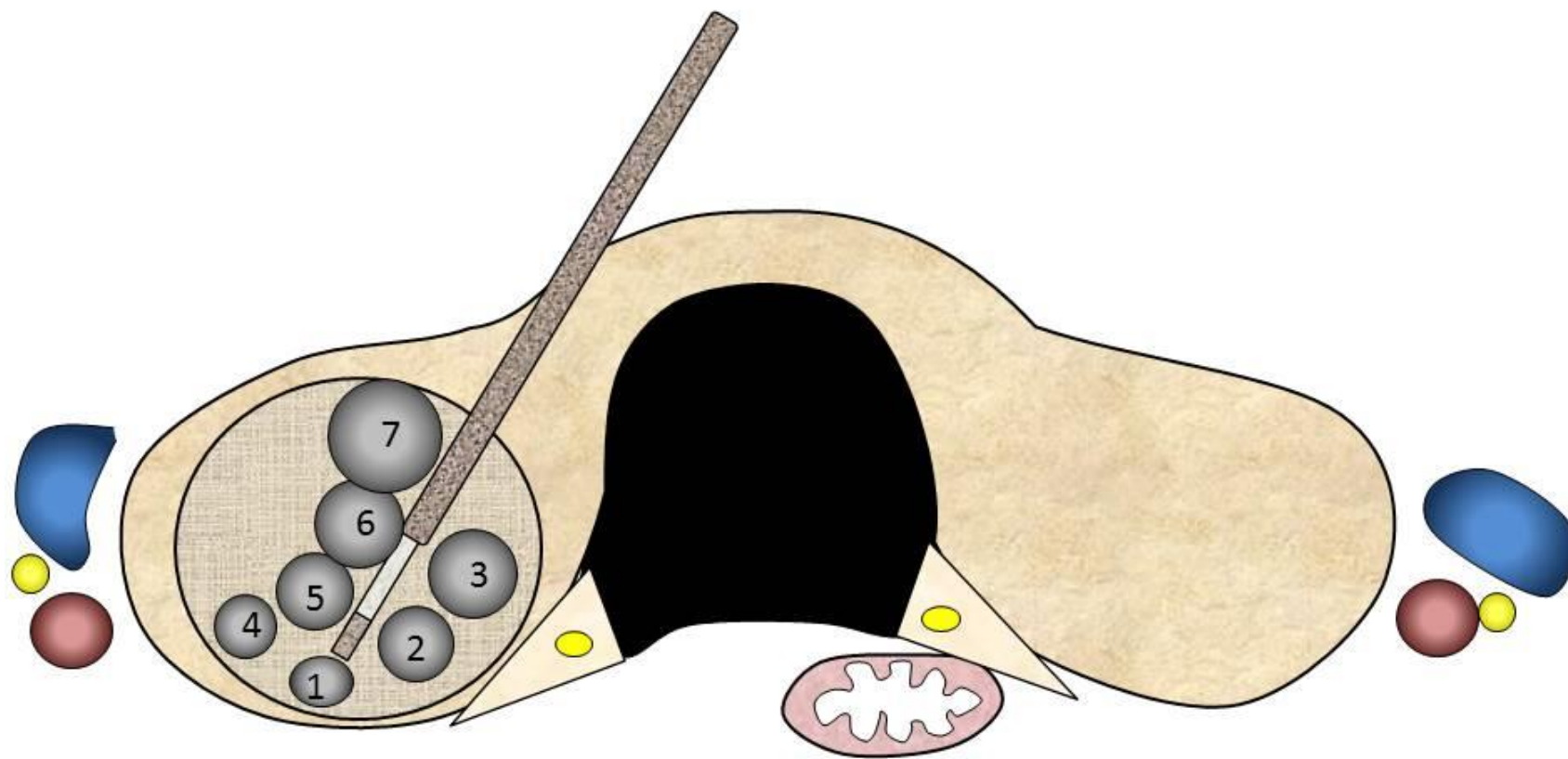
# Bethesda System for Reporting Thyroid Cytopathology

		<b>Malignant</b>
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<sup>®</sup>, ThyroSeq<sup>®</sup> ThyGeNEXT<sup>®</sup> + ThyraMIR<sup>®</sup>)
- Suspicious for a follicular neoplasm
  - Repeat biopsy +/- genetic profiling
- Suspicious for malignancy
  - Hemithyroidectomy or total thyroidectomy
- Malignant
  - Hemithyroidectomy or total thyroidectomy





# Question 1

A 33-year-old male is noted to have palpable enlargement of the right side of his thyroid. Ultrasound reveals a 3.1 cm right midpole thyroid nodule classified as TI-RADS 3. Lab tests show TSH 0.1 mU/L (0.5 - 5.2 mU/L) and T4 11.5 µg/dL (4.6 - 10.7 µg/dL). He reports a history of symptomatic palpitations and weight loss of 5 lbs over the course of 3 months despite an increase in his appetite. He is not taking any medications and has not noted any problems with dysphagia or dysphonia.

# Question 1

What should you do next?

- A. Perform a fine needle aspiration biopsy of the right-sided nodule
- B. Administer a 15 mCi dose of I-131
- C. Refer the patient to a thyroid surgeon
- D. Start methimazole at a dose of 5 mg daily
- E. Check a radioiodine scan and uptake

## 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

# References

- Iwama S et al. Immune checkpoint inhibitor-related thyroid dysfunction. Best Pract Res Clin Endocrinol Metab. 2022 May;36(3)
- Hoang TD et al. Clinical Management of Graves' Disease and Thyroid Eye Disease. Endocrinol Metab Clin North Am. 2022 Jun;51(2):287-304
- Tessler FN et al. Thyroid Imaging Reporting and Data System (TI-RADS): A User's Guide. Radiology. 2018 Apr;287(1):29-36.
- Peeters RP. Subclinical Hypothyroidism. N Engl J Med. 2017 Jun 29;376(26):2556-2565
- Samuels MH. Subacute, silent, and postpartum thyroiditis. Med Clin N Am. 2012. 96(2):223-33