Hyperthyroidism in Primary Care: From Recognition to Individualized Treatment Decisions



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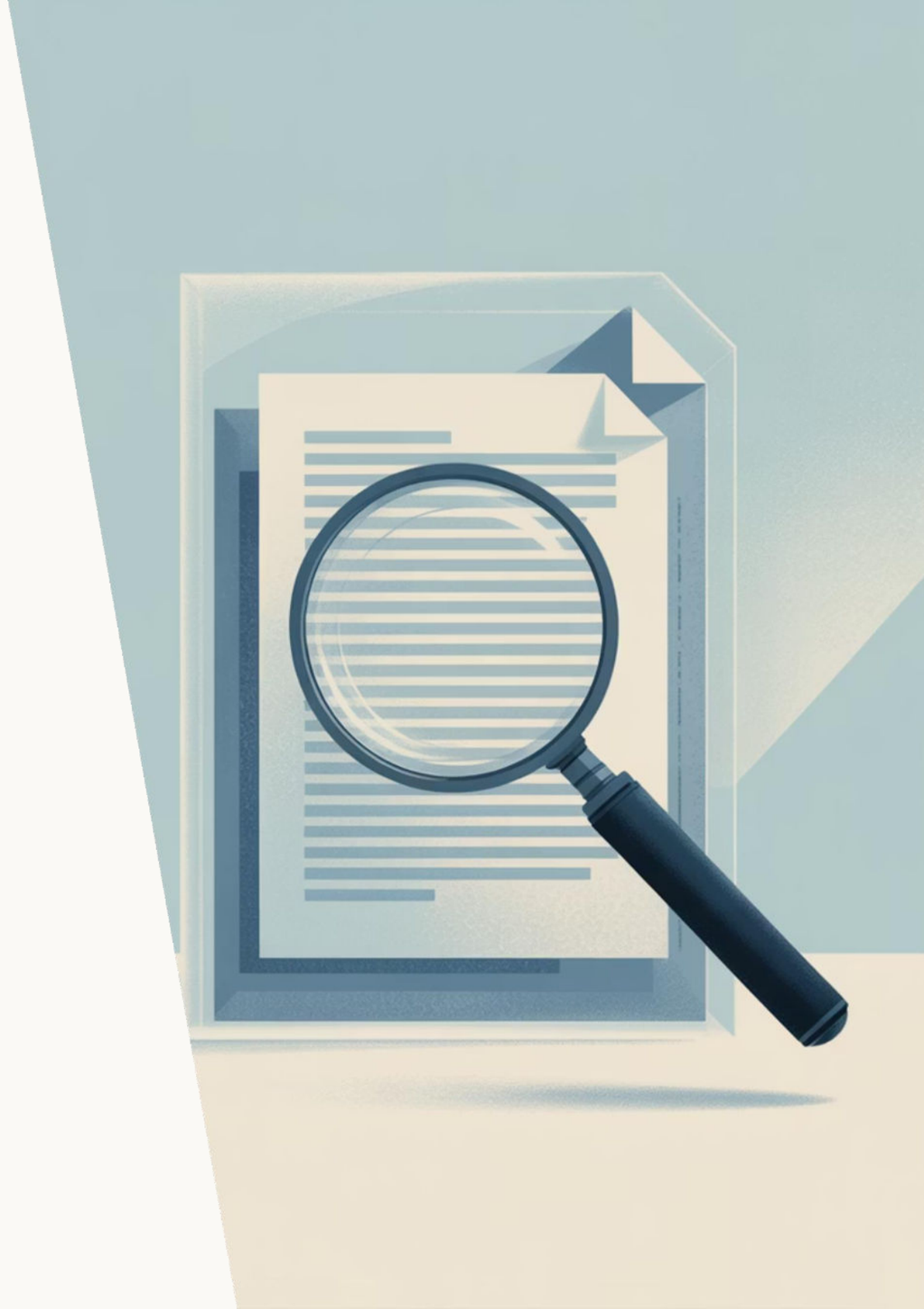
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Disclosures

Insulet (diabetes)



AI Disclosure

Parts of this presentation (and/or its related materials) were generated using AI and are labeled as such, and the faculty have confirmed and validated this information.

Learning Objectives

Recognize

Recognize presenting symptoms and findings suggestive of hyperthyroidism

Categorize

Categorize the most common and most essential causes of hyperthyroidism and navigate challenges to making the diagnosis

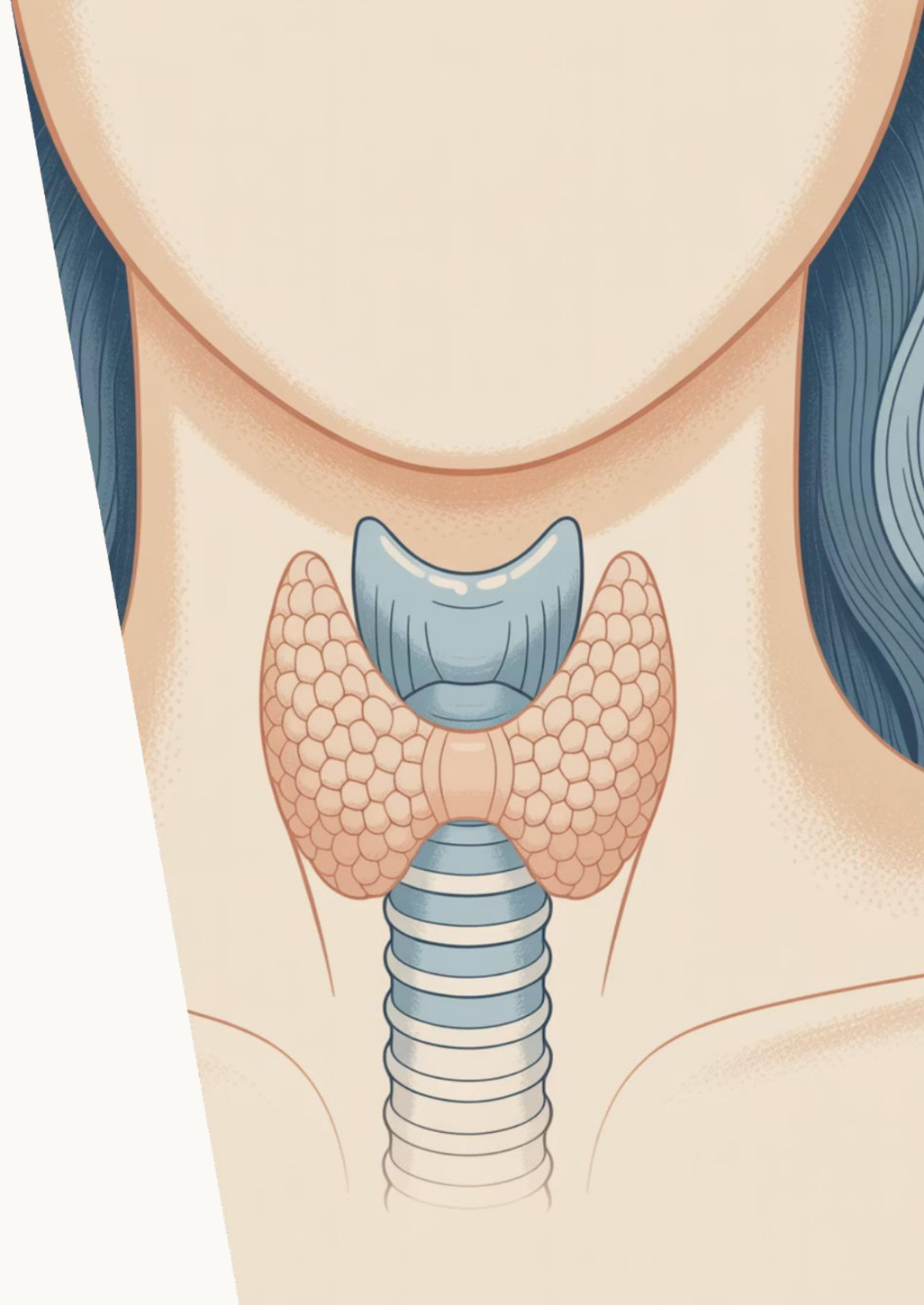
Detail

Detail judicious and most appropriate screening and diagnostic protocols

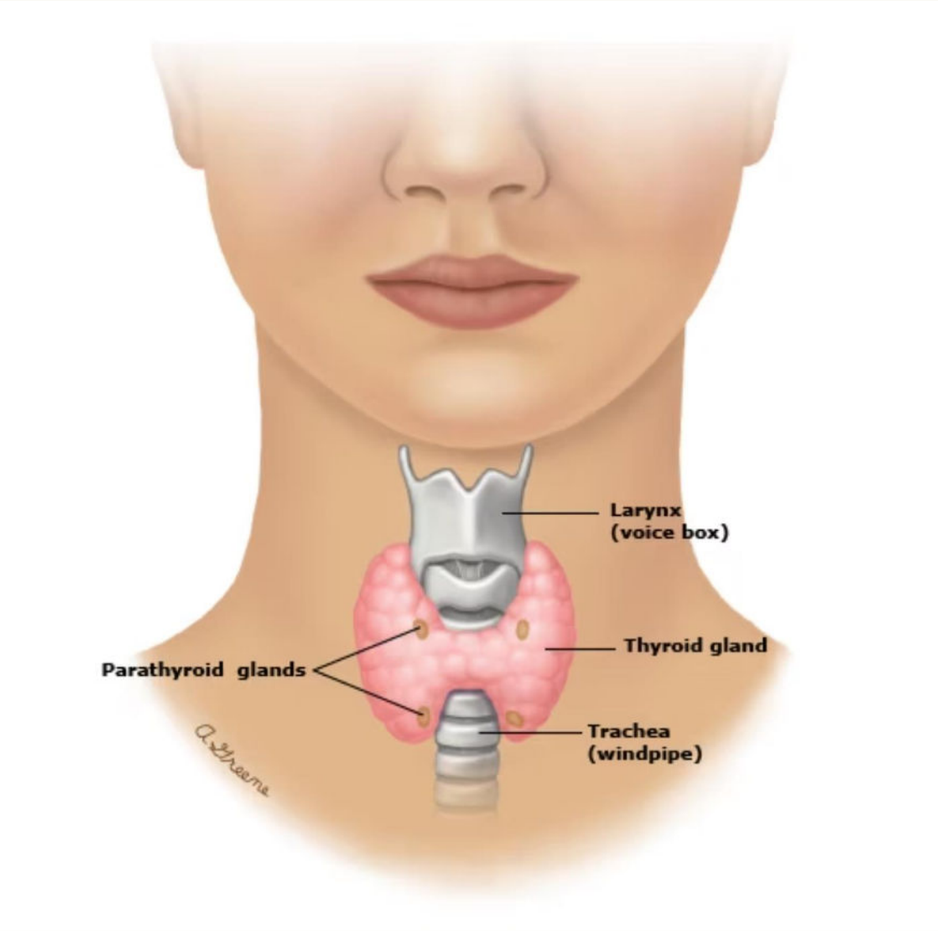
Analyze

Analyze the most appropriate treatment options for hyperthyroidism based on underlying etiology and shared medical decision making

Thyroid Physiology and Pathophysiology



Thyroid Anatomy



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The Thyroid's Role: The Speed of Everything

- Intrauterine and pediatric growth, cognition, and development
- Cardiac rate and function
- Menstrual regularity and fertility
- Activation of nervous system: concentration, reflexes
- Metabolic regulation
- Bone formation and resorption
- Weight regulation
- Muscle metabolism
- Lipid degradation
- Glucose absorption
- Temperature control

Sources:

1. Brent, Gregory MD. "Thyroid Hormone Action." UpToDate.
2. Shahid, Muhammad; Ashraf, Muhammad; Sharma Sandeep. "Physiology, Thyroid Hormone." Stat Pearls.

Thyroid Function

1

2

3

4

Hypothalamus

Thyrotropin Releasing Hormone

Anterior Pituitary: Thyrotrophs

Thyroid Stimulating Hormone (TSH)

Thyroid Gland

Total Thyroxine (T4) > Total triiodothyronine (T3)

Target Tissue

Metabolic effects and feedback regulation

Thyroid Dysfunction

1

2

3

4

Hypothalamus

Thyrotropin Releasing Hormone

Anterior Pituitary: Thyrotrophs

Thyroid Stimulating Hormone (TSH)



Thyroid Gla

Total Thyroxine (T4) > Total triiodothyronine (T3)

Target Tissue

Metabolic effects and feedback regulation

Important: In primary hyperthyroidism, TSH and FT4 are reciprocal

Hyperthyroidism Presentation

1. Asymptomatic
2. Mildly Symptomatic
3. Overtly Clinically Hyperthyroid
4. Thyroid Storm

Note: Symptom presentation and severity can vary significantly irrespective of thyroid assay levels.

Hyperthyroidism Symptoms: "Increased Speed"

METABOLISM

- Weight loss/gain
- Muscle weakness
- Loss of bone density
- Hyperphagia

PSYCHIATRIC

- Anxiety
- Emotional lability
- Irritability
- Restlessness

CARDIAC

- Tachycardia
- Palpitations
- Shortness of breath
- Poor exercise tolerance

VARIOUS

- Tremor
- Hyperdefecation
- Menstrual irregularities

Ross, Douglas S, MD. "Diagnosis of hyperthyroidism." UpToDate.

Hyperthyroidism Conditions/Effects: New or Worsening

METABOLISM

- Myopathy/Sarcopenia
- Underweight/Overweight
- Osteopenia/Osteoporosis

BIOCHEMICAL

- Hypercalcemia
- Elevated alkaline phosphatase
- Hyperglycemia

CARDIAC

- Atrial fibrillation
- Heart failure
- Premature atrial contractions
- Dyspnea on exertion

VARIOUS

- Anxiety
- Fine bilateral tremor
- Oligomenorrhea
- Amenorrhea
- Gynecomastia

Ross, Douglas S, MD. "Diagnosis of hyperthyroidism." UpToDate.

Increased ULN for TSH in Older Individuals

- Population studies: Increased ULN starting at age 50 (females) and 60 (males)
- 50-59 yo → 4.03-4.36 mIU/L
- 60-69 yo → 4.33-4.59 mIU/L
- 70-79 yo → 5.90-5.96 mIU/L
- 80+ yo → 5.94-7.50 mIU/L

Taylor, P.N., Lansdown, A., Witczak, J. *et al.* Age-related variation in thyroid function – a narrative review highlighting important implications for research and clinical practice. *Thyroid Res* 16, 7 (2023). https://doi.org/10.1186/s13044-023-00149-5

Hyperthyroidism Causes

- *Graves' disease: autoimmune thyroid disease (AITD)
- Toxic nodular goiter (TNG): autonomously functioning hyperplasia of thyroid follicular cells
- Postpartum/gestational: postpartum, miscarriage, abortion, gestational trophoblastic disease
- Subacute thyroiditis: post-viral (subacute granulomatous thyroiditis)
  - Elevated ESR, CRP, WBC
  - COVID-19 related?
- Hashitoxicosis: Transient and rare hyperthyroid state associated with Hashimoto's thyroiditis
- Secondary (pituitary) hyperthyroidism: rare

*Most common

Sources

1. Ross, Douglas S, MD. "Diagnosis of hyperthyroidism." UpToDate.
2. Tomer, Yaron; Blackard, Jason T; Akeno, Nagako. "Interferon Alpha Treatment and Thyroid Dysfunction." Endocrinol Metab Clin North Am. 2007 Dec; 36(4): 1051–1066.
3. Lania A et al on behalf of Humanitas COVID-19 Task Force. Thyrotoxicosis in patients with COIVD-19: the THYRCOV study. Eur J Endocrinol. 2020. doi: 10.1530/ EJE-20-0335.PMID: 32698147.

Medication-induced Hyperthyroidism

- **Iatrogenic Hyperthyroidism**
- Factitious Hyperthyroidism
- **Iodine Hyperthyroidism:** following iodine load (CT, angio, myelogram)
- **Amiodarone-induced:** iodine related vs increased thyroid hormone synthesis vs increased thyroid hormone release
    - AITD and TNG are risk factors
- **Graves' Disease**
    - Iodine intake, alemtuzumab (postmarketing), lithium (more commonly hypothyroidism), interferon alpha (AITD vs thyroiditis), COVID-19 vaccine (2 case studies)
- **Misc:** Tyrosine kinase inhibitor, checkpoint inhibitor immunotherapy, Epoprostenol (rare)

Sources

1. Ross, Douglas S, MD. "Diagnosis of hyperthyroidism." UpToDate.

2. Tomer, Yaron; Blackard, Jason T; Akeno, Nagako. "Interferon Alpha Treatment and Thyroid Dysfunction." Endocrinol Metab Clin North Am. 2007 Dec; 36(4): 1051–1066.

Biotin/vitamin B7/vitamin H



Found as a standalone vitamin and in many vitamins including multivitamins, some B-complexes, hair/skin/nail health supplements



May be found in nutritional shakes/supplements



Renders many thyroid function tests inaccurate

TSH, Free T4, Total T3, thyroid antibodies



Does NOT affect the actual thyroid hormone level



***Hold biotin for at least 3 days before testing thyroid levels.**

Katzman BM, Lueke AJ, Donato LJ, Jaffe AS, Baumann NA. Prevalence of biotin supplement usage in outpatients and plasma biotin concentrations in patients presenting to the emergency department. Clin Biochem. 2018 Sep;60:11-16. doi: 10.1016/j.clinbiochem.2018.07.004. Epub 2018 Jul 21. PMID: 30036510.

Hyperthyroidism Evaluation: Where Do We Begin?



Thyroid Diagnostic Studies

To assess function:

- TSH
- Total T4
- Free T4
- Total T3
- Free T3
- Thyroid uptake and scan

To assess structure:

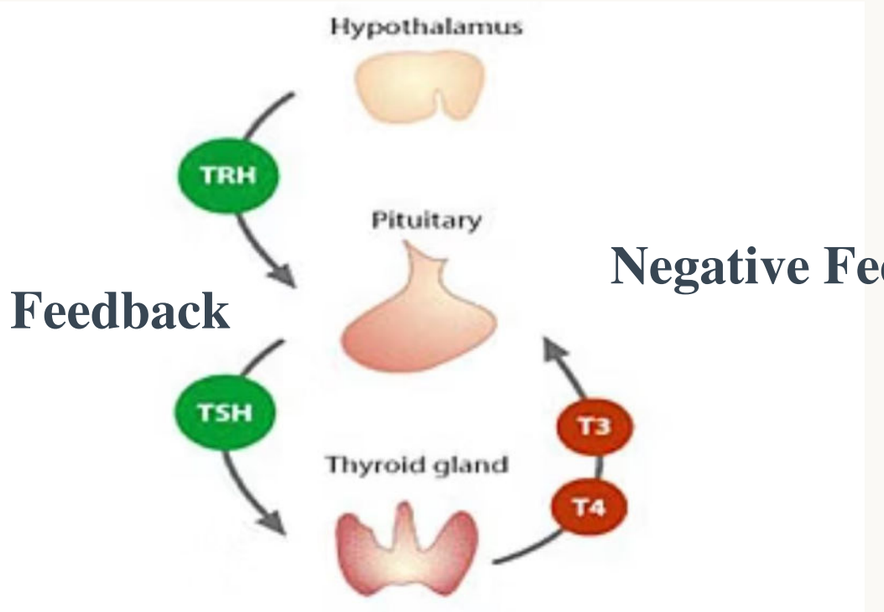
- Thyroid Ultrasound

To assess for AITD:

- Thyroid Peroxidase Antibodies (TPOAb) / Antimicrosomal Antibodies
- Thyroglobulin Antibodies (TgAb)
- TSH receptor antibodies (TRAb)
- Thyroid-Stimulating Immunoglobulins (TSI)

Serological Functional Studies: Thyroid Function Tests (TFTs)

- **Pituitary gland:**
  - TSH
- **Thyroid gland:**
  - Total T4
  - Free T4
  - Total T3
  - Free T3



- <u>Primary</u> deficiency: Pituitary and target hormone values are **reciprocal**

  <u>Central or secondary</u> deficiency: Pituitary and target hormone values are **congruent**

Thyroid Stimulating Hormone (TSH)

The best screening test of thyroid function

Normal: no further serological evaluation

- Use clinical judgement

Elevated: primary hypothyroidism* or secondary hyperthyroidism

- Evaluate for hypothyroidism with free thyroxine (T4) and anti-thyroid peroxidase (TPO) antibodies

Suppressed: primary hyperthyroidism* or secondary hypothyroidism

- Evaluate for hyperthyroidism with free T4 and assessment for underlying causes

*More common

Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

Major Thyroid Hormones: T4 and T3

- Measured after TSH
  - More direct measure of hormone activity and thyroid function
  - Useful in differentiating between primary vs secondary disease
- **T4**
  - *Majority* of thyroid hormone production
  - Deiodination liberates more active T3
- **T3**
  - Small portion synthesized in follicular cells with the majority converted from circulating T4
  - More potent but degraded more quickly

Total vs Free T4 and T3

- **Total T4** = T4 bound to thyroid binding globulin (99.97%) + Free T4
- **Total T3** = T3 bound to thyroid binding globulin (99.7%) + Free T3
  - Thyroid binding globulin (TBG) produced in the liver
  - T4 and T3 bound to TBG act as intravascular thyroid hormone storage pools: **NOT biochemically active**
  - **Free T4 and Free T3** are biochemically active
  - **Total T4 and T3** includes both inactive and active thyroid hormone

Sources

1. Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229. Accessed 5.14.22.
2. Garber, Jeffrey MD; et al. "Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association." ATA/AACE GUIDELINES| VOLUME 18, ISSUE 6, P988-1028, NOVEMBER 01, 2012. DOI:https://doi.org/10.4158/EP12280.GL.
3. Fantz, Corinne; Dagogo-Jack, Samuel; Ladenson, Jack; Gronowski, Ann. "Thyroid Function during Pregnancy." Clinical Chemistry, Volume 45, Issue 12, 1 December 1999, Pages 2250–2258, https://doi.org/10.1093/clinchem/45.12.2250. Accessed 5/14/22.

Thyroid Binding Globulin (TBG)

<u>Decreased TBG</u> (decreased Total T4):

- Androgens, anabolic steroids, glucocorticoids, hepatic failure
- Severe illness, nephrosis, nicotinic acid, L-Asparaginase

<u>Increased TBG</u> (increased Total T4):

- Pregnancy, estrogens (HRT, OCP)
- Hepatitis, porphyria, heroin, methadone, mitotane, 5-Fluorouracil, SERMS, perphenazine, neonatal state

Sources:

1. Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.
2. Garber, Jeffrey MD; et al. "Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association." ATA/AACE GUIDELINES| VOLUME 18, ISSUE 6, P988-1028, NOVEMBER 01, 2012. DOI:https://doi.org/10.4158/EP12280.GL.
3. Fantz, Corinne; Dagogo-Jack, Samuel; Ladenson, Jack; Gronowski, Ann. "Thyroid Function during Pregnancy." Clinical Chemistry, Volume 45, Issue 12, 1 December 1999, Pages 2250–2258, https://doi.org/10.1093/clinchem/45.12.2250.

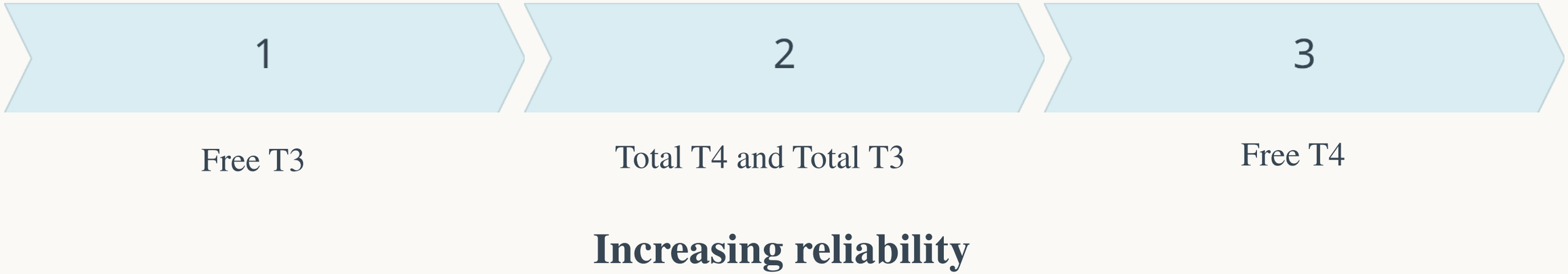
Total vs Free T4 and T3: Clinical Application

- **T4 Assays**
  - Total T4: Reflects **both active and inactive** T4
    - Highly variable due to TBG variations
  - ***Free T4*** *mitigates the confounding factors of TBG variability*
- **T3 Assays**
  - Free T3 is highly variable
  - Generally, T3 is not tested due to variability
  - *If tested, utilize the more reliable* ***Total T3*** (rare: isolated T3 toxicosis)

Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

Total vs Free T4 and T3: Clinical Application

- Free T4 is **best next step** after abnormal TSH



Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

Autoimmune thyroid disease (AITD): Graves' vs Hashimoto's

Graves' Disease:

- Autoimmune-mediated stimulation of TSH receptor via TSH receptor antibodies (TRAb)
- Mimics TSH: Thyroid gland growth and increased thyroid hormone synthesis/secretion
- Subsets:
  - Thyroid-Stimulating Immunoglobulins (TSI)
  - Thyrotropin Binding Inhibitory Immunoglobins (TBII)

Hashimoto's Disease:

- Thyroglobulin Antibodies (TgAB) and Anti-thyroid peroxidase antibodies (TPO Ab)/ Microsomal TPO Antibodies:
  - Also seen in Post-partum thyroiditis

Source

1. Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.
2. Garber, Jeffrey MD; et al. "Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association." ATA/AACE GUIDELINES| VOLUME 18, ISSUE 6, P988-1028, NOVEMBER 01, 2012. DOI:https://doi.org/10.4158/EP12280.GL.

Summary of Thyroid Antibodies

Thyrotropin Receptor Antibodies (TRAb)	Graves' disease
Thyroid stimulating Immunoglobin (TSI)	Graves' disease
Thyroglobulin antibodies (TgAb)	Hashimoto's disease
Anti-thyroid peroxidase antibodies (TPO Ab)	Hashimoto's disease

Sources:

1. Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229. Accessed 5.14.22.
2. Garber, Jeffrey MD; et al. "Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association." ATA/AACE GUIDELINES| VOLUME 18, ISSUE 6, P988-1028, NOVEMBER 01, 2012. DOI:https://doi.org/10.4158/EP12280.GL.

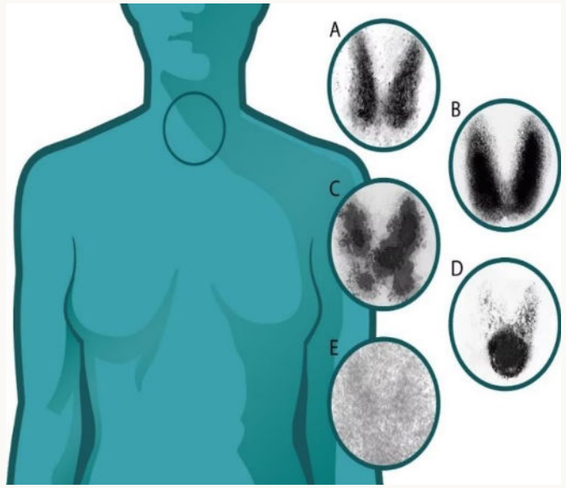
Thyroid Uptake and Scan

✓Refer

Functional study

Indication: suppressed TSH

- AKA Thyroid Nuclear Medicine Scan/ Thyroid Scintigraphy*
- Visualization of thyroid tissue activity after ingestion of radioactive iodine I-123 (tracer)
- Measures radioactive iodine uptake
  - Thyroid tissue
  - Thyroid nodule compared to surrounding thyroid tissue
  - Degree and distribution of uptake
- Not necessary if hyperthyroidism cause is identified unless preparing for radioactive iodine ablation



***Absolute contraindications: pregnancy and breastfeeding**

Source: Ross, Douglas S, MD. "Diagnosis of hyperthyroidism." UpToDate.

Thyroid Uptake and Scan in Hyperthyroidism

Elevated diffuse uptake:

- **Graves' disease**
- Amiodarone use
- Early Hashimoto's thyrotoxicosis
- TSH-mediated hyperthyroidism
- Gestational trophoblastic disease

Localized elevated uptake:

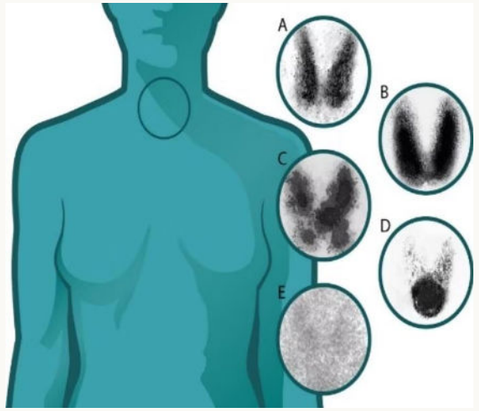
- TNG or "hot" nodule

Low diffuse uptake:

- **Hashimoto's thyroiditis**
- Hashimoto's thyrotoxicosis
- Exogenous iodine exposure
- Amiodarone use
- Thyroiditis
- Factitious hyperthyroidism

Localized decreased uptake:

- "Cold" nodule



Sources:

1. Ross, Douglas S, MD. "Diagnosis of hyperthyroidism." UpToDate.
2. Amiodarone: Drug Information. UpToDate.
3. Davies, Terry. Pathogenesis of Hashimoto's thyroiditis (chronic autoimmune thyroiditis). UpToDate.

Thyroid US

Utility:

- Detection of nodular disease
  - The most sensitive imaging study for evaluating thyroid nodule characteristics
- Color flow doppler
  - Vascular anatomy and flow within blood vessels

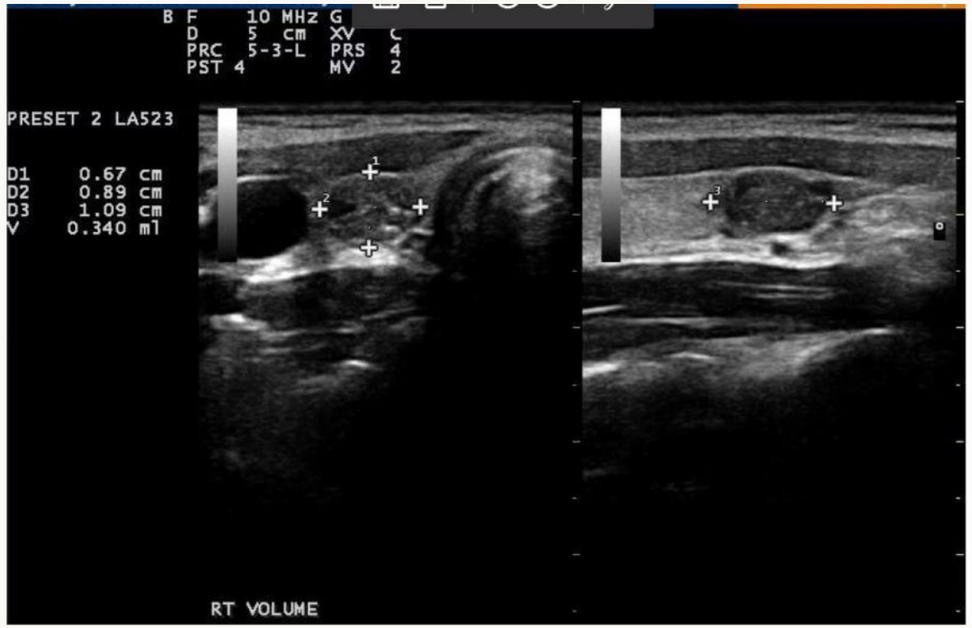


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When it's NOT Hyperthyroidism

MOST COMMON

Altered thyroid binding globulin

Isolated high Total T4

Increased intravascular pool of biochemically inactive thyroid hormone

Elevated TBG level

MOST COMMON

Biotin (B7)

≥ 5,000mcg daily

Asymptomatic and/or inconsistent TFTs mimicking Graves' disease

Interferes with thyroid assays

Stop biotin for at least 2 days and reassess

Factitious hyperthyroidism

Hyperthyroidism without immune markers

Low diffuse uptake

Low thyroglobulin

Pituitary Dysfunction

Intracranial radiation or surgery

Checkpoint inhibitor immunotherapy

Evidence of pituitary disorder

TSH remains inappropriately low or normal

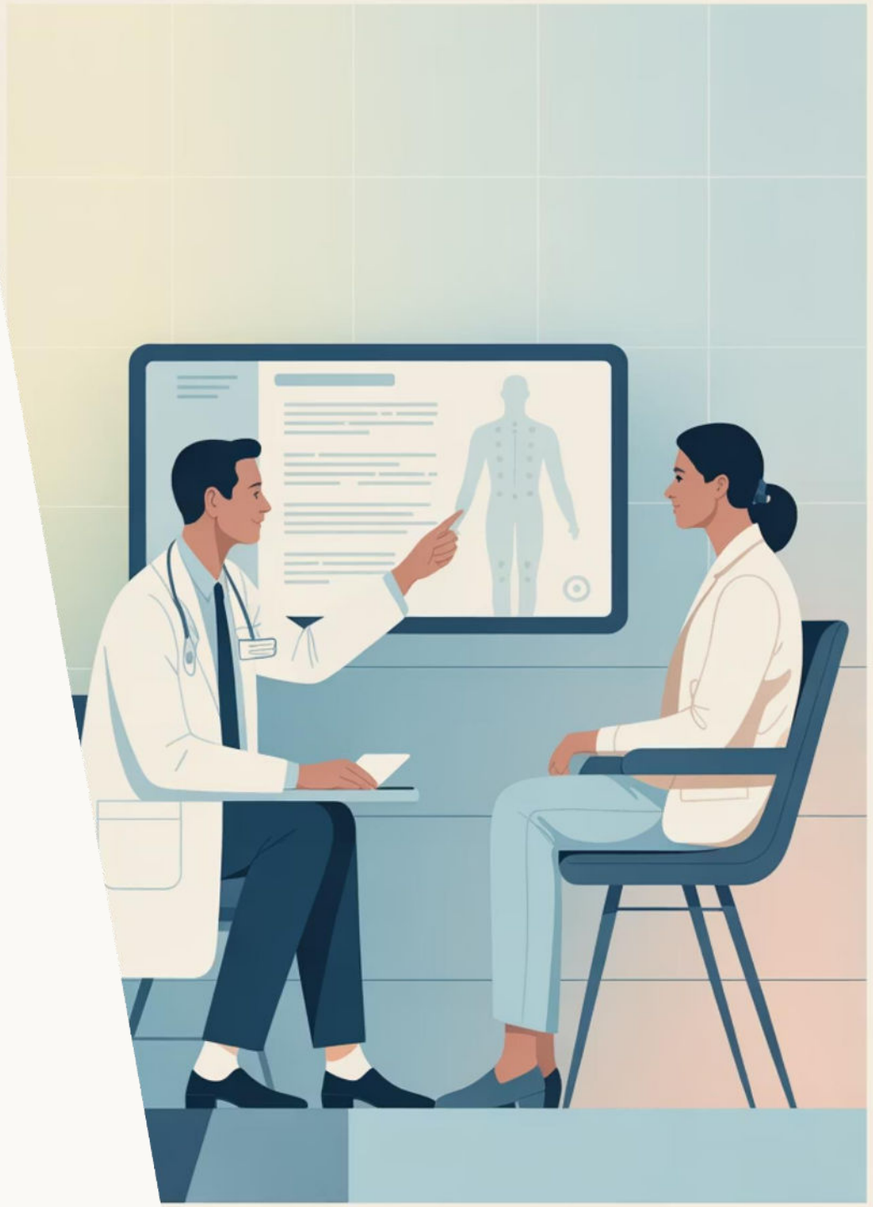
Ross, Douglas S, MD. "Laboratory Assessment of Thyroid Function." UpToDate.

Subclinical hyperthyroidism

- TSH suppressed with normal Free T4
  - Increased risk of cardiovascular mortality, HF, a-fib
  - Variable evidence of osteoporosis and fx risk
  - Especially in more suppressed TSH <0.1 and in older individuals age ≥65
- Etiology: Typically toxic nodular goiter, next Graves' disease
- Confirmation
  - High risk pt: TSH and FreeT4 at 2-6 weeks
  - All others: monitor TSH at 3-6 months
- Management
  - If age ≥65, CVD, osteoporosis, at risk condition, *or* symptoms of hyperthyroidism
    - TSH <0.1, treat
    - TSH suppressed but >0.1, consider tx
  - If age <65 without CVD, osteoporosis, at risk condition *or* symptoms of hyperthyroidism
    - If TSH <0.1, consider tx
    - If TSH suppressed but >0.1, no tx

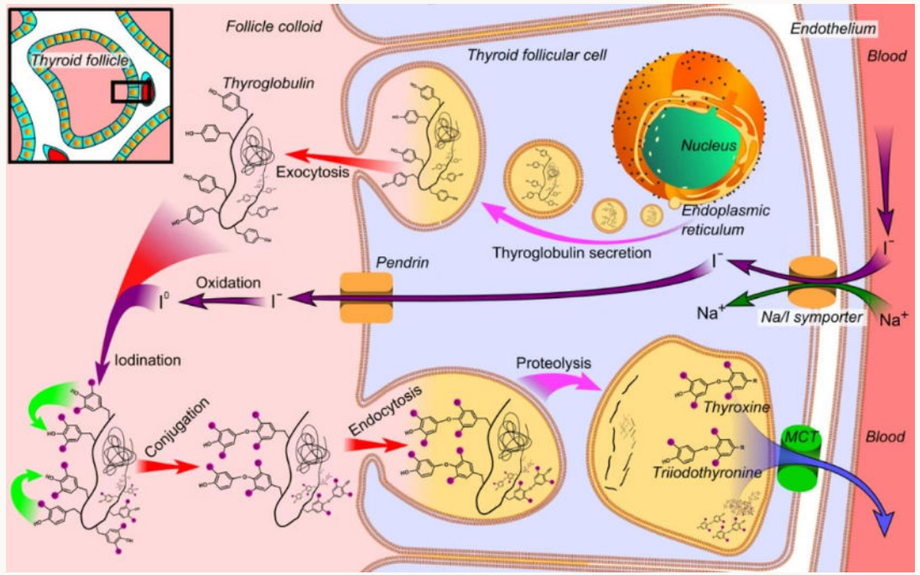
Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

Treatment Approach and Considerations



Medication: Thionamides

- Methimazole, propylthiouracil (PTU)
  - **Methimazole preferred:** less hepatotoxicity, greater efficacy over PTU
- Inhibit thyroid hormone **synthesis**
- **Preferred in:** *pregnant/breastfeeding, unable to isolate, limited life expectancy*
- **Cautions:** pregnancy considerations
  - Both meds are teratogenic
  - PTU preferred: family planning, first trimester
- Side effects:
  - Agranulocytosis
  - Hepatotoxicity
    - Rash, fever, joint pain, n/v



Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

Medication

- **Beta Blockers**
  - *Symptomatic* treatment: tachycardia, palpitations, tremor, anxiety, heat intolerance
  - Elderly, cardiac conditions
  - Cautions: asthma, DM1, CVD
  - Side effects: fatigue, weight gain
- **Steroids**
  - Role in prevention and mitigation of *Graves' eye disease*
    - Prophylaxis after RAI based on shared decision making
    - Active thyroid eye disease
  - *Painful thyroiditis*



Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

✓Refer

Radioactive Iodine

- Ingestion of I-131 leading to destruction of thyroid tissue
  - **Preferred in:**
    - TNG
    - Graves' disease:
      - Women planning pregnancy in >6 months
      - Intolerant to thionamides
      - Previous neck surgery/radiation
- **Considerations**
  - Isolation required
  - Cleaning protocol
  - Repeat TFTs Q4-6 weeks until euthyroid
- **Risks:**
  - Permanent post-ablative hypothyroidism
  - New/worsening thyroid eye disease (TED)
    - Highest risk for current smoking and pre-existing TED
  - Rare: Radiation thyroiditis days-1 week

Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

✓Refer

Thyroidectomy

- Total vs hemithyroidectomy
  - **Preferred in:**
    - TNG (total vs hemi)
    - Graves' disease (total):
      - Goiter/large thyroid nodule/compressive symptoms
      - Planning pregnancy <6 months
      - Thyroid malignancy/additional neck surgery needed
      - Low uptake on nuclear scan

Risks:

- Postsurgical hypothyroidism
- Risk of parathyroid disease or recurrent laryngeal nerve damage
- Surgical/anesthesia risks

Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

✓Refer

Radiofrequency Ablation

- Thermal energy injected via fine needle causing local tissue necrosis and fibrosis
- Approved in 2018
- Non-surgical option
- Moderate efficacy with preservation of normal thyroid function

- **Preferred in TNG if:**
  - *Intolerance to, ineligible for, or opposed to* RAI, surgery, or thionamide tx
  - Recent increase in utilization for benign nodular goiter

Source:
1. Cesareo, R., Palermo, A., Pasqualini, V., Manfrini, S., Trimboli, P., Stacul, F., Fabris, B., & Bernardi, S. (2020). Radiofrequency Ablation on Autonomously Functioning Thyroid Nodules: A Critical Appraisal and Review of the Literature. Frontiers in endocrinology, 11, 317. https://doi.org/10.3389/fendo.2020.0031.
2. Sinclair, Catherine F.; et al. "General Principles for the Safe Performance, Training, and Adoption of Ablation Techniques for Benign Thyroid Nodules: An American Thyroid Association Statement." Thyroid. Vol. 33, No. 10. October 13, 2023. https://doi.org/10.1089/thy.2023.0281

Treatment Based on Etiology

1

Graves' Disease

- Thionamides vs RAI vs Thyroidectomy
- Remission: observation

2

TNG

- RAI vs Thyroidectomy preferred over Thionamides

3

Thyroiditis

- Painless and minimally symptomatic: Observation
- Beta blockers as needed
- Painful thyroiditis: NSAIDs vs Corticosteroids

Source: Ross, Douglas; et al. "2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis." THYROID Volume 26, Number 10, 2016 ª American Thyroid Association ª Mary Ann Liebert, Inc. DOI: 10.1089/thy.2016.0229.

Questions?

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