

Hyperthyroidism

The thyroid gland is a butterfly-shaped endocrine gland that is located in the lower front of the neck. which synthesis thyroid hormones. Thyroid hormone helps our bodies to use energy, stay warm, and keep our brain, heart and other organs working as they should.

Hyperthyroidism presents as a constellation of symptoms due to higher levels of circulating thyroid hormones. The elevated hormone levels may occur despite otherwise normal thyroid function, as in instances of inappropriate exogenous thyroid hormone or excessive release of stored hormone from an inflamed thyroid gland.

Due to the many actions of thyroid hormone in various organ systems in the body, there is a wide range of clinical signs produced by the condition. The symptoms may be subtle and non-specific, making it difficult to diagnose hyperthyroidism at an early stage without the help of laboratory screening.

Pathophysiology:

Normally the hypothalamus produces thyrotropin-releasing hormone (TRH), which stimulates the anterior pituitary gland to secrete thyroid-stimulating hormone (TSH); that triggers the thyroid gland to synthesize thyroid hormone.

Concentration of thyroid hormone is regulated by negative feedback. Also, TRH secretion is partially regulated by cortical centers.

The thyroid gland produces the prohormone thyroxine (T_4), which is de-iodinated by the liver and kidneys to its active form triiodothyronine (T_3). Also, the thyroid gland produces a small amount of T_3 directly. T_4 and T_3 exist in two forms: a free (active form) and bounded to thyroid-binding globulin (TBG). Despite consisting

of less than 0.5% of total circulating hormone, free T₄ and T₃ levels correlate with the patient's clinical status.

Symptoms:

- Weight loss, heat intolerance, sweating (due to stimulating metabolism and heat production).
- Tremor, Nervousness, anxiety, or emotional lability, Psychosis, Disorientation & Fatigue (CNS overactivity).
- Cardiac features caused by β -adrenergic sympathetic activity: palpitations, tachycardia and arrhythmias.
- Increased perspiration, dyspnea & Chest pain - Often occurs in the absence of cardiovascular disease
- Menstrual irregularity
- Weakness - Typically affects proximal muscle groups
- Edema
- Frequent bowel movements
- Eye signs:
 - Minimal/mild: Soft tissue edema, chemosis.
 - Very prominent (sever exophthalmos, corneal ulcers & diplopia).
 - Ophthalmopathy is usually bilateral, but may only involve one eye
- Pretibial myxedema, thyroid acropachy, vitiligo and alopecia are rare.

Laboratory results that indicate hyperthyroidism:

- Low TSH levels and high free T₃ & T₄ levels (thyroid function test)
- Positive serology for thyroid autoantibodies (Graves's disease).
- Hyperglycemia, hepatic function abnormalities

- Low serum cortisol, leukocytosis & hypokalemia.

Etiology:

- TSH-Secreting pituitary adenoma.
- Autoimmune stimulation (Graves' disease)
 - Thyroid-stimulating antibodies (IgG) [Thyrotropin receptor antibodies (TRAb)] bind to TSH receptor and stimulate thyroid cells to produce & secrete excessive amounts of thyroid hormones.
 - Thyroid gland hypertrophies and becomes diffusely enlarged
 - The autoimmune process leads to mucopolysaccharide infiltration of the extra-ocular muscle and may lead to exophthalmos.
- T₃, T₄ Secreting site on the thyroid.
 - Nodular in multinodular goiter (Plummer's Syndrome)
 - Adenoma or (very rarely) carcinoma.
- Thyroiditis (large amounts of preformed hormones are released after the destruction of follicles, with transient thyrotoxicosis).
- Exogenous intake of thyroid hormones (factitious thyrotoxicosis).

Treatment:

Each treatment modality has advantages and disadvantages that need to be considered. These options are preference-sensitive meaning that the patient and provider must discuss the tradeoffs for each individual.

- **Antithyroid drugs (ATD).**

ATD are used as Inhibitors of hormone synthesis

1. Carbimazole and Methimazole

Carbimazole is a prodrug metabolized to methimazole.

Hyperthyroidism	<ul style="list-style-type: none"> • Mild: 15 mg/day PO divided q8hr initially • Moderate: 30-40 mg/day PO divided q8hr initially • Severe: 60 mg/day PO divided q8hr initially • Maintenance: 5-30 mg/day PO divided q8hr
Graves' disease	10-20 mg/day PO once; after euthyroidism is achieved, reduce dosage by 50% and administer for 12-18 months; may subsequently taper or discontinue if TSH levels are normal
Thyrotoxicosis	15-20 mg PO q4hr during first day as adjunct to other agents; reduce frequency to qday or q12hr once patient is stable
Contraindications: Hypersensitivity & Breastfeeding.	

2. Propylthiouracil

Hyperthyroidism	<ul style="list-style-type: none"> • 300-450 mg/day PO divided q8hr initially (may require up to 600-900 mg/day) • Maintenance: 100-150 mg/day divided q8hr
Graves' disease	<ul style="list-style-type: none"> • 50-150 mg PO q8hr initially • Maintenance: 50 mg PO q8-12hr for up to 12-18 months; then taper and discontinue if euthyroidism restored (TSH) is normal.
Thyrotoxic Crisis	<ul style="list-style-type: none"> • Initial 200-300 mg PO q4-6hr initially on Day 1 (may require 800-1200 mg/day), then reduce gradually; some practitioners propose an initial dose of 600-1000 mg with gradual dose reduction after initial response • Maintenance: 100-150 mg/day PO divided q8-12hr.

- **Beta blockers**

β -blockers block hyperthyroidism manifestations mediated by adrenergic receptors and block the conversion of T₄ to T₃ (less active). Used to treat symptoms like tachycardia, palpitation and tremors.

Propranolol	10-40 mg	3-4 times\day	<ul style="list-style-type: none"> • Longest experience. • May block T₄ to T₃ conversion at high does. • Preferred agent for nursing and pregnant mothers.
Atenolol	25-100 mg	1-2 times\day	<ul style="list-style-type: none"> • Relative b-1 selectivity. • Increase the compliance. • Avoided in pregnancy.
These drugs contraindicated in bronchospastic asthma.			

- **Radioactive iodine (¹³¹I).**

Radioisotope iodine is given to destroy thyroid cells. The RAI is usually administered as a small capsule once orally. Over time (weeks to months), the thyroid cells stop working. Cure rates with RAI are as high as 95%.

A typical average dose of RAI is 10–15 mCi. The dose can be given in a fixed dose or calculated based on the RAIU by the thyroid gland and the size of the gland with comparable successful treatment outcomes.

RAI contraindicated in children (younger than 10 y.o), pregnancy & sever eye disease.

- **Surgical (Thyroidectomy).**

Indication

- Relief of local compressive symptoms.
 - Cosmetic deformity.
 - Prevention of progressive thyroid enlargement.
- Total Thyroidectomy.
(for Graves' disease) indicated for patient who aren't candidates for ¹³¹I therapy. It's the treatment of choice in those with eye diseases and patient where control of symptoms has been difficult on medication. Slightly higher risk of recurrent laryngeal nerve injury and hypoparathyroidism (due to increased vascularity of the gland and local fibrosis).
 - Thyroid lobectomy.
for isolated nodules or adenomas.