



Graves disease

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Definition

- **Hyperthyroidism**
- An inappropriately high synthesis and secretion of thyroid hormone by the thyroid
- **Thyrotoxicosis**
- **Clinical manifestations of inappropriately high thyroid hormone action in tissues.**

Graves' disease

- Accounts for 10–15% of all childhood thyroid abnormalities
- Its incidence peaks between age 11 and 15 years
- Predominantly affecting females

Graves Disease

- About 30% of GD patients have family members who also have GD or Hashimoto's thyroiditis.
- **Twin** studies have shown that 80% of the susceptibility to GD is genetic
- Monozygot twins have higher incidence than dizygot twins
- The incidence of Graves' disease in a sibling of the index case is 11/6-fold higher than that in the general population

Associated disorders

is associated with

- Type 1 diabetes
- Celiac disease
- Addison disease
- systemic lupus erythematosus
- Hashimoto thyroiditis
- pernicious anemia
- Down syndrome
- Turner syndrome


Associated disorders

- **is associated with**
- Hepatitis c
- Congenital rubella
- Y.entocolitis
- Helicobacter
- Retroviral

Clinical manifestation

- Fatigue
- Excessive sweating
- irritability
- Nervousness
- Emotional lability
- poor concentration
- Sleep disturbance





Diagnosis is easily overlooked in teenage girls with weight loss who are assumed to have an eating disorder

Cardiac manifestation

Childhood

- Blood pressure, tachycardia, precordial thrill, and an ejection murmur due to functional insufficiency of the mitral valve
- wide pulse pressure
- Palpitations

Neuromuscular disease

- Hyperactive DTR
- Fine tremor

Neuromuscular disease

- Hypokalemic periodic paralysis
- May be associated with myasthenia gravis and thymic enlargement

Bone disease

- osteoporosis
- Restoration to normal for **two years** on ATD treatment

Ophthalmologic manifestation

- Children present milder ophthalmic abnormalities than adults, mostly
- staring eyes
- soft tissue involvement
- Retraction of the upper lid
- wide palpebral aperture
- **Exophthalmos (proptosis)**



Ophthalmologic manifestation

- **Diffuse goiter** symmetric ,firm and uniformly smooth, without tenderness



Gastrointestinal involvement

- The prevalence of celiac disease and IBD is probably modestly increased
- .

Clinical manifestation

- Reduction in menstrual flow or oligo-menorrhea
- **urinary frequency**
- **Gynecomastia**
- Weight loss despite increased appetite

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Clinical manifestation

- Increased perspiration
- Heat intolerance
- Warm, moist and smooth skin
- palmar erythema
- **Thin and fine hair**

- Vitiligo and alopecia areata
- softening of the nails



Pathogenesis

- is autoimmune disease whose major manifestations are owing to circulating Ab that stimulate TSH-R
- . **TSH stimulating Ab** leading to the release of TH and thyrocyte growth.

Diagnosis

Serology

- Serum TSH has the highest sensitivity and specificity for assessing TH excess.
- **should be** used as an initial screening test
- Accuracy improves when TSH and free T₄ are assessed at the time of the initial evaluation.

TSH Receptor Antibody

- TSH-R-Ab are specific biomarkers for **diagnosis of GD**.
 - **95 % of clinical GD will have positive TRAB**



TSH Receptor Antibody

- TRAb is a sensitive and specific tool for rapid and accurate diagnosis and differential diagnosis of Graves' hyperthyroidism.
- for prognostic purposes
- for monitoring ATD therapy
- for timing of stopping therapy
- Allows long term ATD therapy in some cases
- Excellent predictive value for relaps

Thyroid Peroxidase Antibody

- TPOab
- The most sensitive serologic test for detecting autoimmune thyroid disease

Imaging

- Thyroid US is a convenient, noninvasive, rapid, and accurate tool in the initial work-up of GD patients
- It aids in the **diagnosis**, without exposing the patient to ionizing irradiation, and assists in determining the underlying etiology of thyrotoxicosis and **detecting concomitant thyroid nodules** that may change management

Imaging

- characterized by **diffuse thyroid enlargement** and by normal echo or **hypoechoogenicity**, both assessed by US and conventional grey scale analysis

Imaging

- A color-flow Doppler shows vascular patterns and quantifies thyroid vascularity.

Thyroid scintigraphy

- Typical US patterns combined with positive TSH-R-Ab **obviate** the need for scintigraphy in the vast majority of cases.
- There is **no indication** for CT scan, MRI, or PET-CT of the thyroid gland



When and How to Treat



How to Choose Treatment?

- What are treatment choices?
- How to select treatment?

Key Points before Treatment

- Discuss with pt logistics, benefits, speed of recovery, drawbacks, potential side effects and cost
- Final decision on choice of treatment depends on resources pt preference and physician experience

Key Points before Treatment

- Patients should refrain from sporting activities until thyroid function normalizes.

After this normalization, no particular restrictions are needed except for participating in **vigorous sporting activities**.

Key Points before Treatment

- Check WBC & liver profile before treatment
- Routine recheck not necessary
- Absolute neutrophil counts should exceed $1000/mm^3$ and liver enzyme should be no higher than three times the upper limit of the normal range

Choice of treatment

❖ **Safety**

❖ **Efficacy**

Improvement

Cure

Management

Graves' hyperthyroidism is treated by reducing

- TH synthesis by using antithyroid drug (ATD)
- The destruction of thyroid tissue with **RAI or total thyroidectomy**

Medical Treatment

Thionamides

inhibit the function of thyroperoxidase

Reduce TSH-RAb and enhance rates of remission compared to no therapy.

Table 1. Mechanism of action of antithyroid drugs

Intrathyroidal inhibition of:

Iodine oxidation/organification

Iodotyrosine coupling

Thyroglobulin biosynthesis

Follicular cell growth

Extrathyroidal inhibition of T₄/T₃ conversion (PTU)

Methimazole

- **Methimazole is preferred because of**
 - **its longer duration of action allowing for once daily dosing**
 - **More rapid efficacy**
 - **lower incidence of side effects**
 - **The **half-life** in plasma of methimazole is **about 9 hours**, whereas that of propylthiouracil is about **1/5 hours****

Monitoring of children taking MMI

- Measure FT₄ and T₃ every 4 to 6 weeks initially.
- . Repeated test in 4-6 weeks until thyroid function is normal.

After thyroid function has normalized

Repeat free T₄, T₃, and TSH at 2-3 month intervals

Clinical response

- Normalizing thyroid hormone **within six weeks**
- Clinical response becomes apparent **in 3-6 wk**
- Adequate control is evident **in 3-6 mo**
- **T₃ levels** are important to **monitor initially**

Clinical response

- TSH generally becomes detectable in the serum after two to four months
- Patients with persistently low serum TSH after more than six months of therapy are unlikely to have a remission
- consider drug discontinuation

Beta-Adrenergic Blockade

- Propranolol
- Atenolol/bisoprolol, β - β_1 selective, are useful to control adrenergic symptoms such as palpitations and tremor

Criteria for Antithyroid Drug Discontinuation

- if normal thyroid function is maintained with the maintenance dose of an antithyroid drug approximately Δ mg of MMI/every other day to Δ mg/d for more than 6 mo
- Consider discontinuation of the drug.

Criteria for Antithyroid Drug Discontinuation

- If the **goiter decreases in size and negative TRAb** results are maintained, the patient may have achieved remission

How long ATDs should be used in children ?

long-term treatment for up to 10 years

we prescribe MMI indefinitely **till**

leaving home for college

The comparison between three modalities

	Advantage	Hypothyroidism	Disadvantage	Cost
ATD	Nonablative	Low	Recurrence side effects	+
RAI	Definitive	100%	Fear	++
Surgery	Definitive	100%	Complications	+++

Conclusion

Diagnosis of graves is based on

- Clinical manifestation
- TSH Rab
- Throid function Test
- Sonography

Criteria for Antithyroid Drug Discontinuation

- TSH Rab
- Size of thyoid
- Dose of Methimazole
- Concentration of thyroid hormone

