

Hyperthyroidism in Children — Symptoms and Treatment

[See online here](#)

Hyperthyroidism in children is a rare condition. The most common etiology is Graves' disease. Children usually present with weight loss, heat intolerance, sweating, and hyperactivity. Symptoms and signs suggestive of congestive heart failure are rare in children. Thyroid function testing is indicated to confirm the diagnosis of hyperthyroidism and the treatment of choice is antithyroid medication. Surgical management with subtotal thyroidectomy should be reserved for children with severe hyperthyroidism who do not respond to medical therapy.



Overview

Hyperthyroidism can be defined as the **overactivity of the thyroid gland** which is associated with increased release and/or production of thyroid hormones and accelerated peripheral metabolism.

Thyrotoxicosis is a specific disorder of thyroid hormone overactivity that is characterized by an **increased amount of unbound thyroid hormones which can be endogenous or exogenous**. Most cases of hyperthyroidism in children are caused by Graves' disease, but the condition is rare.

Epidemiology of Hyperthyroidism in Children

The estimated prevalence of hyperthyroidism in children is around 1 in 10,000 in the United States' pediatric population. Almost all cases of hyperthyroidism in children are caused by **Graves' disease**, hence we will focus on this etiology in our discussion. Approximately 5 % of all cases of Graves' disease occurs in children.

Causes of Graves' disease

The concordance in monozygotic twins for Graves' disease is around 50 %. Because of this, most scholars agree that Graves' disease is a condition that is caused by a **complex interplay between genetic predisposition and unknown environmental exposures**.

Increase of Graves' disease

The incidence of Graves' disease is increased in certain subpopulations in children. **Children with autoimmune diseases such as diabetes mellitus type 1, Addison disease, systemic lupus erythematosus, and rheumatoid arthritis are at an increased risk** of developing hyperthyroidism due to Graves' disease. The only chromosomal abnormality known to increase the risk of Graves' disease is trisomy 21.

Clinical hyperthyroidism

The incidence of clinical hyperthyroidism in the United States is estimated to be around 0.44 per 1000 in children and 0.59 per 1000 in adolescents. According to some epidemiological studies of hyperthyroidism, a peak in incidence is observed in children aged between 10 and 15 years.

Graves' disease is **more common in girls** compared to boys, with a female to male ratio of 3-6:1 reported in studies. However, other causes of hyperthyroidism have no male to female variation.

The prognosis of Graves' disease in children is excellent with a very low risk of congestive heart failure. Unfortunately, **neonatal Graves' disease has a worse prognosis**. Hypothyroidism after treatment with radioiodine or surgical sub-thyroidectomy is the most common complication seen in children with Graves' disease.

Etiology of Hyperthyroidism in Children

The causes of hyperthyroidism in the pediatric population are classified into:

A. Thyroid causes of hyperthyroidism:

- a. Graves' disease is the most common cause of hyperthyroidism in children
- b. Toxic adenoma
- c. Subacute viral thyroiditis
- d. Chronic lymphocytic thyroiditis
- e. Bacterial thyroiditis
- f. McCune Albright syndrome

B. Pituitary causes:

- a. Pituitary adenoma

b. Pituitary resistance to T4

C. Exogenous causes of thyroid hormone secretion:

This happens among patients with previous history of hypothyroidism who are being treated with thyroid hormone replacement therapy. Adolescents are the most likely to develop hyperthyroidism due to exogenous thyroid hormone intake.

D. Iodine-induced hyperthyroidism (Jode-Basedow Phenomenon)

E. Human chorionic gonadotropin secreting tumors

Pathophysiology of Hyperthyroidism

The exact etiology of Graves' disease is unknown, but an autoimmune pathology is most likely.

Graves' disease is characterized by the **overstimulation of the thyroid gland by thyroid-stimulating immunoglobulins (TSIs)**. The exact trigger for the formation of TSIs is unknown, but environmental exposures along with genetic predisposition are the most likely mechanism.

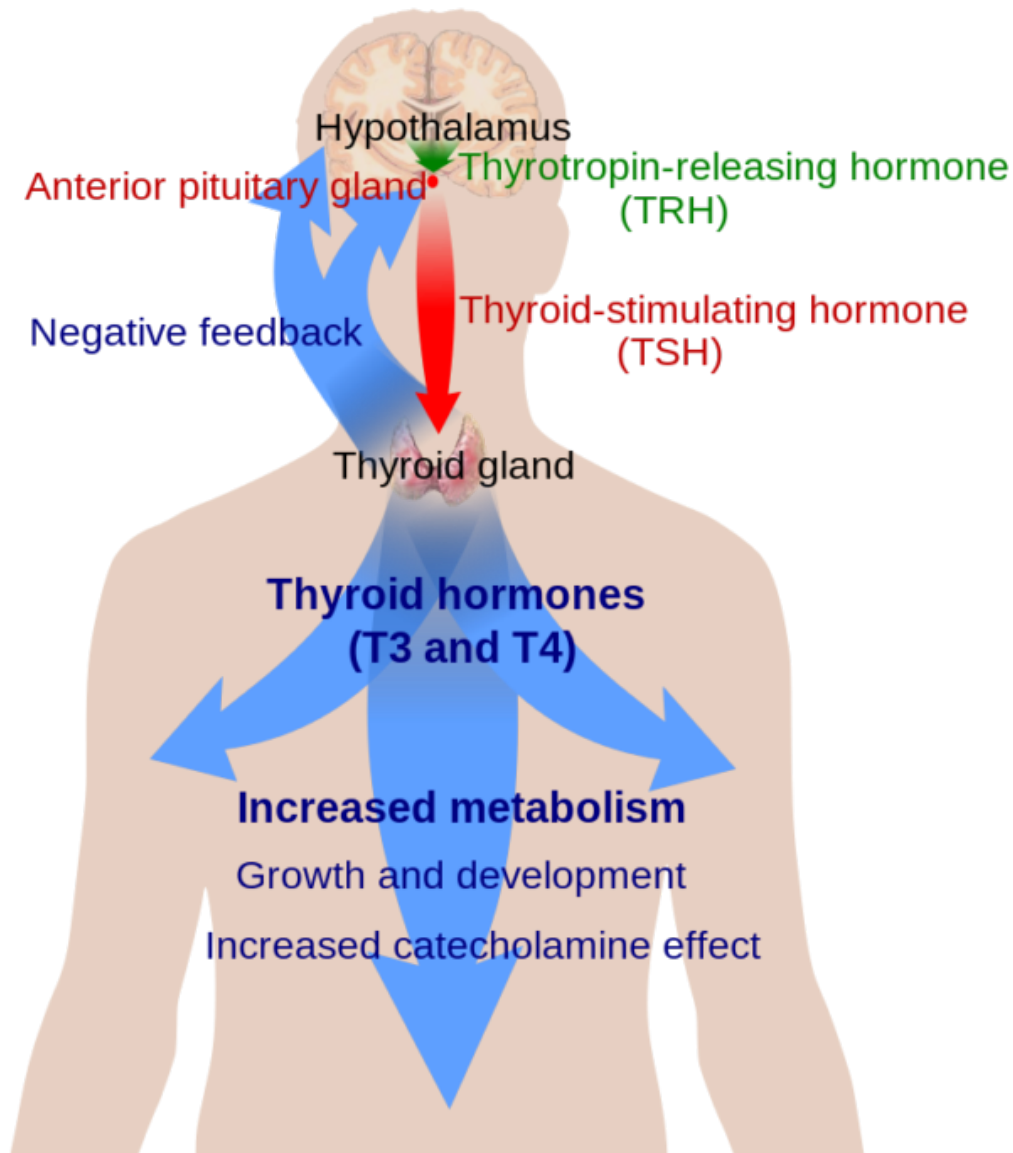
These antibodies bind and activate the thyroid-stimulating hormone (TSH) receptor, which leads to follicular growth and release of thyroid hormones that exert peripheral effects.

Hyperthyroidism symptoms are the **consequence of the activation of transcription of certain cellular proteins that increase the basal metabolic rate**. This is associated with a response that is like the one caused by catecholamines' excess, and adrenergic receptors blockage is known to improve the symptoms of such patients.

Graves ophthalmopathy presented as lid retraction and lid lag is caused by the sympathomimetic effects of the thyrotoxicosis autoimmune reaction and the resulting accumulation of inflammatory infiltrate in the periorbital space.

The increased production and release of the thyroid hormones can be caused by any of the previously mentioned etiologies and the endpoint and pathophysiology are the same regardless of the etiology.

Thyroid system



Overview of the thyroid system

Clinical Presentation of Hyperthyroidism in Children

The diagnosis of hyperthyroidism in children is difficult to make for several reasons. Firstly, the **typical symptoms of hyperthyroidism are usually attributed to attention deficit hyperactivity disorder** instead of hyperthyroidism. Secondly, the **severity of the symptoms is usually lower in children** compared to adults. Finally, the onset of the symptoms in children is usually insidious and not acute.

The most common symptom of hyperthyroidism in children is **weight loss despite an increased appetite**. Sweating, hyperactivity and heat intolerance are also common symptoms of hyperthyroidism in children. Diarrhea and fatigue are less common in children with hyperthyroidism compared to adults. Palpitations are described in one-third of the cases.

Adolescent females with hyperthyroidism might complain of **menstrual irregularities** or **amenorrhea**. Hair loss can be also seen in patients with Graves' disease.

Graves' ophthalmopathy is rarely severe in children, but eye symptoms such as pain on movement or diplopia are common. Patients with Graves' ophthalmopathy might experience worsening of their ophthalmopathy even after the correction of the hyperthyroidism state.

Upon physical examination of the neck in children with hyperthyroidism, **Goiter is present in almost all cases**. Auscultation of the thyroid gland might reveal an audible bruit. Such a bruit is present in up to half of the cases of hyperthyroidism.

Tachycardia and wide pulse pressure are present in most patients with hyperthyroidism, including children. Signs suggestive of congestive heart failure are rarely seen in children. Systemic hypertension might be seen in some children with Graves' disease.

Neurological examination of the child might show tremors, muscle fasciculations, proximal muscle weakness, and exaggerated deep tendon reflexes.

Diagnostic Workup for Hyperthyroidism in Children

Thyroid function tests include the **measurements of T4, T3, T3 resin uptake and thyroid-stimulating hormone levels**. Patients with hyperthyroidism due to Graves' disease have elevated T4, T3 and T3 resin uptake and almost undetectable levels of thyroid-stimulating hormone.

When measuring T4 levels, it is important to **measure total T4 and free T4 hormone**. This is important for differentiation between patients with true hyperthyroidism and those with elevated levels of total T4 but normal free T4 levels.

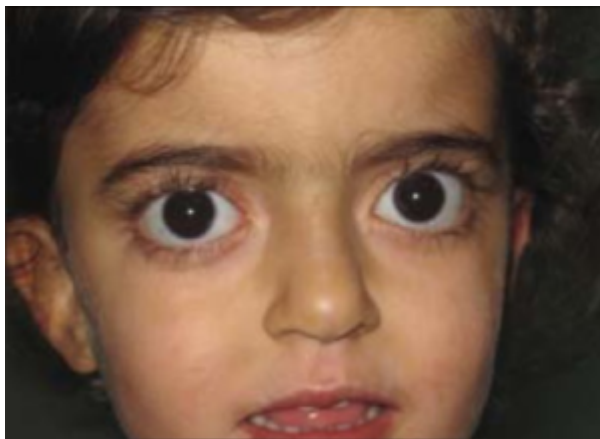


Image: "Photograph of a patient showing exophthalmia. Graves disease with exophthalmia in a two-year old child." by Yalçın H, Akçora B, Balcı A - Mol Imaging Radionucl Ther (2011). Licence: [CC BY 2.5](https://creativecommons.org/licenses/by/2.5/)

The diagnosis of Graves' disease is based on the findings obtained from the physical examination and thyroid function tests. The measurement of TSI levels is rarely needed but is available for clinical practice. An elevated TSI level in a hyperthyroid patient has a sensitivity of 95 % and a specificity of 96 % for Graves' disease.

Patients with chronic lymphocytic thyroiditis might have hyperthyroidism in the acute stage. During the hyperthyroid stage, elevated levels of anti-thyroglobulin and anti-thyroid peroxidase antibodies are seen. TSI levels are usually normal.

A **complete blood count** is indicated in all patients with Graves' disease to get a

baseline. Antithyroid therapy is known to cause agranulocytosis in a few patients, and it is important to differentiate between Graves' disease induced mild leukopenia and anti-thyroid therapy-induced agranulocytosis.

Nuclear imaging is rarely performed in children with Graves' disease as the condition can be diagnosed clinically and biochemically.

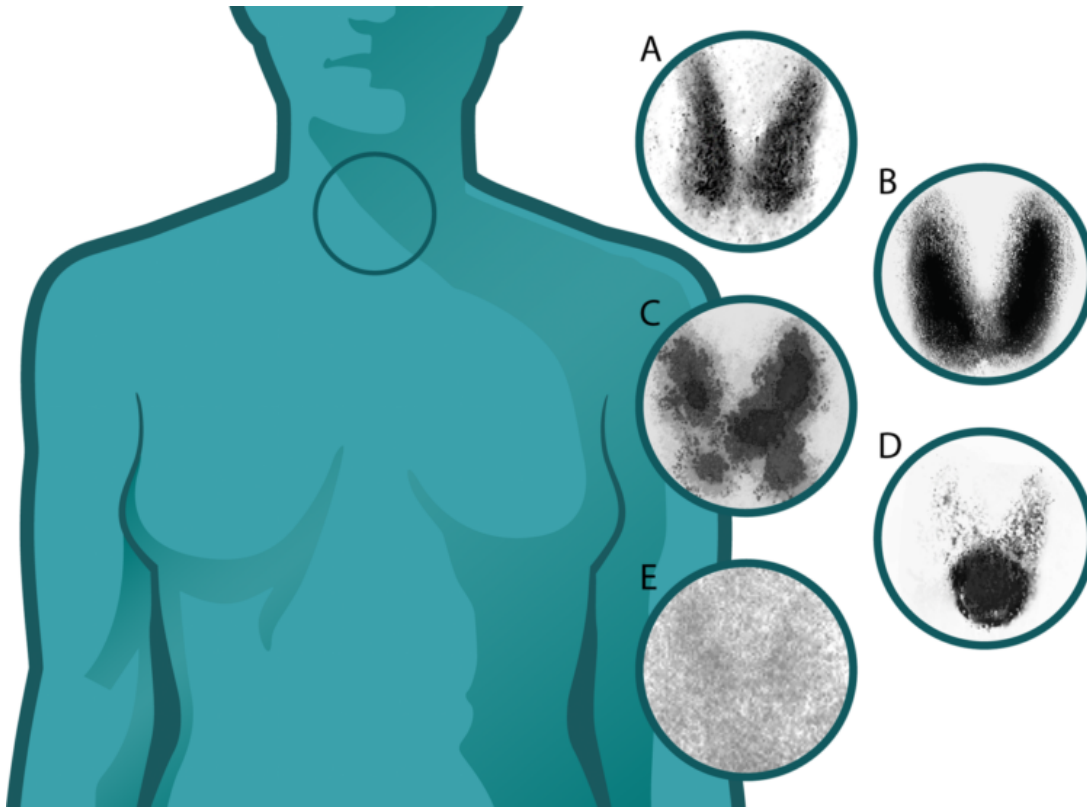


Image: "Technetium 99 Thyroid Uptake Scans

(A) Normal.

(B) Graves disease: diffuse increased uptake in both thyroid lobes.

(C) TMNG: "hot" and "cold" areas of uneven uptake.

(D) Toxic adenoma: increased uptake in a single nodule with suppression of the surrounding thyroid.

(E) Thyroiditis: decreased or absent uptake." by Giovanni Maki. Licence: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

Treatment of Hyperthyroidism in Children

The treatment options for hyperthyroidism in children include **antithyroid medication, radioiodine ablation, and thyroidectomy**. Symptomatic treatment of hyperthyroidism is also indicated in severe cases in children. Propranolol is the beta-blocker of choice for the symptomatic treatment of hyperthyroidism in children. The children are kept under close monitoring for recurrence of the disease, development of hypoglycemia and the imminent risk of osteoporosis and fractures.

1. The treatment of choice for hyperthyroidism in children is antithyroid medication. **Methimazole is the only antithyroid medication available in the United States.** The typical dose of methimazole in children is around 0.4 to 0.7 mg/kg/day. Methimazole is usually given once daily whereas PTU is given three times a day. PTU is no longer recommended in the management of hyperthyroidism in the United States due to its adverse side effects profile.
2. **Radioactive iodine ablation of the thyroid gland in children is not recommended.** However, it should be noted that the risk of malignancy is not

increased after radioactive iodine ablation therapy. Children with severe hyperthyroidism who do not respond to antithyroid medication and who are not good surgical candidates might benefit from this treatment option. Radioactive iodine ablation therapy is the treatment of choice for Graves' disease in adults.

3. Children with Graves' disease who do not respond to antithyroid medication should undergo **surgical subtotal removal of the thyroid gland**. Most children will end up with hypothyroidism, which can be treated easily with lifelong T4 replacement therapy. Generally, the patients receive antithyroid agents preoperatively to reduce the gland's functions and hormonal levels. Iodide is also administered before surgery to reduce the gland's vascularity and allow for excellent surgical outcomes.
4. Self-limited causes of hyperthyroidism, such as sub-acute thyroiditis and exogenous administration of thyroid hormones, can be treated symptomatically. Beta adrenoceptor therapy is administered to control cardiovascular symptoms as the disease subsides.

Prognosis and complications of hyperthyroidism

The prognosis of Graves' disease in children is excellent with a very low risk of congestive heart failure. Unfortunately, **neonatal Graves' disease has a worse prognosis**. Hypothyroidism after treatment with radioiodine or surgical sub-thyroidectomy is the most common complication seen in children with Graves' disease. Untreated disease results in congestive heart failure, developmental delay, and hypercalcemia, among other adverse effects.

References

Medscape: <http://emedicine.medscape.com/article/921707-overview>

Legal Note: Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).