Hyperthyroidism (Overactive Thyroid) in Children — Symptoms and Guidelines

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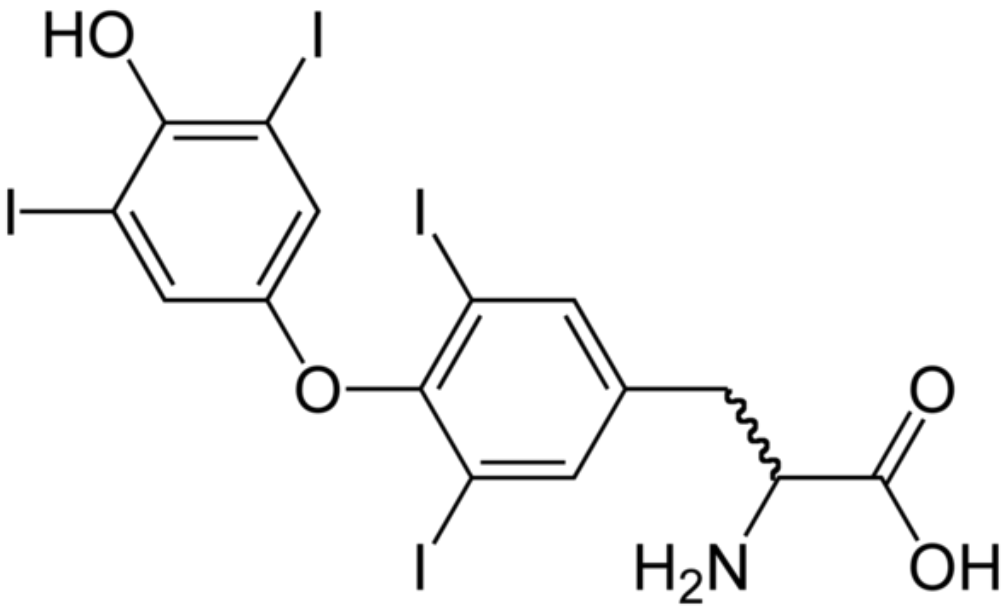
Hyperthyroidism in children is a rare condition. The most common etiology is Graves' disease. Children usually present with weight loss, heat intolerance, sweating, and hyperactivity. Symptoms and signs suggestive of congestive heart failure are rare in children. Thyroid function testing is indicated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



Overview of Hyperthyroidism in Children

Hyperthyroidism can be defined as the **overactivity of the thyroid gland** which is associated with the **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 occur 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 of 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 estimated incidence of clinical hyperthyroidism in the United States is 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 10–15 years. Graves' disease is more common in girls compared to boys.

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 **most common** etiology of hyperthyroidism in children is **Graves' disease**. Other less common causes of hyperthyroidism in children include:

- toxic adenoma
- subacute viral thyroiditis
- chronic lymphocytic thyroiditis
- bacterial thyroiditis.

The exact etiology of Graves' disease is unknown, but an autoimmune pathology is most likely.
Other rarer causes of hyperthyroidism in children include **pituitary adenoma and the exogenous use of thyroid hormone**. Patients with a previous history of hypothyroidism who are being treated with thyroid hormone replacement therapy and adolescents are the most likely to develop hyperthyroidism due to exogenous thyroid hormone intake.

Graves' disease is characterized by the **over-stimulation 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.

Pathophysiology of Hyperthyroidism in Children

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.

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**.

Clinical Presentation of Hyperthyroidism in Children

The **diagnosis** of hyperthyroidism in children is **difficult** to make for several reasons.

Symptoms

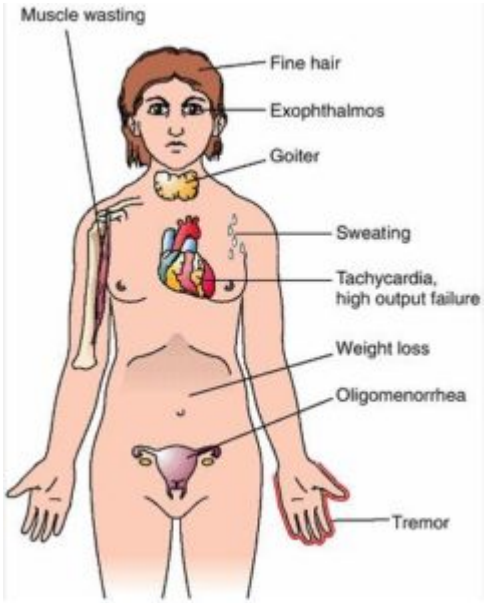


Image: "Hyperaldosteronism Symptoms" by Madhero88. License: CC BY 3.0

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 less 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 reported 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 have worsening of their ophthalmopathy even after the correction of the hyperthyroidism state.

Image: "Proptosis and lid retraction caused by Graves' Disease" by Jonathan Trobe, M.D. License: CC BY 3.0

Physical examination

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

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

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 update and almost undetectable levels of thyroid-stimulating hormone.

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

	Total T4	Free T4	TSH	Other Labs

Primary	⇓	⇓	⇑	Thyroid autoantibody test
Secondary	⇓	⇓	⇓⇔	
Sick euthyroid syndrome	⇓⇔	⇔	⇔	Low T3

High reverse T3**TBG Deficiency**⇓⇔⇔Decreased TBG levels

Diagnosis of Graves' disease

The diagnosis of Graves' disease is **based on the findings obtained from the physical examination and thyroid function tests**. The measurement of TSIs levels is rarely needed but is available for the 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 antithyroglobulin 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. Anti-thyroid 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.

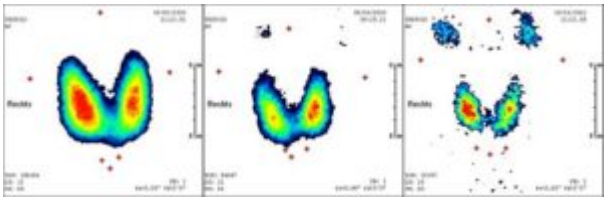


Image: "Serie Radiojodtherapie Basedow" by Drahreg01. License: CC BY-SA 3.0

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.

Medication treatment

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 0.4–0.7 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**.

Radioactive iodine ablation therapy

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.

Surgical Treatment

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.

References

Sinha, Sunil Kumar, MD. 2015. "Pediatric Hyperthyroidism." Available at: http://emedicine.medscape.com/article/921707-overview

Notes