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Graves' Disease

National Endocrine and Metabolic Diseases Information Service



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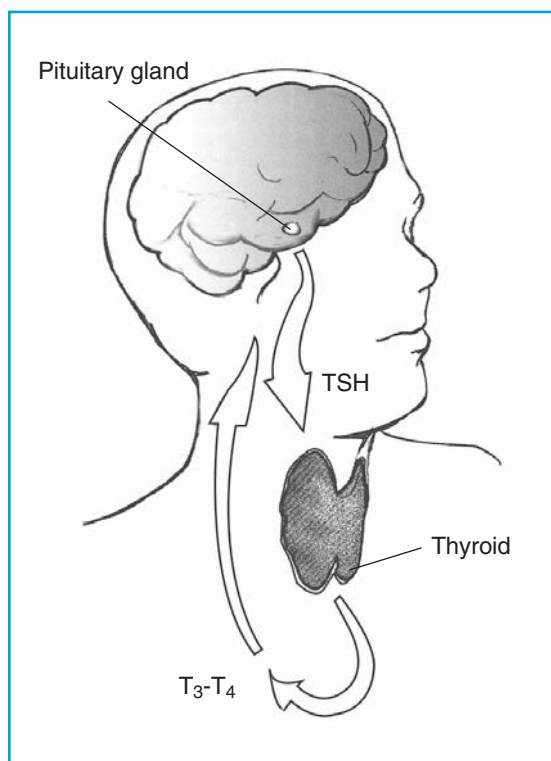
What is Graves' disease?

Graves' disease, also known as toxic diffuse goiter, is the most common cause of hyperthyroidism in the United States. Hyperthyroidism is a disorder that occurs when the thyroid gland makes more thyroid hormone than the body needs.

The thyroid is a small, butterfly-shaped gland in the front of the neck below the larynx, or voice box. The thyroid gland makes two thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4). Thyroid hormones affect metabolism, brain development, breathing, heart and nervous system functions, body temperature, muscle strength, skin dryness, menstrual cycles, weight, and cholesterol levels.

Thyroid hormone production is regulated by another hormone called thyroid-stimulating hormone (TSH), which is made by the pituitary gland located in the brain.

Graves' disease is an autoimmune disorder, meaning the body's immune system acts against its own healthy cells and tissues. In Graves' disease, the immune system makes antibodies called thyroid-stimulating immunoglobulin (TSI) that attach to thyroid cells. TSI mimics the action of TSH and stimulates the thyroid to make too much thyroid hormone. Sometimes the antibodies can instead block thyroid hormone production, leading to a confusing clinical picture. The diagnosis and treatment of Graves' disease is often performed by an endocrinologist—a doctor who specializes in the body's hormone-secreting glands.



The thyroid gland's production of thyroid hormones (T_3 and T_4) is triggered by thyroid-stimulating hormone (TSH), which is made by the pituitary gland.

What are the symptoms of Graves' disease?

People with Graves' disease may have some of the common symptoms of hyperthyroidism such as

- nervousness or irritability
- fatigue or muscle weakness
- heat intolerance
- trouble sleeping

- hand tremors
- rapid and irregular heartbeat
- frequent bowel movements or diarrhea
- weight loss
- goiter, which is an enlarged thyroid that may cause the neck to look swollen

In addition, the eyes of people with Graves' disease may appear enlarged because their eyelids are retracted and their eyes bulge out from the eye sockets. This condition is called Graves' ophthalmopathy.

A small number of people with Graves' disease also experience thickening and reddening of the skin on their shins. This usually painless problem is called pretibial myxedema or Graves' dermopathy.

What is Graves' ophthalmopathy?

Graves' ophthalmopathy (GO) occurs when cells from the immune system attack the muscles and other tissues around the eyes. The result is inflammation and a buildup in tissue and fat behind the eye socket, causing the eyeballs to bulge. In rare cases, inflammation is severe enough to compress the optic nerve that leads to the eye, causing vision loss.

Other symptoms of GO include

- dry, irritated eyes
- puffy eyelids
- double vision
- light sensitivity
- pressure or pain in the eyes
- trouble moving the eyes

About 25 percent of people with Graves' disease develop GO, which is usually of mild to moderate severity.¹ This eye disorder usually lasts 1 to 2 years and often improves on its own. GO can occur before, at the same time as, or after other symptoms of hyperthyroidism develop and may even occur in people whose thyroid function is normal. GO is severe in 3 to 5 percent of people who have the disorder, and smoking makes GO worse.²

¹Yeung SJ, Habra MA, Chiu AC. Graves disease. Available at: www.emedicine.com/med/topic929.htm. Updated July 28, 2005. Accessed September 18, 2007.

²Bartalena L, Pinchera A, Marcocci C. Management of Graves' ophthalmopathy: reality and perspectives. *Endocrine Reviews*. 2000;21(2):168–199.

Who is likely to develop Graves' disease?

Scientists don't know exactly why some people develop Graves' disease, but they believe factors such as age, sex, heredity, and emotional and environmental stress are involved.

Graves' disease usually occurs in people younger than age 40 and is five to 10 times more common in women than men.³ An individual's chance of developing Graves' disease increases if other family members have it.

Researchers have not been able to find a specific gene that causes the disease to be passed from one generation to the next. Scientists know that some people inherit an immune system that can make antibodies against healthy cells, but predicting who will be affected is difficult.

People with other autoimmune diseases have an increased chance of developing Graves' disease. Type 1 diabetes, rheumatoid arthritis, and vitiligo—a disorder in which some parts of the skin are not pigmented—are among the conditions associated with Graves' disease.

How is Graves' disease diagnosed?

Doctors can sometimes diagnose Graves' disease based only on a physical examination and a medical history. Laboratory tests confirm the diagnosis.

The ultrasensitive TSH test is usually the first test a doctor performs. This test detects even tiny amounts of TSH in the blood and is the most accurate measure of thyroid activity available. Another blood test used to diagnose Graves' disease measures T₃ and T₄. In making a diagnosis, doctors look for below-normal levels of TSH, normal to elevated levels of T₄, and elevated levels of T₃.

Because the combination of low TSH and high T₃ and T₄ can occur with other thyroid problems, doctors may order other tests to finalize the diagnosis. Two of these tests are based on the fact that the thyroid gland uses iodine to make thyroid hormone. Both tests use small, safe doses of radioactive iodine.

- The radioactive iodine uptake test measures the amount of iodine the thyroid collects from the bloodstream. High levels of iodine uptake can indicate Graves' disease.
- A thyroid scan shows how and where iodine is distributed in the thyroid. In Graves' disease, the entire thyroid gland is involved so the iodine shows up throughout the gland. Other causes of hyperthyroidism such as nodules—small lumps in the gland—will show a different pattern of iodine distribution.

Doctors may also consider the thyroid-stimulating immunoglobulin test, although this test usually isn't necessary to diagnose Graves' disease. This test, also called a TSH antibody test, measures the level of TSI in the blood. Most people with Graves' disease have this antibody, but people whose hyperthyroidism is caused by other conditions do not.

³American Association of Clinical Endocrinologists. Hyperthyroidism. Available at: www.aace.com/pub/thyroidbrochures/pdfs/Hyperthyroidism.pdf. 2006. Accessed September 18, 2007.

How is Graves' disease treated?

Doctors may prescribe one or more of the three treatment options: radioiodine therapy, antithyroid drugs, or thyroid surgery. Radioiodine therapy is the most commonly used treatment for Graves' disease in the United States.

Radioiodine Therapy

In radioiodine therapy, the patient takes radioactive iodine-131 by mouth. Because the thyroid gland collects iodine to make thyroid hormone, it will collect the radioactive iodine from the bloodstream in the same way. Iodine-131—stronger than the radioactive iodine used in diagnostic tests—will gradually destroy the cells that make up the thyroid gland but will not affect other tissues in the body.

Many doctors use a large enough dose of iodine-131 to shut down the thyroid completely, but some prefer smaller doses to try to bring hormone production into the normal range. More than one round of radioiodine therapy may be needed. Results take time and a person undergoing this treatment may not notice improvement in symptoms for several weeks or months.

People with Graves' ophthalmopathy should talk with their doctor about any risks associated with radioactive iodine treatments. Several studies suggest that radioiodine therapy can worsen ophthalmopathy in some people. Other treatments such as steroids may prevent this complication.

Although iodine-131 is not known to cause birth defects or infertility, radioiodine therapy is not used in pregnant women or women who are breastfeeding. Radioactive iodine can be harmful to the fetus' thyroid, and it can be passed from mother to child in breast milk.

Almost everyone who receives radioactive iodine treatment eventually develops hypothyroidism, which occurs when the thyroid does not make enough thyroid hormone. People with hypothyroidism must take synthetic thyroid hormone.

Medications

Doctors may prescribe a drug called a beta blocker to reduce symptoms until other treatments take effect. Beta blockers act quickly to relieve symptoms such as hand tremors, rapid heart beat, and nervousness. These drugs act by blocking the effects of thyroid hormone on the body, but they do not stop thyroid hormone production.

Two antithyroid drugs, methimazole and propylthiouracil (PTU), interfere with the way the thyroid gland uses iodine to make thyroid hormones. Doctors sometimes use antithyroid drugs as the only treatment for Graves' disease, but these drugs usually do not produce permanent results and their use requires frequent monitoring by a health care provider. More often, antithyroid drugs are used to pretreat patients older than 60 or those who have other health problems before beginning radioiodine therapy, or as a supplemental treatment after radioiodine therapy.

Because pregnant and breastfeeding women cannot receive radioiodine therapy, they are usually treated with an antithyroid drug instead. Pregnant women should not take methimazole and should be monitored if they take PTU. Women who are breastfeeding should take the smallest dose necessary of either drug.

Antithyroid drugs can cause side effects in some people. Allergic reactions such as rashes and itching are the most common side effects. Rarely, antithyroid drugs cause liver failure or a decrease in the number of white blood cells, which can lower resistance to infection.

Thyroid Surgery

Surgery is the least-used option in treating Graves' disease. However, doctors sometimes choose surgery to treat pregnant women who cannot tolerate antithyroid drugs, people in whom thyroid cancer is suspected, or those who fail other forms of treatment. Graves' disease itself does not cause cancer.

When surgery is used, many doctors recommend the entire thyroid be removed, thus eliminating the chance that hyperthyroidism will return. If the entire thyroid is removed, lifelong thyroid hormone replacement is necessary.

Although uncommon, certain problems can occur in thyroid surgery. The parathyroid glands could be damaged because they are located very close to the thyroid gland. These glands help control calcium levels in the body. Damage to the laryngeal nerve, also located close to the thyroid gland, could lead to voice changes or breathing problems. When surgery is performed by an experienced surgeon, less than 1 percent of patients have permanent complications. To find a surgeon, contact one of the organizations listed under For More Information.

Graves' Disease and Pregnancy

After treatment with surgery or radioactive iodine, thyroid-stimulating antibodies can still be present in the blood even though thyroid levels are normal. In a pregnant woman who received either of these treatments, the antibodies she produces may travel across the placenta to the baby's bloodstream and stimulate the fetal thyroid. A pregnant woman who has been treated with surgery or radioactive iodine should inform her doctor so her baby can be monitored for thyroid-related problems later in the pregnancy.

Eye Care

The eye problems associated with Graves' disease may not improve following thyroid treatment, so the two problems are often treated separately.

Eye drops can relieve dry, gritty, irritated eyes—the most common of the milder symptoms. If pain and swelling occur, doctors may prescribe a steroid drug such as prednisone. Other drugs that suppress the immune response may also provide relief. Special lenses for glasses can help with light sensitivity and double vision. Patients may be advised to sleep with the head elevated to reduce eyelid swelling. For people who are unable to fully close their eyelids, taping the eyelids shut at night can help prevent dry eyes.

In more severe cases, external radiation applied to the eyes may be used to reduce inflammation. Like other types of radiation treatment, the beneficial effects are not immediate, but most people feel relief from symptoms as soon as 1 to 2 months after treatment.

Surgery may be used to improve the protrusion of the eyes and correct the vision changes caused by pressure on the optic nerve. A procedure called orbital decompression makes the eye socket bigger, giving the eye room to sink back to a more normal position. Eyelid surgery can return retracted eyelids to their normal position.

More information about hyperthyroidism, hypothyroidism, and related topics is available at www.endocrine.niddk.nih.gov.

Points to Remember

- Graves' disease is the most common cause of hyperthyroidism in the United States and mainly affects young women.
- In Graves' disease, the immune system stimulates the thyroid gland to make too much thyroid hormone.
- Common symptoms of hyperthyroidism include nervousness or irritability, heat intolerance, rapid and irregular heartbeat, frequent bowel movements or diarrhea, weight loss, and goiter.
- People with Graves' disease may also have bulging eyes, a condition called Graves' ophthalmopathy.
- Graves' disease is most often treated with radioiodine therapy, which gradually destroys the cells of the thyroid gland. Antithyroid drugs and surgery to remove the thyroid are sometimes used.
- The eye problems associated with Graves' disease may require additional treatment.

Hope through Research

Researchers are investigating the natural history, clinical presentation, and genetics of thyroid function disorders to further understand thyroid diseases. Scientists continue to study treatment options for Graves' disease and Graves' ophthalmopathy. For information about current studies, see www.ClinicalTrials.gov.

For More Information

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The Endocrine Society

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Internet: www.endo-society.org

The Hormone Foundation

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