

Graves' Disease

National Endocrine and Metabolic Diseases Information Service



U.S. Department
of Health and
Human Services

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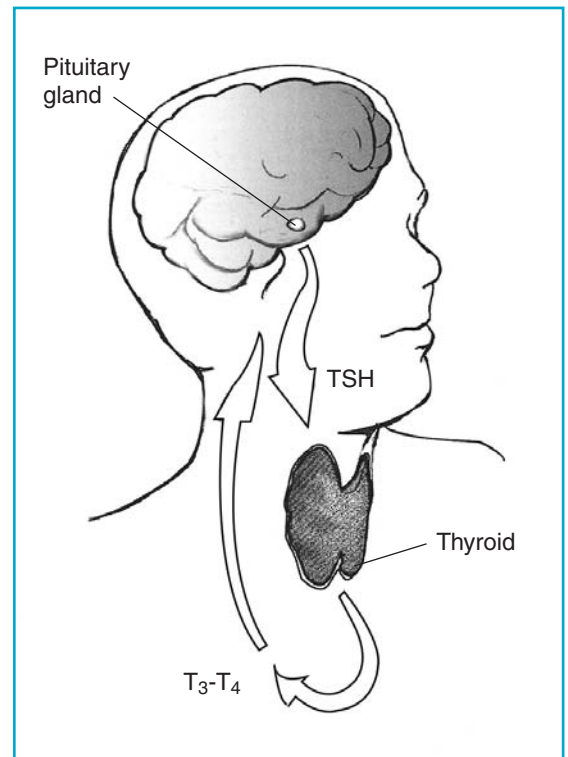
What is Graves' disease?

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

The thyroid is a 2-inch-long, butterfly-shaped gland in the front of the neck below the larynx, or voice box. The thyroid makes two thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4). T_3 is made from T_4 and is the more active hormone, directly affecting the tissues. Thyroid hormones circulate throughout the body in the bloodstream and act on virtually every tissue and cell in the body.

Thyroid hormones affect metabolism, brain development, breathing, heart and nervous system functions, body temperature, muscle strength, skin dryness, menstrual cycles, weight, and cholesterol levels. Hyperthyroidism causes many of the body's functions to speed up.



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

Thyroid hormone production is regulated by another hormone called thyroid-stimulating hormone (TSH), which is made by the pituitary gland in the brain. When thyroid hormone levels in the blood are low, the pituitary releases more TSH. When thyroid hormone levels are high, the pituitary responds by decreasing TSH production.

Autoimmune Disorder

Graves' disease is an autoimmune disorder. Normally, the immune system protects the body from infection by identifying and destroying bacteria, viruses, and other potentially harmful foreign substances. But in autoimmune diseases, the immune system attacks the body's own cells and organs.

With Graves' disease, the immune system makes an antibody called thyroid-stimulating immunoglobulin (TSI)—sometimes called TSH receptor antibody—that attaches to thyroid cells. TSI mimics TSH and stimulates the thyroid to make too much thyroid hormone. Sometimes the TSI antibody instead blocks thyroid hormone production, leading to conflicting symptoms that may make correct diagnosis more difficult.

What are the symptoms of Graves' disease?

People with Graves' disease may have 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 and can interfere with normal breathing and swallowing

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.

In addition, the eyes of people with Graves' disease may appear enlarged because their eyelids are retracted—seem pulled back into the eye sockets—and their eyes bulge out from the eye sockets. This condition is called Graves' ophthalmopathy (GO).

What is Graves' ophthalmopathy?

Graves' ophthalmopathy is a condition associated with Graves' disease that occurs when cells from the immune system attack the muscles and other tissues around the eyes.

The result is inflammation and a buildup of tissue and fat behind the eye socket, causing the eyeballs to bulge out. Rarely, inflammation is severe enough to compress the optic nerve that leads to the eye, causing vision loss.

Other GO symptoms are

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

About 25 to 30 percent of people with Graves' disease develop mild GO, and 2 to 5 percent develop severe GO.¹ This eye condition 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. Smoking makes GO worse.

¹Yeung SJ, Habra MA, Chiu AC. Graves' disease. eMedicine website. www.eMedicine.medscape.com/article/120619-overview. Updated 2010. Accessed December 10, 2011.

Who is likely to develop Graves' disease?

Scientists cannot predict who will develop Graves' disease. However, factors such as age, sex, heredity, and emotional and environmental stress are likely involved.

Graves' disease usually occurs in people younger than age 40 and is seven to eight times more common in women than men.¹ Women are most often affected between ages 30 and 60. And a person's chance of developing Graves' disease increases if other family members have the disease.

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

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

How is Graves' disease diagnosed?

Health care providers can sometimes diagnose Graves' disease based only on a physical examination and a medical history. Blood tests and other diagnostic tests, such as the following, then confirm the diagnosis.

TSH test. The ultrasensitive TSH test is usually the first test performed. This test detects even tiny amounts of TSH in the blood and is the most accurate measure of thyroid activity available.

T₃ and T₄ test. Another blood test used to diagnose Graves' disease measures T₃ and T₄ levels. In making a diagnosis, health care providers 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, health care providers may order other tests to finalize the diagnosis. The following two tests use small, safe doses of radioactive iodine because the thyroid uses iodine to make thyroid hormone.

Radioactive iodine uptake test. This test measures the amount of iodine the thyroid collects from the bloodstream. High levels of iodine uptake can indicate Graves' disease.

Thyroid scan. This scan shows how and where iodine is distributed in the thyroid. With Graves' disease the entire thyroid is involved, so the iodine shows up throughout the gland. Other causes of hyperthyroidism such as nodules—small lumps in the gland—show a different pattern of iodine distribution.

TSI test. Health care providers may also recommend the TSI 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.

More information about testing for thyroid problems is provided by the National Endocrine and Metabolic Diseases Information Service (NEMDIS) in the fact sheet, *Thyroid Function Tests*, available at www.endocrine.niddk.nih.gov.

How is Graves' disease treated?

People with Graves' disease have three treatment options: radioiodine therapy, medications, and thyroid surgery. Radioiodine therapy is the most common treatment for Graves' disease in the United States. Graves' disease is often diagnosed and treated by an endocrinologist—a doctor who specializes in the body's hormone-secreting glands.

Radioiodine Therapy

In radioiodine therapy, patients take 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—gradually destroys the cells that make up the thyroid gland but does not affect other body tissues.

Many health care providers 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 people undergoing this treatment may not notice improvement in symptoms for several weeks or months.

People with GO should talk with a health care provider about any risks associated with radioactive iodine treatments. Several studies suggest radioiodine therapy can worsen GO in some people. Other treatments, such as prescription 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 can be passed from mother to child in breast milk. Experts recommend that women wait a year after treatment before becoming pregnant.

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, a medication that replaces their natural thyroid hormone.

Medications

Beta blockers. Health care providers may prescribe a medication called a beta blocker to reduce many of the symptoms of hyperthyroidism, such as tremors, rapid heartbeat, and nervousness. But beta blockers do not stop thyroid hormone production.

Antithyroid medications. Health care providers sometimes prescribe antithyroid medications as the only treatment for Graves' disease. Antithyroid medications interfere with thyroid hormone production but don't usually have permanent results. Use of these medications requires frequent monitoring by a health care provider. More often, antithyroid medications are used to pretreat patients before surgery or radioiodine therapy, or they are used as supplemental treatment after radioiodine therapy.

Antithyroid medications can cause side effects in some people, including

- allergic reactions such as rashes and itching
- a decrease in the number of white blood cells in the body, which can lower a person's resistance to infection
- liver failure, in rare cases

Stop your antithyroid medication and call your health care provider right away if you develop any of the following while taking antithyroid medications:

- fatigue
- weakness
- vague abdominal pain
- loss of appetite
- skin rash or itching
- easy bruising
- yellowing of the skin or whites of the eyes, called jaundice
- persistent sore throat
- fever

In the United States, health care providers prescribe the antithyroid medication methimazole (Tapazole, Northyx) for most types of hyperthyroidism.

Antithyroid medications and pregnancy. Because pregnant and breastfeeding women cannot receive radioiodine therapy, they are usually treated with an antithyroid medication instead. However, experts agree that women in their first trimester of pregnancy should probably not take methimazole due to the rare occurrence of damage to the fetus.

Another antithyroid medication, propylthiouracil (PTU), is available for women in this stage of pregnancy or for women who are allergic to or intolerant of methimazole and have no other treatment options. Health care providers may prescribe PTU for the first trimester of pregnancy and switch to methimazole for the second and third trimesters.

Some women are able to stop taking antithyroid medications in the last 4 to 8 weeks of pregnancy due to the remission of hyperthyroidism that occurs during pregnancy. However, these women should continue to be monitored for recurrence of thyroid problems following delivery.

Studies have shown that mothers taking antithyroid medications may safely breastfeed. However, they should take only moderate doses, less than 10–20 milligrams daily, of the antithyroid medication methimazole. Doses should be divided and taken after feedings, and the infants should be monitored for side effects.²

Women requiring higher doses of the antithyroid medication to control hyperthyroidism should not breastfeed.

²Ogunyemi DA. Autoimmune thyroid disease and pregnancy. eMedicine website. <http://emedicine.medscape.com/article/261913-overview>. Updated March 12, 2012. Accessed April 10, 2012.

Thyroid Surgery

Surgery is the least-used option for treating Graves' disease. Sometimes surgery may be used to treat

- pregnant women who cannot tolerate antithyroid medications
- people suspected of having thyroid cancer, though Graves' disease does not cause cancer
- people for whom other forms of treatment are not successful

Before surgery, the health care provider may prescribe antithyroid medications to temporarily bring a patient's thyroid hormone levels into the normal range. This presurgical treatment prevents a condition called thyroid storm—a sudden, severe worsening of symptoms—that can occur when hyperthyroid patients have general anesthesia.

When surgery is used, many health care providers recommend the entire thyroid be removed to eliminate the chance that hyperthyroidism will return. If the entire thyroid is removed, lifelong thyroid hormone medication is necessary.

Although uncommon, certain problems can occur in thyroid surgery. The parathyroid glands can be damaged because they are located very close to the thyroid. These glands help control calcium and phosphorous levels in the body. Damage to the laryngeal nerve, also located close to the thyroid, can lead to voice changes or breathing problems.

But when surgery is performed by an experienced surgeon, less than 1 percent of patients have permanent complications.¹ People who need help finding a surgeon can contact one of the organizations listed under “For More Information.”

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, health care providers may prescribe a steroid such as prednisone. Other medications that suppress the immune response may also provide relief.

Special lenses for glasses can help with light sensitivity and double vision. People with eye symptoms may be advised to sleep with their head elevated to reduce eyelid swelling. If the eyelids do not fully close, taping them shut at night can help prevent dry eyes.

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

Surgery may be used to improve bulging 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 and gives the eye room to sink back to a more normal position. Eyelid surgery can return retracted eyelids to their normal position.

Can treatment for Graves' disease affect pregnancy?

Treatment for Graves' disease can sometimes affect pregnancy. After treatment with surgery or radioactive iodine, TSI antibodies can still be present in the blood, even when thyroid levels are normal. If a pregnant woman has received either of these treatments prior to becoming pregnant, 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 health care provider so her baby can be monitored for thyroid-related problems later in the pregnancy. Pregnant women may safely be treated with antithyroid medications.

For more information about pregnancy and antithyroid medications, see "Medications" under the section titled "How is Graves' disease treated?" More information about pregnancy and thyroid disease is provided by the NEMDIS in the fact sheet, *Pregnancy and Thyroid Disease*, available at www.endocrine.niddk.nih.gov.

Eating, Diet, and Nutrition

Experts recommend that people eat a balanced diet to obtain most nutrients. More information about diet and nutrition is provided by the National Agricultural Library available at www.nutrition.gov.

Dietary Supplements

Iodine is an essential mineral for the thyroid. However, people with autoimmune thyroid disease may be sensitive to harmful side effects from iodine. Taking iodine drops or eating foods containing large amounts of iodine—such as seaweed, dulse, or kelp—may cause or worsen hyperthyroidism. More information about iodine is provided by the National Library of Medicine in the fact sheet, *Iodine in diet*, available at www.nlm.nih.gov/medlineplus.

Women need more iodine when they are pregnant—about 250 micrograms a day—because the baby gets iodine from the mother's diet. In the United States, about 7 percent of pregnant women may not get enough iodine in their diet or through prenatal vitamins.³ Choosing iodized salt—salt supplemented with iodine—over plain salt and prenatal vitamins containing iodine will ensure this need is met.

To help ensure coordinated and safe care, people should discuss their use of dietary supplements, such as iodine, with their health care provider. Tips for talking with health care providers are available at the National Center for Complementary and Alternative Medicine's Time to Talk campaign at www.nccam.nih.gov.

³Zimmerman MB. Iodine deficiency in pregnancy and the effects of maternal iodine supplementation on the offspring: a review. *American Journal of Clinical Nutrition*. 2009;89(2):668S–672S.

Points to Remember

- Graves' disease is the most common cause of hyperthyroidism in the United States.
- In Graves' disease, the immune system stimulates the thyroid gland to make too much thyroid hormone.
- Common symptoms of hyperthyroidism include nervousness or irritability, fatigue or muscle weakness, heat intolerance, trouble sleeping, hand tremors, 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 (GO).
- Graves' disease is most often treated with radioiodine therapy, which gradually destroys the cells that make up the thyroid gland. Antithyroid medications and surgery to remove the thyroid are sometimes used.
- The eye problems associated with Graves' disease may require separate treatment.
- A pregnant woman who has been treated with surgery or radioactive iodine prior to becoming pregnant should inform her health care provider so her baby can be monitored for thyroid-related problems later in the pregnancy.

Hope through Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports research into many kinds of disorders, including Graves' disease. Researchers throughout the United States and the world are working to better understand, prevent, and treat this disease.

National Institutes of Health (NIH)-supported scientists 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 GO.

The following federally funded research studies and clinical trials are currently under way:

- Evaluation of Patients With Thyroid Disorders, funded under NIH clinical trial number NCT00001159
- Trial of Rituximab for Graves' Ophthalmopathy, funded under NIH clinical trial number NCT00595335
- Phase II Randomized Controlled Study of Sequential Orbital Radiotherapy for Graves' Ophthalmopathy, funded under NIH clinical trial number NCT00004660

Participants in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research. For information about current studies, visit www.ClinicalTrials.gov.

For More Information

American Academy of Otolaryngology— Head and Neck Surgery

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Phone: 703-836-4444
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American Association of Clinical Endocrinologists

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You may also find additional information about this topic by visiting MedlinePlus at www.medlineplus.gov.

This publication may contain information about medications. When prepared, this publication included the most current information available. For updates or for questions about any medications, contact the U.S. Food and Drug Administration toll-free at 1-888-INFO-FDA (1-888-463-6332) or visit www.fda.gov. Consult your health care provider for more information.

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