

# ADULT GROWTH HORMONE DEFICIENCY



**Human  
Growth  
Foundation**

The Human Growth Foundation is a non-profit organization. Its mission is to help children and adults with disorders related to growth or growth-hormone through education, research, support and advocacy.

- ◆ Support of research
- ◆ Family education and service
- ◆ Public education
- ◆ Education of health care professionals

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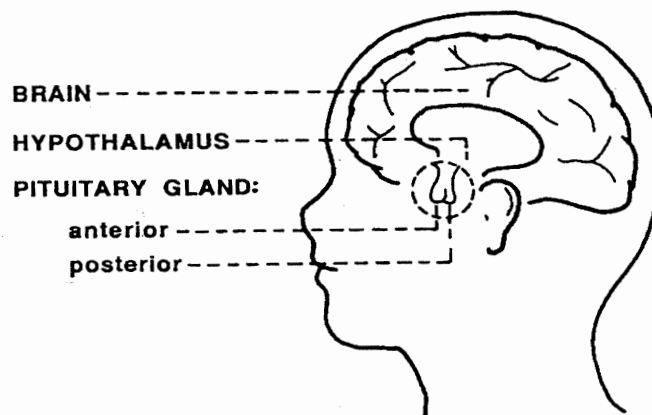
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**HYPOTHALAMUS/PITUITARY**

The **pituitary gland**, known as the “master gland,” produces several hormones that control the functions of other glands. It is located in the middle of the skull below the part of the brain called the **hypothalamus**, to which it is connected. The pituitary gland secretes its hormones in response to a chemical message from the hypothalamus. The pituitary gland has two distinct parts: the anterior (front) lobe and the posterior (rear) lobe. The anterior lobe produces six major hormones: one for the production of breast milk, two for reproduction, one for thyroid function, one for adrenal function, and one for growth. This latter hormone is called somatotropin or growth hormone (GH) and influences growth and metabolism (chemical and physical processes to maintain life). The hypothalamus stimulates hormone release from the anterior pituitary, and these hormones then act elsewhere in the body. When the pituitary gland is removed or destroyed, hormone secretion is lost. When one or more hormones are lost, this is known as **hypopituitarism**. When the pituitary gland is completely removed or

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destroyed and all hormone secretion is lost, this is referred to as **panhypopituitarism**.



*Location of the hypothalamus and pituitary gland*

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## SECRETION PATTERNS OF GH

Pituitary secretion of growth hormone is both age- and sex-dependent. The amount of growth hormone produced and secreted is normally high right after birth and decreases slightly until puberty. At puberty there is a surge of growth hormone secretion, but during adulthood growth hormone levels decrease with age, so that they are quite small by age 50. Women appear to have higher levels of growth hormone than men do.

## EFFECTS OF GH

In children the most obvious effect of growth hormone is linear growth. In adults, the role of growth hormone is more subtle, but still important. In general, growth hormone is *anabolic*; that is, it promotes processes that result in building up the body, rather than breaking it down. Growth hormone promotes lipolysis (fat breakdown) and protein synthesis. It has an anti-insulin effect on metabolism of carbohydrate (sugars) and

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in preventing hypoglycemia (low blood sugar).

## SIGNS AND SYMPTOMS OF ADULT GHD

For many years, growth was considered the final endpoint of growth hormone administration. Recent investigation including multiple clinical studies have now led endocrinologists to better understand the role of growth hormone in adult life. Growth hormone deficiency has been shown to be associated with a number of changes in body composition, which include an increase in the percent of body fat, a decrease in lean muscle mass, decrease in exercise performance, and osteoporosis (bone thinning). Although some studies have shown that the quality of life may be reduced in adults with growth hormone deficiency, others have not. Additional studies are underway to better define this effect of GH deficiency.

Adults with growth hormone deficiency may experience several different symptoms, many of which involve mood and emotions. Here are some of the symptoms most commonly reported by people with GHD:

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### **PHYSICAL SYMPTOMS:**

- ◆ Lack of energy or fatigue
- ◆ Muscle weakness
- ◆ Weight Gain
- ◆ Decreased sexual desire
- ◆ Sleep problems

### **Psychological Symptoms:**

- ◆ Shyness
- ◆ Withdrawal from others
- ◆ Nervousness or anxiety
- ◆ Sadness or depression
- ◆ Feelings of hopelessness

Growth hormone (somatotropin) is often the first hormone to be lost or reduced in pituitary and hypothalamic disorders.

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### **CAUSES OF GROWTH HORMONE DEFICIENCY**

**TUMOR**—Many adults with growth hormone deficiency have had a tumor in the pituitary gland. This tumor may damage the gland, or the gland may be damaged at the time of surgery to remove the tumor.

**SURGERY**—Surgery may be required to remove a tumor from the pituitary as mentioned above. If surgery in the area of the pituitary or the hypothalamus is needed for other reasons, the pituitary gland may also be injured, causing growth hormone deficiency.

**RADIATION**—Exposure to radiation, usually given as treatment for a tumor within the head or as part of a bone marrow transplant, can damage the pituitary gland and lead to growth hormone deficiency.

**CONGENITAL**—Some infants are born without the ability to produce growth hormone. These infants will continue to have growth hormone deficiency after they reach adulthood.

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**IDIOPATHIC**—Many children with growth hormone deficiency develop it for unknown reasons. This is called “idiopathic”. Many of these children will continue to have growth hormone deficiency as adults.

**INFLAMMATION**—This is an uncommon cause of growth hormone deficiency. Inflammation of the pituitary gland may be caused by chronic infections or by chronic inflammatory disorders such as histiocytosis and sarcoidosis.

**AUTOIMMUNE**—Injury to the pituitary gland may occur because the body’s immune system reacts against the pituitary. This usually occurs in women, generally during or after pregnancy.

### **DIAGNOSIS OF GROWTH HORMONE DEFICIENCY**

Who should be tested for growth hormone deficiency? In addition to growth hormone deficient children who have received growth hormone during childhood for improvement of growth, there are other groups of people for whom the diagnosis of growth

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hormone deficiency should be seriously considered. People who have known pituitary tumors, tumors in the region around the pituitary, or any disease involving the pituitary gland may be at particularly high risk for adult onset growth hormone deficiency. This is particularly true if they have lost other anterior pituitary hormones controlling the thyroid, adrenal glands or gonads (ovaries or testicles). Similarly, patients who have received radiation therapy involving the pituitary gland may also be at risk.

Doctors learned how to measure the amount of GH in blood in the 1960s, but the development of that lab test did not solve the problem of diagnosing GH deficiency. Two factors complicate the situation: 1) GH is released by the pituitary gland in bursts and 2) it does not last long in the blood. This means that the amount of GH in a single, random blood sample is likely to be undetectable, unless by chance the blood was drawn just after the pituitary released a burst of it.

Two proteins, IGF-1 and IGFBP-3, are used in screening for GH deficiency in children. Growth hormone stimulates their production, so they reflect the amount of GH that body tissues are being exposed to. They are also more stable in the blood, and they

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are present at higher levels than GH, which makes them easier to measure. However, in contrast to children with GH deficiency, IGF-1 and IGFBP-3 concentrations are often in the normal range in GH deficient adults, so they are not very useful as screening tests. Growth hormone stimulation tests are needed to confirm the diagnosis.

Doctors have found several drugs and chemicals that can be used to stimulate the pituitary gland to produce a burst of GH in most normal people. This allows for the use of GH stimulation testing, which has been the basis of diagnosing GH deficiency for 30 years. The individual is given a GH stimulant, and several blood samples are obtained over a period of time to check the amount of GH being released. Because a person may not always respond to a single stimulant, a second stimulant may also be used. The second stimulant is given after the effect of the first has worn off, followed by another period of blood sampling. Adults who had GH deficiency during childhood need to be re-tested before resuming or continuing GH treatment. Studies have shown that as many as 60-70% of children with GH deficiency will have normal GH secretion upon re-evaluation.

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If needed, stimulation tests to check other pituitary hormones may be performed at the same time as GH testing, without interfering with the results. Examples include the ACTH stimulation test to check adrenal cortisol production, the thyroid hormone releasing factor (TRF) test to check pituitary THS production and thyroid status, and the luteinizing hormone releasing factor (LHRH or LHRF) test to check pituitary LH production, which controls sex hormones.

No two doctors perform the same test in exactly the same way, but there is a general procedure that is used commonly in the United States. The patient's doctor or nurse will explain the details of the procedure that will be used. The endocrinologist needs to be informed about all the medications being taken, because some medicines can interfere with GH testing. The endocrinologist will tell the person undergoing the test whether he or she should take or skip medication doses on the morning of testing.

Most people can be tested safely as outpatients, but sometimes an overnight hospital stay is needed. Growth hormone testing is performed in the morning after an overnight fast (water is allowed). A nurse will check weight, blood pressure and pulse. Because

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there is a risk of low blood sugar and low blood pressure, most centers ask people being tested to stay sitting or lying down in recliners or beds.

An IV (intravenous line) is usually inserted into an arm or hand vein for drawing blood. Drugs may be given through the IV, depending on the GH stimulants being used. Often a bag of saline (sterile "salt water") is hooked to the IV to keep it working. Sometimes the IV is used as a "heparin lock", which means that it is not attached to any fluid bag, and dilute heparin (an anti-clotting drug) or saline is used to clear the IV of blood after every blood sample. An IV may not be needed depending on the drugs being used and the number of blood draws.

After the IV is secured in place, a baseline blood sample will be drawn through it and the first GH stimulant will be given. Blood samples will continue to be drawn as ordered. A second stimulant may be given after the first sampling period ends, with more blood drawing. The patient's condition, blood sugar, blood pressure, and pulse will be checked as needed during the testing. Most centers ask that patients stay until they are alert, and can walk without dizziness, and have eaten a snack or lunch (ask if

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this will be provided or if something should be brought from home). Testing may take from 2-6 hours depending on the drugs being used. The patient may feel tired the rest of that day, but should be able to return to normal activities the next day.

Compiled below is a list of the most commonly used GH stimulants, along with information about how they are given. The dose of each medication is based on body weight. Any of these drugs may cause side effects, so only doctors and nurses familiar with their use should perform this testing.

**ARGININE** is an amino acid (protein building block) which is given intravenously over 30 minutes. Allergic reactions are rare, but possible. Local irritation at the IV site, flushing, nausea and vomiting can occur, especially if infused too rapidly. The results of the test will not be valid if the infusion is not completed.

**CLONIDINE** is a drug used to treat high blood pressure in adults. It is presumed to cause GH release by stimulating certain nerve cells in the brain. It is a small pill given by mouth. Drowsiness and a mild drop in blood pressure, lasting 2-3

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hours, are the most common side effects. Patients may feel light-headed when standing up. Blood pressure and pulse will be checked during testing and should return to normal before discharge. Clonidine is not as effective in stimulating GH release in adults as in children, so it is not used often in adults.

**GLUCAGON** is a naturally occurring hormone that raises blood sugar. It is given intramuscularly (an injection into a muscle) or subcutaneously (a shallow injection under the skin). Nausea and vomiting are uncommon side effects. Although it takes longer to work, glucagon is safe and well tolerated, even by very young children.

**GRF** (growth hormone releasing factor) is produced by the hypothalamus and directly stimulates pituitary GH production. It is given intravenously. Local irritation at the IV site and flushing and warmth are the most common side effects.

**INSULIN** is a naturally occurring hormone that lowers blood sugar. It has been used as a GH stimulant since the 1960s. It is given IV. Complications such as

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seizures and heart rhythm problems can occur if the blood sugar drops too low, so blood sugar is checked frequently during the test. Common side effects include sweating, hunger, and rapid heart rate, lasting about 20 minutes after the dose. Insulin is not used with young children or those with seizure disorders, kidney, lung, or heart problems because of the risks. Despite the temporary discomfort for the patient, the results of several studies have shown that insulin is the most reliable GH stimulant in adults, even when used alone.

**L-DOPA** is a drug used to treat Parkinson's Disease. It is presumed to cause GH release by stimulating certain nerve cells in the brain. It is a pill given by mouth. Possible side effects include nausea, vomiting, drowsiness, and a mild drop in blood pressure, which can cause dizziness. Blood pressure and pulse will be checked during testing and should return to normal before discharge.

**SLEEP** is another GH stimulant. About two thirds of daily GH production occurs at night during periods of deep sleep. Monitoring GH production for 12-24 hours is time consuming but may reflect the usual pattern of GH release better than

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stimulation tests. Sleep tests may be performed during an overnight hospital stay or in the home by a home health nurse. The main drawbacks of sleep testing are the number of blood samples, the length of testing, and the lack of clear division between normal and abnormal results.

There are no rules about what stimulants to use. Most endocrinologists use the same two or three drugs for most of their patients, based on their own experience of which produce the best GH response with the fewest side effects. L-dopa and arginine are frequently used in combination in the United States. Insulin is not used as frequently in children as it once was because easier and safer options now exist, but it is still the "gold standard" for some doctors, especially for testing adults. The use of GRF is increasing because it has become more readily available. The doctor or nurse will discuss which GH stimulants will be used and why.

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## **DIAGNOSTIC CRITERIA AND GROWTH HORMONE DOSING**

Most endocrinologists agree that a GH peak of less than 3-5 ng/mL indicates GH deficiency in adults, although there is some overlap between normal and abnormal responses. GH deficiency is not diagnosed only on the basis of stimulation test results; these results are one part of a large picture that includes the person's medical history, physical findings, and other test results. Growth hormone therapy in the adult is only advised when growth hormone deficiency can be clearly established by endocrinologic tests. As with all medical therapies, the risks versus the benefits should be determined by the individual and his or her physician. Growth hormone should be viewed in the context of the person's entire health picture. If a person has a true deficiency in growth hormone and has symptoms of this, treatment should be initiated to try to reproduce what the growth hormone levels would be normally and relieve the symptoms. Research into the diagnosis and treatment of adult GHD is continuing as doctors try to learn how best to help their patients live healthy and happy lives.

The initial dose of growth hormone used in adults with newly diagnosed GH deficiency

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is much lower than that used to treat GH deficiency in children. The standard dose for children is 0.04 milligrams of GH for every kilogram of body weight each day. However, when this dose is used in adults, there is a high rate of side effects. The adult dose has been determined through many clinical studies. The currently recommended starting dose of growth hormone is 0.003-0.004 milligrams per kilogram of body weight per day. This dose may be gradually increased based on the individual's response. It is unusual for the dose to exceed 1.0 milligram per day.

Because giving too much growth hormone commonly causes side effects, it is important to monitor the effect of growth hormone on the body. This is done by measuring the amount of IGF-1 in the blood. IGF-1 is used to diagnose GH deficiency in children, but as discussed above, it is not often helpful for this purpose in adulthood. However, this test can be used to show that the GH dose is excessive. When the dose is too high, the IGF-1 level will be high as well. Current recommendations advise that the IGF-1 level be maintained in the normal range for the age of the individual.

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## **EFFECTS OF GROWTH HORMONE TREATMENT**

When an individual with GH deficiency begins treatment with growth hormone, the symptoms and physical signs of GH deficiency tend to gradually improve.

There is usually a decrease in body fat during the first few months of treatment. At the same time the amount of muscle mass increases. The amounts of change in these two components of the body tend to offset each other, so the total body weight may not change. However, the result may be a somewhat leaner body build. Along with the increased muscle mass comes an increase in strength and endurance. There may also be an improvement in the function of the heart.

The density of the bones usually increases during treatment of a GH deficient patient. Whether this will lead to a lower risk for broken bones is not known at this time.

Adults with GH deficiency have higher cholesterol levels than other people. When these individuals are given growth hormone, the cholesterol levels generally come

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down. In addition, the levels of LDL cholesterol (the so-called “bad cholesterol”) come down. However, there is not a strong effect of growth hormone on the levels of HDL cholesterol (the “good cholesterol”). Furthermore, growth hormone does not affect levels of fats in the blood, called **triglycerides**.

Growth hormone treatment may result in an improvement in mood and energy levels. It has also been shown to decrease social isolation and increase physical mobility, which are problems for many people with GH deficiency. In addition to growth hormone, other treatment may include medication to help reduce depression or anxiety and a type of counseling called cognitive-behavior therapy in which the individual learns to change his or her feelings by reorganizing and re-framing dysfunctional thoughts.

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## **ADVERSE REACTIONS TO GROWTH HORMONE TREATMENT**

Growth hormone deficiency in adulthood, as with other adult hormone deficiency conditions, may require chronic therapy. For this reason, it is particularly important for patients to have accurate scientific assessment of the benefits versus risks. The most common side effects of growth hormone administration involve salt and water retention. These side effects include weight gain, swelling of the feet or hands called edema, and a sensation of tightness in the skin of the hands. Some individuals may develop carpal tunnel syndrome because of swelling in the wrist that may compress the nerves leading to the hand. This may produce pain, numbness, or weakness in the hand. Some people who are taking growth hormone may also complain of muscle aches and joint pains.

High doses of growth hormone may cause problems with blood sugar, particularly if the person has diabetes. Growth hormone interferes with the way insulin works in the body, blocking its action. However, this is not generally a problem at the doses of GH that are usually used.

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Other rare side effects that have been reported include high blood pressure, headache due to an increase in the pressure inside the skull, and breast development in men.

The side effects that are seen with growth hormone are much more common at higher dose. As discussed above, the dose of GH should be low at the beginning of treatment and gradually increased in order to relieve the person's symptoms. The level of IGF-1 should be used to avoid increasing the dose too much and to avoid the development of side effects. If side effects are noticed, the dose of GH should be reduced. Such a reduction usually allows the side effects to improve.

Little is known about the use of growth hormone replacement during pregnancy. In the absence of information about this situation, it would be advisable to use GH during pregnancy only if it is needed and if so, to use the lowest possible dose.

Growth hormone replacement should not impair fertility. However, people who have growth hormone deficiency may have fertility problems, because the pituitary gland also controls the function of the ovaries and testicles. Fertility problems noted during

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growth hormone treatment are likely to be caused by the pre-existing pituitary problem.

There have been concerns that growth hormone could lead to more rapid growth of tumors. Long term studies of GH use in children have not shown any evidence of increased rates of cancer. There is not much information available regarding the use of GH in adults, but it does not seem to increase the risk of developing new tumors or accelerate the growth of existing tumors. Any person receiving growth hormone should visit a doctor regularly and follow recommendations regarding cancer prevention and early detection.

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## RESOURCES

- ◆ Visit the Human Growth Foundation's Web site at <http://www.hgfound.org>. This web site outlines the activities of the Human Growth Foundation and contains
- ◆ instructions for joining the e-mail list server for patients with adult growth hormone deficiency.
- ◆ For further information on counseling:

American Psychological Association  
(800) 374-2721 [www.http://apa.org](http://www.apa.org)  
(202) 336-5500

Pituitary Network Association  
(805)-499-9973  
[www.http://pituitary.org](http://pituitary.org)

American Psychiatric Association  
(888) 357-7924 [www.http://psych.org](http://psych.org)  
(202) 682-6000

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