

ACROMEGALY

YOUR QUESTIONS ANSWERED



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What is acromegaly?

Acromegaly is a rare disease characterized by excessive secretion of growth hormone (GH) by a pituitary tumor into the bloodstream.

What does growth hormone do?

Growth hormone (GH) is responsible for growth and development of the human body especially during childhood and adolescence. In addition, GH has important functions during later life. It influences fat and glucose (sugar) metabolism, and muscle and bone strength. Growth hormone is produced in the pituitary gland which is a small bean-sized organ located just underneath the brain (Figure 1). The pituitary gland also secretes other hormones into the bloodstream to regulate important functions including reproduction, energy, breast lactation, water balance control, and metabolism.

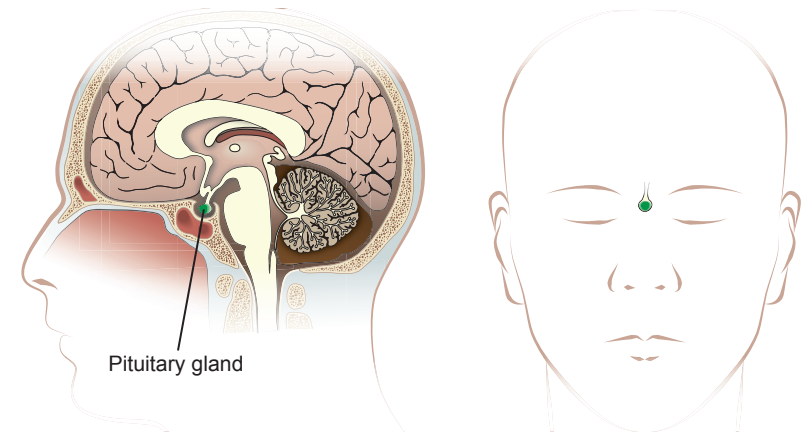


Figure 1. Location of the pituitary gland.

What causes acromegaly?

Under normal circumstances, GH secretion is carefully controlled by a number of factors produced in the brain or elsewhere in the body. Almost all cases of acromegaly are caused by a tumor in the pituitary gland that produces too much GH. These tumors are almost always benign (non-cancerous).

Very rarely, tumors elsewhere in the body can produce a substance called growth hormone releasing hormone, or GHRH, which can also cause acromegaly by stimulating the pituitary gland to overproduce GH.

What are the signs and symptoms of acromegaly?

Excess circulating GH can cause a variety of undesirable effects. In childhood, excess GH results in gigantism, or abnormally large skeletal growth before the growth plates have a chance to close. The signs of gigantism are relatively easy to notice (Figure 2a). However, if the GH excess occurs during adulthood, the signs and symptoms are more subtle. In many cases, because the progression of changes in physical features is so gradual, patients, families, coworkers, and even treating physicians may think that these changes are just the natural results of aging (Figure 2b).

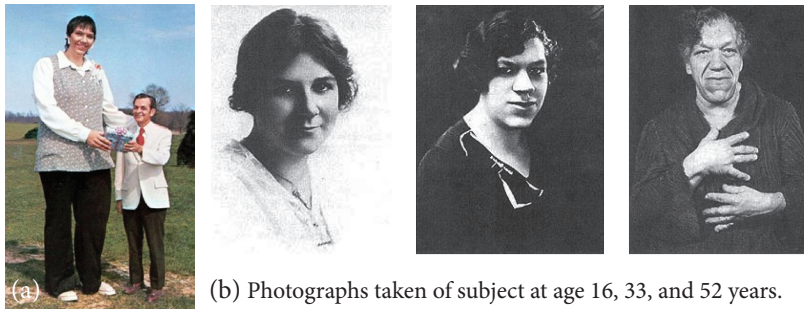


Figure 2. Signs of GH excess in childhood (a) and adulthood (b)

Because the growth plates have already closed in adulthood, bone structure may be altered and surrounding connective tissue increased leading to enlargement of the hands and feet and coarsening of the facial features, ie, protruding forehead and jaw and widening of nose and tongue (Figure 3).

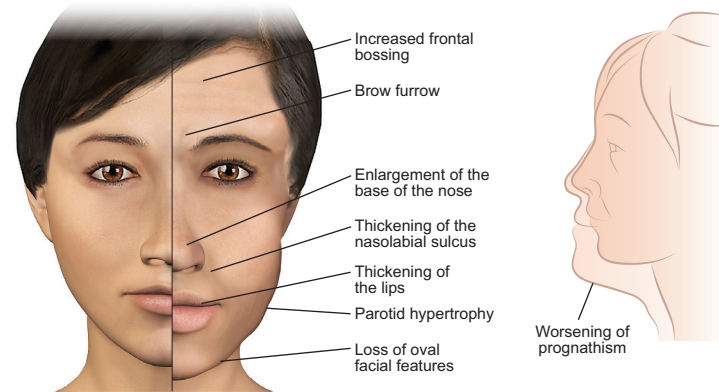


Figure 3. Changes in facial features in acromegaly

An enlarging pituitary tumor can cause problems due to 1) compression of nearby structures; and/or 2) changes induced by excessive growth hormone levels in the blood (Figure 4).

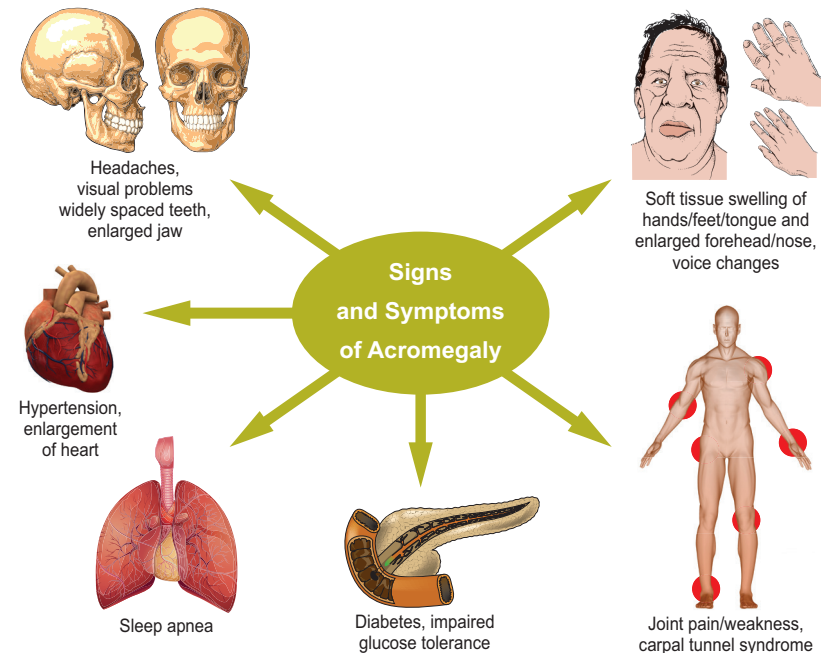


Figure 4. Common signs and symptoms of acromegaly

Compression by the Pituitary Tumor

A growing pituitary tumor can cause pressure on surrounding brain tissues or nerves (Figure 5). As a result, you may experience severe headaches. If the tumor continues to grow, it can affect certain cranial nerves, like the optic nerve, which can cause loss of peripheral vision. In addition to pressure on cranial nerves, considerable growth of the pituitary adenoma may also result in compression of the healthy pituitary gland, causing a deficiency in other pituitary hormones (see *The Pituitary Society’s Patient Information Booklet on Hypopituitarism*). The pituitary gland is often called the ‘master gland’ since it controls most other endocrine glands in the human body. In addition, excess GH can affect other glands in the skin which can lead to excess oiliness and sweating. If healthy parts of the pituitary gland are affected by a pituitary tumor, you may experience deficiencies in certain hormones like the stress hormone cortisol, thyroid hormones, and the sex hormones testosterone or estrogen. These hormone deficiencies may lead to clinical symptoms like impaired sexual function, lack of strength, and changes in metabolism which can be life-threatening.

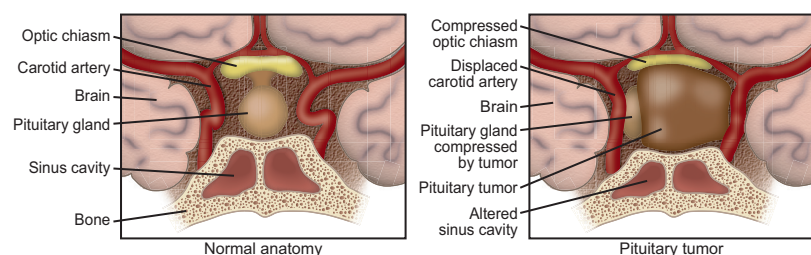


Figure 5. Local compression of brain structures by pituitary tumor

Excess Circulating Growth Hormone

As previously described, too much GH in the circulation can cause hands and feet to enlarge as a result of increased connective tissue. In addition, bones can thicken resulting in enlargement of the forehead, jaw, and elsewhere. Too much GH can also cause arthritis and joint pain. Excess GH can induce metabolic changes in your body such as high blood sugar or diabetes mellitus, sexual dysfunction, and hypertension (high blood pressure). Increased soft tissue swelling of the lips, tongue, and throat can lead to the development of obstructive sleep apnea, a potentially serious sleep disorder characterized by repeated stops and starts in breathing. Because this disorder alone is associated with increased risk of heart and lung disease, you should tell your doctor if you snore loudly and

experience extreme drowsiness during the day. The majority of patients with acromegaly have sleep apnea and may not be aware of it. Patients with acromegaly also have an increased risk of developing certain tumor types including colon polyps as well as tumors of the prostate and thyroid gland.

How is acromegaly diagnosed?

The diagnosis of acromegaly has been standardized and follows published guidelines. However, blood test results should be interpreted by an endocrinologist experienced in diagnosing acromegaly.

If you have experienced enlargement of hands and fingers, increase in shoe size or snoring, or other features discussed above, you should tell your doctor. Because GH levels fluctuate throughout the day, an initial blood test will be performed to measure the level of insulin-like growth factor 1 (IGF-1), a protein made by the liver in response to GH, which is the most accurate clinical marker of acromegaly. If your IGF-1 levels are elevated when compared to normal levels for age and gender, further evaluation is warranted, this time using a test called the “GH suppression test”. This test is performed by drinking a solution of glucose (sugar water) after an overnight fast followed by blood draws every 30 minutes for 2 hours. In healthy individuals, GH levels will be suppressed after ingestion of glucose. If you have acromegaly, your GH levels will continue to be elevated. The findings of increased circulating IGF-1 and GH confirm the diagnosis of acromegaly. The next step is to determine the reason why your IGF-1 and GH values are abnormal. This is typically done by performing a magnetic resonance imaging (MRI) scan of the brain, focusing on the pituitary region (Figure 6).

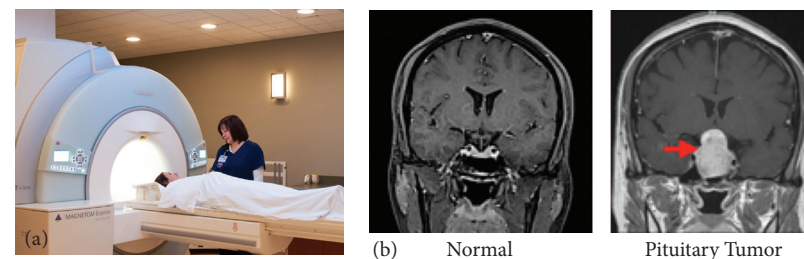


Figure 6. Magnetic resonance imaging for detection of pituitary adenoma (a) Patient undergoing an MRI scan; (b) Coronal MRI showing normal pituitary and presence of a pituitary adenoma.

What are the treatment options for acromegaly?

Treatment of acromegaly aims to reduce tumor size and its clinical consequences, and to control GH secretion, thereby improving the clinical condition and preventing disease complications.

Potential treatment options for acromegaly include surgery to remove the tumor (Figure 7 [1]) and/or medical treatment that either reduces the amount of GH that the pituitary tumor secretes (Figure 7 [2]) or blocks the excess circulating GH from binding to receptor sites (Figure 7 [3]). The binding of GH to its receptor sites leads to increased production of IGF-1 by the liver. Too much IGF-1 causes the clinical manifestations of acromegaly. In most cases, medical therapy is used after surgery; however, medical treatment may also be used as either an alternative to surgery, or prior to surgery, in selected patients. Radiation to destroy the tumor is used, but less often.

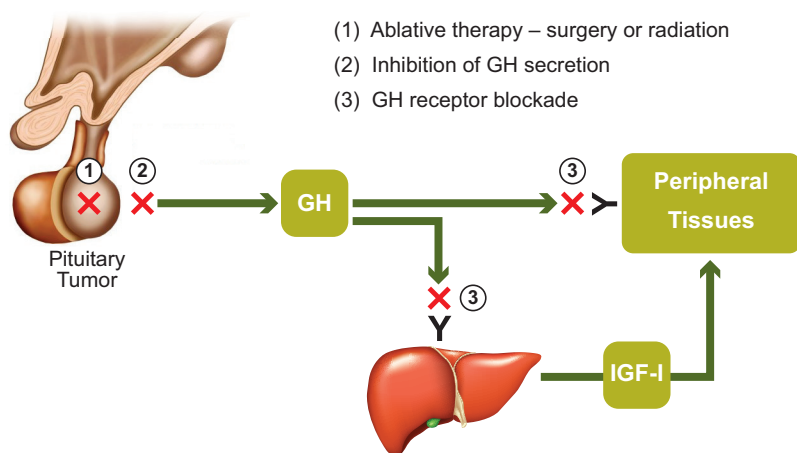


Figure 7. Therapeutic options for the treatment of acromegaly

(1) Ablative Therapy (Surgery, Radiation)

Surgery

A clear diagnosis of an underlying pituitary tumor should be established by an endocrinologist. Many patients are referred to a neurosurgeon highly experienced in pituitary surgery. Surgical removal is potentially curative, but the chances of complete removal of the tumor depend on its size and extension. Except in the case of very large tumors, surgical removal

of the tumor will be done using a minimally invasive approach called ‘transsphenoidal surgery’. Your neurosurgeon will locate the tumor visually through a microscope or endoscope and use small instruments inserted through the nose and air-filled bony nasal sinuses to remove the tumor mass (Figure 8). A neurosurgeon experienced in this approach will attempt to completely remove the tumor while avoiding damage to, or removal of, healthy pituitary tissue or sensitive structures in the area. Surgical success and the risk of complications are largely related to the experience of the surgeon and the number of procedures s/he has performed.

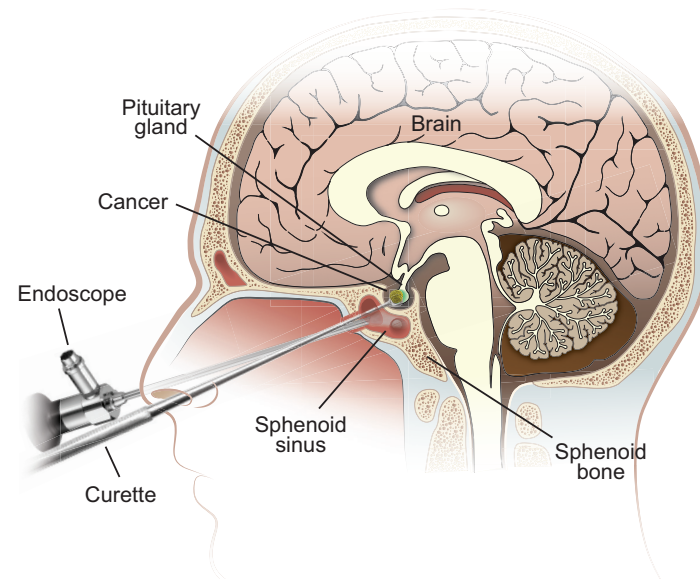


Figure 8. Transsphenoidal surgery

Radiation

For some patients, focused radiation may be used in an attempt to shrink the tumor mass and reduce GH secretion. This is a slow process that may take years to adequately control the GH secretion. Medical treatment is required until radiation takes effect. Radiation can also damage the normal pituitary gland. As a result, patients might require replacement for reduced or missing hormones.

(2) Medical Therapy (Inhibition of GH Secretion)

As shown in Figure 7 (2), somatostatin analogs and dopamine agonists work by directly blocking GH secretion. Commonly used drugs are listed in the table below.

How They Work	Type of Medication	Generic Drug Names
Directly inhibit GH secretion	Somatostatin analogs	Octreotide, Lanreotide
	Dopamine agonists	Bromocriptine, Cabergoline

Somatostatin is a naturally occurring peptide hormone that inhibits GH secretion in your body. Specific drugs called ‘somatostatin analogs’ that mimic the action of natural somatostatin have been developed to lower GH levels in patients with acromegaly. Somatostatin analogs are administered by routine intermittent injection. These analogs lower GH and IGF-1 levels in over half of all patients. These drugs often reduce tumor size.

Dopamine agonists may also decrease GH secretion and, therefore, also decrease IGF-1. These are taken orally; however, they are generally less effective than somatostatin analogs.

Both are relatively well-tolerated agents that have been used for many years. The most common side effects of somatostatin analogs include the development of gallstones in some patients as well as transient nausea and some abdominal discomfort. Use of dopamine agonists can sometimes cause gastrointestinal side effects and low blood pressure.

(3) Medical Therapy (GH Receptor Blockade)

There is only one medical treatment option that works by blocking the actions of GH on the liver, thereby lowering IGF-1 levels in the circulation (Figure 7 [3]).

How They Work	Type of Medication	Generic Drug Name
Blocks the GH receptor rendering GH ineffective	GH receptor antagonist	Pegvisomant

The GH receptor antagonist, pegvisomant, decreases IGF-1 levels in more than two-thirds of patients and is generally well tolerated. It is administered daily by injection and side effects include liver function abnormalities and infrequent development of fatty tissue deposits under the skin.

Will I need treatment with any other hormones?

It is possible that patients with acromegaly may simultaneously develop deficiencies in other pituitary hormones as a result of surgical intervention or inadvertent damage after radiation therapy, or by compression of the normal pituitary by a large tumor. You may require long-term replacement of those hormones. For additional information, you can request copies of other Patient Information Booklets produced by The Pituitary Society that address other pituitary disorders. Of particular interest to patients with acromegaly would be the booklet on *Hypopituitarism*.

How can I expect to feel after treatment?

After surgery or initiation of medical therapy, you can expect initial weight loss, reduced soft tissue swelling, improved headaches, reduced joint pains, lower blood sugar levels, and improved sleep apnea. If your heart function was affected by acromegaly, it, too, will likely improve. Unfortunately, hard bony changes will not be altered by effective treatment. Cosmetic maxillo-facial surgery may be required to correct biting disturbances and improve jaw alignment.

How should patients with acromegaly be followed after initial treatment?

You should undergo regular follow-up visits with your endocrinologist to ensure control of your pituitary hormones in addition to controlling GH and IGF-1 levels. Periodic MRI scans should be performed to check for any remaining tumor tissue, or sometimes, tumor recurrence. A colonoscopy should be performed at the time of diagnosis, with follow-up examinations at your doctor’s recommendation. Regular cardiac, breast, and prostate follow-up examinations should be undertaken. It is important to maintain GH and IGF-1 in the normal range. Additionally, elevated glucose levels and high blood pressure should be controlled.

What do I need to do if I have acromegaly?

- **Get involved**
Make sure that you understand the rationale for the treatment of acromegaly. This might include surgery, medical treatment and sometimes radiation. As with any pituitary tumor, some patients also have deficiencies in pituitary hormones that will require replacement and monitoring.
- **Be attentive**
Make sure to report ongoing or new symptoms to your doctor. Also discuss whether the acromegaly treatment is effective.
- **Cooperate**
Take medication as prescribed and at the correct times.
- **Stick with it**
Attend regular visits with your endocrinologist.
- **Follow up**
Have appropriate tests (blood tests, MRI scans) to determine if the tumor size is stable or reduced, as this might change.

Acromegaly FAQs

Is a pituitary adenoma the same as a brain tumor?

No, pituitary adenomas are benign pituitary tumors that are not cancerous or malignant. The pituitary gland is situated directly below the brain and is not part of it.

What are the major side effects of somatostatin analogs?

Common side effects observed with the use of somatostatin analogs include development of gallstones in some patients as well as transient nausea and abdominal discomfort.

What are the major side effects of dopamine agonists?

A drop in blood pressure when standing can occur. After initially taking these medications, your blood pressure should be monitored both while laying down and standing. Gastrointestinal side effects can occur as well.

What are the major side effects of a GH receptor antagonist (GHRA)?

Common side effects observed with the use of GHRA include usually reversible liver function abnormalities and infrequent development of fatty tissue deposits under the skin.

What are the advantages and disadvantages of transsphenoidal surgery?

Transsphenoidal surgery is potentially curative (as opposed to medical therapy, which requires lifelong treatment), but the chances of a cure depend on the size and invasiveness of the tumor and experience of the surgeon. In addition, surgery can often remove a considerable amount of the tumor and immediately relieve compression of the surrounding structures, which is important if there are visual problems. If surgery is unsuccessful, medical and/or radiotherapy will be required. The risks of surgery include damage to the pituitary which might require new hormone replacement and small risks of a serious complication including worsening vision or stroke.

What are the advantages and disadvantages of radiation therapy?

Radiation treatment is potentially curative, but takes many years to be effective. In the meantime, medical treatment to control GH levels is required. In addition, radiation therapy has a significant chance of damaging the normal pituitary, which may require additional hormone replacement.

Is acromegaly hereditary?

Acromegaly may sometimes affect several members of a single family due to genetic changes, or mutations, in your DNA. Some of those mutations have been identified, for example, in the *AIP* gene in patients with familial acromegaly or in the *menin* gene in patients with multiple endocrine neoplasia type 1 (MEN1). If you have family members with pituitary tumors or other endocrine disorders, be sure to tell your doctor so that s/he can attempt to identify the genetic changes and talk to you about the results.

For Further Information:

The Pituitary Society produces Patient Information booklets on other pituitary disorders. The booklet on Hypopituitarism may be of particular interest to patients with acromegaly in providing important information regarding hormone deficiencies.

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www.pituitarysociety.org

Glossary

Acromegaly	A rare disease in adults characterized by excessive secretion of growth hormone (GH) during adulthood (ie, after the growth plates have closed) into the blood circulation.
Dopamine agonists	A form of medical treatment commonly used for patients with prolactin-producing tumors (see <i>Prolactinoma</i> Patient Information booklet). It sometimes is also beneficial in acromegaly. In acromegaly, this drug works to block GH secretion and, therefore also decrease IGF-1 levels.
Endocrinologist	A medical specialist who deals with the diagnosis and treatment of diseases related to hormones.
Gigantism	An excess secretion of growth hormone (GH) during childhood resulting in continued increased height.
Growth Hormone Receptor Antagonist	A form of medical treatment for patients with acromegaly. This drug works by blocking the actions of GH on the liver, thereby lowering blood IGF-1 levels.
Mutations	Genetic changes that occur either in a patient’s DNA that may result in the occurrence of acromegaly among members of the same family, or may occur only within the tumor.
Pituitary adenoma	A (usually) benign tumor of the pituitary gland.
Pituitary Endocrinologist	An endocrinologist that specializes in diseases of the pituitary gland
Pituitary gland	A small, soft tissue projection situated below the base of the brain. The pituitary secretes growth hormone as well as hormones that control the thyroid, ovaries, testes and adrenal glands. As a result, the pituitary is often referred to as the ‘master gland’, or ‘conductor of the endocrine orchestra’.
Somatostatin analogs	A form of medical treatment for patients with acromegaly. These drugs work by lowering both GH and IGF-1 levels and often shrink the tumor.
Transsphenoidal surgery	A surgical procedure to remove a pituitary adenoma whereby small instruments are passed through the nose and air-filled bony nasal sinuses where the tumor is visualized by microscope or endoscope and subsequently removed.



Educational booklets available from The Pituitary Society:

Acromegaly

Cushing's Syndrome and Cushing's Disease

Hypopituitarism

Prolactinomas

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