# GROWTH HORMONE DEFICIENCY

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# Cause of the Project

Growth Hormone Deficiency is a rare disease that impairs the body's growth. Isolated growth hormone deficiency is estimated to occur in 1/4,000 to 1/10,000 children and affects about 1/3,500 to 1/10,000 live births

Rare diseases are those that affect up to 65 people per 100,000. Together they affect about 400 million people in the world, 13 million of them in Brazil. There are about 8,000 categories of rare diseases. They have a difficult and lengthy diagnosis; this is due to factors ranging from limited diagnostic methods, difficult access to health services, lack of specialized services and professionals. About 95% of rare diseases do not have a specific treatment and are dependent on rehabilitation services that help bring a better quality of life. Among the others that can be treated, the cost is high.

- National Policy for the Comprehensive Care of People with Rare Diseases

In 2014, Ordinance 199 was drawn up, which established the National Policy for Comprehensive Care for People with Rare Diseases, from which it was possible to recognize rare diseases, draw up Clinical Protocols and Therapeutic Guidelines, expand specialized health services and organize care for patients. The objectives include guaranteeing the principles of SUS to rare disease patients, improving access to health services and quality of life, and reducing morbidity and mortality (the rate of deaths due to a disease).

The health care for rare disease patients must be based on the Guidelines for Comprehensive Care for People with Rare Diseases in SUS, which establishes the Health Care Networks, in which Primary Care and Specialized Care stand out as the main services.

Despite the advances, Brazil still has difficulties regarding the network of diagnostic tests, guarantee of drug supply, capacity to meet the demand, and training of health teams.

Another difficulty is the organization of a network that provides preventive measures, avoiding incorrect and ineffective treatments.

According to Dr. Simone Sakura Ito, Pediatrician and Pediatric Endocrinologist, "The estimated incidence of growth hormone deficiency associated with short stature is 1:4000 to 1:10,000. The causes can be varied, from brain tumor, genetic mutation, brain malformation, trauma, or idiopathic (no cause discovered). Unfortunately the incidence is estimated and has a large variation of studies, because how to diagnose the disability is still controversial and the causes of the disability are very varied."

# Introduction

Growth Hormone Deficiency is the lack of growth hormone, which impairs its growth because the pituitary gland does not produce enough of it. It can be associated with heredity (inherited from a family member), lesions in the brain region, absence of the pituitary gland, and deficiency of other hormones. More common in children, it dyes 1 in every 4,000 to 10,000 children in the world, diagnosed after the age of two. It presents with slow growth and short stature and may look younger than it is. It can be isolated or accompanied by pan-hypopituitarism, and can have a deficiency of one or more hormones, genetic causes, or be acquired from lesions that affect the pituitary gland, such as tumors and infections. The treatment is hormone replacement and removal of any causative tumor.

In addition to children, adults can also suffer from GH hormone deficiency, which can be the result of some injury. Thus, surgery or radiation therapy near the pituitary gland can cause damage, in which the brain stops producing the necessary amount of the hormone.

As the years go by, the natural production and release of the hormone relapses. From the age of 21 the release of the hormone is reduced. After the age of 40, only half of the hormone is available in the body. And finally, at the age of 60 the production is less than 50%.

Children with GH deficiency in childhood who have not received treatment can suffer in adulthood. In this case, they can start or continue therapy as adults. Those who suffer from long-term lack of the hormone may increase the risk of some diseases, loss of muscle mass, weight gain that increases the risk of diabetes, reduced bone density, increasing the risk of fractures, depression, and sleep disruptions. The treatment is injectable done daily with applications done under the skin. As a result, some patients with may benefit throughout their lives.

# Growth Hormone

Growth hormone, GH (Growth Hormone) is a protein and stimulating hormone in humans and vertebrate (spinal) animals. It is produced in the pituitary gland, a small gland about the size of a pea, and weighs between 0.5 and 1.0 g. It is considered the master gland of the organism, because its main function is to produce hormones that regulate the body's functioning. During the growth phase, under the action of this hormone, almost all the cells increase in volume and number, propitiating the growth of tissues, organs and, consequently, body growth. Which is located in the lower part of the brain. It is responsible for the physical growth of the human body and also for cell growth. It continues to act on the body's construction throughout life. For this reason, its presence needs to be constant.

Deficiency of this hormone can cause dwarfism. While in excess, GH can cause exaggerated growth of some parts of the body, known as gigantism.

In children, the hormone is responsible for their physical development, which can be seen in the increase in body size.

On the other hand, adults with ideal size, who present increased body fat, loss of lean mass, and increased cholesterol, can be exposed to GH deficiency.

# Reactions in the Individual

Adults who suffer from a long-term lack of the GH hormone can increase the risk of some diseases. Besides loss of muscle mass, weight gain increases the risk of diabetes. Especially in the elderly, bone density is reduced, increasing the risk of fractures. Other unwanted effects resulting from reduced growth hormone production include cognitive disturbances (difficulties in processing information, including mental tasks such as attention, reasoning, and memory), depression, and sleep disruptions.

# Nanism

NANISM

A lack of growth hormones, causing the body to not grow and develop as it should. Characterized by short stature and surgery (it must be performed by an orthopedist and helps to correct alterations in the direction of growth of some bones and to lengthen the bones).

CLASSIFICATION

- HYPOPHYSARY OR PITUITARY - disorders in hormones and metabolism by deficiency in the production of growth hormone or by resistance of the body to the action of the hormone.
- PROPORTIONAL - the symptoms appear in the first years of life, since its main cause is an alteration in the production of growth hormone, present from birth.
- PRIMORDIAL - extremely rare, it can be identified before birth, since the growth of the fetus is very slow, being smaller than expected for the gestational age.
- DISPROPORTIONAL - the most common type is achondroplasia: a syndrome that prevents the normal growth of the bones, causing the parts of the body to grow unequally. Besides short stature, the person has short legs and arms, a large head and small hands, short fingers, and a long and narrow trunk.

CAUSES

As well as familial short stature, other forms of short stature without a defined cause can occur due to delayed skeletal growth at puberty, or due to restricted fetal growth.

It is necessary to consider that the growth process can be altered by events in childhood. Malnutrition, chronic diseases, hormonal deficiencies, and genetic syndromes can become an obstacle for the child to grow and develop normally.

This is not the case with achondroplasia, which has a genetic cause. All it takes is one of the parents to carry the defective gene, and with each pregnancy the probability of passing on a copy of this gene to a descendant, who will also manifest the disorder, rises to 50%.

Inherited characteristics tend to appear in every generation of the same family, and either the father or the mother can pass the affected gene on to their children. Babies who receive this gene from both their father and mother usually live only a short time, no longer than a few months.

PREVENTION AND CONTROL:

- Follow-up should involve pediatricians, endocrinologists, orthopedists, physical therapists, psychologists, dentists, etc.
- Growth hormone is not always the solution to accelerate the child's growth rate
- Genetic counseling is an indicated resource for couples who intend to have children and have a family history of achondroplasia. However, the fact that spontaneous genetic mutations exist, makes it very difficult to talk about absolute prevention of the disorder.

According to the Genome Research Institute, in most cases this change occurs randomly. In such cases, the father and mother are normal height, are not carriers of the mutated gene, and are unlikely to have another child with the same category of mutation.

DIAGNOSIS

It is based on the clinical examination and the results of skeletal X-rays. The signs are usually visible at birth or in the first years of life. Even during pregnancy, they can be observed starting in the sixth month through imaging exams.

It is extremely important to establish the diagnosis of achondroplasia with other forms of dwarfism that also cause short stature and short limbs. The earlier this is done, the better the results of the clinical follow-up, respecting the peculiarities of each condition.

CHARACTERISTICS AND SYMPTOMS

- Short stature
- Short legs and arms compared to the normal size of the torso
- Large head and flattened upper nose
- Short and thick fingers
- Small hands
- Small and wide feet
- Severe kyphosis and lordosis
- Forward displacement of the jaw
- Misalignment of the teeth
- Delay to start walking, which can occur between 18 and 24 months.

TREATMENT

When short stature is related to the absence or small production of growth hormone, the administration of this hormone has been shown to produce beneficial effects.

The treatment can be extended for several years and must be closely monitored by a physician specialized in the area, because adverse reactions to the use of the medication can occur.

Growth hormone is part of the list of high-cost medications that are distributed free of charge by SUS, provided that the person proves that he or she has precise medical indications for hormone replacement.

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Dwarfism can affect women and men who have preserved intellectual capacity and can lead a normal and good quality life.

In many situations, people with dwarfism are forced to deal with prejudice and social discrimination and to overcome access difficulties in environments prepared to receive taller people. Because of this, they need help to perform simple tasks, such as using the ATM or public transportation, for example.

People with disproportionate dwarfism used to be called midgets, which greatly impairs their self-image and socialization

# Gigantism

A disorder caused by excessive secretion of growth hormone, resulting in excessive growth of arms, legs, and increased height throughout the body that occurs due to the over-release of growth hormone or the malfunction of the hormone responsible for inhibiting the release of the GH hormone. Children with gigantism will grow abnormally, and many will experience delayed puberty.

Researchers have found traces of the largest primate that ever lived and named it Gigantopithecus, some specimens of the species were as tall as 3 meters and weighed 300 kilograms, coexisting at the same time with Homo erectus about 5 million and 100 thousand years ago. Some people believe that this species of primate is still alive and call it Yeti and Bigfoot.

Hereditary defects that prevent normal bone development during puberty allow growth to continue, resulting in gigantism. Why does the secretion of growth hormone decrease the capacity of the gonads? People affected by any category of gigantism have muscle weakness and vascular problems in the upper legs.

When the pituitary gland (which controls physical growth and development) is not functioning properly, the body experiences problems with growth. Depending on the hormones affected, these conditions can lead to changes in appearance or unrestricted growth.

- Larger than normal hands, feet, and lips
- Thick facial features

Excess growth hormone can also cause:

- Tingling or burning in the hands and feet
- Excess glucose in the blood
- High blood pressure
- Joint pain and swelling
- Excessive fatigue
- Regular headaches
- Vision problems
- Decreased sexual desire

The cause of increased growth hormone production is in 98% of the cases due to the presence of benign tumors in the Hypophyseal Gland, located in the brain. Prevention in these cases is done by routine examinations. It is not yet known what factors lead to the development of the tumor in the brain. Meanwhile, irreversible damage may be being done to the body.

In order for the disease to be detected, it is necessary to pay attention to the signs. The face and extremities acquire very specific characteristics over time. Performing routine examinations makes it possible to monitor the human body well. But at the same time it can be difficult for parents, because the condition does not cause other unusual signs. If the family is a tall family, this can simply be attributed to a growth spurt or genetic makeup.

Surgery becomes the indicated method, with a chance of cure of up to 90% when the tumors are up to 1 cm. When they are larger, the chance of cure drops to 50%. If after the surgery the hormonal indexes do not regularize, it is necessary to continue a complementary treatment with medication. There is radiotherapy, which is indicated in critical cases when the tumors cannot be removed surgically, or if surgery and clinical treatment do not yield satisfactory results.

# Causes

- Injury to the neighboring areas of the pituitary gland.
- When the gland does not develop properly before the child is born
- A mass or tumor that disrupts the way the pituitary gland works
- Radiation to treat a brain tumor or other category of brain cancer
- Inflammation of the pituitary gland
- Genetic diseases that interrupt the function or development of the pituitary gland
- Surgical interventions in the sensitive area of the gland that can cause a growth hormone deficiency
- Severe psychological stress
- Insufficient production of the releasing hormone
- Deficiency in the production of growth hormone by the pituitary gland.
- Defects or changes in the growth hormone receptor
- Lack of oxygen at birth
- Abnormalities in the growth hormone receptor
- Cases in which growth hormone deficiency is caused by an alteration in pituitary hormone deficiencies can lead to other disease processes.

# Signs and Symptoms

- Short stature with slow growth rate
- Thin hair
- Sharp voice
- Delayed development of bones and teeth
- Low blood sugar
- Lack of or delayed sexual development at puberty
- Headaches
- Excessive thirst
- Increased amount of urine
- Facial abnormalities (rare)
- Weight gain out of proportion to growth, resulting in relative obesity
- Reduced amount of muscle

# Diagnosis

Performed on the basis of a clinical evaluation with blood and radiological studies. Changes in synthesis or activity of the hormone can cause wide clinical variation.

In children with low concentrations, GH deficiency is usually confirmed by measuring GH concentrations. Because baseline GH concentrations are typically low or undetectable, random GH levels are not useful and GH assessment requires provocative testing. However, provocative tests are not physiological, are subject to laboratory error, and are poorly reproducible. In addition, the definition of a normal response varies by age, sex, and testing center and is based on limited evidence.

Imaging studies are done when growth is abnormal, bone age should be determined by an X-ray of the left hand. In GH deficiency, evaluation of the pituitary gland and hypothalamus with MRI is indicated to rule out tumors and structural abnormalities.

Unlike many endocrine deficiencies in which hormone levels are diagnostic, random GH levels are of little use in diagnosing growth hormone deficiency.

PROVOCATIVE TEST
Because GH responses are usually abnormal in patients with reduced thyroid or adrenal function, the provocative test should only be done in these patients after adequate hormone replacement.

Since no single test is 100% effective in causing GH release, two provocation tests should be performed. GH concentrations generally peak 30 to 90 minutes after insulin administration or the start of arginine infusion, 30 to 120 minutes after levodopa, 60 to 90 minutes after clonidine, and 120 to 180 minutes after glucagon.

Because GH levels increase during puberty, many children who fail provocative GH stimulation tests before puberty may have normal results after puberty or when primed with gonadal steroids.

Stimulus tests may miss discrete defects in the regulation of GH release. For example, in children with short stature secondary to GH secretory dysfunction, the stimulus test for GH release is usually normal. However, serial measurements of GH concentrations over 12 to 24 h indicate abnormally low integrated GH secretion over 12 to 24 h. However, this test is expensive and uncomfortable, so it is not the test of choice for GH deficiency.

If decreased GH release is confirmed, secretion tests of the other pituitary hormones and (if abnormal) peripheral endocrine gland hormones with pituitary imaging should be done, if not already done.

Diagnosis of growth hormone deficiency is done through blood tests, which measure hormone levels in the body, and imaging tests, such as x-ray and MRI, which assess the child's bone age and can show possible changes in the brain, for example, where the pituitary gland is located. It is also important to monitor the height through the growth pattern of children of the same age and sex.

PATIENTS WHO SHOULD UNDERGO EVALUATION

The diagnosis should be considered in individuals with evidence of disease, trauma and/or surgery in the hypothalamic-pituitary region, in patients undergoing cranial radiotherapy. In patients with microadenomas without evidence of other associated pituitary hormone deficiency and/or clinical suspicion of DGHA, evaluation for DGH may be waived.

The interaction between the somatotrophic axis and the other pituitary hormones has clinical and laboratory repercussions. Therefore, assessment of the normality of the other pituitary axes should be ascertained before the investigation of DGHA is initiated

STIMULATORY TESTING

The provocative test with GHRH and arginine is considered the alternative of choice. The cut-off values for the glucagon test have been validated, making it an additional option in diagnosis. The reliability of using arginine alone has been questioned, and clonidine is not recommended in the evaluation of adults. The use of other stimuli tests requires validation of the cut-off values.

Performing this test, which stimulates the hypothalamus and pituitary gland, may result false-negative for DGH. This also applies to patients undergoing radiation therapy, in whom the hypothalamic lesion precedes the pituitary lesion, which occurs later. In adults, the normative cut-off values of the peak GH response in stimulus tests depend on body mass index (BMI). Overweight or obese patients may have false-positive results for DGHA and lean patients false-negative results

# Prognosis

Untreated deficiency causes the child to become smaller than his or her parents. In addition, other organ functions can be impaired, and life expectancy reduced. If treated in time, normal height will be possible and most complications of the disease will be avoided.

In adults, therapy can significantly improve the quality of life of those affected.

Most patients develop normal hormone release. For this reason, the diagnosis Growth hormone deficiency

If there is a deficiency, and it goes untreated, the child's growth will be severely compromised. The greater the degree of deficiency, the lower the level of growth. On the other hand, if the deficiency of this hormone is treated at an early stage, it is likely that the child will be able to gain a few centimeters that will allow him/her to set the height level for his/her age

# Treatment

Replacement of the deficient hormone. However, the response to treatment is individual. The dose and duration of treatment should be individualized, according to tests and patient response. Hormone therapy generally responds best when started in pre-puberty.

The goal of treatment is to obtain the final stature, in the normal population, which consequently interferes with the self-esteem of the child or adult.

Treatment with recombinant GH is indicated for all children with short stature who have growth hormone deficiency as a result of pituitary radiotherapy for cancer has a risk of causing cancer recurrence. However, studies have not shown a higher than expected incidence of new cancers or a higher recurrence rate. GH replacement can be safely instituted at least 1 year after successful anticancer treatment has ended. Response to treatment is individualized.

It is controversial whether young children with clinical features of growth hormone deficiency should be treated with GH. Several experts recommend a trial of GH treatment for 6 to 12 months, only continuing it if there is a 3 cm/year increase in pre-treatment growth velocity.

DOSE

Starting treatment with a fixed low dose depending on the clinical and laboratory response has similar benefits, with fewer side effects. Although some studies recommend replacement on alternate days or for only five to six days a week, the consensus recommends daily administration subcutaneously at night, seeking to mimic physiological GH secretion.

CLINICAL EFFICACY PARAMETERS

The response to clinical treatment also varies depending on the timing of the onset of the deficiency, the degree of GH deficiency on the stimulus test, and the presence of other pituitary deficiencies, for example. Patients with craniopharyngioma respond well to GH replacement treatment in lean mass and quality of life. Clinical efficacy parameters include assessment of body composition, bone density, cardiac performance, cardiovascular risk factors, and quality of life. Most patients report benefits after three months of treatment.

BODY COMPOSITION

The evaluation of body composition confirms that in GH there is an increase in total body fat with a predominance of fat in the trunk, a decrease in lean mass, muscle strength, and total body water. The fat mass in these patients is 6.5 kg higher than that observed in normal adult controls matched for sex and age, representing 8% excess.

CARDIAC PERFORMANCE AND RISK FACTORS

A statistical technique suitable for combining results from different studies, evaluated 16 clinical trials involving 468 patients, on the effects of GH replacement on cardiac parameters using Doppler echocardiography. Overall, in half of the studies there is improvement and in half there is no difference in these risk factors. In order to replace the lack of the hormone, injection in its synthetic version can help the changes caused, done daily with applications under the skin. As a result, some patients can benefit from this replacement throughout their lives. In some cases, surgery may be necessary. This is when brain tumors are responsible.

# Use of Medications

Somatropin is used to treat growth hormone deficiency in children and adults who lack natural growth hormone. This includes people with short stature due to Noonan syndrome, Turner syndrome, Prader-Willi syndrome, or short stature at birth without growth recovery.

POSSIBLE SIDE EFFECTS

- Headache
- Muscle pain
- Pain at the injection site
- Weakness and stiffness of the hands or feet
- Fluid retention.
- Increased insulin resistance, leading to diabetes with increased blood glucose and glucose in the urine.

WHO SHOULD NOT USE

People with:

- Hypersensitivity to Somatropin or any component of the product formula.
- People with diabetes mellitus
- Carriers of malignant tumors.
- Short stature due to a brain tumor that may cause hypopituitarism and low secretion of growth hormone.
- Patients with critical illnesses due to complications caused by abdominal or cardiac surgeries or accidental trauma.
- Pregnant women without medical advice.

HOW TO USE SOMATROPIN?

It can be applied to the skin or muscles as directed by your doctor. The dose and administration schedule are individual for each patient and established by the doctor. The injection site should vary and the same site should not be repeated at short intervals.

The weekly dose should be divided into 3 or more injections. It is important to change sites between each injection to avoid injection site reactions such as redness or swelling.

In general, children with disabilities, the recommended dosage is 0.5-0.6 IU (0.17- 0.21 mg) /kg body weight per week or 12 IU/m2 per week. The weekly dose should be divided into 3 to 6 injections under the skin.

SIDE EFFECTS AND REACTIONS

Side effects were observed in about 10% of the short children who participated in the clinical studies. In adults, side effects were observed in 30-40% of patients. These events appeared after the start of treatment and their frequency of appearance decreased as treatment time increased, rarely influencing daily activities. Reports of patients who may develop hypothyroidism during treatment with Somatropin should be considered.

- COMMON REACTIONS

The effect with the use of Somatropin has been related to fluid retention and stiffness of extremities. In general, these effects are mild to moderate in severity, appearing during the first few months of treatment and diminishing spontaneously or with dose reduction.
The incidence of these effects is related to the dose administered, patient age, and inversely related to the age of the patient at the onset of growth hormone deficiency.

- UNCOMMON REACTIONS

Pain at the site of application of Somatropin has been reported to be uncommon.

- RARE REACTIONS

Rare cases of benign intracranial hypertension and type 2 diabetes mellitus have been reported, as well as

1. Headache
2. Arthralgia
3. Nausea

- VERY RARE REACTIONS

Very rare cases of peripheral edema (accumulation of fluid that causes swelling), development of cases of hyperthyroidism during treatment, muscle pain, weakness, hyperglycemia, leukemia, abdominal pain, fever, increased development of breast cancer have been reported.

OVERDOSAGE

Acute overdose could result in hypoglycemia and hyperglycemia. It may be accompanied by tremors or muscle tremors, cold sweats, increased hunger, headaches, dizziness, weakness, tachycardia, and nausea. In the long term, it can result in acromegaly.

INTERACTION WITH OTHER DRUGS

Because the hormone can induce a state of insulin resistance, patients should be observed for evidence of diabetes or glucose intolerance. Patients with pre-existing diabetes or glucose intolerance should be monitored during Somatropin therapy.

CARE

- Patients with cardiac and renal disease should be monitored
- Patients with maturity diabetes with onset in youth or a family history of Diabetes Mellitus.

HYPOTHYROIDISM CAN INHIBIT THE EFFECT

Patients with hypothyroidism should be examined frequently and should have their thyroid functionality tested and treated with thyroid hormone. Hypothyroidism may occur during treatment with growth hormone, making it necessary when there are symptoms that lead to this suspicion.

HOW IT WORKS

It resembles the natural hormone. It stimulates skeletal growth, increases the size and number of muscle cells, and reduces fat stores. It decreases insulin sensitivity, influencing carbohydrate metabolism. It also increases red blood cells through stimulation of erythropoietin.

RISKS VS. BENEFITS

- Diabetes Mellitus (insulin resistance may occur; may need to adjust insulin doses);
- Untreated hypothyroidism (interferes with response; treat hypothyroidism before or simultaneously)
- Psoriasis
- Headache
- Weakness
- Muscle pain
- Pain at the injection site
- Slight increase in blood glucose
- Slight swelling
- Presence of glucose in urine
- Development of antibodies

IMPORTANT CONSIDERATIONS

- Vary the site of application to avoid occurrence of local reaction.
- The product must be used for long-term treatment.

DRUGS WITH SOMATROPIN IN ITS COMPOSITION

- Biomatropin
- Genotropin
- Hormotropin
- Humatrope
- Norditropin Simplex
- Saizen
- Somatropin


The Ministry of Health has been working to increase access to medicines and health products considered strategic for SUS by strengthening the country's industrial complex. To this end, it has established in Brazil, Partnerships for Productive Development, which are carried out between public and private national institutions in order to transfer technology of drugs, previously imported, to finally become national production.

This policy, in addition to expanding access to SUS, means a series of advantages for the health of Brazilians and for the country's economic scenario. From the partnership between Bio-Manguinhos/Fiocruz and Laboratório Cristália, the first genuinely Brazilian biological product was born. It is Somatropina Criscy, Recombinant Growth Hormone, which will very soon be distributed, via the Ministry of Health, to SUS units all over Brazil.

From the initial research to the pivotal phase III study, it was conducted according to the strictest international development standards, and received registration from ANVISA in May 2019.

The final study had Pfizer Laboratory's original product (Genotropin) as comparator and also had an extension study that proved its interchangeability with the reference, this one in final phase for publication.

Somatropin will be distributed in SUS by centralized acquisition by the Ministry of Health, which thus unifies the standardization of the Bio-Manguinhos / Fiocruz / Cristália PDP product throughout the country, in the presentations of 4 IU and 12 IU, in vials with lymphatic powder, whose dilution requires 1 mL of diluent. Please note that some State Health Departments may have in their stocks presentations from another laboratory, whose dilution requires 2 mL of diluent.

Thus, it is essential that the physician be aware of the correct reconstitution of the product being distributed, for proper guidance of their patients, avoiding overdose of the drug.

The launching ensures access to a quality product for the population, reducing the cost to the health system and guaranteeing Brazilian autonomy for the hormone, since its production is entirely national.

# Possible Complications

The deficiency can be congenital, that is, the child is born with this alteration, or develop after birth due to other health problems that affect the pituitary gland, such as infections and tumors.

Treatment with somatotropin can allow children to reach normal height. In adult patients, therapy can relieve symptoms such as increased fat accumulation in the abdomen, decreased performance, and decreased bone density.

In some cases, the treatment may have other effects. Local reactions such as tingling and redness at the injection site, headache, convulsions, generalized pain, and bronchial asthma may occur. In patients with cancer, growth hormone therapy can cause another tumor

Generally, significant side effects are rare with artificial hormone therapy. However, the treatment should be closely checked at least every two months.

# Quality of Life

The compromised quality of life of patients has been observed in reports of patients with hypopituitarism without GH replacement. In the last decade, studies comparing healthy adult individuals with patients with the deficiency have shown compromised physical disposition, sleep quality, irritability, fatigue, lack of initiative, concentration and memorization difficulties, and difficulty socializing.

Through validated methods for depression, patients have been observed to have depressive symptoms, which improve with GH replacement. The criticism is that they may not detect specific changes in quality of life. Thus, the quality of life assessment of gh deficiency in adults, a specific questionnaire recently developed for the disabled, was validated.

For some authors, the improvement in quality of life is the main parameter, both for indication and goal to be achieved in the treatment.

GH replacement, even at low doses, leads to an improvement in the psychological well-being of these patients. The mechanisms responsible for this improvement remain unknown. Contributing factors include improved body composition, exercise capacity, metabolic changes, and the central effect of GH.

Thus, replacement for at least six months is recommended before a new evaluation is performed. Psychological improvement is maintained with long-term treatment, as observed in ten-year follow-up studies of patients.

# Organizations

The Human Growth Foundation is a non-profit organization that provides support for people with growth disorders. It is funded primarily by Genentech and Caremark. In 1994, it published a study that concluded that 20,000 children needed human growth hormone because of their growth deficiencies.

The MAGIC Foundation is a non-profit organization that provides support for people with conditions and diseases that affect child growth. It helps families of children diagnosed with a wide variety of growth-impacting medical conditions through education, networking, medical referrals, and various other services. It was founded in 1989. It is maintained by a network of volunteers and a full-time staff of five. Its services include public education and awareness, quarterly newsletters, national networking, an annual convention, disorder-specific brochures, and a Children's program. The foundation has a membership network of more than 25,000 families. The disorders that MAGIC families have are grouped into primary categories. They include: congenital adrenal hyperplasia, precocious puberty, growth hormone deficiency, pan-hypopituitarism, McCune-Albright syndrome, Turner syndrome, Russell-Silver syndrome, thyroid disorders, optic nerve hypoplasia, and other rare diseases.

The National Institutes of Health is the medical research organization of the United States. They maintain accurate and up-to-date information on various health topics forming the government biomedical research agency of the U.S. Department of Health and Human Services, headquartered in Bethesda, Maryland. It is the largest biomedical research center in the world, with about twenty thousand employees.

# Curiosities

The growth hormone not only acts in the physical growth of the human body, it also participates in the regulation of the metabolism, influencing important aspects for the development of a healthy life, and for this reason, its presence needs to be constant.

An important study published in The Journal of Clinical Endocrinology & Metabolism identified that the replacement of GH in individuals who presented GH deficiency was able to reverse the progression of atherosclerosis, the accumulation of fatty plaques on the artery walls. Other publications have also demonstrated that its replacement improves cardiac performance, strength, muscle mass, skin health, mood, immune protection, and even sexual functions in patients.

To evaluate the rate of development, doctors use the speed of growth. For this it is necessary to have at least two measurements of height and a time interval between them. In the first months of life the measurements can be monthly, but then every three or four months. During the first two years of life, the child grows about 25 cm, with a deceleration of the growth speed, but at puberty it accelerates again. The follow-up with the pediatrician is fundamental to detect any alteration in the speed of growth, and thus allow the early diagnosis of diseases that affect growth. When growth is slower than expected, the ideal is to consult a specialist. The sooner the problem is detected, the better the chances of recovery.

One of the ways to identify growth problems is to observe that the child is taking a long time to change the size of his clothes and shoes, or when he becomes the smallest in the school class. These are important signs that should encourage parents to see an endocrinologist.

Children must be measured, and the weight and height data must be put on charts to be interpreted in the right way. Only then is it possible to compare the child's measurements with those of other children of the same age and sex, and also with the height of the parents.

Growth occurs until the growth of cartilages close, which is a special region of the bones. The time at which growth stops will depend very much on the age at which puberty begins and at which puberty ends. Once the cartilages of the long bones have closed, there is no possibility to grow anymore, even by taking GH. In this case, besides not growing, the use of GH is not safe and can be harmful to health.

Adults with GH deficiency can take the growth hormone replacement. In these cases the GH treatment produces other health benefits, such as improved physical capacity, increased lean body mass, reduced body fat and improved quality of life. Because of these benefits, some people use GH to treat obesity, reduce the aging process, and improve physical performance. The medication is contraindicated for these purposes because it is not considered safe. In sports, its use is considered illegal and punishable.

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