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Growth Hormone Therapy

Growth hormone (somatotropin), a principal stimulator of body growth, is produced by the pituitary (or master) gland, a small glandular structure located at the base of the brain. Insufficient production of growth hormone in children causes slow growth. Because growth hormone deficiency produces striking effects in children, it has been a recognized condition for many years. We usually associate the term growth hormone deficiency with children and with the process of statural growth. Growth hormone, however, is also secreted in adult life, and adults need GH to maintain health. Adults who produce insufficient growth hormone can be called as having adult growth hormone deficiency.

Causes of Growth Hormone Deficiency

Growth hormone deficiency in some adults is due to the continuation of a process that began in infancy or childhood, or it may occur during adulthood. The most common form of growth hormone deficiency beginning early in life is termed "idiopathic", meaning that the cause is not known. Known causes beginning in childhood include developmental defects in the region of the pituitary gland, genetic abnormalities with the production of growth hormone, damage to the pituitary area resulting from tumor, surgery, irradiation, etc. The most common causes of adult-onset growth hormone deficiency are tumors in and around the pituitary gland and hypothalamus. Such tumors may compress and damage the remaining pituitary gland, and growth hormone deficiency may follow after surgery is performed to remove the tumor. Other causes of damage to the pituitary gland in adults include brain irradiation, infection, bleeding in the skull base, bleeding into the tumor and head injury.

The Adult Who Was Growth Hormone Deficiency During Childhood

In the many decades that growth hormone has been used as treatment, the emphasis has been on treating the short stature in GH deficient children. For the most part, these patients have been led to believe that the only purpose of growth hormone therapy was to promote growth so that they would achieve an acceptable adult height and that therapy would not be needed once their final adult height is reached. Experience, however, has led to the conclusion that a substantial number of adults who were GH-deficient during childhood need to continue GH therapy in adult life due to persistence of growth hormone deficiency.

Several findings have led to this conclusion:

- When growth hormone deficiency therapy is stopped, the young GH-deficient adult tends to gain weight and become relatively obese. This excess of body fat tends to accumulate around the abdomen.
- This relative deficiency of muscle mass results in diminished strength and physical performance, changes that may be manifested as decreased ability to perform tasks such as lifting heavy loads or to sustain physical tasks for long periods of time. Adults with growth hormone deficiency have impaired ability to consume oxygen and expend their body energy, both at rest and at work.
- Adults with growth hormone deficiency also may have lower mineral content in their bones, predisposing them to osteoporosis and fractures in their later years in adulthood. All of us lose bone mineral and have increased tendency to fracture our bones as we age, but this natural process may be

accelerated with GHD. Additionally, if the growth hormone deficient adult had insufficient growth hormone during childhood when bones normally accumulate mineral, he/she is likely to begin adult life with low bone mineral content. This, superimposed on the loss of mineral during adulthood, eventually results in lower-than-normal bone mineral content and a greater predisposition to fractures.

- Blood lipid profiles in adults with growth hormone deficiency are such that they are likely to be predisposed to develop atherosclerosis in later years of adulthood. Their blood levels of total cholesterol, low-density lipoprotein cholesterol, and triglycerides are higher than individuals who have normal growth hormone secretion, suggesting that these findings are significant in contributing to the shorter lifespan seen in adults with hypopituitarism (growth hormone deficiency associated with deficiencies of other pituitary hormones). This is because, despite treatment of the thyroid, adrenal and gonadal hormones, the excess death rate is due mainly to cardiovascular problems.
- Young adults who were growth hormone deficient during childhood may have signs and symptoms of impaired physical and psychological well-being. These include feelings of depressed mood, emotional instability, social isolation, anxiety, low self-esteem and reduced vitality.

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Treatment of the Growth Hormone Deficient Adult Who Had Growth Hormone Deficiency in Childhood

Although children who have growth hormone deficiency may continue to be growth hormone deficient in adulthood, the capacity of some patients to secrete growth hormone improves over time. Some patients, therefore, will not need growth hormone therapy in adult life. This is why it is very important that as each GH-deficient child that reaches adulthood, growth hormone treatment should be stopped for at least 1 month and re-testing with a GH stimulation test should be performed to determine the need for continuing therapy in adulthood. The extent and nature of testing needed for this purpose will vary from one patient to another. During this time, the patient may switch over from seeing a pediatrician to seeing an adult endocrinologist. This time is crucial for the pediatrician to prepare the patient to transition over his/her care to an adult endocrinologist.

If treatment is needed in a patient with persistent GH deficiency in adulthood, a variety of beneficial effects can be anticipated:

Effects on Body Composition and Bone Mineral Content

Growth hormone therapy may decrease body fat, with the greatest reduction occurring in the abdomen. Concurrently, the reduced lean tissue mass is increased by treatment with growth hormone. This change is reflected in large part by improvement in muscle mass. The improvement in body composition may help in reducing the risk of developing future diabetes. Although improvements in bone mineral density would be an anticipated effect of growth hormone replacement therapy, systematic studies have not shown that this occurs. This may be because bone changes can take a long time to detect. Therefore, longer periods of observation are needed to assess changes in bone mineral density.

Effects on Physical Performance

Growth hormone therapy in adults has been shown to improve exercise performance, oxygen consumption and cardiac output that is likely to be due to its direct beneficial effects on skeletal and heart muscle.

Effects on Blood Lipids

Growth hormone therapy has been shown to improve blood lipid profile, especially when combined with a statin. Specifically, total cholesterol and low density (bad cholesterol) lipoprotein cholesterol are reduced. The extent to which these changes decrease the development of future atherosclerosis are not yet known.

Effects on Psychological Well-Being

One of the striking effects of growth hormone therapy in adults with growth hormone deficiency is the improvement in psychological well-being reported by these patients. Some, but not all, patients experience an improvement in their psychological well-being. Improvements in mood and in the level of perceived psychological distress has also been documented.

Other Considerations

Treatment with growth hormone requires that the hormone be injected daily into the fat tissue beneath the skin usually at bedtime. This is made relatively simple by the need for small volumes of growth hormone and the availability of fine, small-bore needles with a pen device. Over the years, research studies have shown that growth hormone therapy is relatively safe. Growth hormone therapy in adults, especially in low doses, has uncovered few adverse effects of the hormone. In adults who are treated with high doses of growth hormone, edema (collection of fluid in tissue) and discomfort in the joints are sometimes observed. Decreasing the dosage temporarily can relieve these. Because growth hormone antagonizes the action of insulin, high growth

hormone doses can raise blood glucose levels. This has not proven to be a significant problem in adults particularly if blood glucose levels are monitored and lower growth hormone doses are used. Because growth hormone can cause tumors to grow, this raises the concern that long-term growth hormone treatment might promote the development of tumor growth. These concerns, however, have been unfounded as long-term follow-up studies in adults with growth hormone deficiency have not shown this to be the case.

Summary

- Adults still produce and need growth hormone. It is just that they do not need as much growth hormone as children.
- Adults who are deficient in growth hormone accumulate excess fat centrally, have decreased lean tissue, have lower bone mineral content, have an unfavorable blood lipid and glucose profile, and experience undesirable psychological effects.
- Treatment with growth hormone reverses/attenuates many of the effects of growth hormone deficiency, and may lead to better physical performance and a healthier psychological status.
- Use of growth hormone in adults and children for over 20 and 40 years, respectively, indicate that it has a high degree of safety.

The Transition from Child to Adult with Growth Hormone Deficiency



Patient Information

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