HORMONES AND ME

GROWTH HORMONE DEFICIENCY IN ADULTS

SERONO SYMPOSIA AUSTRALASIA

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Australasian Paediatric Endocrine Group

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About this Book

Growth Hormone Deficiency in Adults is intended to provide adults who have growth hormone deficiency with information about their condition and the potential benefits of treatment with growth hormone. Growth hormone deficiency in adults is one of the areas where growth hormone replacement therapy is being shown to be of benefit. There are now a number of medical reasons to suggest that growth hormone treatment should be continued into adult life in certain individuals. The reader is encouraged to discuss any additional questions or areas of concern with the doctor after reading this booklet.

Serono Symposia Australasia is pleased to bring you ***Growth Hormone Deficiency in Adults***, which is part of their "Hormones and Me" educational booklet series. We hope that you will find it a valuable and helpful resource.

We wish to express our gratitude to Serono Laboratories (UK) Ltd and the Child Growth Foundation for allowing the distribution of this booklet, which was updated and reproduced for Australian and New Zealand readers in 2000. Special thanks to the original authors and editors, Dr Richard Stanhope (Great Ormond Street Hospital for Children and the Middlesex Hospital, UK), Professor Peter Sonksen (St Thomas's Hospital, UK), Mrs Vreli Fry (Child Growth Foundation, UK) and the British Society of Paediatric Endocrinology (BSPE).

This booklet was reviewed and edited with the help of Associate Professor Ross Cuneo (Princess Alexandra Hospital, Brisbane, Australia) - an Endocrinologist specialising in metabolic disorders.

Dr Margaret Zacharin, a Paediatric Endocrinologist (Royal Children's Hospital, VIC, Australia) has reviewed the booklet range on behalf of the Australasian Paediatric Endocrine Group (APEG).

Introduction

In normal individuals, levels of growth hormone are relatively high during childhood and reach a peak during the adolescent growth spurt. They progressively decrease to quite low levels during adult life. It is becoming increasingly evident that even low levels of growth hormone may play an important role in maintaining the body's normal functions during adulthood. This booklet will discuss the functions of growth hormone and the benefits growth hormone treatment offers in growth hormone deficient adults.

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This booklet is intended to provide information for adults with growth hormone deficiency who:

- received growth hormone treatment in childhood for improving growth but ceased treatment when growth stopped; or
- developed growth hormone deficiency during their adult life as a result of various medical conditions.

All adult patients who are to be considered for growth hormone treatment should be tested for their growth hormone production regardless of whether they have received growth hormone during childhood. Studies have shown that a number of children who were diagnosed with growth hormone deficiency during childhood have relatively normal levels when retested as young adults. In addition, there are many children who are not growth hormone deficient but who received growth hormone treatment during childhood to help them grow as a result of other medical conditions (e.g. girls who have Turner Syndrome). As these individuals have relatively normal growth hormone levels, once they have stopped growing there is no need for further growth hormone treatment.

Currently, growth hormone has been approved as an indication for treatment of adults but to date no financial support is available in Australia or New Zealand. Anybody who believes that growth hormone treatment will help them in adulthood, should discuss this with an endocrinologist.

Growth Hormone and its Functions

Hormones are chemicals produced by the body, which carry messages from one cell to another in the bloodstream. Growth hormone promotes the growth of bones, tissues and organs. Another name for growth hormone is somatropin.

Growth hormone is secreted by the pituitary gland, a small pea-sized gland at the base of the brain. The hypothalamus (a part of the brain that directs the pituitary gland) controls the secretion of this hormone and other hormones by triggering the pituitary gland into producing the required hormones. Growth hormone deficiency occurs when the pituitary gland fails to produce adequate levels of growth hormone. This may be the result of problems in the hypothalamus, with the link to the pituitary gland, or with the pituitary gland itself (see Diagram 1).

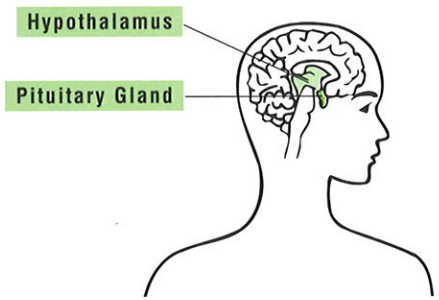

Diagram 1

One of the main functions of growth hormone is to stimulate growth in children. Growth hormone however, also has other

functions, which are important during childhood and adulthood. Growth hormone maintains normal levels of sugar in the blood. This is important during everyday life, especially during periods of prolonged fasting (e.g. severe dieting or religious practices) or after the consumption of alcohol. Growth hormone also has effects on the metabolism of sugar, fats and protein and is important in the building up of tissues in the body, including muscle and bone. Growth hormone also supports the immune system, helps the body to fight infection and helps the kidney to control salt and water balances.

Causes of Growth Hormone Deficiency

In early childhood, growth hormone deficiency may occur if the pituitary gland stops working properly and does not produce adequate levels of growth hormone and the other pituitary hormones. In this age group, the reason the pituitary gland stops working is usually unknown or may relate to a genetic disorder, with a very small or absent pituitary gland.

In older children, growth hormone deficiency may result from irradiation therapy for leukaemia, or from damage by a tumor in or near the pituitary gland. In these children, the irradiation treatment may damage the hypothalamus and the pituitary gland, which affects growth hormone production and secretion.

Growth hormone deficiency from either of these causes will continue into adolescence and adulthood.

In adults, growth hormone deficiency may be caused by tumours in or around the pituitary gland, either as a direct effect of the tumour itself or resulting from surgery and / or radiotherapy used in the treatment of the tumour. Production of other hormones by the pituitary gland may also be affected.

Symptoms of Growth Hormone Deficiency in Adults

Many of the symptoms of growth hormone deficiency in adulthood are subtle or not specific enough to be easily recognised by the doctor or specialist.

The symptoms of growth hormone deficiency are similar in patients who developed this problem during adulthood or during childhood. In the latter, there may be the additional problem of short stature. Growth hormone deficiency (and growth hormone treatment) in adults does not affect stature.

Symptoms of growth hormone deficiency in adults may include poor muscle strength and difficulty in carrying out normal physical activities. Many young adults with growth hormone deficiency are frequently aware of a general lack of energy and vitality. These problems can affect academic performance and subsequent qualifications, or create problems with careers and work prospects. If an adult with growth hormone deficiency is experiencing these problems, they are described as having Adult Growth Hormone Deficiency Syndrome.

"Symptoms of growth hormone deficiency in adults may include poor muscle strength and difficulty in carrying out normal physical activities."

An improvement in general health and quality of life may only become apparent if growth hormone deficiency syndrome is suspected and a trial of replacement hormone therapy given.

It is important to emphasise that not all young adults with growth hormone deficiency experience these problems but for those who do, we hope this booklet will provide help in explaining the condition and the possible benefits treatment with growth hormone may offer.

The deficiency of other hormones may exaggerate some or all of the symptoms and the need for appropriate hormone replacement therapy should be evaluated by an endocrinologist before the value of growth hormone treatment can be assessed.

It must be emphasised that this is an area of active research. A considerable amount of information has already been gained but medical knowledge is constantly being updated. An endocrinologist can provide advice about any new information.

Benefits of Growth Hormone Treatment in Adults

Currently, growth hormone has been approved as an indication for treatment of adults but to date no financial support is available in Australia or New Zealand. Active measures are underway to ensure that patients who will benefit from growth hormone treatment have access to this medication. Any adult with suspected growth hormone deficiency should consult their general practitioner and / or endocrinologist to discuss whether they may benefit from growth hormone therapy.

"Currently, growth hormone has been approved as an indication for treatment of adults but to date no financial support is available in Australia or New Zealand."

It is very important to appreciate that an adult with growth hormone deficiency, may not be fully aware of the psychological impact of this condition until after starting growth hormone replacement therapy. These people may then realise that how they felt before was not 'normal'.

Some of the benefits of growth hormone treatment in adults are listed on the following pages.

1. Quality of Life & General Well-Being

The results of questionnaires, which measure 'perceived ill health' and quality of life have shown that adults with growth hormone deficiency have more than the usual number of symptoms of a poor quality of life including:

- reduced energy and vitality
- poor general health
- impaired ability to cope
- disturbed emotional reactions
- increased anxiety

These symptoms can often lead to a lack of positive well-being, depressed mood and feelings of social isolation. It has been shown that these symptoms can improve or even disappear during growth hormone treatment.

2. Hypoglycaemia (low blood sugar)

In children and adults who are growth hormone deficient and are not receiving growth hormone treatment, symptoms of hypoglycaemia may be experienced if there has been insufficient food intake. Irritability is most often noticed. This usually disappears after eating. Excessive sweating at night and waking up with a headache may also be symptoms. Hypoglycaemia can be a serious condition and the doctor should be informed if a person is experiencing any of these symptoms.

It is important that adolescents with growth hormone deficiency are counselled about excessive alcohol consumption as alcohol reduces blood sugar, which may lead to severe hypoglyceaemia. Alcohol lowers the blood sugar levels very quickly and in some individuals a bad 'hangover' may be felt after only one glass of wine!

Growth hormone is important in preventing the occurrence of low blood sugar if food is not taken regularly. This may be of importance in religious customs where food intake is particularly restricted. Growth hormone also helps control the accumulation of fat so weight gain can be a frequent problem for individuals with growth hormone deficiency. Slimming is difficult and in most cases unsuccessful, as patients with growth hormone deficiency must not have prolonged periods of fasting. The doctor can offer advice on how to avoid low blood sugar levels occurring during the night and early in the morning when there has been a relatively long period without food. Hypoglycaemia, however is a less frequent problem in adults with growth hormone deficiency than it is in childhood.

"Growth hormone is important in preventing the occurrence of low blood sugar if food is not taken regularly."

During growth hormone treatment, control of blood sugar levels generally improves, fat distribution alters and weight control becomes considerably easier and alcohol is better tolerated in normal amounts.

Occasionally adults who have been growth hormone deficient all their lives, may continue to experience episodes of severe hypoglycaemia particularly during periods of stress such as acute illness. They may lose consciousness or have a fit if this is not recognized. This is a particular problem if growth hormone has been stopped at the end of linear growth.

3. Bone Quality

Growth hormone is important for building up the strength of bones. Adults with growth hormone deficiency may develop osteoporosis (thin or brittle

bones). Osteoporosis may develop into a painful and disabling condition and the prevention of this condition may be one of the most important reasons for continuing growth hormone therapy into adult life. Current research suggests that growth hormone deficiency results in a moderate reduction in bone density in adults and that growth hormone replacement therapy for a number of years results in a progressive improvement in bone density.

4. Muscle Strength & Energy

It has been well documented that adults with growth hormone deficiency have reduced muscle size, strength and performance. These problems can often be overcome with growth hormone replacement therapy. While the improvement in muscle strength following short-term growth hormone treatment may not be noticeable to some patients, the improvement in exercise performance can be quite significant. People can perform activities such as walking up stairs much easier than before starting growth hormone treatment.

5. Cardiovascular Disease

Adults with growth hormone deficiency may have a higher risk of illness from heart disease and it is possible that long-term treatment with growth hormone will decrease this risk.

6. Blood Cholesterol

Treatment with growth hormone has been shown to lower the level of cholesterol in the blood. This may be of benefit to growth hormone deficient adults who have an increased number of the risk factors for cardiovascular disease including increased weight gain and high cholesterol levels.

7. Psychological Problems

Children with growth hormone deficiency may have emotional problems during childhood and adulthood. Some of these problems are associated with coping with their short stature and its effect on self-esteem, potential achievement and physical and emotional immaturity.

Growth hormone deficiency in adults is also associated with a high incidence of psychological problems, particularly anxiety, depression and lack of motivation. There is evidence that this is different to normally accepted clinical depression as it appears that the physical deficiency of growth hormone is contributory. This is supported by the often remarkable change in outlook seen in some growth hormone deficient adults once they have started growth hormone replacement therapy. A large Australian study confirms the findings that growth hormone replacement therapy improves the psychological outlook of many patients.

As growth hormone treatment may reduce many of the psychological problems associated with adult growth hormone deficiency syndrome, it is important that these adults discuss their feelings and concerns about quality of life with the specialist so that a psychological assessment can be arranged if needed.

8. Premature Ageing

It has been proposed that one of the reasons physical signs of normal ageing occurs is related to the decrease of growth hormone secretion with age. Some preliminary research has suggested that growth hormone treatment may reverse some of these changes, however, much more information is needed before any recommendations can be made.

Diagnosis of Growth Hormone Deficiency in Adults

If an adult or his / her doctor suspects a diagnosis of growth hormone deficiency, it will need to be confirmed with blood tests. Currently the most accepted test is the insulin tolerance test (ITT). Insulin is given to briefly lower blood sugar level, which should trigger the release of growth hormone from the pituitary gland. Adults with growth hormone deficiency will not produce increased levels of growth hormone in response to this test. There are alternative tests which stimulate the release of growth hormone that may be preferred by the specialist. In addition to testing for growth hormone deficiency, some tests also indicate if any other pituitary hormones are also deficient.

"Currently the most accepted test is the insulin tolerance test (ITT)."

Treatment of Growth Hormone Deficiency in Adults

If an adult has been diagnosed with growth hormone deficiency and it is believed that he or she may benefit from growth hormone replacement therapy, this needs to be discussed with a specialist familiar with these problems to assess the person's individual needs. Although treatment with growth hormone has been shown to be beneficial in many adults with growth hormone deficiency, some do not experience any problems and therefore do not need treatment.

The general practitioner can usually recommend specialists who have knowledge and experience treating growth hormone deficiency in adults. If there are difficulties in finding a specialist, the Endocrine Society of Australia may also be able to offer recommendations.

Doses of Growth Hormone Given

The specialist will determine the dose of growth hormone to be administered. The dose will be based on the person's body size and may be increased or decreased at follow-up clinic visits depending on how well the first dose is tolerated. The dose will vary between individuals and is different between men and women. If a person received growth hormone as a child, the dose used in adulthood will be lower because it is being used for different reasons and not to promote growth. Minor side effects such as fluid retention (with

swelling of the ankles) and occasionally raised blood pressure have been reported in some adults given a dose similar to that given to children. A slight reduction in the dose will relieve these symptoms.

Administration

Growth hormone is given daily by an injection just under the skin (subcutaneous). The injections hold a very small volume of fluid and are best injected in the thighs, upper arms or abdomen. The needles used for the injections are very small (about 1cm long) and fine. They are similar to those used by diabetics. For people who are nervous about injections there is a device available, which hides the needle and delivers the dose automatically. There are a number of injection devices including autoinjectors and pens which may be helpful in giving these injections. Please discuss the options available with the doctor.

Monitoring

Whilst receiving growth hormone treatment, regular visits with the doctor are required to check blood pressure, blood glucose levels and for the occurrence of any side effects. In addition, the doctor may wish to check levels of insulin-like growth factor 1 (IGF-1) to assist in fine-tuning the dose of growth hormone.

Further research is required as there are several unanswered questions about growth hormone treatment in adults and these include:

- identification of patients in whom growth hormone treatment would be beneficial
- how long treatment should be continued
- the dose required for the best results

Questions and Answers

Q *Are there any side effects to growth hormone treatment?*

A This is a replacement hormone therapy (replacing a substance which the body would normally make) and therefore very few side effects are expected. In adults with growth hormone deficiency, growth hormone replacement may initially cause fluid retention, with swelling of the ankles, and arthralgia or aching in some of the small joints (particularly in the wrists and hands) if the dose is too high. This is the reason why relatively low doses are used in adults compared to those used in children. The specialist should monitor this closely and make any necessary dose adjustments. Thus any side effects are usually temporary, dose related and often avoidable. The doctor will carefully monitor blood pressure and blood glucose levels, particularly if there is a family history of hypertension or diabetes.

Q *Is there any method of giving growth hormone except by injection?*

A No; growth hormone is a protein and if given by mouth it would be destroyed in the stomach, therefore it has to be injected. For those experiencing problems with ordinary needles and syringes there are injection devices which can make the process less stressful. These devices can be shown to you by the specialist.

Q *Will growth hormone make an adult feel younger?*

A It has been suggested that one of the reasons physical changes of ageing occurs is due to the gradual decrease in growth hormone secretion with age. Very limited short-term studies have shown that some of the ageing processes may be slowed or even reversed with growth hormone treatment. It is important however, to remember that an increased level of energy and vitality will make a person feel younger.

Q *Will growth hormone help lose weight?*

A Growth hormone treatment itself will not result in weight loss. It will however, alter the distribution of body fat around the body and it will noticeably reduce the fat in the abdominal area (there is commonly a reduction in waist measurements!). This should give a person a greater control over their weight, particularly if they follow a calorie-controlled diet. Other replacement hormones (cortisol, testosterone, oestrogen, or thyroxine) may also affect weight.

Q *Can an adult with growth hormone deficiency drink alcohol?*

A Yes, providing it is sensible amounts. The recommended 'maximum safe' alcohol intake is 4 standard drinks daily for men and 2 for women with at least two alcohol free days per week. One standard drink contains 10g of alcohol, e.g. a nip of spirits, a small glass of wine, a glass (285mL) of regular beer. If excessive alcohol is consumed it can cause hypoglycaemia and in growth hormone deficient individuals this is an extremely dangerous situation as unconsciousness may result.

Q *Will growth hormone make adults grow?*

A Not if the person has already completed puberty and is physically mature. However, if the person is in his / her early twenties and in very exceptional circumstances, it may be possible to achieve some extra growth. The specialist will discuss this.

Q *Will growth hormone treatment in adults give them more vitality?*

A This may indeed happen. It is important however, that any other hormone deficiencies are properly replaced before starting growth hormone treatment, as these too can affect how a person feels, including their 'get up and go'.

A Patient's Story

How it feels to be a Growth Hormone Deficient Adult

I was given growth hormone for growth as a child and then spent 10 years without it before taking part in a clinical trial last year. I would like to describe here how I felt in the 3 months after the trial before I started GH long-term.

The GHD feeling is not an easy one to describe. Indeed, for the decade that I was off GH, I was not only unaware that my lack of energy was due to a hormone deficiency, I was not even aware that I did lack energy. I thought this was the way everybody felt.

GHD produces a physical feeling in me of being completely drained, that spills over into the mood of apathy and resignation. I feel the tiredness most in my legs. I wake up with it and it increases throughout the day so that by late afternoon, I just want to lie down and go to sleep.

But more difficult to handle are the psychological symptoms, the most unpleasant being depression and anxiety. My natural mood off GH is consistently very low without any provocation and on top of this, I often feel panicky even if there is little cause to be stressed.

I've felt many other effects from GHD:-

- physical or mental activity quickly brings exhaustion
- muscles tire out almost immediately when lifting heavy weights
- lack of concentration, particularly at work
- poor memory
- fear of the future
- minor illnesses (such as a cold) are quite debilitating
- alcohol intolerance
- persistent baby shape to my body

The best description of the GHD feeling I've heard is that it is like 'going uphill with the brakes on'. I would liken life without growth hormone to the experience of driving my old Austin Allegro; it gets me to work and back every day but I couldn't describe it as a pleasure to drive. Similarly, I can make it through the day without growth hormone and can hold down a job but I have no energy left to pursue my interests outside work and I am simply not enjoying my life.

This is surviving, not living, and yet that's an important distinction some doctors have yet to learn.

Since starting GH, I have felt profound effects: At work, programming computers, I now have energy up to the end of the day. I can concentrate. I am no longer hampered by anxiety and panic attacks. Thinking no longer tires me out! My solutions are more creative, come more easily and I can implement them more quickly. Overall, I seem to work with three times the efficiency I once did.

At home I feel more positive, I'm not scared anymore and I have the energy and inclination to go out in the evening. But now I have to drink twice as much beer to get the same effect!

It must be emphasised that this is how one person is affected and we know that not all 'GHD adults' feel this way. This is a classical story and reads very well; it probably represents the view of >50% of GHD adults!

Further Reading

Australasian Paediatric Endocrine Group (APEG)
www.racp.edu.au/apeg

Australian Medicines Handbook 2000

The Endocrine Society
www.endo-society.org

The Hormone Foundation
www.hormone.org

The Magic Foundation
www.magicfoundation.org

UK Society for Endocrinology
www.endocrinology.org

Glossary

Adolescence
The period in development between the onset of puberty and adulthood.

Arthralgias
Any pain affecting a joint.

Cardiovascular Disease
An abnormal condition characterised by dysfunction of the heart and blood vessels.

Cholesterol
A steroid found in animal fats and oils.

Cortisol
A steroid hormone produced by the adrenal cortex. There are a number of hormones made by the adrenal gland and they are called corticosteroids.

Endocrinologist
A doctor who specialises in disorders of the endocrine glands.

Growth Hormone
A hormone released by the pituitary gland, which promotes growth.

Hormones

Blood chemicals that stimulate growth and sexual development and help to regulate the body's metabolism. Normally the body carefully controls the release of hormones as too much or too little may disrupt the body's delicate balance. They are produced by endocrine glands and carry messages from one cell to another via the bloodstream.

Hormone Replacement Therapy

Treatment of diseases with substances which simulate hormonal effects.

Hypoglycaemia

A less than normal amount of glucose in the blood.

Hypothalamus

Part of the base of the brain that controls the release of hormones from the pituitary gland.

Immune System

A system in the body that protects the body against pathogenic organisms and other foreign bodies.

Insulin

A naturally occurring hormone secreted by the pancreas in response to increased levels of glucose in the blood.

Leukaemia

A malignant cancer of the blood.

Oestrogen

A group of female hormones that are produced by the ovaries from the onset of puberty and continuing until menopause, which controls female sexual development.

Osteoporosis

A condition that is characterised by thin, brittle bones.

Pituitary Gland

A pea-sized gland at the base of the brain, which releases a number of important hormones related to normal growth, development and fertility, including growth hormone.

Somatropin

Growth hormone.

Subcutaneous Injection

An injection given beneath the skin.

Syndrome

A syndrome is a collection of characteristics that occur together and characterise a particular condition.

Testosterone

Most potent male sex hormone, which is produced in the testes (testicles) and controls male sexual development.

Thyroxine

A hormone produced by the thyroid gland.

Turner Syndrome

A chromosomal disorder occurring in females caused by the absence or abnormality of one X chromosome. Short stature is a common symptom in girls with Turner Syndrome.

Organisations

Australian Pituitary Foundation
PO Box 4792
North Rocks NSW 2151 Australia
Tel: 02 9630 7423

Endocrine Society of Australia
145 Macquarie Street
Sydney NSW 2000 Australia
Tel: 02 9256 5405

UK Child Growth Foundation
2 Mayfield Avenue
Chiswick London UK
Email: CGFLONDON@aol.com

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Serono Symposia Australasia are proud to bring you this booklet from their "Hormones and Me" educational booklet series. We aim to provide readers with a healthy understanding of the issues relating to endocrine disorders particularly in children. We hope that you find it a valuable and helpful resource.

Please ask your doctor or nurse for further information on the resources available to you.

We wish to express our gratitude to Serono Laboratories (UK) Inc for allowing the distribution of this booklet, which was reproduced in Australia in 2000. We would also like to especially thank the Paediatric and Adult Endocrinologists who gave their time and experience to review and edit the booklets for Australian and New Zealand readers. Special thanks to all those involved in this process.

The views expressed in the "Hormones and Me" booklet series are not necessarily Serono Symposia Australasia's, but those of the qualified clinicians working in the field of paediatric and adult endocrinology.

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