

# ADULT GROWTH HORMONE REPLACEMENT



**THE PITUITARY  
FOUNDATION**

*working to support  
pituitary patients*

# THE PITUITARY FOUNDATION

## AIMS AND OBJECTIVES

Most disorders of the pituitary gland are relatively rare, but they are often puzzling and sometimes distressing, both for patients and for families and friends. The Pituitary Foundation can help:

- **By acting as a source of information on pituitary conditions and treatment as well as lifestyle and social issues faced by pituitary patients and their families.** Our HelpLine aims to find answers to the many and diverse questions which patients, their families and advisers may have. We also provide a comprehensive range of written information. Lastly, an Endocrine Nurse Service provides more specialist support (but not medical advice).
- **By providing support for patients and their families and carers.** We support a network of Local Support Groups, Rural Support Networks and Telephone Support, all provided by volunteers who have personal experience of different pituitary conditions.
- **By increasing public awareness of pituitary disorders which, because of their rarity, can be bewildering.** Through a network of volunteers we are actively involved in highlighting the conditions, their symptoms and diagnosis, treatment and implications. We do this both through general media campaigns and by informing GPs, dentists, opticians and other professionals who might identify symptoms.
- **By working to understand and represent the experiences and views of pituitary patients in order to improve services and policies to meet their needs.** Patients and their carers are the experts in understanding the impact of these conditions, and we are here to support and promote the Patient Voice.

## ABOUT THIS LEAFLET

The aim of this leaflet is to provide general information about Adult Growth Hormone Replacement. It is written in general terms so not all of it will apply to you. Hopefully, you will find it helps you understand your treatment better and gives you a basis for discussion with your GP and endocrinologist.

## WHAT IS GROWTH HORMONE?

The scientific name for growth hormone (GH) is somatotrophin, derived from the Greek words for body and nourishment. It is made in the pituitary gland and passes from there into the blood stream. As its Greek name suggests, GH has effects on virtually all the organs in the body. It was given its common name, growth hormone, from its first use in the 1950s and 1960s in helping very short children grow. As GH is a protein and would be digested if taken by mouth, it has to be given by injection subcutaneously (under the skin), usually once a day.

## WHY DO ADULTS NEED IT?

GH affects body composition – the proportion of fat, muscle and bone in the body. GH-deficient adults have more adipose (fatty) tissue and less lean body mass (muscle) than people without pituitary disease. The fatty tissue is deposited in the abdomen increasing the size of the waist which is known to increase the risk of death from heart disease amongst the normal population. The effects of GH-deficiency on body muscle lead to a decrease in strength and stamina. The loss of the beneficial effects of GH on heart muscle may also be a factor in decreasing the ability to exercise.

GH has a major effect on bone. It is vital for normal growth in children, but once growth has stopped (adult peak bone mass is achieved at around age 25) GH is still important for increasing and maintaining bone mass up to the age of 60. There is accumulating evidence to suggest that GH-deficient adults have an increased bone fracture rate. However, it will take some years to show whether GH treatment can reduce fracture rate in hypopituitary adults.

Lack of GH causes changes in blood cholesterol concentrations and also a number of other factors in the blood which, in other studies, have been associated with an increased risk of heart disease.

GH-deficient adults have been shown to suffer from excessive tiredness, anxiety, depression and generally feeling unwell, as well as having feelings of social isolation and a tendency to be easily upset. This can be severe enough to lead to an inability to work or to maintain a basic acceptable lifestyle. These factors have led most studies to conclude that GH-deficiency results in a reduced 'quality of life'. This is very difficult to measure, but several studies have shown that GH treatment of GH-deficient adults results in improved 'quality of life'.

## WHAT CAUSES AN ADULT TO BE DEFICIENT IN GH?

It is estimated that about three in every 10,000 of the adult population are GH-deficient. About one third of those will have developed the deficiency during childhood. In adults the most frequent cause of GH deficiency is a benign tumour of the pituitary gland. GH deficiency is usually caused by damage to the pituitary gland or the part of the brain which controls this gland (the hypothalamus) by the tumour itself or by the surgery and/or radiotherapy used to treat it. Other causes include problems with blood supply, for example haemorrhage or ballooning of the arteries (aneurysm). In many cases this leads to deficiencies of several hormones. Idiopathic (no obvious cause) GH deficiency is the most common cause in children, followed by radiotherapy used to treat leukaemia or a brain tumour. It is important to bear in mind that the effects of radiotherapy in both children and adults may not be apparent for some years, so it is important that pituitary function is monitored regularly, by specialists, after treatment.

## WHO SHOULD BE TESTED FOR GH DEFICIENCY AND WHAT TESTS ARE USED?

Two groups of patients should be considered at risk of growth hormone deficiency in adult life:

- Those at risk of abnormal pituitary function as a result of a tumour in the pituitary region, pituitary surgery or radiotherapy.
- Any adult that had GH deficiency during childhood and received GH replacement therapy to help them grow.

The risk of severe GH deficiency increases as the number of other pituitary hormone deficiencies increases, so a patient on sex steroids, hydrocortisone and thyroxine will almost certainly have GH deficiency. The diagnosis of GH deficiency is confirmed by performing a special test to try and increase GH release from the pituitary. The test involves giving a drug which, in normal individuals, provokes an increase in GH production over a short period of time. Typically blood is taken before the drug is given and then every 30 minutes for up to three hours. Such tests are known as 'pharmacological', 'provocative' or 'dynamic' tests.

The most frequently used test is the insulin tolerance test or ITT. A peak GH blood level of less than nine milliunits per litre (9mu/l), or three micrograms per litre (3 µg/L), indicates severe GH deficiency for which GH replacement therapy should be considered. Some patients (for example, those who have had a fit or have angina) cannot have an ITT and in this case an alternative, such as a glucagon test is normally used. A glucagon test checks how effectively the pituitary gland is regulating the release of GH and cortisol. Both tests must be carried out by experienced staff in a specialised unit. The insulin test is associated with feelings of faintness, hunger, sweating and palpitations, whilst glucagon may induce mild feelings of nausea. A number of other tests, including arginine, GHRH and GHRP, may be used in specialist centres that are assessing new and potentially better tests.

The publication from the National Institute of Clinical Excellence (NICE) has provided guidelines on identifying patients who can receive GH replacement therapy. Patients over the age of 25 must not only be GH deficient but also must complete a questionnaire to demonstrate a certain degree of impairment in quality of life in order to qualify for a short trial of GH. They then need to show a specific improvement in quality of life following the trial to qualify to continue treatment. Full details are given later in this leaflet 'The NICE Guidelines'.

## **HOW IS GH ADMINISTERED AND ARE THERE ANY SIDE EFFECTS?**

GH is given by injection under the skin (subcutaneously, sub-cut, sc) before you go to bed at night. This is normally self-administered after some initial instruction from a nurse. There are a number of pen-devices to make injection easy and virtually painless. Doses vary. Typically, the starting dose would be a single daily injection of 0.8iu (approximately 0.25 mg; 'iu' is an International Unit) with regular reviews at intervals to determine response, side-effects and any necessary dose alterations. Clinics will help you when you start treatment.

As the GH used has the same structure as normal human growth hormone and the doses used are low to mimic the body's production of the hormone, side effects are unusual and minor. They can include mild swelling of the hands and feet (oedema) with some joint discomfort (arthralgia) or tingling in the fingers (parasthaesia), but these are likely to be temporary or will settle when the GH dose is reduced. Effects on blood pressure or blood glucose can occur and will be monitored by your endocrinologist.

Whilst you are on GH replacement treatment you will be regularly monitored by your endocrinologist.

## WHAT ARE THE BENEFITS OF GH REPLACEMENT?

Medical scientists discover the role of a particular hormone in the body by studying what happens in its absence and by ensuring that these changes are reversed when it is replaced (usually by injection). Therefore the benefits of replacement are the reversal of the effects described in the section on “Why do adults need GH?”.

Independent reviewers conclude that GH improves exercise capacity, the ratio of muscle to fat, bone mineral density and cardiovascular health. The difficulties in measuring changes in the ‘quality of life’ have already been mentioned. It should also be borne in mind that the patients willing to volunteer for studies may not be typical of all those attending a particular clinic. However, within these limitations, several studies have shown that GH replacement improves this difficult-to-define measurement. It is the experience of many endocrinologists that the amount of benefit derived from GH treatment cannot necessarily be predicted from the degree of GH deficiency measured by any of the means available. However, it has to be said that few people are willing to inject themselves on a daily basis without any perceived benefit.

Not all GH-deficient people feel short-term benefits from GH replacement, some do not respond at all. Early trials suggested that 30-50% of patients did not choose to continue after the initial trial period, but endocrinologists advise us that some of the people who stopped taking GH have since asked to restart it.

Many patients within The Pituitary Foundation have reported improved quality of life since starting GH replacement.

## AFTERCARE

Patients who are on GH replacement require long-term monitoring and this will be shared between your endocrinologist and GP. Because pituitary conditions are relatively rare, you might find that you will be the only patient using GH replacement that your GP is treating and (s)he might find it helpful to have a copy of our *Pituitary Disease Factfile for General Practitioners*.

You may find you are dealing with psychological and emotional issues associated with pituitary disease or having a long-term condition. It may help to talk to your partner or your GP/endocrinologist. You may also wish to request our leaflet *Psychological Issues in Pituitary Disease*.

## HOW IS GH MANUFACTURED?

The GH used today is known as recombinant human growth hormone (rhGH). This means it is synthetically produced, but has the same structure as the natural human growth hormone and has the same effects. Before this was available, far fewer patients could be treated with the natural human GH. In the mid 1980s, advances in biomedical science, together with the recognition that the use of the natural hormone could occasionally be associated with the development of Creutzfeld-Jacob disease (CJD), led to the sole use of the manufactured product. There is no risk of CJD from the type of synthetic GH now in use.

## GROWTH HORMONE IN ADULTS: THE NICE GUIDELINES

In August 2003 The National Institute of Clinical Excellence (NICE) published their guidance on the use of growth hormone in adults. The full document can be obtained from the NICE website at [www.nice.org.uk](http://www.nice.org.uk). The guidance states that:

1. Recombinant human growth hormone treatment is recommended for the treatment of adults with growth hormone (GH) deficiency only if they fulfill all three of the following criteria.

- They have severe GH deficiency, defined as a peak GH response of less than 9 mU/litre (3 ng/ml) during an insulin tolerance test or a cross-validated GH threshold in an equivalent test.
- They have a perceived impairment of quality of life (QoL), as demonstrated in the disease-specific 'Quality of life assessment of growth hormone deficiency in adults' (QoL-AGHDA) questionnaire.
- They are already receiving treatment for any other pituitary hormone deficiencies as required.

1.2 The QoL (quality of life) status of people who are given GH treatment should be re-assessed 9 months after the initiation of therapy. GH treatment should be discontinued for those people who do not demonstrate a predefined improvement in QoL-AGHDA score.

1.3 Patients who develop GH deficiency in early adulthood, after linear growth is completed but before the age of 25 years, should be given GH treatment until adult peak bone mass has been achieved, provided they satisfy the biochemical criteria for severe GH deficiency (defined as a peak GH response of less than 9 mU/litre (3 ng/ml) during an insulin tolerance test or a cross-validated GH threshold in an equivalent test). After adult peak bone mass has been achieved, the decision to continue GH treatment should be based on all the criteria in Section 1.1.

1.4 Patients currently receiving GH treatment, for the management of adult onset GH deficiency, whether as routine therapy or as part of a clinical trial, could suffer loss of well being if their treatment were to be discontinued at a time they did not anticipate. Because of this, all NHS patients who are on therapy at the date of publication of this guidance should have the option to continue treatment until they and their consultant consider it is appropriate to stop.

1.5 Children with GH deficiency should be treated as outlined in the Institute's guidance on the use of GH in children (NICE Technology Appraisal Guidance No. 42). At completion of linear growth (that is, growth rate < 2 cm/year), GH treatment should be stopped for 2–3 months, and then GH status should be re-assessed. GH treatment at adult doses should be re-started only in those satisfying the biochemical criteria for severe GH deficiency (defined as a peak GH response of less than 9 mU/litre (3 ng/ml) during an insulin tolerance test or a cross-validated GH threshold in an equivalent test), and continued until adult peak bone mass has been achieved (normally around 25 years of age). After adult peak bone mass has been achieved, the decision to continue GH treatment should be based on all the criteria set out in Section 1.1.

1.6 Initiation of GH treatment, dose titration and assessment of response during trial periods should be undertaken by a consultant endocrinologist with a special interest in the management of GH disorders. Thereafter, if maintenance treatment is to be prescribed in primary care, it is recommended that this should be under an agreed shared care protocol.

## **WHAT DO THESE GUIDELINES MEAN FOR ME?**

The NICE guidelines have defined the reasons why GH replacement therapy can be used in adults:

1. To maximize bone mass in young adults who either:
  - (a) received GH replacement therapy for growth and are shown to have persisting severe GH deficiency.
  - or
  - (b) developed GH deficiency after completing growth, but before the age of 25
2. To improve quality of life in adults over the age of 25.



If you are a patient who falls into group 1a you will be tested to see if you have severe GH deficiency. If you fall into group 1b then your GH will be stopped for two to three months before you are retested. In either case, if severe GH deficiency is confirmed then you will be offered GH replacement therapy which you can take until you are 25 years old. At that point the GH will have to be withdrawn for a period of time so that a baseline assessment of quality of life can be made. GH therapy will be restarted if you fulfill the quality of life criteria given by NICE and the guidelines for using GH in adults over 25 will be followed.

If you are over 25 then you will be asked to complete a questionnaire that asks questions about how you feel and how you function on a day-to-day basis. If you achieve an appropriate score then you will be offered a trial of GH replacement therapy. After nine months you will be asked to complete the same questionnaire to demonstrate a beneficial change in your quality of life. If there is sufficient improvement then you will be allowed to continue on GH replacement therapy, if not you will be asked to stop your GH.

## **WHAT IF I DO NOT FULFILL THE CRITERIA?**

Not everyone will fulfill the criteria to start or continue GH replacement therapy as determined in the NICE guidelines. If you strongly believe that you have symptoms that may be caused by GH deficiency then talk to your endocrinologist. NICE provides a guideline so it may be possible to offer a trial of GH replacement therapy in patients who do not fulfill all the NICE criteria.

## QUESTIONS AND ANSWERS

*Q What if I am ill or forget to take an injection?*

A If you have a cold, flu or on antibiotics, you should continue taking your GH as usual, unless your doctor tells you otherwise. Forgetting the odd injection will not affect your treatment, but the best results are achieved with regular injections. If you do forget, take your injection the following day as usual. You don't need to double dose to make up for the missed injection.

*Q What about travelling?*

A If you leave home on a trip make sure you take enough growth hormone with you. If you are going abroad you can get a letter from your doctor in order to avoid problems taking needles and drugs through customs. Also, check with the airline regarding their flight policies.

Some brands of growth hormone need to be kept in the fridge; others do not. Ask your endocrine nurse for advice on what's available. If your GH does need to be kept in a fridge, it is advisable to carry it in a cool bag, whilst travelling. Hotels will usually be happy to keep your GH in a fridge for you, though you may wish to check this is possible before you leave home. Carry your GH in your hand luggage as it could freeze in the hold of an aircraft.

*Q Where do I give the injections?*

A Subcutaneous injections are best given in the fleshy parts of the body such as the thigh, buttocks or abdomen. It is important to vary the sites of the injections each day, otherwise the area used will become sore and lumpy.

## **OTHER FACTORS TO CONSIDER**

### **ALCOHOL AND REPLACEMENT HORMONES**

There is no interaction between alcohol and GH, and you are allowed to drink in moderation. You should restrict yourself to one to two units of alcohol a day.

### **EMPLOYMENT PROBLEMS**

If your pituitary condition is causing you difficulties in retaining, seeking, or returning to employment, contact the HelpLine or your local Citizens Advice Bureau for the most up to date information about employment rights and where to get advice about benefits.

### **PERSONAL MEDICAL IDENTIFICATION**

If you are taking hormone replacement medication, it is a good idea to wear a medical information bracelet or equivalent as the information will help the doctors if you have an accident and are unconscious.

Members have tried:

- MedicAlert® The MedicAlert Foundation, 1 Bridgework, 156 Caledonian Road, London N1 9UU. Tel: 0800 581420.

Website: [www.medicalert.org.uk](http://www.medicalert.org.uk)

- MediTag, 37 Northampton Street, Hockley, Birmingham B18 6DU. Tel: 0121 200 1616. Website: [www.medi-tag.co.uk](http://www.medi-tag.co.uk).

- Doctag, 31-33 West Pilton Drive, Edinburgh, EH4 4HS. Email: [info@doctag.net](mailto:info@doctag.net). Website: [www.doctag.net](http://www.doctag.net).

## PATIENTS STORY

I am 39, married with two boys.

I started having pituitary symptoms in 1990 and over the next few years became increasingly ill until my illness was diagnosed and treated in 1994. Following surgery and radiotherapy I received replacement hydrocortisone, HRT and thyroxine, but no growth hormone (GH) at that time. Although I was told that my tumour was now under control, I felt terrible all the time, needed help with daily living and was unable to work.

Before Growth Hormone replacement I felt as though I was barely surviving. No matter what I did I felt terrible, like an old woman, and that my life was over. I was hardly able to look after myself, let alone anyone else. I was constantly ill and unable to work. I felt exhausted all the time, no matter how much I slept. My muscles were weak and I got frequent cramps and muscle strains. I was unable to walk 100 yards without stopping and resting. I just tried to put a brave face on things but felt that every day was a struggle just to cope with the practicalities such as shopping and housework. My husband had to assume household tasks and take numerous days off work to help me physically cope, attend hospitals, and attend my GPs.

I remember looking at my mother-in-law, who was over 70 and envying her vitality and energy.

My Consultant suggested that I went for tests to see if I was GH deficient. I was sceptical, did not like the idea of daily injections and was worried about side effects. On the practical side I was so exhausted that even the thought of driving to the hospital and having more tests seemed just too much.

The specialist nurse phoned and persuaded me to have the tests. My husband also talked me into going and took time off work to take me. I was found to be producing no GH at all and arrangements were made for me to go on GH replacement.

I never expected it but GH has given me my life back and I have become a net contributor to my family and community. The quality of life of so many people is affected by my restored health – my children, my husband, our parents, friends, the local community and children overseas.

I feel great, energetic and keen to get on with living. I feel that once more I have my whole life ahead of me to plan for. I have all the normal energy and vitality any 39 year old would expect to have. I have the energy to play with my children again.

I am able to go on holiday. I hardly see my GP any more (average number of appointments have decreased from 14 to one per year).

Rather than being a burden on society, I can now work again and of course pay tax! I look after my sons, my husband and my house with no problem whatsoever. I am even pleased to be able to do the housework!

It's not all 'roses' though as taking GH inconveniences me a great deal.

My main supply of GH has to be stored in a fridge which is stressful during winter power cuts. I have to go through an embarrassing performance at airports, etc. explaining my needles and medicines. I have to remember to take it at night. I can't just doze off; I have to give myself an injection first. My leg often looks like a pincushion.

I need a cool box or car fridge to transport the GH on holiday as it can only be out of the fridge for nine hours before becoming ineffective. GH 'miniquicks' came out recently for travel purposes, but they still have to be kept under 25 degrees C which eliminates central or southern Europe, for example.

These are minor inconveniences however compared to the benefits of GH. I really appreciate just feeling 'normal' each morning. Every day is like Christmas Day just knowing I can concentrate on things other than my own health.

## OTHER SUPPORT ORGANISATIONS

Child Growth Foundation	2 Mayfield Road, Chiswick London W4 1PW Tel: 020 8995 0257 www.childgrowthfoundation.org
National Osteoporosis Society	Camerton, Bath BA2 0PJ Osteoporosis Helpline 0845 4500230

## GLOSSARY

Adipose tissue	Fatty tissue, as opposed to muscle.
Cortisol	One of the main hormones produced by the adrenal glands, which controls a number of functions and is particularly important in times of stress.
Endocrine system	The body-wide system of hormone-producing glands, and the hormones they make, which control many aspects of life, including growth and reproduction.
Endocrinologist	A doctor who specialises in treatment of diseases of the endocrine system.
Growth hormone (GH)	A hormone produced by the pituitary gland (mainly while you are asleep), which controls the rate of growth in children. Even after growth has ceased, growth hormone has important effects during adult life.
Hypothalamus	The part of the brain which controls pituitary hormone production.
NICE	National Institute for Health and Clinical Excellence
Osteoporosis	Thinning of the bones with increased risk of bone fracture. The condition is associated with deficiency of oestrogen or testosterone, and research suggests it is probably also caused by growth hormone deficiency.
Pituitary gland	A gland, as small as a pea, located at the base of the brain. It controls the hormone production of many other glands in the body.
Pituitary tumour	A tumour, almost always non-cancerous, of the pituitary gland.
Recombinant human GH	Synthetically produced growth hormone, which has the same structure as natural human growth hormone.
Somatotrophin	Growth hormone produced by the pituitary gland.

# The Pituitary Foundation

*Our **Helpline** is available*  
Mon – Fri 9:00am – 5:00pm  
**0845 450 0375**

We also provide information on our web site [www.pituitary.org.uk](http://www.pituitary.org.uk)  
**Other support can be accessed via the Helpline.**

## Information leaflets currently available:

The Pituitary Gland and its Hormones	Acromegaly
Adult Growth Hormone	Cushing's Syndrome
Patient Fact File	Diabetes Insipidus
Fact File for General Practitioners	Hypogonadism and Infertility: A Guide for Men
Psychological Issues for Pituitary Patients	Hypopituitarism and Replacement Therapy
Pituitary Surgery	Kallmann's Syndrome
Radiotherapy for Pituitary Patients	Prolactinoma
Information Pack for Carers	

The Pituitary Foundation is funded by voluntary donations, sponsorship and membership. For further information about membership, to make a donation or support us in our fundraising activities please contact the Helpline

Disclaimer:

All information is general. If you, or your carer, have any concern about your treatment or any side effects please read the Patient Information Leaflet enclosed with your medication or consult your GP or endocrinologist.

The Pituitary Foundation  
PO Box 1944, Bristol BS99 2UB  
Tel/Fax 0845 450 0376  
Email: [helpline@pituitary.org.uk](mailto:helpline@pituitary.org.uk)  
[www.pituitary.org.uk](http://www.pituitary.org.uk)

Registered address:  
86-88 Colston Street  
Bristol BS1 5BB  
Registered Charity Number 1058968

Company limited by guarantee  
Registered in England Number 3253584

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