



Growth Hormone Deficiency

A Guide for Parents and Patients



SERIES 1



SERIES 2



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SUMMARY

This booklet is intended to provide a better understanding of some of the issues associated with your child's condition and information which will enable you to learn more about your child's treatment which gives you a basis for discussion with your child's specialist.

If you require further general information about growth hormone deficiency, the *Child Growth Foundation* and *The Growth Hormone Group* are there to help you.



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GROWTH HORMONE DEFICIENCY - Series No: 2 (Revised January 2003)

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The British Society for Paediatric Endocrinology and Diabetes (BSPED) is an association of specialists who deal with hormone disorders in children.

CGF INFORMATION BOOKLETS

The following titles are also available:

- Series No 1 Growth and Growth Disorders
- Series No 2 Growth Hormone Deficiency
- Series No 3 Puberty and the Growth Hormone Deficient Child
- Series No 4 Premature Sexual Maturation
- Series No 5 Emergency Information Pack for Children with Cortisol and GH Deficiencies and those Experiencing Recurrent Hypoglycaemia
- Series No 6 Congenital Adrenal Hyperplasia
- Series No 7 Growth Hormone Deficiency in Adults
- Series No 8 Turner Syndrome
- Series No 9 The Turner Woman
- Series No 10 Constitutional Delay of Growth & Puberty
- Series No 11 Multiple Pituitary Hormone Deficiency (MPHD)
- Series No 12 Diabetes Insipidus
- Series No 13 Craniopharyngioma
- Series No 14 Intrauterine Growth Retardation (IUGR)
- Series No 15 Thyroid Disorders

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The use of growth hormone has been reviewed by the Government Agency called the **National Institute of Clinical Excellence** (NICE). Full approval for its use has been given for all the licenced indications in childhood.

At the back of the booklet are a selection of relevant recommendations.

‘Guidance on the use of human growth hormone (somatropin) in children with growth failure’.

See Appendix “A”

GROWTH HORMONE DEFICIENCY

Hormones are the chemicals that carry messages from one cell to another via the blood stream. Growth hormone, also known as somatotropin, acts directly and indirectly on the growth of bones, tissues and organs.

Growth hormone deficiency or insufficiency occurs when the *pituitary gland*, a small pea sized gland at the base of the brain, fails to produce adequate levels of growth hormone. Part of the brain called the *hypothalamus* controls the levels of hormones in the blood by triggering the pituitary gland into producing the required hormones. This low level of growth hormone may be due to problems with the *hypothalamus* or with *the link between the hypothalamus and the pituitary gland* or with the *pituitary gland* itself (see diagram on next page). Where a child's growth hormone level is very low or not present, the child is said to be **GROWTH HORMONE DEFICIENT**. Where the level of growth hormone production is inadequate, the child is said to be **GROWTH HORMONE INSUFFICIENT**. The level of growth hormone insufficiency may vary from mild to severe but as growth hormone is now available in large quantities, all children whose growth hormone levels are inadequate should be able to receive appropriate replacement treatment.

Children with growth hormone deficiency are very short but with normal body proportions, facial appearance and intelligence. Prior to treatment the child may also be “chubby” as growth hormone helps to control the fat under the skin. These children may look young for their age as physical development and bone age is delayed and consequently the skull will be immature producing the facial proportions of a younger child.

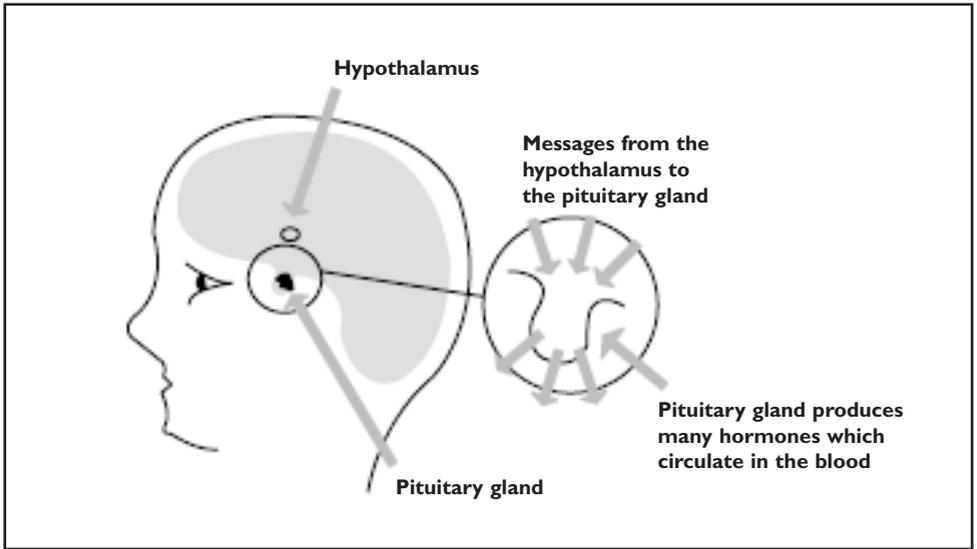
Bone age is assessed by taking an Xray of the left hand and wrist to establish how much growth may still be possible. For example a bone age delayed by 2yrs means that a child has an additional 2yrs of growth which will occur in the teen age years before growth is completed.

There are many causes of growth hormone deficiency. Most cases are called ‘idiopathic’ – of unknown origin. This term includes a number of causes. The pituitary gland or the connections to it may have been damaged at birth or by severe head injury. Sometimes there are problems with the development of the foetus resulting in absence or under-development of the gland. The condition may be hereditary in some cases (about 3% of GHD children have brothers or sisters with the condition). For no known reason, the deficiency appears to be much more common in boys than in girls.

As a consequence of certain brain or pituitary tumours, and their treatment with surgery or irradiation, the function of the pituitary gland is affected, causing hormone deficiencies, of which the commonest is growth hormone deficiency. Treatment for leukaemia, with radiation of the whole head, may also result in the pituitary gland failing to function adequately.

A deficiency of growth hormone may occur alone or it may be associated with other hormone deficiencies. Frequently, the sex hormones are affected but no treatment or diagnosis is required for this until the changes of puberty should commence. The thyroid stimulating hormone (TSH) is sometimes also affected and, much less frequently, the hormone which stimulates the adrenal gland (ACTH), can be involved. All these hormones can be replaced by regular medication.

Booklet No 11 covers information on the Multi Pituitary Hormone deficiencies



DIAGNOSIS OF GROWTH HORMONE DEFICIENCY

Normal levels of growth hormone (GH) in the blood fluctuate from hour to hour and are therefore very difficult to assess. Growth hormone is released in a pulsatile action, as a series of 'spurts' throughout the day and night especially during sleep. These spurts occur approximately 6 to 9 times in each 24 hours and last for 10 to 20 minutes. In order to detect and measure the levels of growth hormone, blood must be taken when a surge of growth hormone has been provoked, or blood must be taken at very frequent intervals. There are two fundamentally different types of tests of growth hormone secretion:

Provocation tests: There are many such tests which provoke the necessary surge of GH including the insulin tolerance test (ITT), as well as tests with glucagon, clonidine, arginine and growth hormone releasing factor. All of these tests stimulate the release of growth hormone from the pituitary gland. However, none is totally effective which is why there are so many alternatives. Insulin (ITT) and glucagon work by altering the level of blood sugar which will make your child feel a little uncomfortable as he/she will feel hot and sweaty and very hungry.

The Department of Health in England has expressed doubts about the safety of insulin tolerance tests as a test of GH secretion in childhood when performed outside specialist centres. This should probably be extended to other tests, such as glucagon, which also alter blood sugar concentrations. Certainly tests such as these should, as stated above, only be done in specialist growth centres.

Physiological tests: Exercise tests (measuring blood GH concentration after a short period of exercise) are still in use. However, an assessment of how much GH a child produces naturally, either overnight or throughout a 24 hr period, is theoretically a more realistic assessment of GH production. Such tests are time consuming and expensive and usually confined to specialised centres. It is still uncertain whether these tests have any advantage over provocation tests for identifying which children will respond to GH treatment. Measurement of GH in a timed collection of urine may be a useful indicator of GH secretion, although its reliability is still being investigated.

There are many different methods of measuring GH secretion and your growth specialist will discuss which test is most appropriate for your child.

Interpretation: A peak level of growth hormone over 15-20 mU per litre of blood is usually assessed as normal but dependent on the methodology of how the growth hormone was measured, each centre will have its own range. Where the level is between 8 and 14 mU/litre, diagnosis is difficult and doctors may decide to monitor the child's growth rather than treat with biosynthetic growth hormone. Where the level of growth hormone is 7 mU/litre or below, treatment with growth hormone for Growth Hormone Deficiency (GHD) is clearly indicated. However, the normal ranges for growth hormone levels are ill-defined and when doubt arises, particularly as it is well appreciated that there is no distinct cut-off value between GH insufficiency and normal, more emphasis should be placed on growth rate than on blood measurements of GH.

Other features of growth hormone deficiency may be helpful in the diagnosis; such as abnormalities of the pituitary gland on scanning (MRI or CT) or low concentrations of growth dependant growth factors (IGF I) in the blood, and low urinary concentrations.

The most important indication for specialist referral is the growth pattern and not the hormone measurements.

It is usual for the appropriate hormone measurements of pituitary failure to be performed by the specialist centre.

TREATMENT OF GROWTH HORMONE DEFICIENCY

TYPES OF GROWTH HORMONE AND COMPANIES INVOLVED

The following versions of growth hormone are currently marketed in England:

<i>Genotropin</i> (somatropin rbe)	produced by Pfizer
<i>Humatrope</i> (somatropin rbe)	produced by Eli Lilly
<i>Saizen</i> (somatropin rmc)	produced by Serono
<i>Simplex</i> (somatropin epr)	produced by Novo Nordisk
<i>Zomacton</i> (somatropin rbe)	produced by Ferring

All these versions of growth hormone are biosynthetic and are identical in structure to the natural human growth hormone. They are manufactured using gene technology. There is no known difference in growth response between any of the five products. However, there are differences in support services, teaching and injection systems offered which should be discussed with your growth specialist.

Prior to 1985 biosynthetic growth hormone was not available and treatment was given using pituitary-derived human growth hormone, i.e. extracted from the brains of cadavers (dead people). Although pituitary-derived human growth hormone is still used in a few countries of the world, it is not used in the United Kingdom. Distribution in the UK was halted in 1985 when it was discovered that this source of human growth hormone carried a risk of infection. The problem does not occur with biosynthetic human growth hormone.

Dosage, frequency and timing

The dosage of growth hormone varies according to the weight/size of your child. This means that the dose given to your child will increase as he/she gets older and larger. In certain circumstances, the growth specialist may increase the dose if your child's response to treatment is poor but this will depend on several factors.

Growth hormone is usually prescribed to be taken daily, by subcutaneous injection. As a child normally produces most of their own growth hormone when asleep, growth hormone is usually recommended to be injected in the evening, just before bed time.

SUPPLY OF GROWTH HORMONE

Growth hormone treatment has been reviewed by a government agency called [National Institute for Clinical Excellence \(NICE\)](#) and full approval has been given for all the licenced indications in childhood.

Sources and supply

Growth hormone is often regarded as expensive and some parents have experienced difficulties in obtaining supplies. If you find yourself with supply problems, always inform your specialist immediately. The Child Growth Foundation will try to help you if your problems continue after you have taken this step.

Three ways that growth hormone is prescribed

- Growth hormone is usually prescribed by the [general practitioner](#). He is asked to prescribe in a “shared care” agreement with the growth specialist or the consultant paediatrician. The areas of responsibilities for the medical monitoring and patient care of those on growth hormone are set out by most specialists for GP’s in what is termed a “shared care protocol”.
- Very rarely growth hormone may be prescribed by a growth [specialist](#) and supplied by the hospital pharmacy. Very few patients are supplied in this way as hospital pharmacy budgets are not large enough to cater for the purchase of large quantities of growth hormone.
- Growth hormone is sometimes available to patients taking part in a trial associated with one of the pharmaceutical companies. In such cases, it is supplied by the pharmaceutical company conducting the trial. If you are asked to allow your child to be part of a trial, this will be fully explained by your growth specialist and you almost certainly will have been asked to sign a consent form. However, we advise you to make sure you have determined both the length of treatment and whether growth hormone will be available for your child after the trial is completed if your child is seen to benefit from its use.

Quantities prescribed

When medicines/treatments are required on a continuous basis, GPs usually prescribe a month's supply on one prescription. Some GPs may prescribe for a longer period and some may prescribe fortnightly or weekly. If your GP is prescribing for less than two weeks at a time, and this situation causes difficulties, speak to your Consultant as he/she may be able to help. If you are experiencing difficulties on the quantity prescribed and your consultant is not able to help, contact The Child Growth Foundation for advice. If you will require a larger than normal quantity on prescription because of a holiday away, please be sure to discuss this with your GP well in advance of your holiday departure date. For a holiday abroad, it is often advisable to ask your specialist to write a covering letter for Customs to explain the possession of both growth hormone and syringes or pen injection devices.

Injection dosage

The dosage of growth hormone can be confusing as sometimes this will have been quoted to you in units of growth hormone and sometimes as mls of reconstituted growth hormone. As the amount of diluent required to mix an amount of growth hormone may vary between products, it is not possible to provide standard conversions. The older units of growth hormone has now changed to a mg basis (3 international units = 1mg). Some pharmaceutical companies produce syringes marked in units or mg of GH, and not mls, which may add further confusion.

It is important to ensure that your consultant has quoted the dosage in terms you understand, preferably in both mg/units and mls. The clinic nurse will advise you if you experience difficulties.

STORAGE OF GROWTH HORMONE

There are a number of companies marketing growth hormones and the storage instructions may differ for each. It is important to read the manufacturers instructions.

Normally growth hormone should be kept cool, usually in a refrigerator (but not too near the freezer compartment). The drug is more affected by heat after having been mixed with the diluent, therefore any growth hormone that needs to be kept out of the fridge for any length of time (when travelling etc.) should, if possible, be in powder rather than liquid form. Small cool bags are available for the transportation of growth hormone. Some of the pharmaceutical companies supply these to patients. They may also be obtained from The Yellow Cross Company and Owen Mumford (See page 10 for addresses).

All growth hormone still in powder form can withstand removal from “fridge” conditions for some period of time and it is important not to worry unduly if power cuts, etc. occur. If your growth hormone has been exposed to high temperatures contact your child's specialist for advice. Do not let growth hormone come into contact with direct sun light.

Storage requirements of the newer versions of growth hormone need to be confirmed with your growth nurse, as some preparations do not need to be kept in a fridge.

Always check the expiry date on your vials of growth hormone.

INJECTION OF GROWTH HORMONE

The pharmaceutical company that produces the growth hormone your child has been prescribed will supply all the necessary equipment directly to the family. Some companies on the receipt of the doctor prescription, will also arrange the supply of the GH directly to the family too.

Pen Injector Systems - Pen injection systems for growth hormone treatment have been available since 1991. This has been a development from pens for insulin treatment in diabetes which have been available for many years. Pen systems are so named as the device appears like a large writing pen which contains a cartridge of growth hormone. They offer the convenience of pre-measured doses, and some children find them both practical and attractive. Some of these pen devices have “needle shields” that fit onto the end of the pen covering the needle. some pen devices have an attachment that inserts the needle automatically, the dose is administered separately. Some devices are fully automatic. See autoinjector.

There are also devices which do not require a needle. The growth hormone is passed through the skin by pressure.

Each pharmaceutical Company has their individual design of pen and method of identifying and giving the dose.

The pharmaceutical companies manufacturing growth hormone have produced a number of booklets and videos to help you with the task of giving growth hormone. The appropriate booklet for the growth hormone you are using should be given to you by your child's specialist or growth nurse when treatment commences. If you have spoken to your growth clinic/hospital and are unable to obtain a booklet, contact the Child Growth Foundation.

ADDITIONAL EQUIPMENT AVAILABLE

There are a number of devices available that are alternatives to the pen systems that may be of help to you and your child with the management of injections. Some are made available through the pharmaceutical companies who make growth hormone. It is important that you discuss all the options available with your growth specialist. A brief description of these devices is given below:

Autoinjection devices - These devices use mainly the Microfine insulin syringes, however, the Autoject 2 also has a version for use with the interchangeable needles and syringes. Autoinjection devices completely enclose the needle and syringe so they cannot be seen. At the touch of a button the needle is inserted through the skin and the growth hormone is automatically injected. This is a quick and usually painless procedure. These devices have helped many children with the transfer to self injection.

The Hypoguard Injector - This simple device, which also uses the insulin syringes, conceals the needle and makes injecting more comfortable.

These devices have helped parents experiencing difficulties with injecting younger children and children injecting themselves. Such devices can be very successful at alleviating the discomfort and fear of injections and the only disadvantage is that parents and children using them will usually become dependant on the device as part of the injection procedure. It is therefore important to also learn to inject without using the device.

Autoinjection devices are available, free of charge, from some of the pharmaceutical companies and you may wish to discuss this with your specialist. Alternatively, you may wish to purchase one of these devices direct from the manufacturer:

(Auto Injector & Autoject 2)	(Hypoguard)	The Yellow Cross Co Ltd (Cooler Bags)
Owen Mumford Ltd, Brook Hill	Hypoguard Ltd, Dock Lane	WW Unit 1, 5 Highclere Road Knaphill
Woodstock, Oxford OX7 1TU	Woodbridge, Suffolk IP12 1PE	Woking, Surrey GU21 2PN
Tel: 0199381 2021	Tel: 01394 3733	Tel: 0125233 2005

If you are unhappy with your current system of administration you should mention it to your growth nurse or specialist as there may be other options to discuss.

SCHOOLS AND ACTIVITIES

Schools, play groups, etc., are sometimes unaware of the problems that children who are very small for their age have to deal with such as practical difficulties of being unable to reach a peg or desk or sit on the toilet. They may also experience psychological problems of not being accepted by friends of the same age or being treated like a toy and picked up by other children. (This problem is not only an annoyance but also means physical danger. Serious accidents have occurred when children are carried inappropriately in the playground.) It may be advisable to visit your child's school or play group to discuss your child's condition as this can help teachers and carers to plan the support and avoid problems before they arise. If problems do occur, and you feel unable to cope, contact the CGF who will put you in touch with other parents with similar problems who may be able to give practical help and support. If the problem becomes more severe, help may be available from an educational psychologist from the school or a child psychiatrist in association with your specialist growth centre. Most of us tend to adjust our expectations for a child that looks younger and sensible discussion of this problem can help to counteract this natural tendency and ensure that your child is treated in a manner appropriate to his/her age.

GROWTH MEASURING AND RECORD KEEPING

If your child is short but no referral has been discussed yet, it is a good idea to keep your own record of his/her growth measurements, particularly as the NHS does not provide a national screening programme. These measurements can provide valuable evidence of the child's growth history which may not be available from any other source. Although these records may be of enormous importance for your growth specialist, we would advise you to retain a copy. Once your child has been referred to a growth centre and regular measurements are taken you may still wish to keep your own record. This can be a sensible backup to hospital records and provide interesting information for you and your child.

It is important not to take measurements too frequently as this can become stressful for your child and is of little, if any, value. Everyone's height naturally reduces very slightly during the day and, as a result, our evening height is less than our morning height. The small changes that occur in height if you measure from month to month will present a confused picture because of seasonal variations. A half yearly measurement will show a clear picture of your child's overall growth and will not put pressure on your child or exaggerate the importance of height.

The Child Growth Foundation produces a leaflet on measuring and record keeping called '**Your Child's Growth**'. Copies of this leaflet, and growth charts for plotting your child's growth, are available for parents from the Foundation.

TREATMENT DURING ILLNESS (and missed injections)

Growth hormone should, if possible, be continued during illness but if your child is too ill to inject without considerable upset, and you miss a day or two, do not worry as long as its just a one off. Any consistent missed injections will effect growth. However, do tell your child's consultant when next you see him if your child has missed more than one or two injections.

IMPORTANT

It is extremely important that **no** injections are missed if your child has low blood sugar associated with growth hormone deficiency which will have been identified by your specialist.

If your child has multiple pituitary hormone deficiencies (MPHD), treatment during illness is more complex but continuation of some growth hormone treatment will certainly be helpful.

The emergency information pack for children with cortisol and GH deficiencies and those experiencing recurrent hypoglycaemia (available from the CGF) gives details on how to cope with illness for this group of children.

Booklet No. 11 is for those with Multi Pituitary Hormonal Deficiencies

PUBERTY

About 50% of children who have 'isolated' growth hormone deficiency usually have some deficiency also of the hormones affecting sexual development (gonadotrophins) and will require additional treatment to initiate puberty.

Nearly all children with multiple hormone deficiencies will require help with puberty.

Puberty will normally be induced if there are no signs of spontaneous puberty by about the age of 14. In the child for whom an early diagnosis of gonadotrophin deficiency is made, puberty should begin to be induced at a younger age than 14yrs so there is little difference between the beginning of their puberty, and the onset of puberty of their peer group.

Modern treatment for this condition is now more successful at inducing fertility as well as sexual characteristics.

This is a complex subject and the Child Growth Foundation has produced a booklet No. 3 explaining the management of puberty for these children. It is advised that all parents with a growth hormone deficient child obtain this booklet prior to the expected start of puberty in their child.

ADULTHOOD

In the paediatric clinic there should be a routine mechanism for the handover of care to an adult endocrinologist. This will vary from centre to centre as to the different ways this is organised and at what age this transfer will be managed. The name of an adult endocrinologist should always be given to the young adult before leaving the care of the growth clinic and an appropriate referral for the transfer of care made.

Research into the use of GH in adults who are growth hormone deficient is ongoing but it does appear that in some adults when growth hormone replacement is stopped, there is a deterioration of "well-being". There is now strong evidence to suggest that growth hormone treatment may aid the prevention of osteoporosis (brittle bones) in adults with GHD. Trials are taking place to test bone density, muscle mass, stamina and the subject's own views on his/her vitality, energy and quality of life.

[See Booklet No 7 Growth hormone deficiency in adults](#)

SIDE EFFECTS

Biosynthetic growth hormone is a comparatively new drug and any new drug can carry the risk of unrecognised side effects. However, synthesised versions of growth hormone have now been tested and used for a number of years without any side effects arising. A few patients report a localised skin reaction at the site of injection but this can usually be treated by varying the injection site or changing the chemical preservative in the diluent.

The only known side effect of growth hormone is "benign intercranial hypertension". Rarely benign intercranial hypertension does occur in the first 6 months of treatment due to growth hormone affecting the retention of fluid in the body which can cause symptoms of headaches, very rarely visual disturbance and vomiting can occur. If growth hormone treatment is stopped these symptoms rapidly resolve and treatment can then be restarted with a very low dose which is then gradually increased to the required replacement dose.

This gradual increase in dose until maintenance level is reached is nearly always used in adults requiring growth hormone replacement. In general children seem to tolerate the full replacement dose from the start, with the significant exceptions.

For the last 15 years there has been a concern that growth hormone treatment could be associated with the onset of sugar diabetes. However, there is now the benefit of long term follow up in many thousands of patients receiving growth hormone in North America and Europe. There is no evidence that growth hormone treatment has any other side effects except the rare raised intercranial pressure.

RIGHTS AND BENEFITS

In certain circumstances, you may feel your child needs additional support to that required for other children of the same age for learning difficulties, behavioural problems or developmental delay. The level and kind of support for children with GHD and MPHD are very individual depending on how severely the child is affected and whether there is any underlying conditions that has caused the deficiency.

Medical care needs to be taken in assessing any additional support if your child has difficulty with symptoms of hypoglycaemia (keeping blood sugar levels stable) these are more associated with MPHD.

The differences in the conditions of GHD and MPHD in the young child are quite dramatic especially in care and replacement medication for the child with MPHD. As the child gets older the issues become more understood and familiar and less daunting.

There are benefits available to help with the extra care that your child may require and the family doctor, health visitor or social services should be able to advise you. The basic benefit available is the disability living allowance. If you apply for this allowance, a doctor will visit you and your child to assess your case.

If the mobility of your child is restricted you may also be eligible for a mobility allowance. Other concessions are available but you would not normally be able to obtain any other financial benefit unless you have first been awarded a disability living allowance. You should discuss this with your growth specialist who may be able to support your application.

DIET AND OBESITY

30% of growth hormone deficient children are overweight. Recent research has shown that these overweight children, in terms of age, size, etc., take fewer calories than the recommended daily intake. It is now recognised that the greater the deficiency of growth hormone secretion the greater the tendency towards obesity. Research has also shown that these children's energy expenditure is less than normal, even when active.

It is important for parents to be aware of this potential problem and to ensure that their child leads an active life and does not eat excessively but eats a well balanced diet with sufficient food to maintain satisfactory growth. If your child is overweight, very low calorie dieting should not be undertaken. A small reduction in calories, together with a slightly increased level of activity, should, in time, produce results. Your growth specialist will arrange an appointment with a dietician if you request this.

The use of growth hormone has been reviewed by the Government Agency called the **National Institute of Clinical Excellence** (NICE). Full approval for its use has been given for all the licenced indications in childhood.

These are a selection of relevant recommendations.

‘Guidance on the use of human growth hormone (somatropin) in children with growth failure’.



**National Institute for
Clinical Excellence**

NICE Technology Appraisal Guidance – No. 42

Guidance

Recombinant human growth hormone (somatropin) treatment is recommended for children with proven clinical diagnosis of growth hormone (GH) deficiency supported by appropriate auxological, biochemical and radiological investigations.

GH treatment is recommended for children with Turner syndrome (TS). The following issues should be taken into consideration in order to maximise the benefit from this treatment:

- diagnosis and treatment at earliest age possible
- appropriate timing and use of oestrogen therapy.

GH treatment is recommended for pre-pubertal children with chronic renal insufficiency (CRI) providing:

- nutritional status has been optimised
- metabolic abnormalities have been optimised
- steroid therapy has been reduced to minimum.

GH treatment is recommended for children with Prader-Willi syndrome.

GH treatment should, in all circumstances, be initiated and monitored by a paediatrician with special expertise in the management of children with GH disorder. Continuation of treatment can be maintained under an agreed shared care protocol with a general practitioner.

Growth hormone (GH), also known as somatropin, is a hormone produced by the anterior pituitary gland. GH is essential for normal growth in children and acts by increasing growth, both by a direct action on the growth plates and via the production of insulin-like growth factors (especially IGF-I) mainly in the liver. GH also has important effects on protein, lipid and carbohydrate metabolism, not only during childhood, but also throughout adult life. Among children who are of very short stature (i.e. at least 3 standard deviations below the population mean), 25% have GH deficiency.

GH deficiency may occur as an isolated hormonal deficiency or in combination with multiple pituitary hormone deficiency (MPHD) as a result of hypopituitarism, tumours in the central nervous system, cranial irradiation or other organic causes. Idiopathic growth hormone deficiency (IGHD) is the most common form, accounting for approximately 50-70% of cases.

Growth failure is a prominent feature in children with chronic renal insufficiency (CRI) and Turner syndrome (TS). Growth failure associated with CRI and TS is thought to be multifactorial, with one of the factors being reduced sensitivity to GH, rather than decreased GH levels. Therefore, supra-physiological doses of GH are required for treatment in children with these conditions. Children with Prader-Willi syndrome (PWS) are considered to have a hypothalamic disorder, and thus GH therapy is intended to replace physiological levels of GH.

The definition of a normal response is still rather arbitrary as there is a continuous spectrum of GH secretion in childhood. In a child with clinical criteria for GH deficiency, peak GH concentrations below 20 mU/litre have traditionally been used to support the diagnosis. However this value will vary depending on the GH immunoassay used and needs to be revised downwards when using newer monoclonal-based assays and recombinant GH reference preparations.

Magnetic resonance imaging of the brain with particular attention to the hypothalamic-pituitary region should be carried out in any child diagnosed as having GH deficiency, to exclude the possibility of a tumour.

GH therapy is currently the mainstay treatment to correct growth failure for children with GH deficiency and with TS. In these groups of children, there are no other active treatment options to increase stature. Oxandrolone may be added to GH treatment regimens for treatment of girls with TS. In the UK, conservative management strategies for CRI include diet guidance and nutritional supplementation.

The aim of treatment in PWS is to improve the body composition as well as promoting growth, as most children with PWS are obese. Dietary management and appetite suppressants have been tried with very limited success, partly because of the behavioural problems associated with this condition.

To measure compliance locally with the guidance set out in Section I, the following criteria should be used. Technical details on the criteria are given in Appendix D.

- GH treatment is prescribed for children with the following conditions: GH deficiency, TS, CRI or PWS.
- For a child with GH deficiency, the diagnosis is made by auxological, biochemical and radiological findings and is confirmed by two GH provocation tests, with an evaluation of other aspects of pituitary function, except for children with defined CNS pathology, history of irradiation, MPHD or a genetic defect affecting the GH axis, who may need one GH test only.
- For a pre-pubertal child with CRI, treatment should be initiated only if nutritional status has been optimised, metabolic abnormalities have been optimised, and steroid therapy has been reduced to a minimum.
- GH treatment is initiated and monitored only by a paediatrician with special expertise in the management of GH disorders.

- GH treatment is re-evaluated against expected growth. Re-evaluation includes taking account of persistent and uncorrectable problems with adherence to treatment with the therapy and in PWS, body composition.
- GH treatment is discontinued in the following circumstances:
 - the child has a poor response to treatment
 - a child with CRI has a transplantation
 - the child attains final height
- The decision to stop treatment is made by the paediatrician with special expertise in the management of GH disorders in consultation with the patient and carers or therapy is continued until re-evaluation by an adult endocrinologist has been undertaken.

SUMMARY

Now that growth hormone is available in biosynthetic form, there are no restrictions on the quantities available. Its use has full approval for all licenced indications in childhood from the National Institute of Clinical Excellence. This means that children can now be treated with progressively increasing doses related to size and body weight and that dosage can be adjusted to ensure that a good growth rate is maintained. Even with the improved outlook for growth hormone treatment, your child's final height will still be influenced by the age at which treatment commenced and if your child's condition was not diagnosed and treated early, their final height will be less than it would have been if treatment had commenced when your child was very young. However, in many cases, current treatment will achieve a normal height for your child.

Modern treatment for both growth hormone deficiency and multiple hormone deficiency is very successful and all the hormones produced by the pituitary gland can be successfully replaced.

SOURCES OF ADDITIONAL INFORMATION

Pharmaceutical company booklets

The pharmaceutical companies producing growth hormone have produced booklets which provide information on growth hormone treatment and general information on their product. Requests for these booklets can be made initially to your growth nurse at the growth centre you and your child attend or hospital where treatment is obtained but if they are not available at your clinic, the *Child Growth Foundation* should be able to help you.

Books

The following book is available from the CGF.

Foetus into Man - (A detailed description of all aspects of growth providing sections on growth hormone deficiency and the action of hormones. Written by Professor Tanner, Professor of Child Growth from the Institute of Child Health). Price on application

The Child Growth Foundation (CGF) is available to provide support and wide ranging information to anyone with problems related to growth.

The CGF office can be contacted at the following address or telephone numbers:

THE CHILD GROWTH FOUNDATION

(Charity No 1172807)

21 Malvern Drive, Walmley

Sutton Coldfield, B76 1PZ

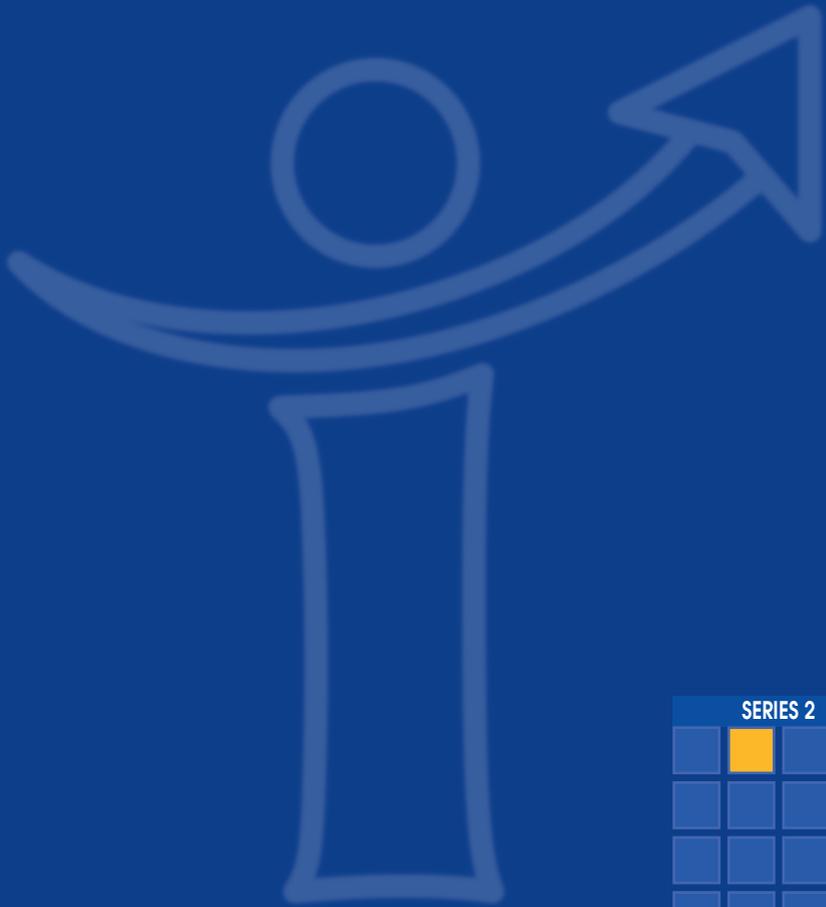
Telephone: +44 (0)20 8995 0257

The CGF supports groups within the foundation which deal with specific conditions. The *Growth Hormone Group* has a voluntary organiser who is available to help with queries or problems relating to Growth Hormone Deficiency.

If you wish to join the foundation there is a network of members who are happy to be contacted.



CHILD GROWTH
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