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**About this Book**

*Growth Problems in Children* should give you a basic understanding of the complex nature of growth and development as well as an overview of the conditions that may affect growth.

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 Problems in Children*, which is part of their “Hormones and Me” educational booklet series. We hope that you will find it a valuable and helpful resource.

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**Introduction**

Growth is the defining characteristic of childhood. Normal growth during childhood depends on a combination of good general health, adequate nutrition and genetics. It is important to remember that there is a wide range of what is considered ‘normal’ in how children grow and develop. Growing, like learning, does not always follow an even course and can occur in spurts.

Although most children who are below or above average size are otherwise normal, there are some important underlying conditions that can cause abnormal growth. These include chromosome abnormalities (genetic disorders), endocrine gland disorders (hormonal abnormalities), cartilage or bone disorders and general chronic disease. Early detection and treatment of underlying conditions with or without growth supplements can enable many children experiencing abnormal growth to reach their full potential.

*Growing, like learning, does not always follow an even course and can occur in spurts.*
Normal Growth

Phases of Growth

Children grow through three phases as can be seen in Diagram 1. Each has a characteristic pattern and each is controlled by a different set of internal mechanisms.

The first phase is from birth through infancy to the pre-school years. This phase is characterised by rapid growth of all parts of the body including the brain and the nervous system. During this time, the rate of growth steadily decreases so that the fastest speed of growth is at the beginning of this phase in the first three months of life. Hence a newborn baby is growing faster than at any other time in childhood or adolescence and illness can severely disrupt growth potential during these early months. A number of hormones control this growth phase - the hormone thyroxine is essential for this phase of growth and development to be complete.

The second phase extends through the school age of children until adolescence begins. The growth rate during this time is fairly steady at about 5cm each year. Most of the growth is in the limbs so that the mid-point of the child moves upwards as can be seen in Diagram 2. In this phase, growth hormone is the most important factor controlling growth and development.
The third phase is the most complicated and stretches through adolescence (puberty) until the bones become solid and adult height is reached. During this phase, the speed of growth picks up rapidly and then falls away to nothing (the growth spurt of adolescence). The sex hormones (testosterone and oestrogen), are the major factors controlling this phase but growth hormone and insulin levels are also important.

The Essentials of Normal Growth

Children grow best when their health, both physical and psychological are optimum. Most important is the provision of adequate nutrition both in quantity and quality so that the energy needs and the specific building blocks are provided to the growing child. Protection from preventable illness is also important (e.g. immunisation against common infectious diseases).

The reasons that our ancestors were shorter than the present generation relates mostly to the lack of the above essentials for growth in their time.

Assessment of Growth

Every child should be measured regularly. If there are any concerns regarding any child's growth, these should be discussed with the local doctor. The doctor will ask about the child’s birth, development and general health, examine the child and may order specific tests to assess the child’s growth (see Table 1).

The measurements taken will depend on the age of the child. Weight, length and head circumference should be measured regularly in infancy. Standing height of the child without shoes is useful from two years of age and should be measured at least every two years. If the growth pattern is abnormal, measurements as often as three monthly will give a more accurate view of the pattern and allow calculation of the speed of growth. The heights of both parents should be accurately measured as these can be used to estimate the familial adult height potential of children.

“Every child should be measured regularly.”
Assessment of Abnormal Growth

**DETAILED MEDICAL HISTORY**

**General Examinations**
- measurement of length, height, weight and head circumference
- body proportions, unusual physical features, pubertal status
- general health

**Screening Investigations**

**Blood Tests**
- full blood count, blood chemistry
- hormone function (e.g. thyroid hormone levels)
- chromosome studies

**Urine Tests**
- microscopic examination
- chemical assessment

**Imaging**
- X-rays to assess bone structure and maturity

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**Centile Charts**

Centile charts are graphs that show the average pattern of growth during childhood. Measurements of height (or length in infants), weight and head circumference should be plotted throughout childhood on the centile chart appropriate for the age and sex of the child. A series of measurements demonstrating the trend in growth is more valuable than one static measurement. The child's growth should usually follow the curve of the centile graph (see Diagram 1). Crossing centile lines is a warning sign of abnormal growth (see Diagram 3).
Short Stature

Short stature - defined as having a height below the 3rd percentile for age and sex - is a common problem affecting up to 5 children out of every 100. Although this may be the normal pattern of growth for an individual child, underlying causes of poor growth should be considered. The following sections will look at the major causes of short stature in childhood.

Familial Short Stature

Children are a reflection of their parents. Parents who are short usually have children whose height is in the lower range of normal. Conversely tall parents usually have children who are tall. As a general rule, a child’s potential adult height is the average of the parents heights with a correction for the parent of the opposite sex to the child. See Table 3 for a formula to calculate a child’s potential height.
To calculate the potential height of a boy, the mother’s height is given an additional 13cm and averaged with the father’s height. This mid parental or ‘target height’ can be plotted on the growth chart to estimate the centile the boy should grow along.

E.g.  
FATHER 180cm  
MOTHER 157cm + 13cm = 170cm  
AVERAGE 175cm = potential height = 50th height centile  
(see Diagram 3)

To estimate a girl’s target height, subtract 13cm from the father’s height and follow the steps above.

Constitutional Short Stature with Slowed Maturation

Constitutional delay of growth is the most common cause of short stature in childhood. This is a variant of normal and is usually associated with a delay in maturation and with late puberty. Constitutional short stature often runs in families and members of the family may have a history of being ‘late bloomers’ with regard to growth and puberty.

Children with constitutional short stature usually have normal weight and length at birth. Between 6 and 30 months of age their growth slows down and falls below the 3rd centile line. After this dip, growth returns to normal and they remain parallel to, but below the 3rd centile line on their growth chart. Intellectual development remains normal for age. Assessment of bone maturity on X-ray will show that the bones are behind in skeletal maturation.

Problems may arise especially around the time of adolescence. While the child’s friends experience the onset of puberty and its associated growth spurt, the child with constitutional short stature will fall further behind his or her peers in growth. This child will eventually enter puberty normally and given time children with constitutional short stature usually reach their genetic height potential. Reassurance and open communication can help deal with the emotional stress of being small.

If reassurance is not enough, there are treatments available. The use of a mild anabolic steroid (oxandrolone) can cause the adolescent growth spurt to occur a little earlier but makes no difference to final height. If lack of pubertal development is the major concern, hormone therapy with a male hormone (testosterone) in boys or female hormones (oestrogen) in girls, can initiate puberty. These forms of therapy require careful monitoring by a paediatric endocrinologist.
Human Genetics (Growth Genes)

The genetics of growth in humans is extremely complex and not all the inherited traits have been identified yet. There are however, many genes on the human chromosomes that affect the way the body proportions develop making no two children grow in the same fashion or look identical (with the exception of identical twins). Clearly some growth traits are dominantly inherited affecting each generation, whereas other traits are recessive and appear only when two parents carry the trait but do not show it themselves. The parents genetic makeup influences the growth of their children much more than that of previous generations or lateral relatives (cousins) so that the growth characteristics of the father and mother are most relevant in determining the growth of their children.

Turner Syndrome

Turner Syndrome is one of the most common genetic (chromosome) abnormalities in girls, affecting 1 in every live 2500 girls born. It is caused by an abnormality of the sex chromosomes so that one of the pairs of X chromosomes found in women is partly or completely missing. This results in short stature and problems with ovarian development. Some affected girls have other physical features. Any girl with short stature should have a chromosome study done to test for Turner Syndrome.

Girls with Turner Syndrome benefit from growth hormone treatment starting as early as possible and later need hormone replacement therapy (HRT) with female hormones to complete their sexual development.

“Any girl with short stature should have a chromosome study done to test for Turner Syndrome.”

Down Syndrome

Down Syndrome is one of the most common chromosome abnormalities affecting around 1 in 1000 babies born worldwide - male and female alike. Down Syndrome is the result of having 3 instead of 2 chromosomes number 21, an abnormality which occurs at the moment of conception. Children with Down Syndrome have a variety of features affecting various body systems and have a characteristic facial appearance. They experience poor growth and special growth charts are available for children with this syndrome. The growth problem in this syndrome can sometimes be worsened by an underactive thyroid gland or by problems with the pituitary gland. Children who grow poorly on the Down Syndrome centile charts need investigation by a paediatric endocrinologist to identify their hormone deficiencies.

Noonan Syndrome

Noonan syndrome is a less common genetic abnormality affecting around 1 in 2000 babies born. It affects both girls and boys and often runs in families.
Children with Noonan Syndrome have characteristic facial and body features, poor growth, sometimes a delay in adolescence and often abnormalities of the heart chambers or valves. All children with Noonan Syndrome should see a children’s cardiologist for heart investigations.

Although children with Noonan Syndrome may have normal weight and length at birth, their growth rate and final height is often less than average. Special height charts are available for children with Noonan Syndrome and from this a paediatric endocrinologist will be able to estimate the child’s final height. Growth hormone may be used to try and improve adult height in some children with Noonan Syndrome. Hormone replacement therapy (HRT) may be necessary if puberty does not occur spontaneously.

Other Genetic Causes

There are many other syndromes and recognizable patterns of growth that are rare but have a genetic basis. These conditions can be recognised by a paediatric endocrinologist or a specialist in human genetics. Often there are specific tests to confirm the doctor’s suspicions of the diagnosis. Growth patterns in this group of disorders vary widely but the diagnosis can be most useful in predicting the outcome for the individual child. Some of these conditions can benefit from growth hormone treatment.

Intrauterine Growth Retardation

Intrauterine growth retardation (IUGR) is a term used to describe the characteristics of a baby who is smaller than normal during pregnancy. Babies with IUGR do not grow at a normal rate within the womb and are born with a weight and length that are inappropriately low for the duration of the pregnancy. For a baby born at full term, this is less than 45cm long and less than 2.5 kilograms weight. Tables of length and weight are available for premature babies.

The growth of a baby within the womb depends on maternal health and nutrition, the placenta that supplies food and oxygen to the foetus and the genetic information stored within the baby’s cells. Sometimes the cause of IUGR remains a mystery, however there are some conditions in the mother that are commonly linked to poor fetal growth. These include high blood pressure or infections during pregnancy, smoking and the abuse of alcohol or other drugs. Babies with genetic or chromosomal abnormalities often have IUGR.

Most babies born with IUGR show catch-up growth over the first two or three years of life, however in around one third of cases this does not occur.
Children who do not experience this catch-up growth can benefit from growth hormone therapy to help them reach their genetic height potential.

**Russell Silver Syndrome**

Russell Silver Syndrome describes a group of children born with IUGR who display a number of specific physical characteristics as well as poor growth. These children tend to be small and thin with triangular faces, prominent foreheads and small chins. Often the limbs are of different lengths and the fifth fingers are very small. There are many other physical traits associated with this syndrome and the number of characteristics varies from child to child. The cause of Russell Silver Syndrome is unknown, although some genes linked with this condition have now been identified and it rarely occurs twice in the same family.

Most children with Russell Silver Syndrome develop normally except in size. They tend to put on weight in middle childhood and experience normal puberty although this may be a little earlier than their peers. Improved care including the prevention of low blood sugar levels, nutritional supplements during childhood and growth hormone therapy will help children with Russell Silver Syndrome reach their full potential. Growth hormone therapy can improve short and long term growth in this syndrome.

"Most children with Russell Silver Syndrome develop normally except in size."

Not only does normal growth depend on good health and nutrition, but the normal secretion of growth stimulating hormones from endocrine glands. The two most important hormones required for growth are growth hormone and thyroid hormone. A deficiency of one or both of these hormones will result in poor growth and short stature.
Growth Hormone Deficiency

Growth hormone deficiency is estimated to affect 1 child out of 5000 and is more commonly recognised in boys. It occurs when the pituitary gland at the base of the brain fails to produce adequate levels of growth hormone. The pituitary gland releases growth hormone (as well as many other hormones) in response to chemical messages from the hypothalamus, the part of the brain to which it is connected (see Diagram 4).

Low levels of growth hormone may be due to a problem within the hypothalamus, the link between the hypothalamus and the pituitary gland or within the pituitary gland itself.

Growth hormone is released by the pituitary gland in spurts over a 24 hour period, mostly at night during sleep and after exercise. Once released into the blood stream, growth hormone acts on the liver, kidneys and other tissues including bones to produce other chemicals known as somatomedins (or insulin-like growth factors). These somatomedins act with growth hormone to promote growth. As well as promoting growth, growth hormone has an important role in the metabolism of fat and carbohydrate and helps to maintain blood sugar levels.

Causes of Growth Hormone Deficiency

It is not always possible to determine the exact cause of growth hormone deficiency. There may have been damage to the pituitary gland or its connections at birth or it can occur following a head injury or infection. When the cause is unknown the term idiopathic growth hormone deficiency is used.

Other causes of growth hormone deficiency include problems with the development of the pituitary gland or the hypothalamus. Sometimes growth hormone deficiency may be inherited or linked to a genetic syndrome. In some cases, damage to the pituitary gland or hypothalamus is caused by trauma, a brain tumour, surgery or X-ray therapy used to treat brain tumours and leukaemia.

It is rare for children to have a complete lack of growth hormone. In most cases there is some growth hormone present but this is insufficient to maintain normal growth.
How is Growth Hormone Deficiency Diagnosed?

Children with growth hormone deficiency are small compared to other children of their age and their growth rate is poor, so they fall behind their peers (see Diagram 3). They tend to be chubby and to have young looking faces due to delayed bone development in the skull as well as in the limb bones.

Any child with suspected growth hormone deficiency should be assessed by a paediatric endocrinologist. This growth specialist will take a medical history including details of the child’s birth, development and general health. It is important to provide as many measurements of the child’s height and weight as possible so a detailed growth chart can be plotted.

A thorough physical examination of the child including accurate measurement of height, weight and body proportions will be performed. X-rays of the child’s left hand will be taken to determine maturation of the skeleton. Blood tests will be taken to look for levels of other pituitary hormones, which may also be low. These include thyroid stimulating hormone (TSH), the sex hormone stimulating hormones (FSH and LH) and the adrenal stimulating hormone (ACTH), insulin like growth factors (IGF1) and their binding proteins (IGFBP3), (see Diagram 5).

As the blood level of growth hormone fluctuates widely over a 24 hour period it is not reliably measured in a single blood test, rather blood must be taken during a growth hormone surge or at frequent intervals over a period of time. The specialist will recommend provocation or stimulation tests, which will involve a day stay in hospital. In growth hormone deficiency there will be a lack of growth hormone production in response to two stimulation tests.

Growth Hormone Treatment

Growth hormone has been used for many years with great success in the treatment of children with growth hormone deficiency. Biosynthetic growth hormone is manufactured using gene technology and is identical to the growth hormone we produce naturally. Before biosynthetic growth hormone was available (prior to 1985), growth hormone was taken from human pituitary glands at autopsy. The use of human growth hormone carried a small risk of infection but this does not occur with biosynthetic growth hormone.

The aims of treatment are two-fold: firstly to catch up height to the normal range and secondly to increase final height. Provided treatment with growth hormone is started at a reasonably early age (before age 6 years) both aims can usually be achieved. Later, treatment before puberty is still appropriate but the results are usually less satisfying than when treatment is started early.

The dosage of growth hormone varies according to the child’s weight and surface area and will increase as he or she grows. It is given by an injection once daily just under the skin using a syringe or special pen with a fine needle. The injection is best given before bedtime to mimic the natural production of growth hormone as closely as possible.

Refer to page 35 for further information on growth hormone treatment.

"Growth hormone has been used for many years with great success in the treatment of children with growth hormone deficiency."
Pituitary Gland Failure (Hypopituitarism)

Around half of all children with growth hormone deficiency will also have some deficiency of the hormones involved in sexual development and will need treatment with sex hormones to initiate puberty. Children with deficiencies of multiple pituitary hormones will need sex hormone therapy to experience normal puberty, thyroid hormone (thyroxine), hydrocortisone for adrenal gland failure and often vasopressin (DDAVP) to balance water loss.

Hypothyroidism

Hypothyroidism is a deficiency of the hormones produced by the thyroid gland - thyroxine (T4) and triiodothyronine (T3). These hormones are essential for normal growth and cell function. A deficiency may be present from birth and the main problem may be either in the thyroid gland itself or in the way the pituitary gland naturally stimulates the thyroid gland. A routine blood test for hypothyroidism is performed on every newborn baby to ensure early diagnosis and treatment but children may develop a thyroid problem later.

Later in childhood, hypothyroidism is usually caused by an abnormality of the immune system that results in damage of the thyroid gland. Sometimes hypothyroidism is due to failure of the pituitary gland to secrete thyroid stimulating hormone (TSH), (see Diagram 5). Low levels of thyroid hormones in hypothyroidism result in a slowing down of growth during childhood resulting in short stature. Other general symptoms of hypothyroidism include tiredness, constipation, dry skin and intolerance to cold. Treatment with oral thyroid hormone (thyroxine) restores normal thyroid function and normal growth.

Cushing Syndrome

Cushing Syndrome is a condition caused by overproduction of the hormone cortisol or the prescription of this hormone or others like it, e.g. hydrocortisone and prednisone, in conditions where such steroids are essential for maintaining health. Conditions such as asthma, inflammatory bowel disease and rheumatoid arthritis are examples. Cortisol is normally produced by the adrenal glands (located on top of the kidneys) and is vital in the regulation of blood pressure, the immune system, metabolism and growth.

Excess production of cortisol can be due to over-activity of the pituitary gland (which stimulates the adrenal glands to produce cortisol) or over activity of the adrenal glands themselves.

Children with too much cortisol will tend to be overweight, (especially around the face and trunk) and experience poor growth. They may also develop excess body hair, greasy scalp hair and acne. This condition is diagnosed by the measurement of cortisol levels in the blood and urine. Treatment depends on locating the source of over-activity and removing it. Following this, supplements of adrenal or pituitary hormones may be necessary. Growth in these children then usually resumes but growth hormone treatment is sometimes required.

In asthma and the medical conditions treated with steroids such as prednisone, growth failure may occur and the physician will attempt to reduce the steroid prescribed to improve growth. Some children however, can not reduce their steroid due to the need for ongoing maintenance treatment of their underlying condition. Growth hormone treatment is sometimes used to improve growth, but may not be successful when the child is using steroids.
There are many cartilage and bone disorders which affect growth. Most of these conditions are rare and many are inherited. They are known as skeletal dysplasias.

**Achondroplasia**

This is the most common type of skeletal dysplasia recognisable at birth. Achondroplasia is due to an abnormality of a single gene, which can occur spontaneously when a baby is conceived or be inherited from a parent with achondroplasia. This inheritance of achondroplasia is autosomal dominant, meaning a person with achondroplasia has a 50% chance of passing the defective gene to their child. If the child inherits the gene he or she will have achondroplasia. When a child with this problem is born to normal stature parents a mutation has generally occurred to cause the genetic abnormality.

Children with achondroplasia share many distinctive features including very short arms and legs, normal length back, a large head and characteristic face. Achondroplasia does not affect intelligence.

There is no cure for achondroplasia, but operations to lengthen the bones of the arms and legs can be successful and improve height. Growth hormone treatment can be of use in the short-term by increasing the rate of growth but has not been shown to increase final height. The best outlook for final height is likely to be achieved by a combination of growth hormone treatment and surgery to lengthen the limbs.

**Hypochondroplasia**

Hypochondroplasia is also a common skeletal dysplasia in which the limbs are less shortened than in achondroplasia. Recognition comes not at birth but from the doctor's measurement of limb length and characteristic X-rays.

Final adult height in this condition is generally less than expected in the family. In the short-term, growth hormone treatment improves height but whether final (adult) height is improved is controversial.

**Other Skeletal Dysplasias**

There are many rare conditions of cartilage and bone development which lead to short stature and poor growth. The particular features can be recognised by paediatric endocrinologists and X-rays used to more clearly define the diagnosis. Some of these conditions (e.g. hypophosphatemic rickets) respond to chemical treatments. Others do not respond to treatment and the use of growth hormone treatment in this group is of controversial value.
Disorders of the Absorption of Food

Any condition that impairs the ability to absorb food resulting in poor nutrition can cause inadequate growth. Food provides the energy source for growth and the specific chemicals that are the building blocks of growth. Coeliac disease and Crohn's disease are two of the most likely conditions causing short stature due to poor nutrition.

There are a number of other gut problems in this category, but unlike coeliac disease and Crohn's disease, the symptoms of the problem will be very obvious. Hence coeliac disease and Crohn's disease are more likely to show up as a child with poor growth.

Coeliac Disease
Children with coeliac disease are sensitive to a protein called gluten, which is present in many grains including wheat foods. The gluten damages the delicate lining of the small bowel making it unable to absorb vital nutrients. As well as experiencing poor growth, children with coeliac disease can become grossly malnourished and develop gut symptoms.

Coeliac disease is diagnosed by a blood test measuring anti-endomysial antibodies followed by a biopsy of the small intestine which can be done using an endoscope. Once diagnosed, it is important to eliminate gluten from the diet. Growth returns to normal with the new diet. Advice about gluten-free eating is available from the Coeliac Society of Australia.

Crohn's Disease
Poor growth is usually present in children with Crohn's disease. It involves long-term inflammation of the bowel wall, which leads to poor absorption of nutrients and there are usually gut symptoms. Inflammation can usually be well controlled with medication and a gastroenterologist should supervise management. Occasionally, surgery is required. Growth returns to normal when the poor absorption is treated.

General Chronic Disease
Almost all chronic disease in childhood can cause short stature for reasons that are not always clear. Some of the conditions in which poor growth can occur are listed in Table 4. Sometimes it is the treatment as well as the disease itself that interferes with normal growth. Long-term therapy with prednisone and other steroids, which are used to control inflammation in many chronic diseases (e.g. asthma), can result in growth disorders (see Cushing Syndrome page 25).

Anorexia nervosa, a common eating disorder, most frequently seen in adolescent girls, can be associated with serious growth failure - partly due to poor growth secondary to lack of nutrition and partly to failure to start or continue with puberty.
CONDITIONS OF CHRONIC ILLNESS ASSOCIATED WITH POOR GROWTH

- Anaemias
- Asthma
- Cystic Fibrosis and Other Lung Conditions
- Heart Disease
- Inflammatory Bowel Disease
- Kidney Disease
- Liver Disease
- Rheumatoid Arthritis
- Other Long-Term Disorders

Mostly, these diseases will be obvious but sometimes poor growth is the presenting problem. Hence the doctor will order screening blood tests for these conditions when a short child is investigated (see Table 1).

Psychosocial Short Stature

Children in situations where home life is severely disrupted or unhappy, often experience emotional stress and poor growth. The growth failure is due to a combination of factors including, a reduction in the secretion of growth hormone, growth hormone’s response in the tissues and poor nutrition. Children with psychosocial short stature may be chubby for their height and have poor eating habits. There is always an associated behaviour disorder.

Often the only solution to this disorder is to remove the child temporarily from the disrupted social situation and provide normal emotional, physical and nutritional support elsewhere. Growth in these children then recovers rapidly.

Tall Stature

Tall stature generally has less disadvantage than short stature. Only very tall or rapidly growing children require assessment. The most likely cause of tallness is a genetic trait from one or both parents. This genetic tendency in height can be calculated by estimating the same sex mid-parental height (see Table 3).

The assessment of tall stature follows much the same lines as for poor growth. After careful body measurements an estimation of final (adult) height is made by X-raying the hand and wrist for the level of skeletal maturation and using the height and a set of tables to predict the final height. When the predicted final height is much greater than the parent’s height, consideration is given to further investigation and to interventions that may limit growth and reduce final height.

Otherwise normal, but very tall boys and girls can have their adult height reduced by advancing maturation (and adolescence) with the appropriate sex hormones in high dosage - testosterone in boys and oestrogen in girls.

Occasionally tall stature is due to an inherited disorder such as Marfan Syndrome, genetic disorders such as Klinefelter Syndrome or Sotos Syndrome, early puberty (precocious puberty) or an endocrine disorder.
Genetic Disorders Causing Tall Stature

Marfan Syndrome
Marfan Syndrome is a rare inherited disorder that may affect many organ systems including bones, eyes, heart and blood vessels. Children with Marfan Syndrome have excessively long limbs with long thin fingers and very mobile joints. They are often long babies at birth. They may be near-sighted (myopic) and at risk of more serious eye disorders. All children with Marfan Syndrome are tall and loose jointed and they may require limitation of their height to improve the mechanics of their loose joints. The diagnosis can be made by DNA (genetic) studies. Some of the most worrying problems occurring in Marfan Syndrome are abnormalities of the heart valves and dilation of the main arteries. All children with Marfan Syndrome need regular check-ups with specialists in various fields to ensure early detection and treatment of any problems.

Klinefelter Syndrome
This syndrome occurs in about 1 in 800 boys and promotes a more rapid growth and tall stature particularly after 8 years of age. The problem is genetic and relates to the boy having 1 extra X chromosome 47XXY.

Other problems can include some learning difficulties and abnormalities in physical development. All men with Klinefelter Syndrome have reduced fertility due to reduced sperm counts and adolescent boys have smaller testicles than normal.

Some boys with Klinefelter Syndrome benefit from male (testosterone) hormone treatment in childhood and /or later in life to promote male physical and behavioural characteristics.

SEX CHROMOSOMES IN HUMANS

<table>
<thead>
<tr>
<th>Boys/Men</th>
<th>Girls/Women</th>
<th>Turner Syndrome</th>
<th>Klinefelter Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>46 XY</td>
<td>46 XX</td>
<td>45 X (or variants)</td>
<td>47 XXY (or variants)</td>
</tr>
</tbody>
</table>

Table 5

Sotos Syndrome
This syndrome is an example of a number of rare conditions where rapid growth and tall stature are associated with an abnormality of the nervous system. Children with Sotos Syndrome have delayed intellectual development associated with large brains and head size and characteristic facial features that a paediatrician can recognise. Fortunately, bone maturation advances faster than normal and although they become tall adults, these children do not remain as huge as they appear in early years. No growth treatment is required.

Other Genetic Causes
There are a number of rarer genetic disorders which result in tall stature. These are either chromosomal disorders (e.g. 47XYY Syndrome) or specific gene defects, which result in a characteristic appearance along with rapid growth and tall stature. These conditions can be recognised by a paediatric endocrinologist or a specialist in human genetics. Often there are specific tests to confirm the doctor’s suspicions of the diagnosis. Growth patterns in this group of disorders vary widely but the diagnosis can be most useful in predicting the outcome for the individual child.
Premature Sexual Maturation

Premature sexual maturation is a term that describes a group of children who grow rapidly (out pace their peers), and cross centile lines on the growth chart in an increasing direction (see Diagram 3). These changes are due to the sex hormones of puberty being produced abnormally early. Another term for this diagnosis is precocious puberty. There are many causes for this problem, including a genetic tendency to early adolescence. The doctor can advise on the treatments available to arrest rapid growth and sexual maturation if necessary.

Any child who is growing and maturing rapidly requires medical assessment as some of the causes have very serious implications.

Other Hormonal Causes

Excessive growth hormone produced by the pituitary gland is usually due to a tumour and will cause rapid growth and advanced bone maturation. Often this rare condition is associated with headaches, problems with eyesight and other nervous system complaints. Urgent medical assessment by a specialist is needed.

"Any child who is growing and maturing rapidly requires medical assessment as some of the causes have very serious implications."

The first sign of thyroid hormone excess may be rapid growth as thyroxine, the main hormone from the thyroid gland, promotes growth of the long bones. An overactive thyroid causes other symptoms including a large thyroid gland (goitre), a rapid heart rate, fatigue and nervousness with behaviour problems including poor attention span. Medical or surgical treatment of the overactive thyroid condition corrects the growth problem.
Some children with poor growth benefit from the administration of growth hormone. The doctor’s recommendation to begin a child on a course of growth hormone is based on many factors including a complete evaluation of the child’s growth pattern, general health, medical and family history, the results of appropriate laboratory tests and the diagnosis. In addition, the child must fulfil conditions set by the Government so that the supply of the hormone can be provided through the public health system.

Availability of Growth Hormone

All growth hormone is called somatropin and is produced by a process called biosynthesis. There are several brands of growth hormone available and although they vary in formulation, all brands of growth hormone have been shown to be equally effective in promoting growth.

The following brands of growth hormone are currently available in Australia:

- Saizen (somatropin rmc) produced by Serono
- Genotropin (somatropin rbe) produced by Pharmacia & Upjohn
- Norditropin (somatropin epr) produced by Novo Nordisk
- Humatrope (somatropin rbe) produced by Eli Lilly
- Scitropin (somatropin) produced by Scigen

Dosage and Administration

The dosage of growth hormone is calculated from the weight or size of the child. This means the dose will increase as the child grows. In certain circumstances the doctor may increase the dose if the child does not respond adequately.

Growth hormone is given by an injection just under the skin. To mimic the body’s natural production, it is recommended that growth hormone be given before bedtime each night.

“Please discuss the options available with the doctor.”

Storage of Growth Hormone

Growth hormone should be stored in the refrigerator at 4°C as it is susceptible to temperature extremes. When out of the refrigerator, growth hormone should be stored in an insulated bag with a cool brick. Incorrect storage can reduce the effectiveness of the growth hormone injections. Please discuss the storage options with the doctor or nurse.

Supply of Growth Hormone

Growth hormone is provided in 3 month supplies once the Government authority has been granted. Supplies are delivered to the doctor or the hospital pharmacy. Every 6 months, the doctor will need to provide details of the child’s response to growth hormone to obtain further supplies.

Growth Hormone Injections

Somatropin can be given with a disposable syringe or by a pen device. The pen injector is generally more flexible as it offers better convenience when...
travelling and therefore children can attend school camps, sleepovers etc. For children who are nervous about injections, there is a device available which hides the needle and delivers the dose automatically. Please discuss the options available with the doctor.

Coping with Injection Problems

It is never easy explaining to children that injections are for their own good but there are ways of making the process easier. Try to develop a routine by injecting at the same time every day, giving the child a familiar toy to hold and using the same location such as a sofa or bed. Take time to create a relaxed atmosphere and explain the process to the child.

It is recommended that the child does not see the injection preparation process and therefore it is usually best for it to be done out of sight. The establishment of a quick, ‘no-fuss’ procedure often ensures that children grow to accept their injections readily. The doctor can provide you with information about injection techniques and hospital growth clinics offer support programmes and other advice.

Questions and Answers

About Growth Hormone Treatment

Q How does growth hormone work?

A Growth hormone increases the size, number and protein content of cells in the growing body. The amount of muscle, bone and connective tissue increases whilst the skeleton lengthens and widens. At the same time body fat is reduced. The child starting on growth hormone loses fat without losing weight and gains muscle strength and bone structure. Some children find that their appetite increases and the increased food intake adds to the effect of the growth hormone.

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

A There are usually no side-effects. Fluid retention may occasionally occur and to avoid this the doctor may start the child on a small dose of the hormone and gradually increase it until the full dosage is reached. Other rarer side-effects can occur, though these usually only happen in children who have a separate pre-existing condition (e.g. Turner Syndrome) and therefore an increased risk of developing these rare effects. Occasionally children develop a local reaction at the injection site, such as pain, numbness, swelling or redness. If this occurs treatment is stopped and recommenced with another brand.
**Questions and Answers**

**Q** Why would the doctor recommend growth hormone treatment?

**A** There are usually three reasons
1. To achieve ‘catch-up’ growth to bring the child in line with peers
2. Improve self-esteem and to reduce social discrimination
3. Long-term to significantly improve adult height
Aims 1 and 2 are always part of the recommendation

**Q** When is treatment with growth hormone stopped?

**A** In certain conditions such as growth hormone deficiency, treatment with growth hormone should be life-long even after reaching final adult height. Currently, growth hormone has been approved as an indication for treatment in adults but to date no financial support is available in Australia or New Zealand. In other conditions, treatment is given until the bones are close to becoming solid. This usually occurs at 13-14 years in girls and 16-17 years in boys, however, bone maturation can occur earlier or later than these ages. In some children, growth hormone treatment is stopped when there has been sufficient ‘catch-up’ growth to bring the child into the normal range for their age.

**Q** Should children give their own injections?

**A** Children should feel involved in the administration of their injections and if they can give their own growth hormone injection it is easier for them to attend school camps and sleepovers etc. Around the age of 9 years, some children may decide to give their own injections. They should, however, always be supervised by an adult.

**Q** Where should injections be given?

**A** Growth hormone injections are given under the skin in the legs, arms, abdomen or buttocks. It is important to use different injection sites every day.

**Q** What if an injection is missed?

**A** There is no adverse reaction to missed injections, just less efficient growth. Wherever possible, injections should be given regularly, however, if 1 or 2 days are missed, these can be caught-up on subsequent days. Talk to the doctor or nurse if an injection is missed.

**Q** Are there any drugs or treatment that should not be taken during treatment with growth hormone?

**A** Tell the doctor if the child is taking any other medication before starting to use growth hormone. Some medication may interfere with the effect of growth hormone, however there are no known drugs which are incompatible with growth hormone as it is made naturally by the body.
Further Reading

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

Australian Institute of Health and Welfare
International Health - How Australia Compares November 1999

Burren CP Werther GA
J Pediatr Endocrinol Metab
1996 Jan - Feb; 9(1): 31 - 40

Commonwealth Department of Aged Care
Schedule of Pharmaceutical Benefits March 1999 - Guidelines for the Availability of Human Growth Hormone (hGH) as a Pharmaceutical Benefit

The Endocrine Society
www.endo-society.org

The Hormone Foundation
www.hormone.org

The Magic Foundation
www.magicfoundation.org

Saizen® Product Information 1996

UK Society for Endocrinology
www.endocrinology.org

Glossary

Anabolic Steroids
Synthetic male sex hormones that promote tissue and bone growth.

Biosynthetic Hormone
Manufactured hormones that are identical to or perform the same function as those made naturally by our bodies.

Cardiologist
A doctor who specialises in the disorders of the heart and circulation.

Cartilage
Soft gristle material at the end of long bones, some of which hardens into bones when growth is complete.

Chromosome
A thread like structure that carries genetic information in the form of genes composed of DNA. Normally, each human cell contains 23 pairs of chromosomes, and one pair of these are the sex chromosomes. Genes and chromosomes are like blueprints for the body’s development, and so play a large part in determining a person’s characteristics.
Congenital
A feature or condition that is present from birth, but not necessarily hereditary.

Corticosteroids
Steroid hormones produced by either the adrenal gland or synthetic process. Examples include cortisone, hydrocortisone and prednisone.

Cyanotic Heart Disease
Heart conditions in which arterial and venous blood mix. The overall oxygen content of the blood is lower resulting in less oxygen delivery to the body.

Cystic Fibrosis
A hereditary disease that affects secretory glands (such as sweat glands, mucus-secreting glands and the pancreas). Children with cystic fibrosis experience frequent chest infections, digestive problems as well as poor growth.

DNA
Stands for Deoxyribonucleic Acid and is the chemical that forms the genetic code.

Endocrine Gland
A gland that makes hormones and releases them into the blood. The pituitary, thyroid, adrenal, testes (testicles) and ovaries are all endocrine glands. All of the glands together make up what is termed the endocrine system.

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

Endoscope
An instrument used to visualise the inside of the body. Most endoscopes consist of a narrow, mobile tube with a light and a camera to transmit the images to the eye or a screen.

Foetus
The developing baby in the womb from the ninth week of pregnancy until the moment of birth.

Gastroenterologist
A doctor who specialises in the disorders of the digestive tract.

Genetic Potential Height
The adult height calculated from the heights of the parents.

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.

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

Idiopathic
The term used to describe the situation when no reason can be found to explain the cause of a disease or disorder.
Intrauterine
Within the uterus (womb).

Karyotype
The chromosome set of an individual. For example the karyotype of a girl with Turner Syndrome is usually 45X.

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.

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

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.

Placenta
The organ which connects the foetus to the wall of the uterus. The placenta provides the foetus with nourishment and eliminates wastes.

Somatomedins
These are hormones made by the liver that deliver the growth message to bones and other tissues. Somatomedins are stimulated by 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.

Thyroid Gland
A butterfly-shaped gland in the front of the neck below the larynx, which makes the hormone thyroxine.

X Chromosome
The female sex chromosome.

Y Chromosome
The male sex chromosome.
Organisations

Association of Genetic Support of Australasia Inc.
66 Albion Street
Surry Hills NSW 2010 Australia
Tel: 02 9211 1462

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

Children's Growth Foundation
PO Box 459
Maroubra NSW 2035 Australia
Tel: 02 9315 7547

Coeliac Society of Australia
PO Box 703
Chatswood NSW 2067 Australia
Tel: 02 9411 4100
Email: info@nsw.coeliac.org.au

Coeliac Society of New Zealand
PO Box 19739
Avondale Auckland New Zealand
Tel: 09 820 5157
Email: dawnb@clear.net.nz

Down Syndrome Association of NSW Inc
PO Box 2356
North Parramatta NSW 1750 Australia
Tel: 02 9683 4333
Email: dsansw@hartingdale.com.au

Growth Hormone Parent Support Group
c / - 432 Scoresby Road
Ferntree Gully VIC 3156 Australia
Tel: 03 9764 0309

Klinefelter Syndrome and Associates Inc
PO Box 119
Roseville CA 95661-0119 USA

Little People of New Zealand
108 Mayfair Avenue
Hastings New Zealand
Tel: 06 878 7506
Email: katy.sinclair@clear.net.nz

Marfan Syndrome Association (NSW)
PO Box 464
St Marys NSW 2760 Australia
Tel: 02 9621 1201

Noonan Syndrome Association
303 Rowe Street
Eastwood NSW 2122 Australia
Tel: 02 9804 6759

Parent and Family Resource Centre
PO Box 13185
Onerahi Auckland New Zealand
Tel: 09 366 0351

Parent to Parent New Zealand Inc
PO Box 234
Hamilton New Zealand
Tel: 07 834 1108

Russel Silver Support Group
PO Box 153
Cooma NSW 2630 Australia
Tel: 068 22 1026

Short Statured People of Australia
Website: www.mpx.com.au/~frank/spa.htm

Sotos Support Group of Australia
Email: rdhope@pnc.com.au

Turner Syndrome Association of Australia Ltd
PO Box 112
Frenchs Forest NSW 1640 Australia
Tel: (02) 9452 4196
Email: turnersty@one.net.au

Turner Syndrome Auckland Support Group
Private Bag 92024
Auckland New Zealand
Tel: 03 307 4949 EXT 5538

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

UK Pituitary Foundation
PO Box 1944
Bristol BS99 2UB UK
Email: helpline@pitpat.demon.co.uk

Victorian Turner Syndrome Association Inc
31 Price Street
Essendon VIC 3040 Australia
Tel: 03 9337 4074 or 03 9777 0185

Girl’s Growth Chart

This chart may be used to plot a female child’s growth pattern and used in consultation with the specialist.
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.
HORMONES AND ME

GROWTH PROBLEMS IN CHILDREN

THIS BOOKLET IS ESSENTIAL READING FOR CHILDREN WHO HAVE HORMONE PROBLEMS, PARTICULARLY THOSE AFFECTING THEIR GROWTH. IT IS ALSO RECOMMENDED READING FOR THEIR FAMILIES AND FRIENDS.