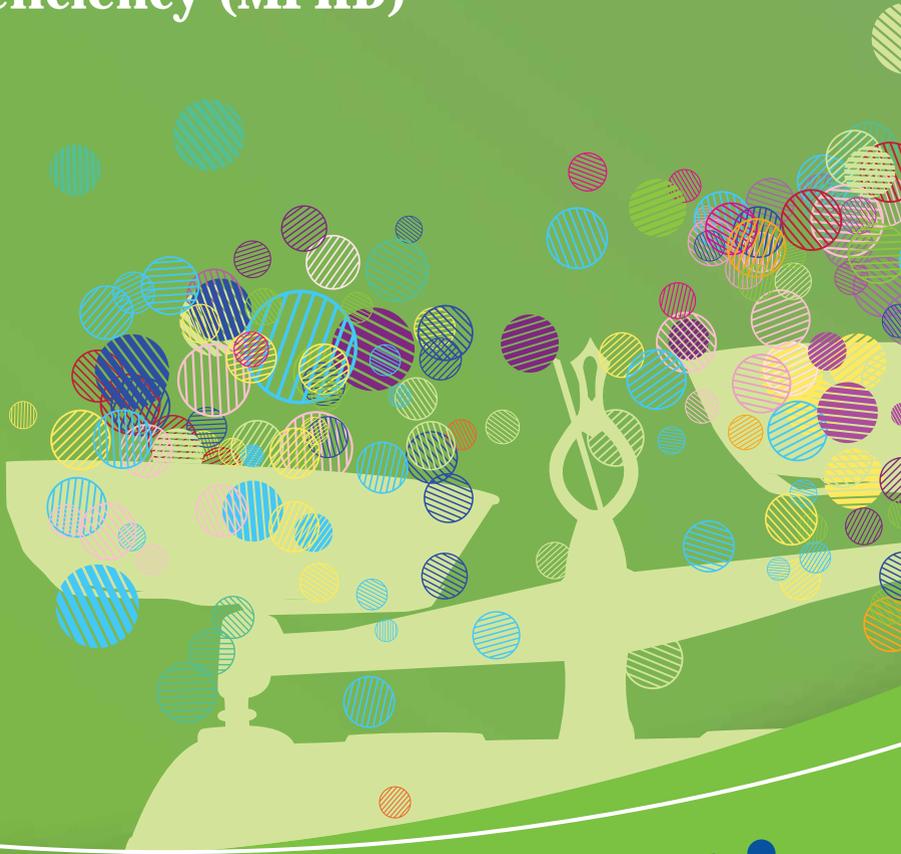


Hormones and Me
**Multiple Pituitary Hormone
Deficiency (MPHD)**



Australasian Paediatric Endocrine Group



Hormones and Me

Multiple Pituitary Hormone Deficiency



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About this book

This booklet, *Multiple Pituitary Hormone Deficiency (MPHD)*, aims to give you a basic understanding of how pituitary disorders may develop and the treatments that are currently available. When children or adults are diagnosed with Multiple Pituitary Hormone Deficiency (MPHD), they may be affected in many different ways. The doctor will advise which sections of this booklet are relevant to you.

We encourage you to discuss any additional questions or areas of concern with your doctor after reading this booklet.

Merck Serono Australia is pleased to bring you this booklet from the *Hormones and Me* educational series. We hope that you find it a valuable and helpful resource.



This booklet was revised in 2011 with the help of Dr Ohn Nyunt (Royal North Shore Hospital, NSW, Australia) and Prof Andrew Cotterill, (Mater Children's Hospital, QLD, Australia), Paediatric Endocrinologists specialising in childhood endocrine disorders and members of the Australasian Paediatric Endocrinology Group (APEG).

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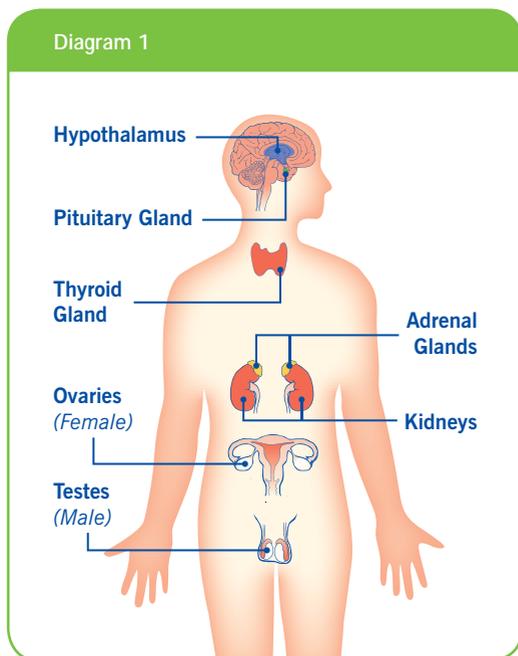
This booklet was first updated and reproduced for Australian and New Zealand readers in 2000 with the help of A/Prof Andrew Cotterill. Special thanks to the original authors and editors, Dr Richard Stanhope (Great Ormond Street Hospital for Children and the Middlesex Hospital, UK), Ms Janis Clayton (Serono Laboratories (UK) Ltd, UK), Mrs Vreli Fry (Child Growth Foundation, UK) and the British Society of Paediatric Endocrinology (BSPE).

Introduction

This booklet discusses how the hypothalamus and pituitary gland are important in the control of growth and development of children and for the maintenance of good health in adults. These can develop abnormally during pregnancy in the unborn child, or they may be damaged in later life by tumours or other injury.

Hormones

Hormones are chemicals that carry messages from one part of the body to another via the blood stream. Hormones are produced by endocrine glands (such as the pituitary gland) and play a vital role in regulating growth, development and metabolism. A low level or deficiency of a hormone can have dramatic effects on the body's growth and functions, especially when more than one hormone is deficient, which occurs in multiple pituitary hormone deficiency (MPHD).



“Low levels, or deficiency of a hormone can have dramatic effects on the body's growth and function, especially when more than one hormone is deficient, which occurs in Multiple Pituitary Hormone Deficiency (MPHD)”

The regulation of hormone production begins in a part of the brain called the hypothalamus, which sends chemical messages to the pituitary

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gland via the pituitary stalk (see *Diagram 1*). In turn, the pituitary gland responds to these messages by producing a number of different hormones. Some of these hormones have a direct action on the body whilst some stimulate other hormone producing glands in the body, such as the thyroid gland, adrenal glands and sex hormone glands (ovaries and testes) (see *Diagram 1*).

Hormone Replacement Therapy

The aim of hormone replacement therapy is to mimic the normal hormone production from the pituitary gland. Growth hormone (GH) is produced mainly in bursts and during night. Therefore, GH replacement therapy is advised in the evening. Adrenocorticotrophin (ACTH) production is more in the early morning and little at night. Therefore, a higher dose of hydrocortisone is usually given in the morning and a smaller dose in the afternoon and evening. Vasopressin production is higher overnight than during the daytime. Therefore larger doses are often taken at bedtime compared to daytime doses. However, thyroxine levels are relatively constant so there is no set time for taking it during the day.

The Hypothalamus

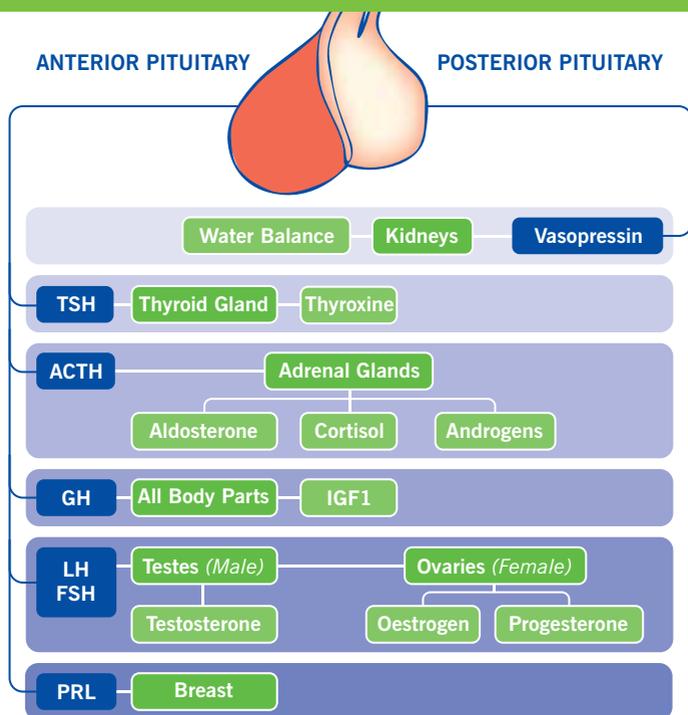
Hormones produced by the hypothalamus stimulate the pituitary gland, controlling release of the pituitary hormones. Some of these are referred to as 'releasing hormones' and include growth hormone releasing hormone (GHRH) and gonadotrophin releasing hormone (GnRH).

The Pituitary Gland

The pituitary is a pea-sized gland at the base of the brain, just below the hypothalamus. The pituitary is divided into two lobes called the anterior (front) lobe and the posterior (rear) lobe. Some hormones are released

by the pituitary gland which then stimulate other glands in the body to release their hormones (see Diagram 2). Some hormones act directly on the organ where its effect is produced.

Diagram 2



TSH Thyroid Stimulating Hormone
ACTH Adrenocorticotropic Hormone
GH Growth Hormone
IGF1 Insulin Growth Factor 1

LH Luteinising Hormone
FSH Follicle Stimulating Hormone
PRL Prolactin

The Role of the Hypothalamus and Pituitary Gland

The hypothalamus and the pituitary gland act like a director. They control and regulate the release of hormones from the pituitary and other glands. They collect messages from the brain, the body and the environment and translate them into hormone signals. These hormone signals are released to specific parts of the body to cause an appropriate action.

During normal growth, the hypothalamus and the pituitary gland, co-ordinate the onset of puberty at an appropriate time for the child. In severe illness the body may divert energy from normal growth to repair itself and cause a delay in the start of puberty. Sometimes the co-ordination of the signals can be disrupted and puberty may start too early, for example after a head injury.

The Development of the Pituitary Gland

The pituitary gland develops in two separate sections, the anterior (front) and posterior (rear) lobes.

In the growing unborn baby (foetus), a small pouch of tissue forms at the back of the nose and grows back to meet the developing brain. This pouch of tissue develops into the anterior part of the pituitary gland.

The posterior pituitary gland develops as an outgrowth from the base of the brain (hypothalamus). It carries with it the pituitary stalk, which connects the pituitary gland and the hypothalamus. When the two parts meet in the developing foetus, the pituitary gland starts to function at about 10 weeks after conception.



This development is sometimes disrupted and causes a condition known as congenital hypopituitarism. The development of the pituitary gland and the hypothalamus are co-ordinated by a number of genes. Some of these genes are vital just for the anterior pituitary and some of these genes are also important for the development of vision and general brain development.

If a doctor suspects a problem with the pituitary gland, they may wish to look at other problems such as vision. Sometimes newborn children who are found to have problems with their vision will be referred to an Endocrinologist for assessment of Pituitary gland functions.

Causes of Pituitary Hormone Deficiency

Pituitary hormone deficiencies can be present from birth (congenital) or may happen later in life as a result of developing problems such as a tumour or injury (acquired).

Congenital

Development of the pituitary gland and hypothalamus are co-ordinated by a number of genes. As research progresses, more and more genetic causes for congenital hypopituitarism are being discovered. The problem is usually found in the first few weeks of the baby's life. Occasionally, if only a few hormones are affected, the disorder may be discovered much later in life.

Anterior Pituitary Hormone Deficiencies

In the majority of cases, no cause is found for abnormal development of the anterior pituitary lobe. Currently, there are several known genetic defects that can cause this problem. They may be inherited.

Panhypopituitarism

This occurs when babies are born with damage to both the anterior and posterior lobes of the pituitary gland. This may be due to trauma during birth or, very rarely, due to the mother having an infection during pregnancy.

Septo-optic Dysplasia

This is a syndrome caused by abnormalities of development of the vision pathways. In some cases, this has been linked to a gene defect, which can be hereditary. The condition is variable in its effects. Some affected people may have many symptoms, whilst others just a few. Not all children with this condition have pituitary gland problems.



Evolving Hypopituitarism

Multiple pituitary hormone deficiency may develop gradually over a number of years, often following a pattern known as evolving hypopituitarism, which affects the anterior lobe of the pituitary gland. The first hormone to be affected is growth hormone (GH) followed by the gonadotrophins (LH and FSH), then thyroid stimulating hormone (TSH) and less frequently, deficiency of adrenocorticotrophic hormone (ACTH).

“Poor growth is often the first sign of an evolving pituitary disorder”

Poor growth, therefore, is often the first sign of an evolving pituitary disorder. Thus isolated growth hormone deficiency diagnosed early in life, may be found later to be associated with other hormone deficiencies. The time period over which this can happen varies depending on the underlying cause. Some pituitary tumours can cause very rapid loss of all hormones whereas MPPHD following irradiation therapy may develop over many years.

Acquired

The most common types of multiple pituitary hormones deficiency are caused by damage to the hypothalamus and / or the pituitary gland, from trauma, tumours and irradiation to this area of the brain.

Trauma

Children or adults suffering severe head injury may develop multiple pituitary hormone deficiency as a result. This occurs most commonly following a fracture in the base of the skull. The pituitary stalk may be damaged at the time of injury. This can result in disconnection between

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the pituitary gland and the hypothalamus. As a result of this damage, the pituitary gland may stop functioning properly because the messages from the hypothalamus cannot get through. Unfortunately, the pituitary stalk, once damaged, is usually unable to be repaired. If this happens, it will then be necessary to replace the missing hormones with appropriate treatment.

Tumour

The effect of tumours or cysts in or beneath the brain is based on their size and location. Some brain tumours can be so large that they press on the hypothalamus or pituitary gland, causing these areas to stop functioning properly. Small tumours may develop in 'vital' areas of the hypothalamus or pituitary gland causing significant damage due to their location. For example a very small tumour in the Pituitary stalk will block the message from the hypothalamus even though it may be the size of a grain of rice.

Irradiation

Surgery to remove a tumour or cyst may be effective. However, damage to the hypothalamus or pituitary gland may occur at time of surgery, either because the tumour is closely attached to these areas, or because the very fine narrow blood vessels are damaged by the surgery or by swelling in the area.

Radiation to the brain as part of treatment for tumours and cysts may have side effects on various parts of the brain, particularly the hypothalamus and pituitary gland. The entire spectrum of damage to the hypothalamus and pituitary gland can evolve up to 20 years after radiation treatment. Therefore, children or adults treated with radiotherapy to the brain always require long term regular follow-up to assess possible changes in pituitary function.



Diagnosing a Pituitary Disorder

When making a diagnosis, the endocrinologist will ask about the person's history and perform an examination and investigations.

MPHD may be diagnosed at several different times of life and with different symptoms.

Babies (infants)

These children may have a history of prolonged jaundice in their first few weeks of life, episodes of low blood sugar levels, have poor growth, lethargy or dry skin. It is important to know if the mother may have experienced difficulties during her pregnancy or labour.

Children and Adolescents

May have any of the following symptoms:

- Poor growth due to lack of growth hormone
- Poor growth, lethargy, dry skin and intolerance to cold (a sign of thyroid hormone deficiency)
- Hypoglycaemia (a sign of cortisol and growth hormone deficiency)
- Failure to go into puberty (a sign of gonadotrophin deficiency with no message to the sex organs)

A history of head injury, infections (e.g. meningitis) or symptoms suggestive of brain tumours is important as well as the type of growth pattern. The doctor will examine for weight, height and signs of growth hormone deficiencies, thyroid hormone deficiency or delayed puberty. An usually small penis in a boy may be a sign of MPHD present from birth.

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Hormone Tests

If a hormone deficiency is suspected, blood tests will be necessary to check the function of the pituitary gland.

Growth Hormone (GH)

GH cannot be checked reliably by a simple "one-off" blood test because levels of GH go up and down at different times of the day and night. If the child is short or growth is poor, a stimulation test should be performed. This may involve exercise or a sleep test in hospital, or the use of drugs to stimulate the production of GH if possible. Use of sex hormone for two days before stimulation test increases the reliability of the test if the child is near the age of expected puberty. Measurements of GH levels over 24 hours are performed in some centres. The doctor will explain what type of test is most appropriate for the child.

Adrenocorticotrophic Hormone (ACTH)

There are many different ways to examine ACTH and cortisol levels. Cortisol production is usually measured during a GH test, or can be checked first thing in the morning. The Synacthen test is a stimulation test to examine ACTH and cortisol levels. Synacthen is a synthetically produced ACTH that stimulates the adrenal cortex to produce cortisol. The overnight Metyrapone test and insulin-induced hypoglycaemia test are other ways of testing for ACTH production but are less frequently used.

Thyroid Stimulating Hormone (TSH)

A thyroid test is a simple blood test and may be done at any time of the day. It measures both TSH and thyroxine levels.

Follicle Stimulating Hormone (TSH) & Luteinising Hormone (LH) (Sex Hormones)

These are not usually measured before the time that puberty is expected, as they are low throughout childhood. The only exception would be a



measurement done in the first month of life for a baby boy with a very small penis and/or undescended testes. In this case, the small penis may indicate a lack of pituitary hormone stimulation around the time of birth. Boys usually have high male hormone levels in the first month of life, so a 'low' test at this time may be diagnostically very helpful.

If puberty is very late (no breast development in girls by 13 years and no testicular development in boys by 14 years of age), a special stimulation test of pituitary FSH and LH production may be helpful, although it is often hard to interpret. Doctors frequently use the physical changes of development as a guideline for whether treatment is needed.

Imaging

Bone Age

Bone age is a measure of biological age or maturity, rather than actual age. It is checked using an X-ray of the child's left hand, and acts as a guideline for the treating doctor. A significant difference between the actual age and bone age increases the suspicion of hormone deficiencies.

Magnetic Resonance Imaging Scan (MRI Scan)

MRI scans are a technique for obtaining high-resolution scans of different parts of the body. There is no exposure to X-rays and they can therefore be repeated in the same person many times. An MRI scan of the hypothalamus and pituitary gland will enable the specialist to see if there are any structural abnormalities. MRI scans of the hypothalamus and pituitary gland also show their size and appearance. This can help determine if there is a structural problem such as a cyst or tumour or whether the pituitary gland is extremely small or absent.

Effects of Pituitary Hormone Deficiencies

The pituitary hormones are vital for healthy growth and development and for regulating the body's metabolism. Each hormone has specific actions and the loss of it will cause particular problems. The following sections examine the effects of each of the hormones and how any loss of them may be managed individually. Management needs to be co-ordinated by either a paediatric endocrinologist for children or by an endocrinologist for adults.

MPHD is lifelong and needs to be followed up regularly through adulthood.



Growth Hormone (GH) Deficiency

Growth hormone (GH) is also known as somatotropin. It is often the first hormone to become deficient in any type of pituitary insufficiency (idiopathic or secondary). The incidence of GH deficiency is around one in 5,000 children, with boys being affected more commonly than girls. Around half of these children will have isolated GH deficiency (meaning no other hormone deficiencies occur).

“The incidence of idiopathic GH deficiency is around one in 5,000 children, with boys being affected more commonly than girls.”

GH 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, GH acts on the liver, kidneys and other tissues including bones to produce growth factors. As well as promoting growth, GH has an important role in the metabolism of fat and carbohydrate and helps to maintain blood glucose (sugar) levels.

Children with GH deficiency are small compared to other children of their age but they have normal proportions. The rate of growth tends to slow at around one year of age and can be seen as a flattening of the growth curve as measured by the doctor. In the first year of life, growth is more dependent on nutrition than on growth hormone secretion and may be normal even if growth hormone deficiency is present from birth.

Even though babies with growth hormone deficiency may have grown normally in their first year of life, some of these babies may have episodes of low blood glucose (hypoglycaemia), which can be very dangerous. Once a diagnosis is made, growth hormone treatment is given to these

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children in order to help restore glucose levels to normal. Hypoglycaemia that persists despite GH therapy may indicate deficiency of another pituitary hormone (adrenocorticotrophic hormone ACTH) which in turn leads to inadequate levels of cortisol. The child may therefore need replacement treatment with cortisol.

Children with MPHD may continue to experience low blood glucose levels during any episode of sickness, throughout childhood and adolescence.

GH therapy has been used for many years with great success in the treatment of children with growth hormone deficiency. Biosynthetic GH is manufactured using gene technology and is identical to the growth hormone we produce naturally. The dosage of GH varies according to the child's weight and will increase as he or she grows. It is given by an injection under the skin once daily, usually before bedtime, to mimic the natural production of GH as closely as possible.

When a child has GH deficiency, treatment with GH results in rapid 'catch up' growth, with the greatest improvement in the first year of treatment, then a normal rate of growth throughout childhood whilst treatment is continued. The best outcome occurs when treatment is started soon after the onset of growth hormone deficiency, but growth will improve if treatment is given any time before the end of puberty. Response to growth hormone is assessed by monitoring the rate and progress of growth compared to other normal children. In both Australia and New Zealand, careful assessment at the start of growth hormone and close follow up is needed so that the respective health departments in both



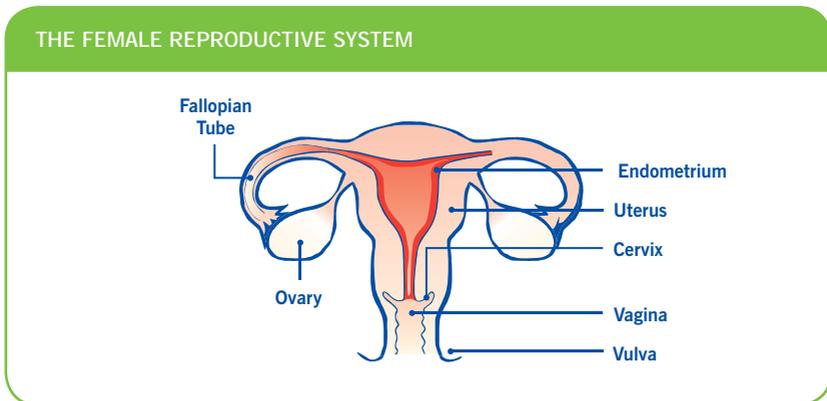
countries continue to fund this treatment. It usually involves 3 monthly clinic appointments, annual blood tests and X-ray. Treatment with growth hormone is normally stopped when puberty is complete and the bone age is considered to be mature.

Treatment for adults with growth hormone deficiency has been approved by the regulatory authorities in Australia and New Zealand but financial assistance may not be available in some countries. In adults, response to growth hormone is assessed using bone density and muscle size (mass).

Gonadotrophin (FSH, LH) Deficiency

The Ovaries

The ovaries are part of the female reproductive system. They produce eggs and sex hormones (oestrogen and progesterone) in a regular cycle, which is regulated by the release of gonadotrophin hormones from the pituitary gland. There are two ovaries, each the size of a large olive in an adult, situated on either side of the womb (or uterus). The ovaries contain many follicles (small secretory glands) in which the eggs (ova) develop and which secrete oestrogen and small amounts of androgen (male sex hormone). Once the egg has been released from a follicle (ovulation), the site which remains secretes progesterone.

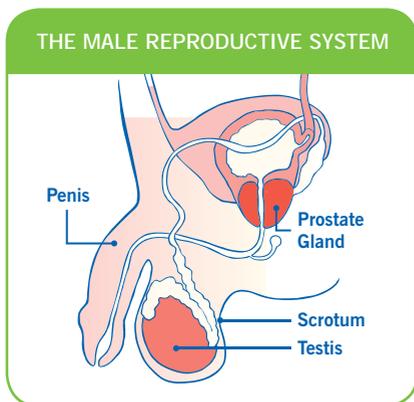


After the age of 8 years in a girl the hypothalamus sends signals to the pituitary gland that puberty should start soon. Then the pituitary gland sends gonadotrophin hormones (FSH, LH) to the ovary. These hormones act on the ovaries to produce the female hormone oestrogen which causes breast development and slowly builds up the lining of the uterus (womb). Later in puberty, the ovary makes a male hormone (androgen), which

stimulates the growth of more pubic hair. Progesterone, another female hormone, stimulates further maturation of the lining of the womb (uterus). After several months the cycle of oestrogen and progesterone is established, causing a change in the pattern of the lining of the womb. At the end of each cycle, both hormones 'switch off', causing loss of the womb lining, known as a 'period'.

The Testes

The testes are part of the male reproductive organs, which produce sperm and secrete the male hormone testosterone in response to gonadotrophin



hormones (LH & FSH) released by the pituitary gland. Before a boy is born, the testes develop within the abdomen, descending into the scrotum (the sac which holds the testes) around the time of birth. After about 9 years of age in a boy, signals from hypothalamus start to be produced that puberty should start. The hypothalamus sends a signal to the pituitary gland which in turn sends

gonadotrophin hormones (LH & FSH) to the testes. The testes will then produce male hormone testosterone which causes development of the penis, increase in size of the testes and pubic hair. Later on it stimulates facial and body hair, deepening of the voice and muscle development.

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Gonadotrophin and Sex Hormone Deficiency

In newborn male children with gonadotrophin deficiency, there may be physical signs such as a very small penis or testes that have not descended. A brief course of treatment with testosterone in the first few weeks of life can increase penis size and may trigger the testes to descend although sometimes surgery is required.

It is much more difficult to detect gonadotrophin deficiency in newborn girls and during the middle-childhood years (between the ages of two and nine years) as there are no physical changes expected and blood tests for gonadotrophin levels are normally low during this period. The problem does not usually become apparent until the time when the child is expected to undergo puberty. If there is no message from the hypothalamus and or pituitary gland, the child will not start to develop or go through puberty. The normal time for beginning of puberty depends on many factors including the health of the child and the ages at which parents had their puberty. However, for children where MPH is suspected, careful monitoring at this time will be needed to assess whether normal progress is occurring.

Some children with apparently 'isolated' growth hormone deficiency in childhood will also have some deficiency of the hormones involved in sexual development. Therefore, children with growth hormone deficiency should have further tests checking for gonadotrophin deficiency from around nine years of age.

In girls, as gonadotrophins stimulate the growth of the ovaries, a pelvic ultrasound may be helpful as it will reveal the size, appearance and maturation of the ovaries and show whether they are of average size for age.



In boys, delayed puberty is quite common. This means it is difficult to tell if there is an actual deficiency of gonadotrophins or if gonadotrophin release is simply delayed.

Even if there is doubt about the actual cause of delayed puberty, treatment with sex hormones should be started to trigger puberty if either a boy or girl has failed to start normal sexual development within the expected range of time for their peers. Once puberty and growth have been completed, it may be advisable to stop the male and female hormone replacement for a few months, in order to assess whether the body will be able to produce its own hormones or whether long term treatment will be needed. This is particularly important in order to give the adolescent an idea of whether his or her future fertility is normal, or whether extra treatment to stimulate fertility may be required in due course.

Initial treatment has involved gradually promoting the development of sexual characteristics through the administration of slowly increasing amounts of sex hormones over a period of around three years. Boys will have testosterone therapy (injections) and girls will have oestrogen (tablets or skin patches) at first, with the addition of progesterone towards the end of puberty.

Recently, a different method of inducing puberty has been used for boys who have gonadotrophin deficiency. This involves replacement of the missing hormones FSH and LH, in gradually increasing doses until puberty is complete and fertility achieved as shown by sperm production. The boy is then changed over to testosterone treatment until he wants to start a family, at which time he can repeat the same treatment that was used to induce puberty. This newer type of treatment is not used for

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girls because all their eggs (ova) are present from birth and the ovaries only need to be stimulated to produce an egg when the girl wants a pregnancy. The endocrinologist who looks after the patient for MPHD may need to refer them to a fertility specialist at this time.



Thyroid Stimulating Hormone (TSH) Deficiency

The Thyroid Gland

The thyroid gland is located in the front of the lower part of the neck and consists of two connected lobes. It secretes thyroid hormone (thyroxine) in response to thyroid stimulating hormone (TSH) produced by the pituitary gland. The thyroid gland is involved in the regulation of metabolic rate which is the speed at which the body breaks down (or metabolises) food, for many normal daily body functions. Metabolic rate varies from person to person and is affected by factors including age, size, diet, and exercise as well as hormone levels.

Thyroid Hormone Deficiency

The thyroid gland produces thyroxine (thyroid hormone), which is very important for normal growth and development throughout childhood. It is essential for normal brain growth in the first two years of life and helps with brain function. Therefore it is very important to monitor the dose of thyroxine with blood tests. Thyroxine also has a vital role in controlling the rate of the body's metabolism in children and adults. Its deficiency may cause sluggishness, weight gain, constipation and dry skin.

If the hypothalamus does not produce enough thyrotropin releasing hormone (TRH), or the pituitary gland does not produce enough thyroid stimulating hormone (TSH), the thyroid will not be stimulated to produce enough thyroxine to meet the body's needs. This is called secondary hypothyroidism.

The treatment of hypothyroidism is relatively simple. To increase the levels of thyroxine in the body, replacement thyroxine is given in tablet form as a daily dose. The dose required varies with body size and dosages may need to be increased as the child grows. Regular blood

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tests measuring the levels of thyroid hormones will be necessary usually 2-4 times a year. The doctor will also regularly assess the rate of growth and bone development as another way to monitor the effectiveness of replacement hormone therapy.

In children with isolated growth hormone deficiency, commencing growth hormone replacement therapy can result in a temporary lowering of thyroxine due to suppression of pituitary hormone release (including TSH). This usually resolves within six months and long-term treatment with thyroxine may not be necessary. Sometimes the thyroid hormone level remains low during growth hormone treatment, so the addition of thyroxine may be required.



Adrenocorticotrophic Hormone (ACTH) Deficiency

The Adrenal Glands

The adrenal glands are two triangular glands that lie close to the kidneys. Each gland is the size of a broad bean and consists of two parts – the medulla (inside part) and the cortex (outside part).

The adrenal cortex is stimulated by adrenocorticotrophic hormone (ACTH) produced by the pituitary gland. In response to this stimulation, the adrenal cortex releases cortisol and, to some extent, aldosterone. Cortisol is important in controlling the body's response to 'stress', the maintenance of blood pressure and the amount of sugar in the blood. Aldosterone controls the concentration of salt in the body but is not usually affected in MPHD.

ACTH Deficiency

Adrenocorticotrophic hormone (ACTH) is one the least common hormones to become deficient in MPHD. When the body is stressed, such as during illness or surgery, the body must produce more ACTH and cortisol to maintain the blood pressure, blood glucose level and generally to be able to cope with the stress. People with untreated ACTH deficiency have low levels of cortisol and can experience episodes of dangerously low blood pressure and low blood sugar levels when the body is stressed. Undiagnosed ACTH deficiency may lead to slow recovery from operations, injuries and illness.

Synthetic forms of cortisol (hydrocortisone or cortisone acetate) are used as replacement treatment for people with ACTH and cortisol deficiency. Tablets are given two or three times a day. The normal release of cortisol from the adrenal glands is higher in the morning. To mimic the body's production of natural cortisol, a larger dose is given first thing in the morning and the remainder in the afternoon and evening.

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It is important to give just the right amount of hydrocortisone to maintain normal growth and metabolism as too much cortisol can result in side effects such as weight gain and slowing of growth in height. Occasionally it may be necessary to perform blood tests to check that the dose is correct. Too little hydrocortisone can cause low energy levels, low blood sugar and low blood pressure.

At times of acute illness, a person with ACTH deficiency cannot respond to the stress of the illness. It is important that extra hydrocortisone is given on these occasions.

Minor Illness

In case of minor illness such as the flu or gastroenteritis, the dose of hydrocortisone should be increased during the illness. The dosage to be used should be discussed with the doctor.

Major Illness

In the case of major illness, such as any major fracture or any general anaesthetic (including for radiological proceeding such as MRI Scans) or when the child cannot take the oral stress dose during minor illness (see above), an injection of hydrocortisone must be given. The endocrinologist will advise the correct dose depending on the age and size of the person. This should be repeated every 4–6 hours until the patient is better. Thereafter, the oral dose should be taken again at an increased dose decided by the doctor.

All people who have MPHD with ACTH deficiency should either wear some form of medical alert bracelet or pendant, and/or carry information with them at all times, giving advice on how to manage a crisis situation.



Many doctors may not have seen a patient with this type of problem and may not be familiar with the correct treatment.

The recommended doses of hydrocortisone for major illness or when oral hydrocortisone cannot be taken are as follows:

Age and Weight (Kg)	Dose of hydrocortisone
≤6 months (≤7 kg)	25 mg
6 months–2 years (8–12 kg)	50 mg
3–10 years (13–30 kg)	100 mg
> 10 years (>30 kg)	100–200 mg

In the event of illness, your doctor will advise when to increase the dose of hydrocortisone/cortisone and what dose is to be given in the event of illness.

Ask your doctor for an instruction letter for minor and major illnesses and for situations when intramuscular hydrocortisone is to be given.

Vasopressin Deficiency

The posterior lobe of the pituitary gland produces vasopressin, also known as antidiuretic hormone (ADH). Vasopressin acts on the kidneys, adjusting how much water is retained in the body or excreted in the urine thereby controlling the concentration of the blood. If the blood becomes too concentrated, vasopressin is produced and the kidneys are signalled to retain water. Vasopressin secretion results in the urine becoming more concentrated and the blood become more dilute. Once the blood concentration is back to normal the pituitary stops producing vasopressin.

Vasopressin deficiency is known as central diabetes insipidus. This condition results in large quantities of dilute urine, as there is no signal to the kidneys to retain water. The blood becomes increasingly concentrated, resulting in extreme thirst and the individual has to drink large amounts of water to make up for the water lost in the urine.

The treatment for diabetes insipidus is replacement therapy with desmopressin (or DDAVP) which is a synthetic form of vasopressin. This can be given as tablets, nasal drops, nasal spray, injection and also as a wafer that goes under the tongue. In most patients oral tablets are the best way to take DDAVP. In young children requiring small doses of DDAVP, the tablets can be diluted in water and the smaller doses given as required, after instruction from the treating doctor. In situations when oral absorption of the drug may not be reliable or predictable (e.g. severe vomiting illness), nose drops containing DDAVP can be considered. Your doctor will advise you on the best way to take DDAVP.



The body will detect the need to drink and balance fluid intake and output by increasing or decreasing thirst appropriately. It is important not to overdose on DDAVP or drink too much water because it will result in dangerous build up of fluid in the body and brain.

For more information, please refer to the *Hormones and Me* booklet "Diabetes Insipidus".

Summary

Not all children with GH deficiency go on to develop further pituitary hormone deficiencies and not all the hormone deficiencies described in this booklet will apply to every child with MPHD. It is important to remember however that the loss of pituitary hormones can occur gradually over long periods of time. Regular medical assessment for signs of other hormone deficiencies in children with isolated growth hormone deficiency is important.



Some Useful Tips

- It is important to treat the child with MPHD as normally as possible and allow him or her to undertake normal age-related activities.
- Children with MPHD should wear a medical alert bracelet stating that they have MPHD. This is particularly important for those children with cortisol deficiency, in addition to GH deficiency, because of the risk of low blood sugar and low blood pressure during stressful situations (e.g. accidents).
- When travelling it is wise to carry a letter from the doctor explaining MPHD, the treatment and the need for carrying drugs or syringes.
- Parents of children who have episodes of low blood sugar or low blood pressure or vomiting associated with MPHD should have injectable hydrocortisone available and know how to administer it in case of an emergency. The doctor will arrange instruction on how to administer the necessary injection.

The doctor will advise of when to increase the dose of hydrocortisone/cortisone and what dose is to be given in the event of illness.

Have an emergency plan and always carry it with you.

Questions and Answers

Are pituitary deficiencies reversible?

No, once pituitary hormones become deficient it is very rare that they can be reversed. They can however be treated very successfully with hormone replacement therapy.

Can hypothalamic and pituitary hormone deficiencies develop in adult life?

Yes, some hormone deficiencies in MPPHD may not appear until later in life. This is why regular medical check-ups are essential right into adulthood. Sometimes during adolescence, the paediatric endocrinologist will refer the child to an endocrinologist who specialises in the care of adults with hormone disorders such as fertility issues.

What is transition?

It is a process of change of care from a children's endocrinology team to an adult endocrinology team just like changing from primary to high school. It is important that you and your child know about this process. You should discuss with your paediatric team and have a plan of how, when and where transition should occur.

Does the rapid development of additional hormone deficiencies suggest that there is a tumour or cyst in the brain?

No, not necessarily. There are many conditions that can result in evolving pituitary insufficiency and sometimes the actual cause remains a mystery (idiopathic pituitary insufficiency). However, rapidly progressive losses of pituitary hormones may indicate presence of a tumour in some people. The specialist will explain the possible causes of pituitary insufficiency and the need for further tests.



What is the cause of diabetes insipidus (vasopressin deficiency)?

Diabetes insipidus results from a problem associated with the posterior (rear) lobe of the pituitary gland. Usually a cause can be identified following tests of hypothalamic and pituitary function along with special X-rays and scans (such as a MRI scan of the brain). The exception is when diabetes insipidus is due to a genetic defect inherited from the parents.

Is it important for the child to have special X-rays or scans of the pituitary gland?

For children with MPHD it is usually recommended that these tests be performed to exclude the presence of pituitary cysts or tumours. Occasionally, in a child who develops diabetes insipidus with or without MPHD, these scans may need to be repeated every 3-12 months for several years to be sure that a small tumour is not developing in the area. The specialist will advise if these tests are necessary.

Will sexual development and function be normal in individuals with MPHD?

Yes, if gonadotrophin deficiency is present, male and female hormone replacement will be given. This will trigger the development of the normal sexual characteristics that occur with puberty. Male and female hormone therapy will continue into adulthood to maintain sexual development as well as libido (sex drive).

Multiple Pituitary Hormone Deficiency

Will a child with MPHD be able to have children in the future?

In most cases, yes, although this will depend on the underlying cause of their MPHD. Specialised hormone treatment can induce fertility, making it possible to have children. The endocrinologist will discuss this as your child grows up and the young adult will need to be aware that he or she may need to see a specialist in the field of fertility when they wish to start a family.

Does a child with isolated growth hormone deficiency need to continue to see an endocrinologist into adult life?

Yes, additional pituitary hormone deficiencies may occur later in life so it is important that he or she is under the care of an endocrinologist who can prescribe appropriate hormone replacement therapy.



Glossary

Aldosterone

A steroid hormone produced by the adrenal gland that helps regulate salt concentration in the body.

Androgens

Male sex hormones including testosterone.

Congenital

A feature or condition that is present from birth, but not necessarily hereditary.

Cortisol

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

Endocrine Gland

A gland that makes hormones and release 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.

Gonads

A term that refers to the sex glands, the ovaries in females and the testes in males.

Growth Hormone

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

Multiple Pituitary Hormone Deficiency

Hormone

A chemical substance that is made by an endocrine gland and carries messages from one cell to another via the bloodstream. Hormones stimulate growth and sexual development and help to regulate the body's metabolism. There are a large number of hormones that have widespread effects on the body, such as cortisol, thyroid hormone and growth hormone. Normally the body carefully controls the release of hormones as too much or too little may disrupt the body's delicate balance.

Hormone Replacement Therapy (HRT)

Hormone medicines which are used for the treatment of diseases when the body cannot make enough hormones by itself.

Hypoglycaemia

A low level of glucose in the blood.

Hypothalamus

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

Hypothyroidism

Low levels of hormones produced by the thyroid gland.

Idiopathic

The term used to describe the situation when no reason can be found to explain the cause of a disease or disorder.



Magnetic Resonance Imaging (MRI Scan)

A technique for obtaining high-resolution scans of the brain and other parts of the body. There is no exposure to X-rays and they can therefore be repeated in the same person many times.

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/hormones in children.

Progesterone

One of the two female hormones that is produced mainly by the ovaries from the onset of puberty and continuing until menopause, which controls uterine bleeding.

Puberty

The process of physical changes when a child's body becomes an adult's body and the child becomes physically capable of reproduction.

Subcutaneous Injection

An injection given beneath the skin.

Testosterone

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

Multiple Pituitary Hormone Deficiency

Thyroxine

A hormone produced by the thyroid gland.

Uterus

Womb.



Support Organisations and Further Reading

Australian Pituitary Foundation Ltd

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Ph: 1300 331 807

Email: support@pituitary.asn.au

www.pituitary.asn.au

Australian Thyroid Foundation

Suite 2, 8 Melville Street, Parramatta NSW 2150

Ph: 02 9890 6962

Email: info@thyroidfoundation.com.au

www.thyroidfoundation.com.au

Australasian Paediatric Endocrine Group (APEG)

www.apeg.org.au

Diabetes Insipidus Foundation, Inc

www.diabetesinsipidus.org

The Endocrine Society

www.endo-society.org

The Hormone Foundation

www.hormone.org

Pituitary Network Association (USA)

www.pituitary.org

Pituitary Foundation UK

www.pituitary.org.uk

UK Child Growth Foundation

www.childgrowthfoundation.org

UK Society for Endocrinology

www.endocrinology.org

The Magic Foundation

www.magicfoundation.org



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Multiple Pituitary Hormone Deficiency

Merck Serono is proud to bring you this booklet from the *Hormones and Me* educational series. We aim to provide readers with a better 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.

The *Hormones and Me* series includes:

1. Growth Problems in Children
2. Turner Syndrome
3. Craniopharyngioma
4. Diabetes Insipidus
5. Puberty and its Problems
6. Delayed Puberty
7. Multiple Pituitary Hormone Deficiency (MPHD)
8. Congenital Adrenal Hyperplasia (CAH)
9. Growth Hormone Deficiency in Adults
10. Management of Emergency or 'Stress' Situations where Hypoglycaemia or Cortisol Deficiency Occur
11. Intrauterine Growth Retardation (IUGR)
12. Congenital Hypothyroidism
13. Klinefelter Syndrome

DISCLAIMER

Speak to an appropriate healthcare professional

The information contained in this booklet is a general guide only and should not be relied upon, or otherwise used, in place of medical advice.

Any medical information contained in this booklet is not intended as a substitute for informed medical advice. You should consult with an appropriate healthcare professional on (1) any specific problem or matter which is covered by information in this booklet before taking any action; or (2) for further information or to discuss any questions or concerns.

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Hormones and Me

Multiple Pituitary Hormone Deficiency (MPHD)

This booklet is valuable reading for anyone
with Multiple Pituitary Hormone deficiency (MPHD).
It is also recommended reading for their family and friends.