HORMONES AND ME

CRANIOPHARYNGIOMA

Australasian Paediatric Endocrine Group

SERONO SYMPOSIA AUSTRALASIA

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Table of Contents

About this Book

Craniopharyngioma should give you a basic understanding of the diagnosis, treatment and associated problems of having a craniopharyngioma.

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 ***Craniopharyngioma***, 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

The aim of this booklet is to provide general information about a type of brain tumour called a craniopharyngioma, its treatment and some of the problems that may be encountered both in the short and long-term following treatment.

It has been written in general terms, therefore, not all of the information provided will be relevant to every reader. Treatment should always be individualised and not everything will apply to every child with a craniopharyngioma.

"Diagnosis of the condition, its treatment and the outcome will vary from person to person."

The information in this booklet hopes to help the reader understand the condition better and give a basis for discussions with the General Practitioner and Specialists.

Although a craniopharyngioma may occur for the first time in adulthood, this tends to be a different type of tumour from the one occurring in childhood. Childhood craniopharyngiomas tend to be more difficult to treat, especially the ones that cause symptoms at a very young age as these

tend to be growing faster. For this reason, the booklet will focus on childhood craniopharyngiomas, however, some aspects of the booklet may be relevant for adults with this condition.

A craniopharyngioma is a type of brain tumour. It is a benign tumour which means it is NOT cancerous and therefore will NOT spread to other parts of the body.

What is a Craniopharyngioma?

A craniopharyngioma is a congenital tumour, which means that it is present from birth. It is thought to form and grow from some misplaced cells collecting in an area of the brain close to the pituitary gland and its stalk (the pituitary stalk), early on in the development of a baby in the womb. There are no known reasons for this to happen, such as taking medications or being ill during pregnancy and the condition is not hereditary (i.e. passed on from parents or grandparents).

Although present from birth, craniopharyngiomas vary in the timing of when the symptoms first appear. The appearance of symptoms indicates that there has been a change in the size of the craniopharyngioma and the effects it is having on other areas of the brain. The impact of a craniopharyngioma may happen at any age, from birth to old age because some grow faster and cause symptoms much earlier than others. In children, most are diagnosed between the ages of 5 - 10 years, the tumour being slightly more common in boys than girls. Even though craniopharyngiomas are fairly uncommon, for children they are the most common tumours in the area of the pituitary gland. They represent about 9% of all childhood brain tumours.

If the symptoms appear in early childhood it means the tumour is growing faster than if the symptoms do not appear until adulthood. A craniopharyngioma

diagnosed during childhood is therefore a more serious condition and can also be more difficult to treat.

The tumour itself is made up of solid parts usually containing pieces of calcium, and cysts which are filled with a thick fluid. Occasionally, a craniopharyngioma may be entirely fluid-filled or more rarely, entirely solid. These tumours are often very 'sticky' and they adhere to the surrounding tissues. This means it can be difficult to remove them surgically without damaging some of the tissues, particularly an area in the brain called the hypothalamus.

"Even though craniopharyngiomas are fairly uncommon, for children they are the most common tumours in the area of the pituitary gland."

Even if it is removed surgically, a craniopharyngioma may regrow at the place where it was first found and therefore need further treatment.

The most commonly occurring symptoms are headaches and disturbed vision, both resulting from pressure the craniopharyngioma causes as it grows and presses against other parts of the brain.

How Does a Craniopharyngioma First Appear?

As shown in Diagram 1, many of the symptoms and potential problems of having a craniopharyngioma result from its position and size in relation to the surrounding parts of the brain. As the tumour grows, it starts to exert pressure against other delicate areas such as the pituitary gland, the hypothalamus, and the connections between them, producing effects which are described on page 11.

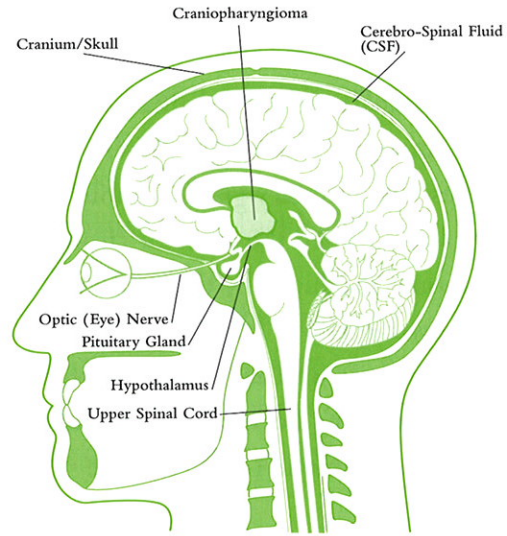


Diagram 1

Hypothalamus

This is an extremely important area of the brain. It influences a number of essential behavioural and functional aspects of the body including temperature regulation, food intake, thirst and therefore water intake, sleep - wake patterns, emotional behaviour and memory. The hypothalamus also serves as the main 'communication centre' for the pituitary gland by sending messages or signals to the pituitary gland in the form of hormones, which travel via the bloodstream and nerves, down the pituitary stalk. These signals in turn control the production and release of further hormones from the pituitary gland, which signal to other glands and organs in the body. The role of the hypothalamus is like that of a director. The hypothalamus has an overall controlling activity and its link with the pituitary gland is very important.

Pituitary Gland

The pituitary gland is linked to the hypothalamus by the pituitary stalk. The pituitary gland releases hormones which trigger other glands in the body to release their hormones. The pituitary gland is about the size of a pea and is divided into two lobes, called the anterior (front) and posterior (rear) lobes. The hormones produced by the anterior lobe include those responsible for growth (growth hormone (GH)), development in puberty (gonadotrophins), as well as hormones which stimulate the thyroid gland (thyroid stimulating hormone (TSH)) and the adrenal glands (adrenocorticotrophic hormone (ACTH)). The

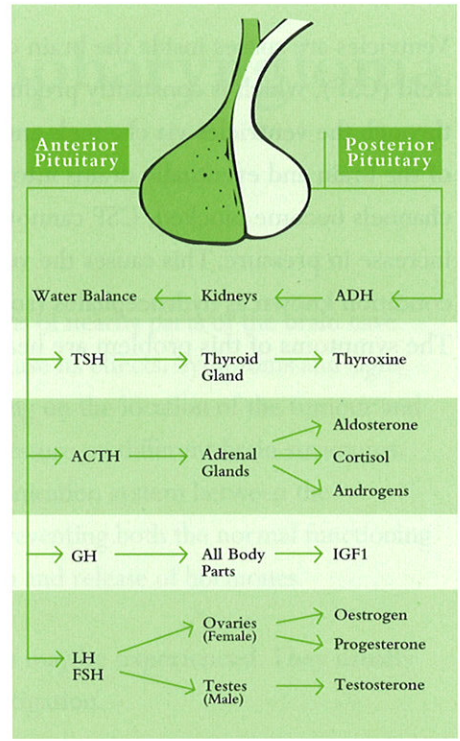
How Does a Craniopharyngioma First Appear?

posterior lobe stores and releases vasopressin, also called antidiuretic hormone (ADH), which regulates the levels of fluid in the body and so the amount of water passing out through the kidneys and into the urine. This determines the amount of fluid within the body, so-called hydration. The hormones released by the pituitary gland can be seen in Diagram 2.

Optic Nerves

The nerves from both eyes, called the optic nerves, meet and cross at the optic chiasm, which is found just above the pituitary gland. From here they carry the visual information to the back of the brain. If there is pressure on the optic nerves from the growing craniopharyngioma, vision can be affected, the most serious outcome being complete loss of sight.

PITUITARY GLAND



DEFINITIONS

ADH	Antidiuretic Hormone
TSH	Thyroid Stimulating Hormone
ACTH	Adrenocorticotrophic Hormone
GH	Growth Hormone
IGF1	Insulin Growth Factor 1
LH	Luteinising Hormone
FSH	Follicle Stimulating Hormone

Diagram 2

Ventricles of the Brain

Ventricles are spaces inside the brain containing fluid known as cerebrospinal fluid (CSF), which is constantly produced and circulated. This fluid flows through the ventricles via channels and openings, circulates over the surface of the brain and eventually drains into the blood-stream. If the ventricular channels become blocked, CSF cannot escape. It accumulates and causes an increase in pressure. This causes the ventricles to enlarge, resulting in a condition known as hydrocephalus (sometimes called 'water on the brain'). The symptoms of this problem are headaches and vomiting.

Symptoms of a Craniopharyngioma

Diagram 1 and the preceding descriptions of nearby parts of the brain have shown how a craniopharyngioma may cause its effects. Symptoms and signs may be different for each child, depending on the location of the tumour and the amount and position of increased pressure on different brain structures. These problems may disturb the communication system between the hypothalamus and the pituitary gland, preventing both the normal functioning of the pituitary gland and the production and release of hormones.

All or some of the following symptoms may be experienced. They usually appear gradually and will require investigation.

Headaches – (with or without nausea & vomiting)

It is particularly significant if these occur first thing in the morning or at night. They are due to increased pressure within the brain caused by the tumour increasing in size. If the tumour or cyst extends far enough upwards, it can cause blockage of CSF circulation in the ventricles which in turn leads to hydrocephalus.

Vision Disturbance

This symptom occurs when the craniopharyngioma is close to the optic nerves and optic chiasm. As the craniopharyngioma grows, it starts to press against the nerves. This stops signals from the eyes reaching the brain and sight can become impaired or lost altogether.

Effects on Hormone Secretion

The pituitary gland, the hypothalamus and / or the connection between them can be affected by the growing craniopharyngioma, resulting in impaired production and release of the pituitary hormones. The following problems may result:

Poor Growth

One of the causes of poor growth in children with a craniopharyngioma is the effect the tumour has on the pituitary gland, which means that there may be growth hormone insufficiency. In these cases normal growth is affected. It is not fully understood why some children with a craniopharyngioma have poor growth but do not have a measurable hormone deficiency.

Delayed Onset of Puberty

Pubertal development includes breast and pubic hair growth in girls and growth of the penis, facial and body hair and muscular development in boys. These events will not occur if the gonadotrophin hormones, which are needed to trigger pubertal development, are deficient as a result of damage to the pituitary gland.

Early Onset of Puberty

An unusually early onset of pubertal changes can occur in some children,

again resulting from the impact of the craniopharyngioma on the hypothalamus and the pituitary gland. This problem is very rarely seen with craniopharyngiomas.

Increased Thirst – (more frequent urination)

A craniopharyngioma can cause pressure on the hypothalamus and posterior (rear) lobe of the pituitary gland or pituitary stalk, causing loss of the anti-diuretic hormone, vasopressin (ADH). This leads to a condition called diabetes insipidus, where an affected person is no longer able to control water loss from the body, due to a lack of the water retaining hormone. The symptoms of this are excessive urine output and increased thirst, causing some children to drink up to 6 - 10 litres of fluid per day.

Other symptoms may include:

- Tiredness and frequent infections which are difficult to 'shake off'
- Intolerance to cold temperatures
- Disturbance of normal sleep patterns with either excessive sleepiness during the day-time or increased waking at night
- Weight loss or weight gain with a normal, decreased or increased appetite
- Behavioural problems such as becoming withdrawn, introverted, aggressive or having poor concentration
- Poor balance or weakness in the arms or legs
- Fits may occur, though this is rare

Diagnosis of a Craniopharyngioma

The following investigations will be needed to confirm the diagnosis:

Brain Scan (X-Ray Scan (CT) and / or MRI Scan)

This will enable the tumour and the surrounding areas of the brain to be seen in great detail. Further treatment, especially surgery, can then be planned very carefully. MRI scan is necessary to completely assess the involved area. CT scan may be suitable as a first step towards diagnosis.

Skull X-Ray

This may be helpful in showing up flecks of calcium which are almost always present in childhood craniopharyngiomas. This investigation however, is not always performed because brain scans give more information and are now much more widely available.

Additional tests that form part of the overall assessment may include:

Visual Assessment

This will be done by the paediatric endocrinologist and an eye specialist to check if the tumour is affecting the child's sight, particularly his or her field of vision.

Diagnosis of a Craniopharyngioma

Height & Weight

The specialist will measure the height and weight of any child diagnosed with a craniopharyngioma to assess their rate of growth. The child's stage of development in puberty will also be checked when appropriate.

Blood Tests

These will be done to check the levels of hormones to see if there are any which are insufficient.

Water Balance

A test is performed to measure the level of fluid in the body. It is done by comparing the concentration of the blood with the concentration of the urine as there is a relationship between the two which should be maintained. If an abnormally high level of salt is present in the blood together with a low concentration of urine, then it may be necessary to perform a specialised test over several hours to check for this problem. It may indicate that the child with a craniopharyngioma has diabetes insipidus resulting from vasopressin insufficiency.

Psychological Assessment

Depending on the severity of the craniopharyngioma and what treatment is planned, it may be important to assess the child's stage of learning, memory and behaviour, as these may be affected by the development of the tumour and / or its treatment.

Hearing Assessment

Occasionally hearing loss or ringing in the ears (tinnitus) can occur as an early symptom of a craniopharyngioma. This may need assessment by a specialist.

Treatments for a Craniopharyngioma

Because of the problems a craniopharyngioma causes, particularly if it is growing rapidly, it is usually best to try and remove it surgically. There are different ways this can be done, although it will usually require a major operation.

Normally the surgeon will try to remove as much of the tumour as possible, but this should not be at the expense of serious damage to nearby areas of the brain. As mentioned previously, these tumours can be very 'sticky' and they attach themselves to the surrounding tissues. Removing them can be a very difficult and delicate procedure.

It may also be necessary to follow the surgery with radiotherapy to help prevent any regrowth of the tumour, but this will also depend on the age of the child.

"Normally the surgeon will try to remove as much of the tumour as possible, but this should not be at the expense of serious damage to the nearby areas of the brain."

Some of the treatments will now be discussed in more detail:

Surgery

Craniotomy

In most hospitals where treatment for a craniopharyngioma is available, the primary treatment is surgery to remove all or part of the tumour. This involves a major operation known as a craniotomy. The skull is opened surgically at the front, or front and side of the head, near the hair-line and usually on the right side. The hair around the area of the incision will need to be shaved, but usually no more than this is needed.

By looking carefully at the scans which were taken before the operation, the surgeon will decide whether it is best to try and completely remove the craniopharyngioma. This is usually the aim. If however, during the operation, it can be seen that there are solid or cystic parts of the tumour stuck very firmly to the optic nerves, the hypothalamus, or a major blood vessel, then it may be far too hazardous to try and remove all of the craniopharyngioma without causing severe damage to these sensitive parts of the brain. Sometimes the tumour can be only partially removed, leaving a significant portion behind. Other treatments, such as radiotherapy or cyst drainage, may then be required. The specialist will discuss these options.

Trans-Nasal Operation

If the tumour is small and confined to the area where the pituitary gland lies, the operation can be done through the nose. It is unusual for this operation to be performed in children, as the tumour in a child is often much larger and more extensive than in older people.

Cyst Aspiration

The cystic part of a craniopharyngioma may be a single cyst or formed by

several cysts joining with one another. Before attempting to remove the tumour, the surgeon may decide to drain or aspirate the contents of the cyst, particularly if there is one major cyst which is pressing against a critical structure and causing symptoms of increased pressure within the brain. This involves a small operation whereby a hole (burr hole) is made in the skull and a tube is passed into the cyst to drain its contents. The surgeon will then go on to perform a craniotomy at a later date. Cyst aspiration may also be done if the cystic part of a tumour regrows.

Drainage of the Ventricles

In about one third to a half of children with a craniopharyngioma, the ventricles of the brain become enlarged due to the build-up of CSF. It may be necessary to re-establish the flow and drainage of the CSF before attempting removal of the tumour itself. This involves inserting a form of drainage system into the ventricles that can be either a temporary or permanent measure. Most commonly, the drainage system is a tube, called a shunt, that connects a ventricle to another body cavity, usually the abdomen (this is then called a ventriculo-peritoneal shunt, as can be seen in Diagram 3). There is an inter-connecting valve so that the speed and pressure at which the fluid drains can be controlled.

Occasionally, after the main operation to remove a craniopharyngioma, it is necessary to insert a shunt. Less commonly a shunt may be needed if the tumour regrows and causes obstruction of the CSF flow.

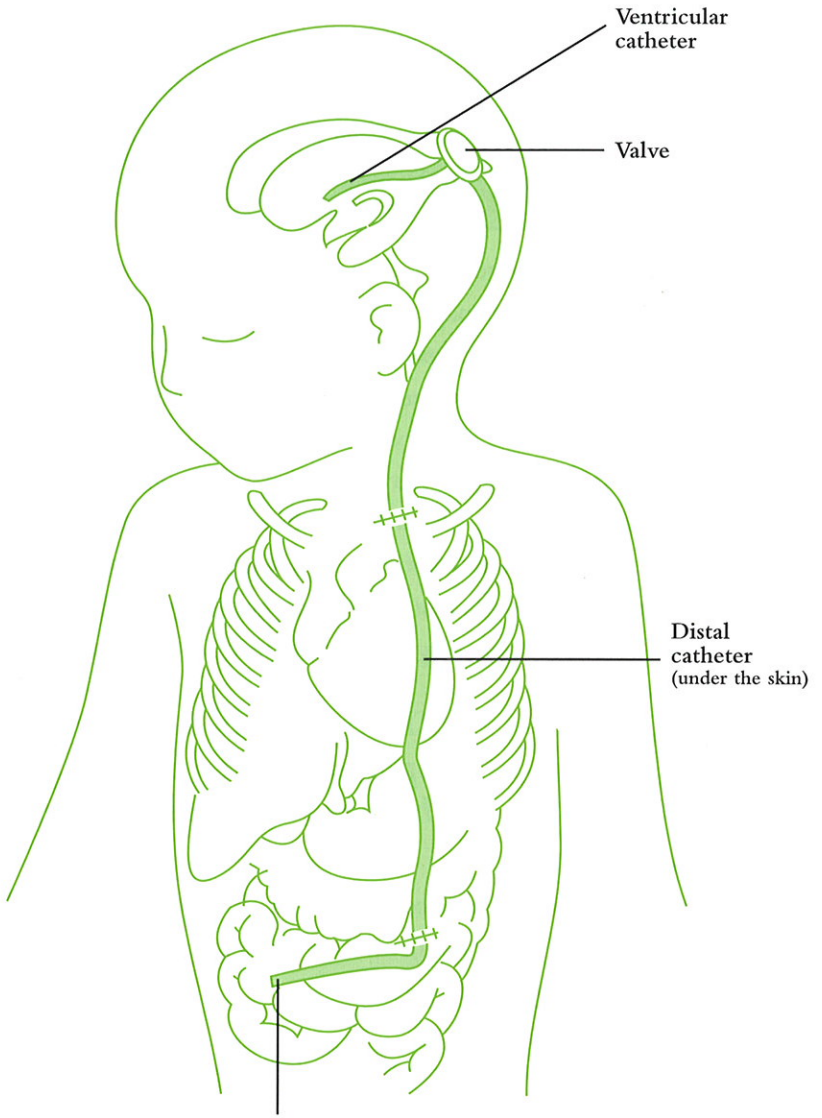
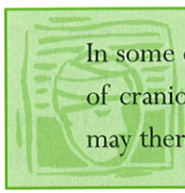


Diagram 3

Radiotherapy



In some centres, radiotherapy is not used at all for the treatment of craniopharyngioma. Some of the information in this section may therefore not apply to the treatment of the child.

Radiotherapy is a way of targeting radiation at a tumour in order to kill the tumour cells with minimal damage to the surrounding normal tissues. This form of treatment is more commonly used for malignant or cancerous types of tumours but has been found to be effective in preventing regrowth of a craniopharyngioma.

Radiotherapy is mainly used in children who have had surgery to remove their craniopharyngioma, especially if it was decided to remove only part of the tumour. It may be that a course of radiotherapy is given as soon as the child has recovered from their surgery. Alternatively, a 'watch and see' policy may be adopted, with the option of giving radiotherapy at a later date if scans show that the craniopharyngioma is regrowing. If the neurosurgeon is confident that all of the tumour has been removed at surgery and this is confirmed on further brain scans, then it is unlikely that radiotherapy will be needed.

"The age of the child is also important when deciding whether radiotherapy is given."

The age of the child is also important when deciding whether radiotherapy is given. It is generally not used for children under 2 years of age and rarely for those under 5 years because of the concerns of the long-term effects of

radiation on the developing brain. However, newer, more refined techniques of giving radiotherapy are being developed all the time so this form of treatment may play a more important role in the future.

A radioactive element, yttrium, is occasionally used as a local implant into a craniopharyngioma cyst to try to prevent re-growth and fluid accumulation.

Chemotherapy

Like radiotherapy, chemotherapy is used only for certain cancers and is currently not used for the treatment of craniopharyngiomas. However, a particular antibiotic-like drug called bleomycin is used in some centres in Europe and Australia prior to surgical removal of the cystic portion of a craniopharyngioma. A month or so before the operation, bleomycin is injected into the cyst to thicken or shrink the wall of the cyst in the hope that it will make surgical removal easier. It is also used sometimes to try and control local cyst growth after surgery.

Initial Treatment

The child may be in hospital for a few weeks, although this will depend upon the individual patient and what treatment he or she receives. Usually, the few days before the operation are spent performing the investigations already described and assessing the results of the brain scans, although most of these tests are now performed prior to hospital admission.

The main operation to remove the tumour may be delayed by a few days or occasionally a few weeks, if insertion of a shunt or cyst aspiration is needed first. This time may be spent in or out of hospital depending on the individual child.

"The child may be in hospital for a few weeks, although this will depend upon the individual patient and what treatment he or she receives."

After the operation to remove the tumour (a craniotomy) the child is likely to be in hospital for 1 to 3 weeks. Again much will depend upon the progress of the individual, and whether there are any new problems after surgery, such as diabetes insipidus.

If radiotherapy is additionally required, arrangements for this will be made once the child has recovered from surgery. The course of treatment takes approximately 6 weeks as small doses of radiation are given every day in order to reduce the side effects of the total dose. The child may not have to stay in hospital for this course of radiotherapy. This will however, depend on the age, cooperation and well-being of the individual child.

Post-Operative Care

As with any major operation, the child will be very closely monitored for the first 24 - 48 hours following surgery. This period of observation may need to take place in an Intensive Care Unit depending on whether the support of a breathing machine is needed. This is usually only the case if the operation has taken several hours as it is often considered better to wake up children more gradually, giving a period of complete rest and stability for the first few hours after surgery.

A careful record of fluid balance, i.e. liquid intake and urine output, will need to be kept during, as well as after, the operation. All urine produced is measured and checked for its concentration. A urinary catheter may be used initially to make this easier and more comfortable for the patient. All fluid taken in, through a drip at first and then by mouth, will be carefully calculated and recorded. Blood and urine samples will be taken at least daily for the first few days to make sure this balance of intake and output is correctly maintained.

After-Effects of a Craniopharyngioma and/or its Treatment

A craniopharyngioma occurs in a part of the brain which is very close to the hypothalamus and the pituitary gland and so most of the after effects are due to damage which has occurred to these very important areas.

Diabetes Insipidus

In a normal person, the hypothalamus monitors the state of water balance in the body. In conditions where the body might become dehydrated, for example in very hot weather, the 'thirst centre' in the hypothalamus is stimulated so that we feel thirsty and drink more water. The hypothalamus also normally signals to the posterior lobe of the pituitary gland to release the hormone vasopressin in larger amounts. This hormone acts on the kidneys in order to prevent water loss, i.e. urine is passed less frequently and appears more concentrated. Without vasopressin the urine would continue to be diluted and passed out frequently and the affected person would feel very thirsty and want to drink almost constantly so as to try and compensate for this lack of control of water loss from the kidneys.

Absent or inadequate production and release of vasopressin disturbs the ability of the body to maintain a normal fluid balance and leads to a condition called **diabetes insipidus**. This is quite different from diabetes

mellitus which is also called 'sugar diabetes'. A very young child with diabetes insipidus is not able to say how thirsty he / she feels and is dependent on carers for the provision of food and drink. In these young children there is a real risk of the child becoming rapidly dehydrated without correct treatment.

As mentioned earlier, the location of a craniopharyngioma is usually very close to the pituitary gland and stalk. During surgery, it may be necessary to cut the pituitary stalk in order to reach the tumour or the stalk can be stretched or damaged due to the size or location of the tumour, which is often adhered to the stalk. If this happens, communication between the hypothalamus and the pituitary gland is disrupted and the pituitary hormones will no longer be produced and released as needed. Vasopressin is one of these hormones and it is therefore extremely common for diabetes insipidus to develop after the operation. This explains why fluid intake and output need to be so closely observed following surgery.

How is Diabetes Insipidus Treated?

Signs of diabetes insipidus are quickly noticed because of the obvious symptoms of increased thirst and urine output. Strict fluid balance records show the increased fluid losses very soon after onset of the problem. Diabetes insipidus is treated by replacing the deficient hormone, vasopressin, with a synthetic form of the hormone, called an 'analogue'. An analogue is a product which has a slight change made to it. It has the same actions as the original hormone but lasts longer and therefore can be given less often. It may also be given in a different way, e.g. by tablets or intranasal drops, rather than by injection.

After-Effects of a Craniopharyngioma and / or its Treatment

During the first few days after surgery, the vasopressin analogue is given as necessary by injection into the vein or muscle. As soon as the child is well enough, the treatment can be given using a nasal preparation, either as a spray which is sniffed up the nose or as drops blown or sniffed from a fine, transparent plastic tube. It is usually required once or twice a day. Alternatively, vasopressin may be given as tablets in some countries and to achieve the very much smaller doses needed in children, the specialist will advise how to break the tablets to give the correct dose. These tablets are not available in Australia at this time.

In the first few days following surgery, the correct fluid balance may be quite difficult to sort out and the child may have periods of feeling very thirsty and wanting to drink frequently. These problems soon settle down once a smoother control has been achieved with the right dose and timing of vasopressin.

Over treatment of diabetes insipidus through giving too much vasopressin, may result in a build-up of fluid in the body and this could result in convulsions (fits). For this reason it is very important not to exceed the dose of vasopressin recommended by the specialist. Under-treatment is less dangerous and just causes the individual to pass more urine and so become extremely thirsty.

Occasionally a patient may have damage to his or her thirst centre as well as having diabetes insipidus. In such cases, although they lose a lot of fluid in large volumes of dilute urine, they do not get a feeling of thirst. This thirst loss is called adipsia. In this unusual event, dehydration may occur quickly if the child does not drink extra fluid. It may be necessary to assist the child to drink more if he or she does not feel a sense or need to drink. The specialist will advise how much fluid is needed each day - this may be called a fluid 'prescription'.

Will the Child Always Need to Take Vasopressin?

Diabetes insipidus is not always permanent. It will become apparent in the first few weeks after surgery whether vasopressin will be needed in the long-term. This depends on the degree of damage to the hypothalamus, the pituitary stalk and the posterior lobe of the pituitary gland. Obviously, if the stalk has been cut, then recovery cannot take place and vasopressin treatment will be required for life. Sometimes diabetes insipidus can occur in the first few days after surgery then disappear completely as brain swelling reduces. Occasionally there can be a 'triple response' where diabetes insipidus occurs in the immediate post-operative days, gets better 7 – 10 days later then recurs permanently about 2 weeks after the operation.

Other Treatments

Anticonvulsants

Rarely, children with a craniopharyngioma have a convulsion as the first sign that there is anything wrong. Medication will then almost certainly be given to cover the period of the operation to prevent any further fits occurring. The medication may be gradually withdrawn a few months after the operation if no further problems arise.

Even if the child has not had any previous fits, any interference with the brain, such as the trauma of an operation, may potentially cause a fit. Therefore, some neurosurgeons like to administer anticonvulsants before and after the operation. The treatment can be gradually withdrawn if there are no problems.

A proportion of children do continue to have problems with fits or develop them later on. In this case they may need medication for a longer time to keep these under control.

After-Effects of a Craniopharyngioma and / or its Treatment

Steroids

Steroids are always given before and after surgery for a craniopharyngioma. There are two main reasons for this:

1. To help reduce the swelling and build-up of pressure within the brain. High doses of either dexamethasone or hydrocortisone are usually given.

2. To cope with stress

Adrenocorticotrophin (ACTH) is one of the hormones produced by the anterior lobe of the pituitary gland. It triggers the adrenal glands to make and release a steroid called cortisol. Cortisol is produced in varying amounts during the day and night but more importantly, it enables us to cope with stress such as illness and trauma. At these times, greatly increased amounts of cortisol are released into the bloodstream.

If the pituitary gland and pituitary stalk are damaged, either by the craniopharyngioma itself or the surgery, then the ability to produce cortisol is lost. The body will then be unable to cope with the stress of an operation unless replacement steroids are given. Cortisol is initially given in high doses following the operation. The dose is then gradually reduced to much smaller doses which are then continued in the form of hydrocortisone tablets until further tests of pituitary gland function have been carried out.

Assessment of Pituitary Gland Function After Surgery

Approximately 2 - 3 months after the operation, some blood tests, usually taking a morning to perform, will be done to assess how well the pituitary gland is working. From the results of these, it should be clear which

hormones will need to be replaced. Treatment, once started, will almost certainly be for life. At the present time however, growth hormone in not yet available in Australia or New Zealand for use for growth hormone deficient adults. Currently it can only be used to promote growth in children.

Thyroid Hormone (thyroxine)

Following the operation, if there has been damage to the hypothalamus, the pituitary gland or the connection between the two, the pituitary gland will be unable to release the hormone necessary to stimulate the thyroid gland. Replacement thyroid hormone treatment will then be needed. This is given in the form of tablets.

Growth Hormone (GH)

Damage to the hypothalamus and / or the pituitary gland may mean that the anterior lobe of the pituitary gland is unable to release growth hormone in sufficient amounts. Replacement treatment may be needed if the child is growing poorly. The only way to give growth hormone treatment is by injection because growth hormone is a protein and if it was taken by mouth it would be digested and not work. These injections are given each evening and the needle goes just under the skin (subcutaneous). The dose of growth hormone needed is calculated according to the size (either body weight or body surface area) of the child. Even when the dose increases the volume of the injection remains very small. Occasionally, after surgery for craniopharyngioma a child continues to grow usually despite a lack of growth hormone measured during testing. If this is the case, the child will not need growth hormone treatment.

Sex Hormones

If there is an insufficiency of the gonadotrophins, there will not be the

After-Effects of a Craniopharyngioma and / or its Treatment

stimulus to the gonads (ovaries in girls, testes in boys) to produce the sex hormones (oestrogen and testosterone respectively) which are needed to trigger the physical changes which occur during puberty. At the appropriate age, replacement treatment will be needed.

When all the pituitary hormones are deficient, the term panhypopituitarism or multiple pituitary hormone deficiency (MPHD) is used. Unfortunately, most children will become panhypopituitary after surgery for a craniopharyngioma. Even if the pituitary gland is still functioning shortly after the operation it is likely with time, that it will gradually stop producing hormones in sufficient amounts, particularly if radiotherapy has been given as well. Careful follow-up is therefore always required by a hormone specialist (endocrinologist). This will need to be continued throughout adult life.

It is very important to remember:

1. Medications MUST always be given regularly as prescribed and do NOT run out of supplies
2. Hydrocortisone is VITAL in helping the body cope with stress. At times of illness, the prescribed dose will need to be INCREASED and if vomiting occurs, the hydrocortisone will need to be given by injection (see the booklet on Prevention and Treatment of Hypoglycaemia in Adrenal Insufficiency and Other 'At Risk' Conditions)
3. Children who are deficient in pituitary hormones and / or who suffer with fits, for whatever reason, should wear an identity necklet or bracelet and carry a medical card

More information about some of these conditions are available in the Serono Symposia Australasia series of educational booklets titled "Hormones and Me".

- Growth Problems in Children
- Delayed Puberty
- Puberty and its Problems
- Management of Emergency or 'Stress' Situations where Hypoglycaemia or Cortisol Deficiency Occur
- Multiple Pituitary Hormone Deficiency (MPHD)
- Diabetes Insipidus

Other Long-Term Follow-Up

Eyes

Problems with sight often improves after surgery and can return to normal. Sometimes however, visual loss may be permanent. Eye tests will therefore be needed at regular intervals. Special help may need to be organised at school if the child's sight is very restricted in one or both eyes.

Growth

Children who have been treated for a craniopharyngioma need to have measurements of their height, weight and pubertal development recorded carefully and regularly. This is best done in a growth clinic by a paediatrician or paediatric endocrinologist. Children who have a craniopharyngioma can grow normally following surgery even though the pituitary gland is no longer producing growth hormone. Normal growth may continue for many months or years but usually slows down after 1 - 2 years, at which point growth hormone injections can be started to re-establish normal growth once more.

Some children who do 'grow without growth hormone' usually gain a lot of weight because they eat very large quantities of food. Some children

however, gain a lot of weight after craniopharyngioma surgery without obvious excessive eating. This is thought to happen as a result of injury to the hypothalamus when the craniopharyngioma was removed during surgery. The eating control centre may have been damaged or a change may have occurred in the metabolic rate of the body, possibly due to a change in levels of the hormone leptin. It is therefore very important to monitor the child's weight and consider reducing the intake of very fatty and sugary foods. Consultation with a nutritionist (dietician) may be helpful.

Other children grow very poorly before and after surgery due to their growth hormone deficiency and therefore need treatment at a much earlier stage than the above children.

Brain Scans

The timing of when further X-ray (CT) or MRI scans are needed will vary between individual children. As a guideline, a scan will be performed within 24 - 48 hours after surgery or before the person is discharged from hospital, to make sure all is well. A repeat scan will probably be arranged 6 months after the operation. Depending on the results of this, scans will be repeated every 6 - 12 months for the next 2 - 3 years and then as recommended by the specialist.

School Progress

It will be very important to monitor the child's progress at school. For various reasons, up to two thirds of children may experience learning problems following treatment of a craniopharyngioma.

Problems may range from:

- Difficulty in catching up on missed work because of the amount of time taken off school
- Difficulties keeping up due to poor sight
- Difficulties with concentration because the child is distracted by thoughts of food
- Difficulties due to learning or memory problems

Learning difficulties may result from injury to the hypothalamus and other areas of the brain during the operation or from the effects of radiation therapy, which may build up over a period of years. Ideally, a psychologist should be involved in the child's care from the beginning so that further tests of learning and memory can be done at intervals after the operation and / or radiotherapy. In this way, any special needs can be picked up early and prompt referral can be made to an educational psychologist so that appropriate support and supervision can be organised at school as soon as possible. Some children's needs may be better met in schools geared to special educational aspects and it is crucial not to let these children struggle for several years before finding this out.

Other Effects of a Craniopharyngioma or its Treatment

Earlier in this booklet, the hypothalamus was mentioned as having a number of important functions and its closeness to a growing craniopharyngioma can be appreciated. At the time of diagnosis, a craniopharyngioma will often have grown so large that it presses against the hypothalamus and this may result in some changes in behaviour such as disturbance of eating and sleep patterns. Neurosurgeons are increasingly aware of the importance of causing as little damage as possible to this area during the operation, even if this means leaving a small amount of the tumour behind. Some damage however, may still occur and this can cause certain behaviour problems. Sometimes, but not always, these problems will improve with time.

"It is extremely common for children to gain some weight after surgery for a craniopharyngioma but the amount varies from child to child."

Increased Food Intake & Obesity

It is extremely common for children to gain some weight after surgery for a craniopharyngioma but the amount varies from child to child. It is much

less likely to be a problem in those children whose tumour is not adhering to the hypothalamus at the time of operation. Increase in weight is due to a combination of the high doses of steroids given around the time of the operation, pituitary hormone deficiencies and / or injury to the 'eating control centre' of the hypothalamus. When this happens, a persistent feeling of hunger results so that these children may feel hungry even if they have just eaten. It seems as though they need to eat much more than normal to try and 'fill-up'.

In those children where there has been an effort to remove all the tumour with resulting damage to the eating control centre, up to 60% become obese because of the change in eating behaviour. The increase in appetite can develop very soon after surgery and they can become totally preoccupied with thoughts of food. Understandably, this may cause distress to the child and their family, particularly if there is a sudden change in body appearance because weight gain has been so rapid. Problems at school may also occur both from poor concentration and from teasing by other children.

In a small minority of children total dietary control is necessary, including locking kitchen doors, cupboards and refrigerators. It is important to discuss the issue openly and to encourage the involvement of the child as much as possible in the ideas of how to deal with it. Appreciating that this is a specific medical problem may help family and friends understand the child's 'need' for food and help plan for when the child becomes more independent. Early referral to a psychologist may be helpful.

Sleep Disturbance

This may mean that the child wakes up several times during the night or falls

asleep at odd times during the day. This symptom is related to the effect of the tumour itself pressing on other areas of the brain and / or due to damage to some of these surrounding areas during surgery. It usually continues even as the child gets older.

The main problems associated with this is the impact on education (they may be very tired during the day when they are at school) and the disturbance to other members of the family, parents, brothers and sisters etc, particularly if the night-time wakefulness is spent looking for food! It may be possible to treat daytime sleepiness effectively in some children, by using an amphetamine derivative.

Impaired Thirst

This is fortunately rare as the inability to feel thirsty is a serious problem, particularly when associated with diabetes insipidus. If both problems are present, carers need to use a 'fluid prescription' with accurate daily measurements of fluid intake and variations in volume depending on the weather.

Memory Disturbance

Memory may be affected either by damage to the hypothalamus or disturbance to other nearby areas of the brain. Short-term memory is usually affected rather than long-term although this may depend on the individual child. Memory 'processing' can be a problem, where new information is stored briefly but cannot be transferred to the long-term memory. This may have a particular impact on schooling, especially in high school, where ongoing learning in some subjects, such as mathematics, build on previously learned information. This problem, if present, needs to be recognised early,

so the child or teenager is not forced to continue trying to succeed at a subject when he or she simply cannot. Other, more appropriate subjects where this type of learning is not so important may need to be chosen.

Impaired Temperature Regulation

This is a rare but serious problem. Family and friends will notice if the child is not sensitive to extremes of temperature. When everyone else is piling on jumpers, the child is walking around in T-shirts or on a hot day they are asking for their jumper! Very occasionally a child may have great difficulty in maintaining a normal body temperature and need an electric blanket or hot water bed to prevent hypothermia.

In the rare case where temperature regulation is seriously impaired, this is often associated with other severe hypothalamic problems, such as impaired thirst. This can be a very difficult problem to manage and parents and carers need to vigilantly monitor fluid needs and to control the room / area temperature - e.g. the child should not be allowed to stay outside in very hot weather because their body temperature will tend to rise in an unusual way and might result in 'hyperthermia' with possible fitting or loss of consciousness.

Mood Swings

Children treated for a craniopharyngioma sometimes find that they have a much 'shorter fuse' than before the operation and have temper tantrums, which are quite out of character. This may be due to the fact that they have been ill although occasionally, damage to the hypothalamus may play a part. In some cases it may be necessary to seek advice from a psychiatrist.

Questions and Answers

Q *What are the signs that a craniopharyngioma is regrowing?*

A The child may have no symptoms at all and a reappearance of the tumour may be found either during a routine follow-up scan or the symptoms that were present at first diagnosis may return. In children, poor growth, despite hormone replacement treatment, may be an early sign of the tumour regrowing.

Q *What are the chances of the craniopharyngioma regrowing and what will happen?*

A If a craniopharyngioma is going to regrow, it usually does so within 3 years from the first treatment, which is why it is important to have regular brain scans during this time. If only a partial removal of the tumour was possible, then there is a higher chance of the tumour increasing in size again. Treatment options will depend on the individual child. Radiotherapy is sometimes used. At times further surgery is necessary as a craniopharyngioma can recur many years after the first treatment whether or not radiotherapy therapy has been given. The treatment plan decided upon will aim for the best possible outcome.

Q *Can a child die from this condition?*

A Approximately 90% of children treated for a craniopharyngioma are alive 10 years from diagnosis. A small proportion of children however, have serious complications following diagnosis and treatment and may die related to these problems. .

Q *Will a child's brothers and sisters have the condition as well?*

A No. A craniopharyngioma is a developmental abnormality that happens by pure chance. It is not familial or hereditary (i.e. passed on from parents or grandparents).

Q *Will the child be able to have children when they grow up?*

A They will almost certainly need hormone replacement therapy (testosterone or oestrogens) in order to go through puberty normally and will need to stay on this treatment to maintain sexual development. It should still be possible for them to have children. Additional hormone treatment of a slightly different type, will be required for both men and women in order to become fertile and this is one of the reasons why they need to remain under the care of an endocrinologist as an adult.

Q *What will happen when a child treated for a craniopharyngioma becomes an adult?*

A As an adult, most of the hormone treatments will need to be continued, including growth hormone. As some of the hormone deficiencies may develop at an older age it is very important that the child is referred to an adult endocrinologist at the appropriate time for continuity of their care.

Q *Why is this tumour different in adults?*

A Although a craniopharyngioma may occur for the first time in adulthood, this tends to be a different type of tumour from the one occurring in childhood as the cells making up the tumour are usually different. Childhood craniopharyngiomas tend to be more difficult to treat, especially the ones that cause symptoms at a very young age, as these tumours tend to be growing faster.

Further Reading

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

Diabetes Insipidus Foundation, Inc
www.onelist.com/community/diabetesinsipidus

John Hopkins University
www.med.jhu.edu/radiosurgery

The Hormone Foundation
www.hormone.org

The Magic Foundation
www.magicfoundation.org

UK Society for Endocrinology
www.endocrinology.org

Glossary

Cerebrospinal Fluid (CSF)

The fluid, which flows through the ventricles and over the surface of the brain, eventually draining into the blood-stream.

Chemotherapy

Medications used to treat various forms of cancers or tumours.

Computerised Tomography (CT Scan)

A type of X-ray which shows a three dimensional view of the area being examined.

Congenital

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

Convulsion

Involuntary muscular contractions and relaxations, also known as a fit.

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.

Dehydrated

Condition resulting from excessive fluid loss by the body, i.e. when fluid intake fails to replace fluid lost by the body.

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.

Gonadotrophins

The sex hormones, i.e. follicle stimulating hormone (FSH) and Luteinising Hormone (LH)

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.

Hereditary

When a genetic characteristic is passed on from parents to their children.

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.

Hyperthermia

A term used to describe an unusually high fever , where body temperature is raised above normal.

Hypothalamus

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

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.

Nerves

Transmit impulses from the brain to the rest of the body to make the body respond in a certain way.

Neurosurgeon

A doctor who specialises in surgery on the brain.

Nutritionist

A health professional who specialises in dietary advice.

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.

Optic Chiasm

The area just above the pituitary gland where the optic nerves from both eyes meet and cross one another.

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.

Puberty

Essentially the period in a young person's life, both male and female, where they become physically capable of reproduction.

Subcutaneous Injection

An injection given beneath the skin.

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.

Tinnitus

Constant ringing in the ears.

Urinary Catheter

A tube inserted into the bladder to remove urine from the body. It is used when the bladder is unable to function properly, or for a hospitalised patient who cannot leave their bed.

Womb

Uterus.

Organisations

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

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

Pituitary Tumor Network of America
16350 Ventura Boulevard # 231
Encino California 91436 USA
Internet: www.pituitary.com

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

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

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

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

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

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

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HORMONES AND ME

CRANIOPHARYNGIOMA

THIS BOOKLET IS ESSENTIAL READING FOR ANY PERSON WHO HAS BEEN DIAGNOSED WITH OR IS RECOVERING FROM A CRANIOPHARYNGIOMA. IT IS ALSO RECOMMENDED READING FOR THEIR FAMILIES AND FRIENDS.

Australasian Paediatric Endocrine Group

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