



Diabetes Insipidus

A Guide for Parents and Patients



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INTRODUCTION

The aim of this booklet is to describe a condition called Diabetes Insipidus which is affecting you or your child. The main symptoms of diabetes insipidus are excessive urine output and thirst. We hope this booklet provides help when dealing with problems or difficulties associated with this condition, and information which will enable you to understand about the treatment and give you a basis for discussions with your GP or specialist when necessary.

HORMONES

Hormones are the chemicals that carry messages from one cell to another via the bloodstream. A part of the brain called the hypothalamus controls the levels of many of the hormones in the blood by triggering the pituitary gland into producing the required hormones. Any low level, or deficiency, of a hormone may be the result of problems in the hypothalamus, or with the link with the pituitary, or with the pituitary gland itself (Figure 1).

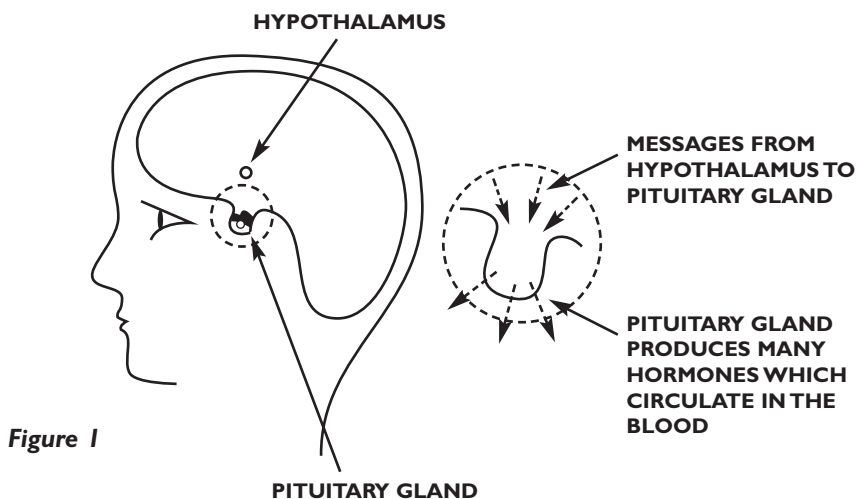


Figure 1

Pituitary gland

The pituitary is a pea sized gland and it is found in the centre of the head at the base of the brain, just below the hypothalamus. It receives signals from the hypothalamus to stimulate the release of hormones which affect many functions in the body.

The pituitary is divided into two areas (lobes) and these are called the anterior (front) and posterior (rear) lobes. Secretion of vasopressin (also called antidiuretic hormone or ADH) from the posterior lobe controls the level of fluid in the blood, and so its

concentration. Another hormone, oxytocin, which, at the end of a pregnancy, triggers the contractions of labour to start, is also released from the posterior lobe.

The hormones released from the anterior lobe of the pituitary are growth hormone (GH), the gonadotrophins (luteinising hormone (LH) and follicle stimulating hormone (FSH)), thyroid stimulating hormone (TSH) and adrenocorticotrophic hormone (ACTH).

Although the terms vasopressin and antidiuretic hormone (ADH) can be used interchangeably, in this booklet we will use the term vasopressin.

WHAT IS DIABETES INSIPIDUS?

Diabetes insipidus is a condition caused by an abnormality of the pituitary gland which leads to a deficiency of the hormone vasopressin. This affects the body's ability to control the level of fluid in the blood and urine. As a result, there is no stimulus for fluid to be retained in the body and so it is lost in the urine which becomes very dilute and is passed in large quantities. As a result of the excessive urine loss, an individual with diabetes insipidus will usually feel very thirsty.

Diabetes insipidus is not the same as the more common condition **Diabetes Mellitus** which is better known as sugar diabetes. Diabetes mellitus is relatively common and is a disorder of the pancreas which means the body is unable to control the level of sugar in the blood. The only similarity with diabetes insipidus is that large quantities of urine are passed and so it can seem quite confusing that they have similar names. In children, the treatment of diabetes mellitus involves regular injections of insulin and careful monitoring of levels of sugar in the blood.

It is very important not to confuse the two conditions called “diabetes” because they have different causes and very different treatments. **This booklet is about the condition Diabetes Insipidus.**

TYPES OF DIABETES INSIPIDUS

There are two types of diabetes insipidus:

- **Cranial diabetes insipidus:** This is caused by a deficiency of the hormone vasopressin. This results in the kidneys not being given the signal to retain fluid and so large quantities of fluid are lost as very dilute urine. Because fluid is being lost from the body in this way, the blood becomes too concentrated.

Normally, this concentration of the blood would be detected by the thirst centre in the hypothalamus and it would send a message to the pituitary to secrete vasopressin. In people with diabetes insipidus, there is a deficiency of vasopressin which means that the only way they can make up for the loss of fluid in the urine, is to drink more fluids. Thus, the hypothalamus detects the concentrated blood and this stimulates a feeling of thirst.

- Nephrogenic diabetes insipidus: This is due to an abnormality of the kidneys such that they are not able to respond to the vasopressin stimulus. This too means that large quantities of fluid are passed out of the body in the form of urine. This is a very different problem and will not be further discussed in this booklet.

HOW ARE FLUID LEVELS NORMALLY CONTROLLED IN THE BODY?

Control of the fluid levels in the body is important so that the blood does not become too concentrated or too dilute. If too much fluid is lost from the body in the form of large quantities of dilute urine, the blood becomes too concentrated. An area of the brain called the hypothalamus recognises that the blood has become too concentrated and as a result it sends a message to the posterior lobe of the pituitary gland to release the hormone vasopressin. This hormone is carried in the blood stream to the kidneys, giving them the message to reduce the amount of fluid being lost in the urine. This means that a smaller volume of more concentrated urine is passed, and the increased level of fluid in the blood means that its concentration returns to normal.

If the blood becomes too dilute, the hypothalamus sends a message to the pituitary to switch off vasopressin secretion. This means that the kidneys will allow more fluid to be lost in the urine, making it more dilute and excreted in a larger quantity. The increase in fluid being lost from the body as dilute urine means that the concentration of the blood returns to normal.

WHAT CAUSES DIABETES INSIPIDUS?

- Diabetes insipidus is usually caused by an abnormality at the base of the brain. This affects the normal function of the pituitary gland and results in vasopressin deficiency. Alternatively, there may be a small cyst or tumour (such as a craniopharyngioma), or an inflammation, and the symptoms of excessive thirst, with the loss of large quantities of urine, may be the first indication that there is something wrong. Diabetes insipidus may occur on its own, or with other pituitary hormone deficiencies (multiple pituitary hormone deficiency or MPHD) as will be described in more detail later.

- Diabetes insipidus may occur when the cause is unknown and this is called idiopathic diabetes insipidus.
- Very rarely, diabetes insipidus is passed from the parents to the child (hereditary). In some cases it may affect the newborn baby who will have problems with dehydration but in other cases the symptoms may not appear until the child is up to 1 year old. This cause is, however, very unusual.
- Finally, diabetes insipidus can result from surgery in the area of the pituitary gland. However, this type of diabetes insipidus is usually temporary, often lasting only a few days and requiring little or no treatment. However, in some cases, depending on the degree of damage following surgery, the diabetes insipidus may be permanent.

Whatever the cause, it is important that all children with diabetes insipidus are assessed by a specialist. The types of investigations they may need include special scans (either CT or MRI) of the brain to check whether a cyst or tumour is present. These scans may need to be repeated every 6 to 12 months.

SYMPTOMS OF DIABETES INSIPIDUS

The most common symptom in individuals with diabetes insipidus is passing large volumes of urine. This often means there is a need to go to the toilet frequently, including through the night which can naturally cause a disturbance of sleep. The individual usually retains control of their bladder so there is rarely a problem with bedwetting. This excessive output of urine means that an individual needs to drink large quantities of fluid and this is triggered by the other main symptom, thirst. So, in individuals with vasopressin deficiency, thirst becomes the regulator of water balance in their body. The amount of fluid which is drunk may be up to six to eight litres (12 to 16 pints) per day, although in partial diabetes insipidus the amounts may be less.

If enough fluid is drunk, the loss of fluid in the urine may not be too much of a problem. However, this may be difficult to recognise and manage in small babies as they do not always have the increased thirst and so the only signs may be constipation and a failure to gain weight as a result of dehydration.

In some people, especially if they have had surgery that has affected their hypothalamus, their thirst centre may also be affected. In such individuals, although they lose a lot of fluid in large volumes of dilute urine, they do not get a feeling of thirst. This is called adipsia. These individuals may rapidly dehydrate if not *made* to drink large quantities of fluid. This situation is potentially dangerous and needs very careful monitoring of fluid intake and loss. It is a common problem following surgery for a type of tumour at the base of the brain called a craniopharyngionia. In such cases the control of fluid balance may be extremely difficult.

HOW IS THE DIAGNOSIS MADE?

The diagnosis of diabetes insipidus can usually be made by comparing the concentration of blood and urine in early morning samples. This needs to be done after an overnight fast, and before your child has eaten or drunk anything.

If the concentration of the blood is high, and the concentration of the urine is low, this shows that there is a lack of control of the body's fluid levels and so suggests diagnosis of diabetes insipidus.

If this test does not confirm the diagnosis, a special test may need to be carried out called a "water deprivation test". This is done in hospital and your child would have to be admitted for the day, but not overnight.

For this test the patient is prevented from drinking fluid for eight hours and during this time the patient's weight, as well as the concentration of the blood and the urine, are checked regularly. Again, if the concentration of the blood is high and the concentration of the urine is low, this confirms the diagnosis of diabetes insipidus.

The administration of synthetic vasopressin at the end of the test will tell whether the cause is cranial or not. If it is cranial, the kidneys will respond to the administered hormone and there will be a rapid reduction in the volume of urine passed. The concentration of the blood will then return to normal.

Note: It is very important that all the urine is collected. However, the test will be stopped if there is too great a loss of urine such that it affects body weight.

Confusion in the diagnosis may occur in young children if they have a urinary infection as this causes large volumes of urine to be passed. Also, children with epilepsy who pass water when they have a fit can be suspected of having diabetes insipidus. Obsessive drinking, also called polydipsia, may also be confused with diabetes insipidus.

The distinction between diabetes insipidus and diabetes mellitus is quite simple as patients with diabetes mellitus have large concentrations of sugar in their urine which can be tested for by using a simple urine test.

DIABETES INSIPIDUS AND MULTIPLE PITUITARY HORMONE DEFICIENCY (MPHD)

Diabetes insipidus usually occurs on its own without any additional pituitary hormone deficiencies being present. However, there are occasions when diabetes insipidus and MPHD occur in the same individual. This is rare when the MPHD is due to an unknown cause (idiopathic) but is more common when the MPHD is secondary to a tumour that is present in the area of the pituitary gland. Also, if there has been damage to the pituitary gland as a result of surgery to remove the tumour, there is the risk of MPHD and diabetes insipidus occurring together. Diabetes insipidus does not occur as a result of irradiation therapy for such a tumour.

However, individuals with MPHD may not always be aware that they also have diabetes insipidus! Cortisol insufficiency (resulting from adrenocorticotrophic hormone (ACTH) insufficiency)~ results in the kidneys being unable to excrete a large volume of urine. So, in individuals with ACTH insufficiency in addition to their vasopressin insufficiency, it is only when they start receiving cortisol replacement that their kidneys start working properly. Large quantities of urine start to be excreted and the additional diagnosis of diabetes insipidus is suspected.

HOW IS DIABETES INSIPIDUS TREATED?

Diabetes insipidus is treated by replacing the deficient hormone, vasopressin, with a synthetic form of the natural hormone. The synthetic hormone may also be an analogue” of the natural hormone. This means it has had a slight change made to it allowing it to have the same actions as the natural hormone but usually it lasts longer and so can be given less often. Also, it can often be given in a different way, eg by tablets or intranasal drops, rather than by injection.

In children and adults vasopressin may be given as tablets, or as a nasal spray or drops. Of course, it is very important to adjust the dose for children and babies/infants as they often need only very small doses.

If someone has a cold or an allergy, their nose often becomes blocked and this may result in poor absorption of the administered vasopressin if it is given by spray or drops. This may affect the control of their diabetes insipidus and it is therefore important to try and clear the nose as much as possible before taking the treatment. Alternatively, your specialist may advise you to take your vasopressin as tablets during this time. The tablets are usually taken three times per day, although in mild, partial diabetes, using them just at night may be enough.

In patients who take vasopressin as a spray or drops, their nose can become very sensitive making it uncomfortable to continue taking their treatment in this form. If so, your specialist may advise you to use the tablets instead.

Sometimes your specialist may advise you to use a combination of these different types of vasopressin analogue if that will help you have more control over your symptoms.

It is very important to have your dose of vasopressin checked every year by your specialist, especially as repeatedly taking too much results in excess water absorption and this is dangerous. In addition, you should make sure that the doses and timings of your treatment ensure that your lifestyle is affected as little as possible. This may mean simply being able to sleep through the night without needing to get up to go to the toilet. Discussion with your doctor should also include advice as to what extra doses to take when your nose is blocked and absorption of treatment is, therefore, less reliable.

It may take some time to discover how to adjust your type of treatment (drops), spray or tablets), as well as the dosage, to cover daytime and night time without problems. This is quite natural and your doctor will advise you about how to do this.

WHAT HAPPENS IF THERE IS NO SENSE OF THIRST?

If the thirst centre has been damaged, as can happen if there is damage to the hypothalamus, particularly following surgery for a craniopharyngioma, diabetes insipidus may be associated with the lack of a sense of thirst, the condition known as adipsia. Very occasionally, adipsia may occur on its own without diabetes insipidus.

It is very important to know whether your child has this condition. Individuals who have no sense of thirst need to be encouraged to drink and your doctor will provide you with an idea of how much fluid is needed each day - this may be called a fluid "prescription". The amount of fluid needed will depend on the size of the individual. In addition, it may have to go up during hot weather and minor infections as at these times extra fluid is lost through sweating.

Generally, the fluid prescription can be managed quite easily by parents, but such added complications do mean that these children need to have regular blood tests to make sure they are not losing too much fluid.

In all children with diabetes insipidus it is important that they drink enough to keep up with their fluid requirements.

DIABETES INSIPIDUS IN SMALL BABIES

Diabetes insipidus in small babies leads to the loss of large amounts of urine and excessive thirst just as it does in older children, but it may be difficult for the parents to recognise this. The problem may result in poor weight gain which then improves when treatment is given.

As with older children, vasopressin can be given to babies in the form of tablets. The dose of each individual tablet is too large for small babies and so your specialist will advise you and your pharmacist how the tablets should be broken to allow a dose which is suitable for babies and infants.

Alternatively, vasopressin treatment can be given as drops into the nose. However, *very much smaller* doses are needed than are given to adults and generally your doctor will ask the pharmacy to make up a diluted solution so that the dose can be accurately assessed and the volume that needs to be given is not too large. It may be difficult to use the small plastic tube in babies and it is often easier to use a 1 ml syringe. The baby is laid on one side and the vasopressin is gently dropped onto the inside of the nose and the baby is left in that position for a few minutes. The baby is then turned onto the other side and the remainder of the dose is again dropped into the inside of the nose.

Measuring urine loss in small babies can be quite difficult. It can be done fairly accurately by weighing nappies but this can be impractical in the long-term. Once the dose of vasopressin treatment has been established, it is usually enough for the parents to check their baby's nappy at regular intervals so that they get a clear idea of when the nappies are fairly dry and when they are wet. In time, most parents can recognise if their baby is passing more or less urine than normal.

It is **always** advisable to treat babies with the lowest possible dose of vasopressin as it is **very important** to avoid any risk of fluid overload.

This means that sometimes extra water needs to be offered to your baby to make sure he/she does not get dehydrated. For example, a breast feeding mother may offer the baby some water at the end of each feed and if the baby is thirsty he/she will take the extra water. In addition, if, for any reason, a baby needs to be fed through a nasogastric tube, it is very important to monitor fluid intake in order to prevent fluid overload.

The problems are much greater in babies who are lacking a sense of thirst and it is very important to establish this at a very early stage. These babies will not take extra free water and they will need to have a water prescription to make sure they get enough fluids each day. The risks of dehydration during very hot weather or illness are quite high in these babies and in all small babies with diabetes insipidus. Illness where vomiting or diarrhoea develops will usually require a short stay in hospital.

QUESTIONS AND ANSWERS

Q1 Is diabetes insipidus permanent?

A Yes, almost always. However, in rare cases, following operations at the base of the brain, diabetes insipidus may develop which is only temporary.

Q2 Are any special precautions needed for travel?

A When travelling to a hot climate, extra fluid intake will be needed due to extra loss of fluid as sweat. Your specialist will need to advise you about this. Usually your normal dose of vasopressin will be sufficient. If you are in a hot climate you will need to store your drops or spray in a cool place (but not in direct contact with ice as it shouldn't be frozen). If you don't have a cool bag, don't worry. Try wrapping the bottle in wet toilet paper and keep it in a plastic bag. Vasopressin tablets can be kept at room temperature.

Q3 Will any adverse effects occur if I leave the medication out of the fridge?

A Intranasal drops and sprays need to be refrigerated. If they are left out for a long time, they may become less effective and a larger dose of vasopressin would therefore be required to achieve the usual effect. Tablets of vasopressin do not require special storage requirements.

Q4 Are there any adverse effects of drinking alcohol?

A Normally, there is an interaction with alcohol which reduces vasopressin secretion so in individuals with partial diabetes insipidus there may be the need for additional treatment. In patients who are deficient in their own vasopressin there will obviously be no interaction. However, drinking large quantities of fluid, even in the form of alcohol, after taking vasopressin could lead to the risk of water overload.

Q5 What happens if I don't feel thirsty?

A If you have the problem whereby you lack the sense of thirst, please read the section on page 10. However, if you are unwell and have difficulty taking fluids or solids then you should seek medical advice as temporary inpatient care may be necessary. In addition, in very hot weather, heat stroke can lead to sleepiness and a reduced thirst. Particular precautions will therefore be needed.

Q6 What happens if I miss a dose or the dose does not get absorbed?

A If this happens you will notice that you start passing a lot of urine and getting thirsty at a time when the vasopressin treatment would normally be working. If this occurs within 2 hours of the time when you normally take the dose, and you are pretty sure that you've missed it or something was wrong with the administration, then it is safe to take half the dose again. If, however, several hours have elapsed, it is probably safer to drink yourself out of trouble. Take a jug of water and keep up with the fluid losses until you would normally take your next dose.

Q7 Is it dangerous to take too much vasopressin treatment?

A Yes. This will cause the retention of too much fluid in the body and will result in an increase in weight, swelling or puffiness of the limbs, an increase in blood pressure and headaches. The increased fluid retention causes a lower concentration of substances in the blood. Hyponatraemia, or low blood sodium, may result in fits. *This can be a serious condition and generally it is safer to give too little vasopressin than too much.*

Q8 Is it important that I carry notification about my condition?

A Yes. An older child or adolescent will need to have an SOS Talisman or Medic Alert necklace or bracelet. Details about these are available from the Child Growth Foundation.

Q9 If I have a cold, will this affect my treatment?

A It may do if your vasopressin treatment is by intranasal spray or drops. If only one nostril is blocked, the other one will be adequate for treatment. If, however, your nose is totally blocked, you may not absorb enough medicine and you will need to consult your doctor. In these circumstances, it may be necessary to change your treatment to tablets, however, such a change will need careful monitoring of fluid balance.

Q10 What extra care will be needed if my child develops diarrhoea and vomiting?

A In young children, diarrhoea and vomiting can very easily upset their fluid balance and this may require special precautions and, possibly, admission to hospital to make sure their fluid balance is adequately controlled. If you have any doubts with a young child, you should take them to the nearest Accident and Emergency Department explaining the situation and asking to see a doctor immediately.

Q11 Do all my child's school teachers need to be told about his/her condition?

A Yes. Each teacher who sees your child needs to be informed and told that your child needs *free access* to both drinks and the toilet, even during examinations. Children with diabetes insipidus cannot hold their urine for long when they want to go to the toilet. If teachers ask the child to wait for a convenient time, it can cause the child great discomfort as well as embarrassment if they wet themselves.

Q12 I am deficient in other pituitary hormones (hypopituitary or multiple pituitary hormone deficient (MPHD)). Can this affect diabetes insipidus?

A Yes, if in addition to your vasopressin insufficiency you have cortisol insufficiency as a result of your adrenocorticotrophic hormone (ACTH) insufficiency. Cortisol is important in enabling the kidneys to excrete large volumes of fluid in the urine. Thus, when you start receiving cortisol replacement treatment, this may unmask your diabetes insipidus because you start excreting the large quantities of urine associated with this diagnosis.

SYNDROME OF INAPPROPRIATE ADH SECRETION (SIADH)

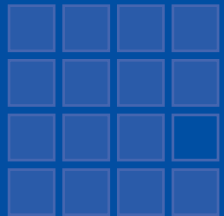
Very rarely, a condition involving the area at the base of the brain may cause an excess of ADH secretion rather than ADH deficiency as has been described.

In patients with this condition, the excess ADH secretion causes an excess of fluid to be retained by the kidneys and this results in severe dilution of the blood. The fluid retention causes weight gain, puffiness of the hands and feet and low sodium levels which can result in fits and unconsciousness.

Treatment of SIADH requires a restriction of fluid intake. Usually SIADH is temporary and after a few days the condition improves, especially if the underlying problem is treated.



SERIES 12



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