



AVP-D

Condition guide 

Arginine Vasopressin Deficiency

(Diabetes Insipidus)

Arginine Vasopressin Deficiency (AVP-D, formerly known as Diabetes insipidus or DI) is caused by a problem with either the production, or action of the hormone vasopressin (AVP).

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What is Arginine Vasopressin Deficiency (AVP-D) and why do we get it?

Arginine Vasopressin Deficiency (AVP-D, formerly known as diabetes insipidus or DI) is caused by a problem with either the production, or action, of the hormone vasopressin (AVP). If you have AVP-D your kidneys are unable to retain water. This leads to the production of large volumes of colourless urine and, in turn, greatly increased thirst.

The body is therefore reliant on only one of its two mechanisms to keep the amount of water in the body at the correct level, namely thirst and drinking (the other being increased AVP production to conserve water). People with AVP-D are thirsty all of the time; they pass large amounts of urine frequently through the day and often have to pass urine several times at night. This can be very inconvenient and can cause dangerous dehydration.

AVP-D can occur at any age but is mostly found in adults. It is a rare disorder, affecting only about 1 in 25,000 people.

To understand AVP-D we need to understand a little about how the body regulates water balance - the difference between how much water the body takes in and how much it passes out. Water balance is very important for the body because it affects every organ, particularly the brain and the kidneys. A large proportion of our bodies are made up of water.

In addition, the amount of water we have in our circulation is a large factor in determining the balance of electrolytes in our bodies (minerals in the blood), particularly sodium. As with any function that is important, the body has a sensitive mechanism for regulating water balance (a process called homeostasis). The mechanism for controlling water regulation is simple and, involves two key components:

- AVP or ADH (anti-diuretic hormone) which causes the kidneys to conserve water.
- Thirst which leads to the behavioural response of seeking water and therefore increased fluid intake.

AVP is a hormone released from the rear part of the pituitary gland (the posterior pituitary). This gland is located at the base of the brain and is about 3 to 5 centimetres behind the bridge of the nose. AVP circulates in the bloodstream and signals to the kidneys to increase the amount that is conserved, and therefore reduce the amount of water that is passed out in urine. Therefore, when AVP levels are high, the urine appears darker yellow because more water is conserved and less passes into the urine. When AVP levels are low, less water is conserved so more is passed and the urine looks pale, often indistinguishable from water.

How AVP and thirst work together is best described with the help of the bathtub analogy. As with a bathtub, the body likes to keep the level of water it contains at the right level for its purposes. There are only two ways the level of water can be altered:

- Water can be let in to the bath by turning the taps on; just as thirst and drinking can allow more water into the body.
- Water can be let out of the bath by taking out the plug; just as the body can reduce the production of AVP and passing more water out of the body as urine. Think of AVP like the plug as it stops water leaking out.



Unlike a bathtub, the body is very good at sensing the level of water it has on board. If it does not have enough and is dehydrated, it triggers us to drink more through activating our thirst (turning on the taps). At the same time, it makes more AVP to reduce water loss in urine (it puts the plug in).

On the other hand, if the body senses the level of water is too high, it turns off the thirst (turning taps off) and makes less AVP (taking the plug out). The level of water is therefore maintained through this combined approach. Clear urine that looks like water pretty much always mean AVP levels are low. This can either be an appropriate response to over-dilution of the blood, or due to a disease that causes AVP-D (usually related to some problem with the pituitary gland).

Together, AVP and thirst maintain water balance very effectively in both situations where water is either easy to find or is scarce. AVP-D occurs when this mechanism regulating water balance breaks down.

What is AVP-Resistance (previously known as nephrogenic diabetes insipidus or NDI)?

AVP-Resistance is similar to AVP-D, but there are some key differences. In AVP-R, there is no problem producing AVP (unlike in AVP-D where levels are low), but the kidneys do not respond to the normal signal (AVP) to reduce water loss. In fact, in AVP-R, AVP levels are usually high because the hormone is trying to work harder to get it to have an effect on a receptor that doesn't fit or work (like a key that can't get into a lock). Because AVP is not working on the kidney, water cannot be absorbed.

The symptoms of AVP-R are exactly the same as AVP-D in that people experience polyuria (passage of large volumes of urine) and polydipsia (excessive thirst and drinking). The difference is that giving AVP will not help in AVP-R because it will not have an effect, unlike in AVP-D when the effect of giving AVP can relieve symptoms at once. Usually AVP-D is treated by kidney doctors (nephrologists) rather than endocrinologists because the problem usually occurs in the kidney rather than the endocrine system.

Why was the name changed?



There has been confusion for a long time between diabetes mellitus (related to blood sugar levels) and diabetes insipidus, which has been detrimental to patient care. Many people will have their own experiences of having their fingers pricked to check glucose levels when telling a medical professional that they have diabetes insipidus, which many people have told us is very frustrating.

After a long campaign involving a working group of endocrinologists, patient representatives, and patient support groups, the new name was decided on: Arginine Vasopressin Deficiency or AVP-D/AVP Deficiency for short. This is a global change. The advantage of this name is that you are more likely to see a specialist endocrinologist early as it implies to the health care professional that this is a rare disease that is associated with a deficiency in AVP levels.

AVP-D is treated with a medication called desmopressin which is abbreviated to DDAVP. The new name may trigger the health care professional to give this drug early. This is good because some people have come to harm because there have been delays in DDAVP administration because of lack of knowledge and awareness of this condition.

During the transition period it is likely that both names will be used whilst clinicians and patients get used to the change. So, it will be called 'AVP-D (Diabetes Insipidus)' until the name beds in. It is expected that eventually diabetes insipidus will stop being used, making way for the new name.

This booklet will refer to only Arginine Vasopressin Deficiency or AVP-D from now on.

What are the causes of AVP Deficiency?

There are several causes for AVP-D:

- Sometimes AVP-D occurs on its own (often due to a gene defect in AVP production)
- The pituitary gland hasn't developed properly (congenital)
- A tumour or other abnormality within or near the gland
- An accident or surgery to, or near to, the gland (post-traumatic)
- Associated with pregnancy

AVP-D may be accompanied by other pituitary conditions or reduced function of other hormones. You can find out more about this on our website: www.pituitary.org.uk/conditions

AVP-D following pituitary surgery may be temporary, only lasting a week or two. This is sometimes called partial AVP-D. Partial AVP-D can also be when you only have symptoms for a part of a day or every few days.



What are the symptoms of AVP Deficiency?

Excessive thirst and need to pass urine

The main symptoms that you will feel are a constant thirst (no matter how much you drink) and the need to pass urine very frequently, even during the night. You will pass large volumes of urine, which can be from 4 to 10 litres per day. The urine will be very clear, colourless, similar to water, although occasionally it can go yellow if there is only a partial deficiency of AVP. There can be many reasons to have symptoms of increased thirst and passing large volumes of urine, so it is important to have blood tests with your doctor. Red flag signs for AVP-D are a sudden change in symptoms over a few weeks or months where you notice more urine output and thirst compared to usual. Anything more than about 3 litres a day of urine is probably too high and needs medical attention.

Some people have a behavioural tendency to drink more fluid, which leads to a secondary increased urine (primary polydipsia) and it is important to distinguish this from AVP-D as DDAVP treatment can be dangerous in primary polydipsia. Usually, primary polydipsia is long-standing and gets worse with stress but sometimes it can be difficult for doctors to tell the difference between this and partial AVP-D, and this needs an opinion by a specialist endocrinologist.

If you have AVP-D, you may well have symptoms of dehydration, for example feeling dry mouthed, shivery and nauseous with headaches. People with AVP-D have mentioned that their constant thirst can be compared with eating 4 or 5 dry cream crackers one after the other, without having anything to drink.

Most people do have a thirst mechanism, but some don't. This is called **hypodipsia** and is very rare. The combination of AVP-D and hypodipsia requires special attention from patients, carers and doctors.

Other symptoms

Other common symptoms of AVP-D include:

- Very pale urine, which is possibly clear and doesn't concentrate
- Preference of icy cold drinks
- Headaches (which may be due to dehydration)
- Exhaustion
- Shivering
- Nausea
- Dehydration symptoms: parched mouth, cracked lips, coated tongue, dry eyes and dry skin
- Most savoury foods are intolerable with a preference to drink fluids
- Weight loss.

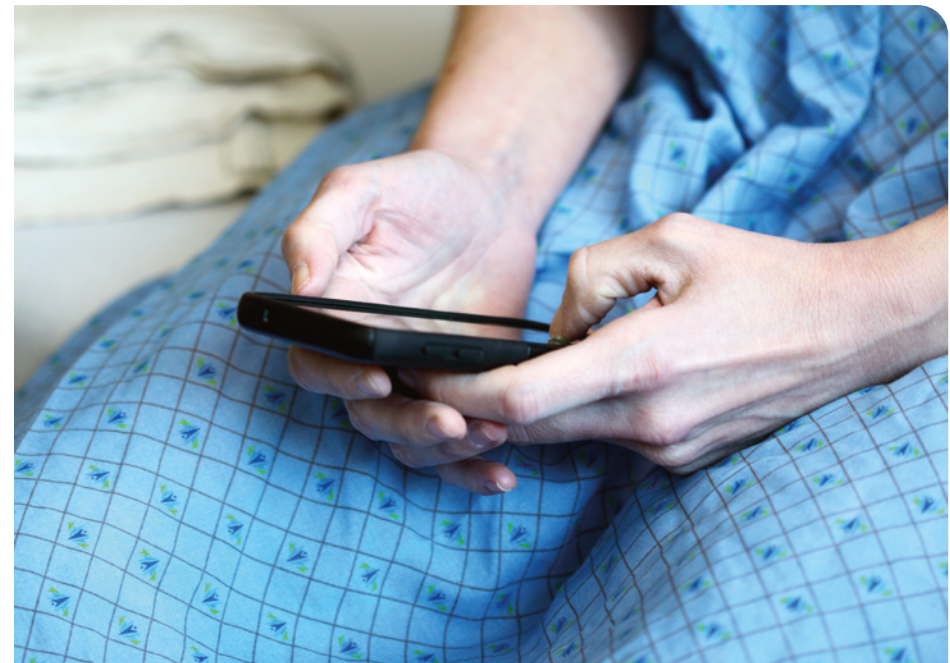


“For three years my thirst dramatically changed and I just simply couldn't quench my thirst. It's drastically worsened over the past year where I could drink multiple pints of water and still not feel hydrated!”

I also had worsening symptoms in regards to urination where I had to be close to a toilet as my bladder couldn't control the amount of water passing through. I went to the GP, he was convinced it was Type 2/1 Diabetes but after loads of tests, there was no answer.

They told me to cut down on my water intake because it could be anxiety related. I tried this thinking there was nothing wrong, my symptoms worsened – debilitating migraines, shaking, nausea/vomiting, fatigue and temperature fluctuations!”

Emily, who struggled to get a diagnosis for AVP-Deficiency



How is AVP-D diagnosed?



There are several tests for AVP-D which can lead to a diagnosis. These include:

- Measurement of 24-hour urine output
- Measurement of plasma and urine osmolality (concentration) from a blood and urine test
- Water deprivation test (under supervised conditions)
- Saline infusion copeptin test (under supervised conditions)
- Arginine stimulated copeptin test (under supervised conditions).

Water deprivation test

This test usually takes about 6 to 8 hours in a hospital setting. During the test you will have no food or fluids. When you arrive at the clinic in the morning, you will be asked to urinate and then have no fluid or food until you are informed you can. You will be weighed and blood and urine samples will be taken regularly. If during the test you lose 3% of your starting weight the test will be stopped.

If your blood sodium and/or blood/urine osmolality reach the set criteria, you will be given a sample dose of desmopressin. In 1 to 2 hours, you will provide another blood and urine sample. If required, additional blood and urine samples will be taken. If your urine osmolality increases to a set criteria, AVP-D is diagnosed. It is important that the test is supervised.

Some people find this test very unpleasant, particularly if there is severe AVP-D.

Hypertonic saline infusion copeptin test

This test usually takes 3-4 hours in a clinic or hospital setting. During the test you will have no food or fluids. You will be asked to lie on a bed and will receive a saline (sodium) intravenous drip (IV). The test is completed when either sampled blood sodium exceeds a threshold or the infusion ends.

Then a blood sample is taken for a copeptin test, which is sent to a specialised laboratory. It can take between 2 and 3 weeks to get your results. There can be some temporary side effects including headache and thirst. The test should and should only be done in a centre that has experience of supervising this test.

Arginine stimulated copeptin test

This test usually takes 2 to 3 hours in a clinic or hospital setting. During the test you will have no food or fluids. You will be asked to lie on a bed and will receive an IV of arginine and low levels of saline over a period of 30-45 minutes. Blood will be taken several times.

If the blood test results reach a certain criterion a further blood sample will be taken for a copeptin test. This is then sent to a specialised lab. It may take 2-3 weeks to get the results. This test is much easier for children than the other tests. It is probably slightly less accurate than the hypertonic saline infusion test but has less side effects and needs less intensive supervision.

How is AVP-Deficiency treated?

AVP-D is treated by the drug desmopressin, which people usually have to take several times a day. Desmopressin, also referred to as DDAVP®, is an AVP-like drug, which acts specifically on the kidneys in the same way as natural AVP. It lasts longer than natural AVP as it is more resistant to breakdown.

A variety of different preparations are available, each of which is given by a different route: injection, nasal spray, tablets to be swallowed, or oral lyophilisates (wafers that melt in the mouth). All are effective and it is a matter of finding the best match for you, based on preference and lifestyle. Depending on the severity of the AVP-D, these are generally taken between 1-3 times a day.

Doses vary between people, again based partly on degree of your symptoms. An ideal aim is for you to pass around 2 litres of urine over 24 hours whilst taking your desmopressin. A good test of satisfactory management of fluid levels is to weigh yourself each morning. A varying body weight on a day-to-day basis can help you monitor fluid balance when you start treatment. Remember that 1 litre of water weighs 1 kilogram.

Name of DDAVP® product	Dosage/ strengths available	Recommended initial dose: how it is taken	Comments
DDAVP® Melt (Ferring)	60 mcg; 120 mcg; 240 mcg	1 x 60mcg Melt 3 times a day. Place under tongue.	Dissolves within seconds, no unpleasant taste. Convenient to store, carry and discreet to take. Relieves symptoms in less than an hour.
Desmospray® desmopressin nasal spray (Ferring)	100 mcg/ml	1 or 2 sprays (10-20mcg) once or twice daily, sprayed up the nostril.	Does not require storing in a refrigerator. Works within 30 minutes to relieve symptoms.
Desmopressin® tablets (Ferring)	0.1 mg and 0.2 mg	1 x 0.1mg tablet three times a day. Take orally with water.	Convenient to store and carry. A dose might take up to an hour to relieve symptoms.

Breakthrough is where your previous dose of desmopressin medication has run out. Symptoms include:

- Full bladder, going to the toilet several times within an hour
- Urine becomes paler, colourless and not concentrating
- Feeling extreme thirst, and drinking lots to try and quench it
- You may feel shivery and irritable.

Allowing yourself to breakthrough before you take your next dose of desmopressin allows any excess fluids that may have built up to leave your body.

Side effects

Treatment has remarkably few side effects. Those who use the nasal spray may find some problems with the drug working when they have a heavy cold. Some people who use the tablets, find they work less well when they have an upset stomach. Some people can run into problems if the balance of treatment means that they are taking in more fluid than they are passing out; this can lead to the gradual development of water overload and a drop in the level of sodium in the blood stream (hyponatraemia). This is best addressed by re-balancing treatment by looking at how much desmopressin is given and how much fluid is being taken in.

You will gradually feel better once you are taking desmopressin (DDAVP) but it may take time to work out the right dose and preparation for you which is an individual thing. The aim is to give you the right dose of DDAVP that returns your body to normal, so you are neither dehydrated or over-loaded with fluid.

If you are thirsty, dry and passing large volumes of pale urine, then you need more desmopressin and/or fluids. If you are feeling headachy, 'thick-headed' and are not passing much urine or it is unusually yellow, then you have probably taken too much DDAVP and/or fluids. The reason for this is that excess water in the blood leads to low sodium levels which can lead to mild or moderate swelling of the brain. In the worst-case scenario this can be severe and lead to seizures requiring immediate medical attention.

It is good practice to make sure you temporarily miss out a dose of DDAVP once a week to let yourself pee and this will allow you to offload any excess water in the blood. This is called a breakthrough or desmopressin escape. Many people with AVP-D have a 'desmopressin escape' time in the week where they purposefully miss out a dose to make sure they do not become over-diluted. A study showed that people who do this are much less likely to come into hospital with low sodium.

Please note that DesmoMelt®, although of the same preparation as DDAVP® Melt, is the product brand name for children or adults who have enuresis, not AVP Deficiency.

Generic versions of desmopressin

There are generic substitutions available for the Ferring DDAVP® range of AVP-D medications. These generic substitutions might present some differences than your usual DDAVP® brand, especially for those who have no thirst mechanism, or for children.

Adults with AVP-D may find that you 'breakthrough' earlier (with more thirst and urine output) or perhaps later (with less thirst and urine output) than they usually do.

Parents with children with AVP-D should look out for any change in behaviour (more/less thirst/urine or simply a personality change - tiredness, grumpiness etc.) which might represent a change in total water balance and a change in serum sodium which will need urgent checking.

Many will find no difference, but some might. If your prescription (or your child's prescription) is changed to a generic version, and you/ your child experience less stability with the medication, then we encourage you to contact your GP or endocrinologist for advice.



“Without sufficient fluids, we can quickly get severely dehydrated. Taking desmopressin, a synthetic hormone medication helps keep fluids in our bodies, but we have to consciously monitor our fluids to make sure we don’t have too much or too little fluid so our organs function properly. In addition, strenuous exercise, such as hiking, can cause heavy sweating and therefore the loss of electrolytes (including sodium), so it is important to keep those in balance.”

Amy, who has AVP-Deficiency and type 1 diabetes climbed Mount Kilimanjaro in 2024.



Long term care

It is possible that your condition will require long-term monitoring, and this will be shared by your endocrinologist and GP. Because pituitary conditions are relatively rare, you might find that you will be the only person with AVP-D your GP is treating and they might find it helpful to have a copy of our Pituitary Disease Fact File for General Practitioners.

It is advisable to have your sodium level regularly tested, around every 6 or 12 months. This may be carried out by your GP.

We have lots more support on living with a pituitary condition on our website: www.pituitary.org.uk/living-with-a-pituitary-condition/

Sick day rules

You should seek medical attention if any of the following happen:

- You have missed or cannot take your desmopressin and have little or no access to fluids
- You have taken your desmopressin as normal but have then had a large intake of fluid
- You have vomiting (more than once) and/or diarrhoea.

The healthcare team seeing you should seek advice from an endocrinologist experienced in AVP-D.

1. You have missed or cannot take your desmopressin and have little or no access to fluids.

This means you will continue to lose water as you will not be able to control your urine output, but you cannot replace this as you have little or no intake. This can very quickly lead to your becoming dehydrated with an increase in your blood sodium level. This would be known as hypernatraemia (high sodium). You may need intravenous fluids which can only be given in a hospital setting so it is important not to let things get to a serious stage before seeking medical attention. By the time sodium is high, it usually means a hospital admission is needed unless you have a rare problem that is already known about by the medical team looking after you.

Why have I developed hypernatraemia?

High sodium is very uncommon unless the body is severely lacking in water. If this is not recognised and treated it can be life-threatening as it can cause problems with the brain and central nervous system.

Hypernatraemia develops when desmopressin is not taken/given and intake of fluid is low or nil. It can also develop if you have an episode of gastroenteritis or repeated vomiting, due to increased fluid loss caused by vomiting and/or diarrhoea. Correcting a too high sodium level should be resolved carefully to prevent too sudden a drop.

What symptoms may I have?

Symptoms of high sodium/hyponatremia can include headaches, fatigue or tiredness, irritability, dry mouth and lips, nausea and reduced appetite, cramps, muscle spasms. If left untreated or not recognised convulsions or seizures may occur.

Seeking help

- Attend your GP without delay if early symptoms of headache, tiredness and irritability occur
- Attend A&E if you have early symptoms and nausea, low appetite, cramps, muscle spasm
- Call 999 if convulsions or seizures occur

2. You have taken your desmopressin as normal but have then had a large intake of fluid

This means you will have excess fluid in your system as you will have reduced your urine output with the desmopressin. Having a high fluid intake after taking your desmopressin can lead to a reduced blood sodium level, known as hyponatraemia. This can lead to seizures.

Hyponatraemia (low sodium) can be graded as mild, moderate or severe. Correcting hyponatraemia has to be resolved very carefully to prevent too sudden a rise in blood sodium.

The level of emergency medical attention needed will depend not only on your sodium levels but also on your symptoms at the time.

Why have I developed hyponatraemia?

When you take desmopressin this signals to your kidney to reduce or stop losing water from your circulation.

Too high a dose or too much of desmopressin can cause too much water to be kept in the body and this can lower your blood sodium levels. If you continue to have a strong thirst, and drink to quench the thirst after taking desmopressin, this can also cause over-dilution of the blood and so lower your blood sodium levels.

Other illness can also cause a shift in your fluid balance and result in a drop in sodium levels, especially so if you have vomiting and/or diarrhoea.

What symptoms may I have?

Symptoms can vary and do not always match the level of blood sodium in their severity. A person with a mild or moderate low blood sodium may have severe symptoms.

Moderate symptoms will include confusion, headaches and nausea without vomiting,

Severe symptoms include vomiting, seizures, reduced level of consciousness and possibly cardiac arrest.

Seeking help

If you have any of these symptoms listed you should seek emergency medical attention.

3. You have vomiting (more than once) and/or diarrhoea.

This will affect your fluid balance levels and the levels of sodium and potassium in your blood. It may become difficult for you to keep control of your AVP-D in these circumstances. This is especially important if you take cortisol replacement, as reduced cortisol levels also have an impact on your blood sodium levels. This situation would need you to attend accident and emergency for urgent assessment and stabilisation. If in doubt, double your dose of steroids if you are on steroid replacement. If you are thirsty and dehydrated then drink according to your thirst. If you are really unwell it can be difficult to know what to do with your desmopressin so in this situation it is important to seek urgent medical attention.



Personal medical identification

If you are taking hormone replacement medication, it is a good idea to wear a medical information bracelet or equivalent as the information will help doctors if you have an accident and are unconscious.

There are various medical emblems available.

The Foundation has produced a small credit-card sized wallet card to help you explain about your AVP-D if you are in an emergency situation. There is also a toilet access card, so explain to people that you may need access to toilets. Both of these can be purchased in the shop on our website.

National key scheme

The National Key Scheme (NKS) offers disabled people independent access to locked public toilets around the country. Toilets fitted with National Key Scheme (NKS) locks can now be found in shopping centres, pubs, cafés, department stores, bus and train stations and many other locations in most parts of the country.

Visit to find out more: www.disabilityrightsuk.org

Common questions

Q: If I just drink less, will I pee out less?

A: No, without your desmopressin, you would continue to pass urine and restricting your fluid could be dangerous (unless medically supervised for a water deprivation test, for example).

Q: What should I do if the spray is blocked or damaged?

A: You should take the whole product to the chemist who will replace it free of charge.

Q: Can I still use the desmopressin spray if I have a cold or hay fever that gives rise to a blocked nose?

A: Only one nostril is blocked, then using the clear nostril should give the right result. If both nostrils are blocked, your doctor may recommend temporary use of the tablets.

Q: I have been having more headaches than normal recently and seem to be putting on weight. Could this be caused by desmopressin?

A: If you drink large volumes of fluids and take too much desmopressin, your body may become overloaded with fluid, which could result in headaches, dizziness and abnormal weight gain. In turn, this could result in a low sodium level in the blood, which is called hyponatraemia. It is important that you contact your doctor if you experience these symptoms as you may be taking more desmopressin than you need. Your doctor will help you to find the right dose of desmopressin and will advise you on the amount of fluid you should drink.

Q: If I can't remember whether I have taken a dose of desmopressin, should I take another one just in case?

A: It is better to miss a dose than to risk taking twice the amount.

Q: Is it safe to take other prescribed medicines alongside desmopressin?

A: If your doctor prescribes any medicines, you should point out that you are taking desmopressin.

Q: If I have an upset stomach while I am on holiday, what should I do?

A: Mild holiday diarrhoea is no problem. Only if you have any vomiting and/or serious diarrhoea do you need to see a doctor.

Q: What happens if I am in a hot climate or taking strenuous exercise which causes me to sweat?

A: As with anyone else, you should increase your liquid intake in such circumstances; your thirst should prompt you to do this.

More information

We have a full range of booklets to support people with their pituitary conditions, as well as information across our website. You can find this at www.pituitary.org.uk.

If you would like more support then we have a range of services that may be suitable:

Endocrine Nurse Helpline

Our specialist endocrine nurses can provide medical guidance.



Information and Support Helpline

Our volunteer and staff run helpline allows you to speak to others with pituitary conditions, and ask practical questions about living with a pituitary condition.



Telephone Buddy

This service provides one to one support with someone with a similar pituitary journey as you. For example someone with the same condition, or a parent of someone with a condition.



Support Groups

We have a number of volunteer-led support groups across the UK, which host meetings with endocrinologists and peer support for patients.



Events

We host online and in-person events with endocrinologists on specific conditions/topics. These give people the opportunity to hear from professionals and ask questions.



About The Pituitary Foundation

We're a dedicated team offering practical, emotional and peer support to everyone living with or impacted by a pituitary condition, to feel empowered and live with a greater sense of wellbeing.

For over 30 years, we've been amplifying voices and striving towards positive developments for the pituitary community. We work alongside healthcare professionals, clinical research teams and specialist organisations to raise the profile of pituitary conditions, finding better solutions for everyone affected by these life changing illnesses now and in the future.

Become a member and support our work

Becoming a member is an excellent way to show your commitment to our work at The Pituitary Foundation.

As members you'll enjoy a range of benefits including free copies of Pituitary Life magazine – full of great articles from endocrinologists and inspiring stories from people living with pituitary conditions. You'll also be able to have a say on how the charity is run, and get early access to our fantastic events.

A yearly donation of £25 allows us to continue our work now and in the future.

You can become a member at: www.pituitary.org.uk/membership

All information in this guide is general. If you have any concern about your treatment or any side effects please read the Patient Information booklet enclosed with your medication, or consult your GP or endocrinologist.

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