

Patient resource

Arginine Vasopressin Disorders (Diabetes Insipidus)

What are Arginine Vasopressin Disorders?

Arginine vasopressin disorders, (formerly known as diabetes insipidus (DI)), are rare conditions that lead to excessive urination and thirst. Parts of the brain known as the hypothalamus and pituitary gland make and release **arginine vasopressin (AVP)** (also known as antidiuretic hormone (ADH)). AVP helps the kidneys balance the amount of water in the body by making the right amount of urine. When there is a deficiency in AVP or when the kidneys do not respond to AVP, the body can lose water, resulting in large amounts of clear urine. This can lead to dehydration and increased thirst.

There are 2 main types of AVP disorders:

1. **AVP deficiency, (AVP-D)**, (formerly known as central DI): When the body does not make any AVP or makes less AVP.
2. **AVP resistance, (AVP-R)**, (formerly known as nephrogenic DI): When the body makes enough AVP, but the kidneys do not respond to it.

AVP disorders are not related to diabetes mellitus (type 1 and type 2 diabetes), which is a condition where blood sugar levels are too high due to the body not producing enough insulin or being resistant to the effect of insulin. To prevent confusion, this was a reason 'diabetes insipidus' was renamed in 2022 to 'AVP disorders'.

What causes AVP disorders?

The different types of AVP disorders have different causes.

AVP deficiency: Damage to the pituitary gland or hypothalamus from:

- brain injury
- surgery
- radiotherapy
- brain tumours, and/or
- infections or inflammation.

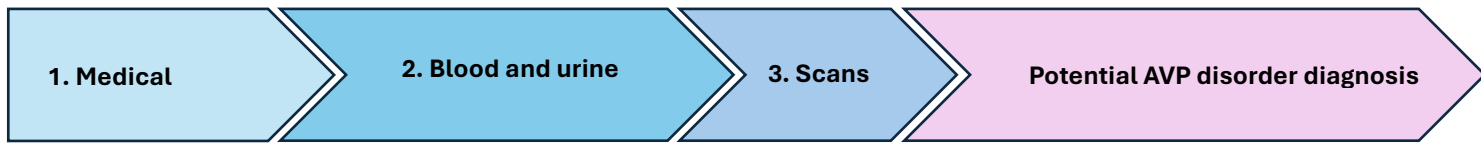
AVP resistance: The pituitary gland releases AVP but the kidneys do not respond to it because of:

- medications such as lithium
- high blood calcium
- low blood potassium, and/or
- genetic conditions.

Symptoms of AVP disorders:

- Feeling very thirsty and drinking large amounts of fluid
- Needing to urinate often, large amounts of clear urine, and/or
- Waking up at night frequently to urinate.

How are AVP disorders diagnosed?



1. Medical history

Your doctor will ask you questions about your health, symptoms and medical history. This includes if you take any medications or use supplements, have other health conditions and your family history.

2. Blood and urine tests

Tests confirming the contents of your blood and urine are often required. The volume of urine and a blood test to check for a hormone called ‘copeptin’ may be requested. **Copeptin** is a molecule produced when the pituitary releases AVP. Before these tests, you may be asked to not drink any fluids overnight.

After these initial tests, a **water deprivation test, arginine stimulation test or a hypertonic saline copeptin test** might be required. These are different tests that measure the response of the pituitary gland in producing AVP.

Water deprivation test: This often requires a stay in the hospital as you will need to be closely monitored and have several blood and urine tests whilst you are asked not to drink any fluids for up to 8 hours. Towards the end of the test, you will be given a medication known as **desmopressin**. Desmopressin acts similarly to AVP. If you have AVP deficiency, your kidneys will respond to desmopressin, and you will notice a reduction in the amount of urine you pass. The test also records your urine volume and any weight changes.

Arginine stimulated copeptin test: A blood test will be taken before you are given arginine which is a medication that normally stimulates the pituitary gland to secrete AVP and copeptin. You will have a blood test one hour after arginine has been given. Your weight, blood pressure and heart rate will also be monitored regularly for 2 hours after arginine has been given.

Hypertonic saline copeptin test: This involves being given a salt solution that aims to raise the blood sodium level. This should stimulate your body to release AVP. Whilst the salt solution is being given through the blood stream, blood tests are taken regularly. Once the sodium level has approached a certain level, blood tests will be taken for the copeptin level and the salt solution will subsequently be stopped. You will then be asked to drink a specified amount of water. A glucose solution will then be given to lower your sodium level back to normal. Your sodium level should be at a safe level before you leave the hospital.

3. Scans

If the blood and urine tests suggest that the problem is AVP deficiency, a detailed look for abnormalities in or near the pituitary gland may be required. This is usually done using a magnetic resonance imaging (MRI) scan.

What do the results mean?

Your body's response as well as comparing your blood tests and urine tests during a period without water will determine if you have an AVP disorder, and, if so, the type of AVP disorder.

The copeptin level may be useful in suggesting an AVP disorder. If the copeptin level is high, this suggests you do not have AVP deficiency. If the copeptin level is low this suggests you have AVP deficiency. If the level is in the middle, your doctor may discuss organising a water deprivation test, arginine stimulation test or a hypertonic saline copeptin test with you.

Normally when the body is deprived of water, the pituitary gland will release AVP to make the kidneys produce less urine, and conserve water. If you are still passing large amounts of clear urine, and despite during the test, when AVP is given to you, you still pass dilute urine, this is suggestive of AVP resistance. When AVP is given, and the urine concentrates (becomes less dilute), it is suggestive of AVP deficiency.

How are AVP disorders treated?

The goal of treatment is to prevent dehydration, relieve thirst and decrease the amount of urine being made overnight so that sleep is less disrupted. The type of treatment depends on the type of AVP disorder you have.

AVP deficiency is usually treated with desmopressin (brand name DDAVP®). This is usually given as a tablet or nasal spray (if available). It replaces the hormone AVP that is not being made by your pituitary gland. The medication is usually taken two to three times a day. Taking the right amount of medication is balanced with the amount of water you are drinking and with the amount of urine you are making. Concentrated urine (darker in colour) is a sign that the desmopressin is working. Dilute urine (pale urine) is a sign the desmopressin has worn off.

A high sodium level can occur if desmopressin is missed and/or you do not drink enough water. On the other hand, taking too much desmopressin or drinking too many fluids can cause your body to retain too much water which can lower blood sodium levels. Low sodium levels can be dangerous. Symptoms of low sodium can include headache, confusion, lethargy, nausea and vomiting. Some doctors may recommend waiting for your urine output to increase again before taking another dose of desmopressin (usually in the evening for convenience), omitting a dose of desmopressin once a week, or delaying a few doses each week. This minimises the risk of having a low sodium. Speak to your doctor about your medication and doses.

AVP resistance is treated differently. The kidneys usually do not respond to AVP. Treating other health conditions can help if they are the cause. Some medications used to treat high blood pressure or glaucoma can help.

Your doctor may advise you to drink a certain amount of water each day and to weigh yourself in the morning. It might take some time to get the dose correct and you may require several blood tests and appointments with your doctor once starting treatment. Once you have the right dose, your doctor will have appointments with you to ensure symptoms are under control, and your sodium level is within the normal range.

What do I do when I am unwell?

When people are sick (with fevers, vomiting and diarrhoea), the sodium level can be affected. Vomiting and diarrhoea may mean that the medication cannot be absorbed properly and will not work as well. It is important to develop a “sick day management plan” with your doctor. If you are worried or unwell, you should present to your nearest Emergency department, as developing either low or high sodium can be dangerous.

What happens if I am in a hot climate or exercising?

Increased sweating can result in excess fluid loss through your skin. Most people will need to increase their fluid intake in these conditions and you should pay particular attention to thirst and drink if thirsty. If you do not have a sense of thirst you will need to discuss these circumstances with your treating doctor and come up with a fluid prescription to manage hot weather and exercise.

Other strategies to help living with AVP deficiency and AVP resistance

- Always carry water and an emergency dose of desmopressin with you.
- When in unfamiliar places, it can be helpful to know the location of toilets and drinking water fountains/coolers.
- When travelling, carry a letter from your doctor outlining why you need to carry water with you.
- Carry or wear identification that alerts medical staff in the event of an emergency situation.

Adipsic AVP deficiency

There is a rare form of AVP deficiency, called adipsic AVP deficiency. People with adipsic AVP deficiency have also lost their thirst sensation. This condition can be more difficult to manage as it can lead to more rapid and substantial changes in the sodium levels in the blood. In addition to taking desmopressin, people with adipsic AVP deficiency are commonly prescribed a daily fluid intake (“fluid prescription”) and are recommended to regularly measure their body weight. Blood tests may be required more frequently to help monitor their condition.

Questions to ask your doctor

- What is causing my AVP disorder?
- How can I treat my AVP disorder?
- How much water or fluids should I drink every day?
- How quickly should the medication work?
- How will I know that the medication is working?
- What is my 'sick day management plan'?

Common terms and definitions

Hypothalamus: An area in the base of the brain that controls the release of pituitary gland hormones.

Pituitary gland: A small gland located underneath the brain that controls hormone production from several other glands such as the thyroid, adrenals, ovaries and testes

Tumour: An abnormal growth in the body. Tumours can be non -cancerous or cancerous.

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