

Diabetes insipidus



The Pituitary Foundation Information Booklets

The
Pituitary
FOUNDATION

Working to support pituitary patients, their carers & families

The Pituitary Foundation is a charity working in the United Kingdom and Republic of Ireland supporting patients with pituitary conditions, their carers, family and friends.

Our aims are to offer support through the pituitary journey, provide information to the community, and act as the patient voice to raise awareness and improve services.

About this booklet

The aim of this booklet is to provide information about *diabetes insipidus*.

You may find that not all of the information applies to you in particular, but we hope it helps you to understand your condition better and offers you a basis for discussion with your GP and endocrinologist.

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What is **diabetes insipidus (DI)** and why do we get it?

Diabetes insipidus (DI) is caused by a problem with either the production, or action, of the hormone vasopressin (AVP). If you have DI your kidneys are unable to retain water. This leads to the production of large volumes of urine and, in turn, greatly increased thirst. DI 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 DI 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. A large proportion of what we are is made up of water. In addition, the amount of water we have in our circulation is a large factor in determining the balance of salt in our bodies. As with any function that is important, the body has a sensitive mechanism for regulating water balance. Like any good mechanism it is also simple, involving two key components:

- **Vasopressin (AVP or ADH - anti-diuretic hormone)** - which regulates the amount of water passed out of the body in urine.
- **Thirst and drinking** - which determines the amount of water the body takes in.



AVP (sometimes called Anti-diuretic hormone or ADH) is a hormone released from the rear most 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 acts on the kidneys to reduce the amount of water that is passed out in urine.

How AVP and thirst work together is best described with the help of the bath tub analogy. As with a bath tub, 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 through turning the taps on; just as thirst and drinking can allow more water into the body

What is **diabetes insipidus (DI)** and why do we get it?



- Water can be let out of the bath through taking the plug out; just as the body can let more water out by reducing the amount of AVP produced and so letting more water to be passed out of the body as urine

Unlike a bath tub, 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 the thirst (turning on the taps). At the same time, it makes more AVP and so reduces water loss in

urine (it puts the plug in). On the other hand, if the body senses the level of water is too much, it turns the thirst off (turning taps off) and makes less AVP (taking the plug out of the plug hole). The level of water is therefore maintained through a combined approach.

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

The two forms of **diabetes insipidus (DI)**

1. Cranial diabetes insipidus (CDI)

CDI is caused by the partial or absolute lack of AVP. The lack of AVP means that the kidneys cannot retain the amount of water that the body needs them to, and produces a lot of dilute urine. 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, thirst and drinking. People with CDI 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.

Sometimes CDI occurs on its own and however in many cases, it is accompanied by loss of other hormones made by the pituitary. This may be through a problem in the development of the pituitary gland; a tumour within or near the gland; or the result of an accident, or surgery to, or near to, the gland.

CDI following pituitary surgery may be temporary, only lasting a week or two. In some cases it may be permanent.

2. Nephrogenic diabetes insipidus (NDI)

NDI is a condition in which the kidneys do not respond to the normal signal (AVP) to reduce water loss. Thus, the kidneys are not able to absorb the water that passes through them.

The primary symptoms of NDI are polyuria (passage of large volumes of urine) and polydipsia (excessive thirst and drinking).

Inherited NDI may show up in the first weeks of life. Symptoms can include irritability, failure to thrive, lack of appetite and vomiting. Investigation can reveal high blood levels of sodium. Up to 90% of the cases of inherited

NDI are the result of mutations affecting the AVP-receptor (V2R) that is needed for the kidney to respond to AVP and reabsorb water. The remaining cases are the result of mutations in the pore in kidney cells through which water is reabsorbed (AQP2). Though each type of inherited NDI has a different genetic cause, the symptoms of each are the same.

Males are the most likely to display symptoms of X-linked NDI, whereas males and females are equally likely to display symptoms of the autosomal recessive form of NDI. This is because the V2R gene is carried on the X-chromosome and males have only one X-chromosome. A problem with a gene on this single X-chromosome can't be counter-balanced by another normal X-chromosome (the position in females). Autosomal recessive NDI is carried on a non-sex chromosome, so males and females are equally likely to inherit the problem.

Acquired NDI is the more common form of NDI and can occur at any time of life. Most often, acquired NDI is a result of the use of the drug lithium. Acquired NDI can also result from the use of other drugs, such as colchicine, methoxyflurane, amphotericin B, gentamicin, loop diuretics and demeclocycline. It can also occur as a result of certain diseases and physical conditions, which can result in either permanent or temporary NDI such as:

- chronic kidney failure
- other kidney diseases
- abnormally low levels of potassium
- abnormally high levels of calcium
- sickle cell disease

The two forms of **diabetes insipidus (DI)**

- And rarely, during pregnancy

Treatment of NDI

There is as yet no cure for inherited NDI. Currently, NDI is managed by:

- ensuring ready access to water
- following a low-sodium (and sometimes low-protein) diet, and
- using thiazide diuretics, alone or in combination with a prostaglandin inhibitor or a potassium-sparing diuretic, to reduce the volume of urine output.

Thiazide diuretics can reduce an NDI patient's polyuria, but they may also deplete the body's stores of potassium. This depletion can cause other symptoms and may be dangerous. When taking thiazide diuretics, the patient's potassium levels must be monitored. To maintain sufficient potassium in the body, the addition of potassium supplements or amiloride (but not both) to the treatment regime may be required.

DI is not related to diabetes mellitus

It is very important to point out that DI is not related to the type of diabetes most people have heard of - **DIABETES MELLITUS** which is very common and can also cause symptoms of passing a lot of urine and being thirsty. In DI, there is **NO** problem with the level of sugar in the blood or urine. This is very important as friends, relatives and health care workers may make assumptions about the condition you have, based on the more common condition.



What does it feel like to have DI?

The main symptoms that you will feel are 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; you may pass as much as 4 - 10 litres of urine a day. It is important that you do not try to prevent this by ignoring your thirst and drinking less, or you will disturb the balance of water in your body.

You may well have symptoms of dehydration, for example feeling shivery and nauseous with headaches. People with DI have mentioned that their excessive thirst can be compared with eating 4 or 5 dry cream crackers one after the other, without any drinks.

Most patients do have a thirst mechanism, but a few patients don't. This is called **HYPODIPSIA**. The combination of DI and hypodipsia is unusual and requires special attention from patients, carers and doctors.

How is DI diagnosed and treated?

How is it diagnosed?

What tests are carried out and how will these feel?

Investigation methods for patients with excessive urine production would be:

- Measurement of 24 hour urine output
- Measurement of plasma osmolality from a blood test (a measure of sodium and glucose circulating in the blood)
- Water deprivation test (described below)
- Therapeutic trial of desmopressin (DDAVP®)

The water deprivation test deprives you of fluid for 6-8 hours to see if there is a reduction in the volume of urine. You can expect to feel quite thirsty during this test. The next stage is to give you a small quantity of desmopressin, usually as an injection. If you have **CDI**, you should notice a reduction in the amount of urine you pass. This shows that your kidneys are responding to the hormone.

If you have **NDI**, this response does not occur or is impaired, as the kidneys don't recognise the effect of the hormone in small doses. Once you are allowed to drink again, you will begin to feel better. If you need other hormone treatments, you will need to continue taking them during the test. This test can be performed as a day case.

How is DI treated?

CDI is treated with an AVP-like drug called desmopressin or DDAVP®. This medication acts specifically on the kidneys in the same way as natural AVP, though 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 drops, nasal spray, tablets to be taken and swallowed, or oral lyophilisates (wafers that melt in the mouth). All are effective and it is a matter of finding the best match for each individual, based on preference and lifestyle. The spray and the tablets are popular choices. Depending on the severity of the DI, these are generally taken between 1 - 3 times a day; some people have to take the medication 4 times a day. Doses vary between people, again based partly on degree of their symptoms. An ideal aim is for a patient to pass around 2 litres of urine over 24 hours whilst taking their 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.

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 water 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. Overall, the treatment of DI is straightforward, but if you are experiencing any difficulty controlling your DI please do talk to your endocrinologist.

How is DI diagnosed and treated?

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.
DDAVP® desmopressin intranasal solution (Ferring)	100 mcg/ml	10 - 20mcg once or twice daily; using thin rhinile to 'sniff' the solution up nostril.	Does require refrigeration but dose can be negotiated. 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.

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 diabetes insipidus.

Generic Versions of desmopressin It has come to our notice that there are generic substitutions available for the Ferring DDAVP® range of diabetes insipidus medication. These generic

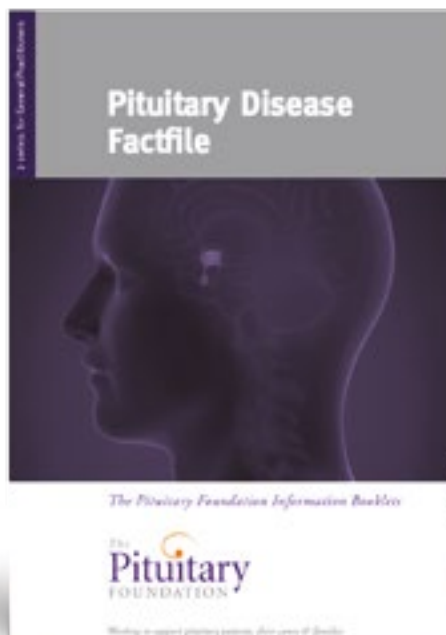
Aftercare

substitutions might present some differences in patients than their usual DDAVP® brand, especially for those who have no thirst mechanism, or for children.

Adults with DI may find that they 'break through' earlier, (with more thirst and urine output) or perhaps later (with less thirst and urine output) than they did when taking, and stabilised, on desmopressin.

Parents with children with DI 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.

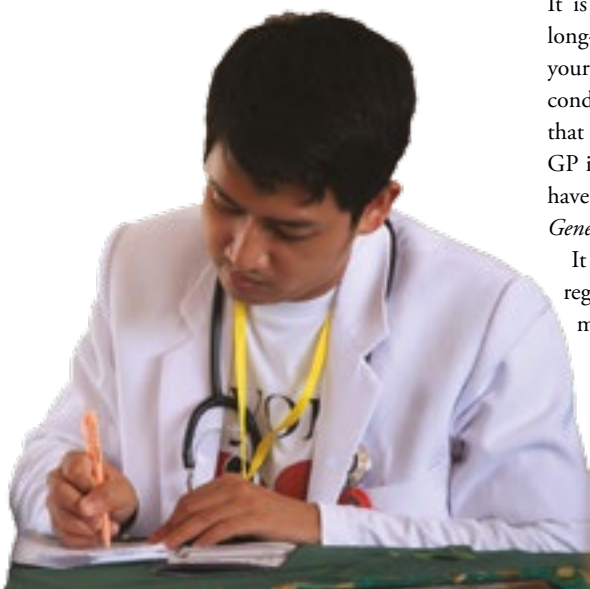
Many will find no difference, but some might. If your prescription (or your child's prescription) is changed to a generic version, and you/your child experience less stability with the medication, then we encourage you to contact your GP or endocrinologist for advice.



Aftercare

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 patient with DI 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, say every 6 or 12 months. This may be carried out by your GP.



How will **diabetes insipidus (DI)** affect my life?

Prescriptions

You will be entitled to free prescriptions as you have DI and take desmopressin

To apply for a medical exemption certificate ask your doctor for an FP92A form. Your GP, or hospital will sign the form to confirm that your statement is correct. At your GP's discretion, a member of the practice who has access to your medical records can also sign the form.

Your certificate will be valid from one month before the date that the NHS Business Authority receives the application form. The MedEx lasts for five years and then needs to be renewed. You may receive a reminder that your certificate needs to be renewed. If you don't receive a reminder, it is your responsibility to ensure that it is renewed.

For more information phone 0300 330 1349 for the prescription services help line



Driving

Find out if your health condition will affect your

driving and if you'll be able to keep your licence. DVLA – Drivers Medical Enquiries Telephone: 0300 790 6806 Monday to Friday, 8am to 5:30pm Saturday, 8am to 1pm

Or write to:

**Drivers Medical Group DVLA Swansea
SA99 1TU**

www.gov.uk/dvla-medical-enquiries

Employment problems

Contact the **Disablement Employment Adviser** (or **DEA**) at your local Department of Social Security. Often the DEAs are also very knowledgeable about benefits and entitlements generally. Also contact your local **Citizens Advice** for the most up to date information on employment rights and benefits.

Insurance and pensions

As a general guide, if you have primary DI with no complications, you should be able to obtain insurance at normal rates. If your DI results from an underlying cause such as pituitary tumour, your case would be assessed and any loadings would depend on your medical condition.

If your tumour has been completely removed you should be accepted at normal rates. Of course, each insurance company will have its own practices. Because of the potential confusion between diabetes mellitus (DM) and diabetes insipidus (DI), particularly in the minds of the insurers, it is important to emphasize that DI is due to vasopressin (anti-diuretic hormone) deficiency and has nothing to do with sugar diabetes. It may help to state you have ADH or vasopressin deficiency to save confusion.

How will **diabetes insipidus (DI)** affect my life?

Pensions can normally be arranged without difficulty. For further information please call The Pituitary Foundation or see our website for up to date insurers' contact details which other patients have used, with success, and have informed us about these companies.



Personal medical information

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; our website includes contact details for several organisations.

Please see reverse for more information

86-88 Colston Street,
Bristol, BS1 5BB
www.pituitary.org.uk
Helpline: 0845 450 0375 Registered charity No. 1058968

Toilet facilities card

The Foundation has produced a small credit-card sized card to help the patient explain about their DI if they are in an emergency situation. Please contact The Foundation if you would like a card. An emergency DI card is also available which explains you have DI and can be kept in your purse or wallet.

Radar Key www.disabilityrightsuk.org

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.

Contact **020 7250 8191** Monday to Friday 10.00-12.30 and 1.30 to 4.00

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 happens if my desmopressin has been kept out of the fridge?*

A: Although intra-nasal desmopressin can be kept at room temperature for a limited period, long term exposure to temperatures above 8 °C may reduce the effectiveness. Please contact your doctor or pharmacist for advice if you are concerned that your medication has been left out of the fridge, or if the fridge is broken. Desmospray, DDAVP melts and the tablet form of DDAVP are stable at room temperatures, so there is no need to store these in a fridge.

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

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

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

A: If 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. You would usually know in a few hours or so by breaking through (your thirst and wanting to pass urine).

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: *Is it OK to take my desmopressin through airport X-ray machines?*

A: Yes, it's fine. For travelling with medication information please see our website.

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.

Q: *Will alcohol cause me any problems?*

A: You should be careful about drinking large volumes of alcoholic drinks. Alcohol tends to reduce vasopressin secretion in non-DI adults, causing dehydration. Check with your doctor for advice on your specific drinking habits.

Q: *My lifestyle means that it is inconvenient to take my desmopressin at the prescribed times and it is also awkward to keep leaving the room to use the toilet. What can I do?*

A: If you have any difficulties with your lifestyle due to DI, do contact your doctor, who will be able to advise you about varying the timing of doses. Don't experiment with this yourself, however.



Q: *If pregnant, do I take more desmopressin?*

A: You may have to increase your normal dose to overcome changes in the body, which have increased concentrations of an enzyme destroying desmopressin.

What DI means to me - one patient's story

My name is Lisa. I'm 26 and I am a pharmacist. Towards the end of 1991 I began to feel unwell, although it was nothing specific. I was also aware that I was drinking more than usual and even waking up in the night to drink and go to the toilet. At first I thought it might go away, but as the weeks passed I began to worry. One of the worst things was the lack of sleep. At this point I decided to visit my GP.

I was aware that I had some of the symptoms of diabetes mellitus, so was not surprised to have the standard tests for it. The results were normal so my GP suggested I come back in a few weeks if no better. During those few weeks I began to believe that no one believed me and that maybe there wasn't anything really wrong as everything seemed so vague and non-specific. By the time I returned to my GP I was feeling dreadful. I was drinking anything between 5-10 litres of water a day, constantly going to the toilet and getting very little sleep. My GP referred me to the Westminster Hospital, and reassured me that, although he did believe there was something wrong, he did not think it was anything sinister.

I had my first appointment at the end of June 1992, explaining my symptoms and how I felt to the consultant who arranged for me to have a water deprivation test the following week. The results showed I had DI.

I started taking medication at the beginning of July 1992. The treatment involves administration of desmopressin which at that time was only available as a nasal solution or spray. The effects were not dramatic but over the next week or so I began to feel a lot better, the amount of water that I was drinking reduced and so did the need to go to the toilet during the night. Over the next year I accepted that I have a medical condition which may or may not be for life and no-one really knows why I developed the problem in the first place!

One of the most difficult things is trying to explain to people what DI is. Most people hear the word 'diabetes' and automatically think of insulin and needles. Insurance companies are the worse - they hear 'diabetes' and either refuse to insure you completely or charge you a fortune! There is very little information on diabetes insipidus to be found, even in medical textbooks, so it's not really surprising that most people have never heard of it. Hopefully the Pituitary Foundation is improving matters by helping people to understand about DI and pituitary disease generally and by providing a self-help group for patients.

Anyway, at least I get free prescriptions!

LISA

Please support The Pituitary Foundation

Join The Pituitary Foundation today and enjoy the benefits of membership!

- ✓ Receive our members' magazine, *Pituitary Life*, three times a year full of the latest information, updates and patient stories, to help you better understand, or manage your pituitary condition.
- ✓ Become an important part of the only charity in the UK providing support to pituitary patients.
- ✓ Receive a welcome pack and a membership card and enjoy discounts to Pituitary Foundation events, such as our conferences.
- ✓ Give us a stronger voice to raise awareness, and understanding, of pituitary disorders.

Individual membership costs **£20.00** for a full year, which is only **£1.66** a month!

(Family, concessionary and life membership rates are also available).

To become a member, please complete the form below and return to us with your payment

(cheques made payable to *The Pituitary Foundation*) to:

**The Pituitary Foundation,
86 Colston Street,
Bristol, BS1 5BB**

If you would like to pay for your membership by standing order, please contact **0117 370 1333**,

or to join online visit **www.pituitary.org.uk**



I wish to become a Member of **THE PITUITARY FOUNDATION**

Title:	First Name:	Surname:
Address:		
Postcode:		
Telephone No:	Email:	

Please tick (✓) the type of Membership you require:

Individual <input type="checkbox"/> £20.00 (annual)	Family <input type="checkbox"/> £35.00 (annual)
Life Membership <input type="checkbox"/> £250.00	Concessionary* <input type="checkbox"/> £10.00 (annual)

Additional donation (optional) £

**(Concessionary rate for people on a state pension, in receipt of state benefits, on low income, students, and under 18s only).*

Gift Aid: I am a UK Taxpayer. Please treat all membership payments and donations I have made for 6 years prior to this declaration and all that I make from this date, until I notify you otherwise, as qualifying for Gift Aid

(please tick)

You must pay an amount of Income Tax and/or Capital Gains Tax for each tax year (6th April one year to 5th April the next) that is at least equal to the amount of tax that the charity will reclaim on your gifts for that tax year.

Signature:	Date:
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Helpline

Monday - Friday 10:00am-4:00pm
0117 370 1320

Endocrine Nurse Helpline

available scheduled hours
0117 370 1317

Website: www.pituitary.org.uk

Email: helpline@pituitary.org.uk

More Information

The Pituitary Foundation publishes a library of booklets on pituitary conditions, treatments and well-being issues.

For more information please visit our website, or call our Helpline.

The Pituitary Foundation

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www.pituitary.org.uk

Company Limited by Guarantee

Registered in England and Wales
No. 3253584

Registered Office:

86 Colston Street

Bristol

BS1 5BB

Registered Charity No. 1058968

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Working to support pituitary patients, their carers & families