CONDITION

Nephrogenic diabetes insipidus

Nephrogenic diabetes insipidus is a condition in which the kidneys cannot conserve water normally.

WHAT IT IS
Kidney resistance to the water-conserving hormone vasopressin

BODY SYSTEM
Kidneys and urinary system

MAIN SYMPTOMS
Extreme thirst, frequent urination, large urine volumes, nighttime urination

WHAT CAUSES IT
Inherited gene changes or acquired kidney resistance

HOW IT IS DIAGNOSED
Blood and urine concentration tests, supervised water-deprivation testing

MAIN TREATMENT
Water replacement, cause treatment, diet changes, selected medicines

CAN IT BE CURED?
Sometimes - acquired forms may improve after cause removal

IS IT AN EMERGENCY?
Sometimes - confusion, seizures, collapse, or inability to drink

LONG-TERM OUTLOOK
Usually manageable; inherited forms need lifelong care

Overview

Nephrogenic diabetes insipidus, often shortened to NDI, is a condition that affects the kidneys' ability to conserve water. It causes the body to make unusually large amounts of pale, diluted urine.

Normally, a hormone called vasopressin tells the kidneys to return water to the bloodstream. Vasopressin is also called antidiuretic hormone, or ADH. In NDI, the body may make enough vasopressin, but the kidneys do not respond to it properly.

Water is therefore lost in urine. This causes frequent urination and strong thirst. If you can drink whenever you need to, your body may keep its water level stable. Dehydration can develop quickly if water is unavailable or you are unable to drink.

Despite its name, diabetes insipidus is not the same as diabetes mellitus, which causes high blood sugar. NDI does not usually involve high blood sugar or glucose in the urine.

NDI may be inherited and begin in infancy, or it may be acquired later because of a medicine, another health condition, or kidney damage.

Symptoms

The main symptoms come from passing more water than usual in the urine. They may develop gradually or become more noticeable after a medicine or health problem affects the kidneys.

Symptoms can include:

Adults with reliable access to water may compensate by drinking enough to match their urine loss. Symptoms can still disrupt sleep, work, travel, and daily activities.

Babies and young children cannot always communicate thirst or obtain water themselves. Possible signs include frequent wet diapers, unusual irritability, poor feeding, vomiting, constipation, fever without a clear cause, poor weight gain, or slower growth. These signs can have many causes, but they need medical assessment.

Symptoms may become more serious during vomiting, diarrhea, fever, hot weather, fasting, surgery, or any situation that limits drinking.

- Passing very large amounts of pale urine
- Urinating frequently during the day and night
- Strong or nearly constant thirst
- Preferring cold drinks
- Interrupted sleep because of drinking and urination
- Signs of dehydration, such as a dry mouth, tiredness, or dizziness

Causes and risk factors

Inherited NDI is caused by a gene change that affects how the kidneys respond to vasopressin.

Most inherited cases involve the AVPR2 gene, which provides instructions for a vasopressin receptor in the kidney. This form is linked to the X chromosome. It most often causes more severe symptoms in males, although females with the gene change can have symptoms ranging from mild to significant.

Other inherited cases involve the AQP2 gene. This gene helps form water channels that allow

kidney cells to move water back into the body. AQP2-related NDI can affect people of any sex.

Acquired NDI develops because something reduces the kidneys' response to vasopressin. Causes include:

Lithium-related NDI may develop during treatment and can sometimes continue after lithium is stopped. Do not stop lithium or another prescribed medicine on your own. Sudden changes can be harmful, and the medicine may be treating an important condition.

Some people have partial NDI, meaning their kidneys retain some ability to respond to vasopressin. Their symptoms and test results may be less pronounced.

- Lithium, a medicine used for some mental health conditions
- High calcium levels in the blood
- Low potassium levels
- Long-term or advanced kidney problems
- A blockage in the urinary tract
- Certain medicines, including demeclocycline and some antifungal medicines

Diagnosis

A clinician will ask about your thirst, urine volume, nighttime urination, medicines, kidney history, and family history. If possible, measuring how much you drink and urinate over 24 hours can provide useful information.

Blood tests may check sodium, glucose, calcium, potassium, and kidney function. Urine tests measure how concentrated or diluted the urine is. A measurement called osmolality shows the concentration of dissolved substances in blood or urine.

The results help separate NDI from other causes of excessive thirst and urination. These include diabetes mellitus, drinking unusually large amounts of water, and central diabetes insipidus. In central diabetes insipidus, the body does not release enough vasopressin.

A supervised water-deprivation test may be used when the diagnosis remains uncertain. During this test, drinking is temporarily restricted while urine output, body weight, blood results, and urine concentration are closely monitored. Desmopressin, a medicine that acts like vasopressin, may then be given.

In central diabetes insipidus, desmopressin usually makes the urine more concentrated. In complete NDI, there is little or no response because the kidneys cannot respond normally. Partial forms can be harder to distinguish.

Water-deprivation testing can cause dangerous dehydration and must not be attempted at home. Some specialist centres use vasopressin-related tests, including a blood marker called copeptin, instead of or alongside traditional testing.

Genetic testing may confirm inherited NDI. It can also help clarify how the condition may affect other family members.

Treatment and management

The central part of treatment is replacing the water lost in urine. You need reliable access to drinking water and toilets. The amount required is based on your losses and circumstances rather than a standard target for everyone.

Fluid restriction is not a treatment for NDI. Restricting water without medical supervision can cause severe dehydration and a high blood sodium level.

When NDI is acquired, treatment focuses on the cause. This may include correcting calcium or potassium levels, treating a urinary blockage, or reviewing a medicine that affects the kidneys. Any medication change should be planned with the clinician who prescribed it.

A lower-sodium diet can reduce the amount of urine the kidneys must produce. In some cases, adjusting protein intake may also reduce the dissolved waste that needs to leave through urine. Children and anyone at risk of poor nutrition should make these changes only with specialist or dietitian support.

Medicines used to reduce urine volume can include:

These medicines require professional monitoring. They can affect blood pressure, kidney function, potassium, sodium, or the stomach. Anti-inflammatory medicines are not appropriate for everyone.

Desmopressin usually has little effect in complete NDI. Some people with partial NDI may benefit from it under specialist care.

Babies and children need close management from paediatric kidney or hormone specialists. Care may involve carefully planned fluids, lower-solute feeding, medicines, and regular checks of growth and blood chemistry.

- Thiazide-type diuretics, which can reduce urine output in NDI despite usually increasing urination in other settings
- Amiloride, which may be particularly useful when lithium contributes to the condition
- Nonsteroidal anti-inflammatory drugs like ibuprofen or naproxen in selected cases

Complications

The most important complication is dehydration. This can raise the sodium concentration in the blood, a problem called hypernatremia. High sodium affects how water moves in and around brain cells.

Early effects may include intense thirst, weakness, irritability, headache, or unusual sleepiness. Severe hypernatremia can cause confusion, muscle twitching, seizures, reduced consciousness, or coma.

Repeated dehydration in infants and young children can interfere with feeding, weight gain, growth, and development. Prompt diagnosis and careful treatment reduce these risks.

Producing very large amounts of urine over a long period can stretch the bladder and the tubes that carry urine from the kidneys. Some people develop urinary leakage, incomplete bladder emptying, or widening of the urinary tract.

Treatment can also cause complications if fluid balance changes too quickly or medicines alter sodium, potassium, blood pressure, or kidney function. Regular blood tests help identify these problems.

Prevention

Inherited NDI cannot currently be prevented. It results from a gene change present from birth. Genetic counselling can explain inheritance patterns, testing options, and possible effects on relatives.

Not every acquired case is preventable. Risk may be reduced by monitoring kidney function and blood chemistry when taking medicines known to affect the kidneys. If you take lithium, attend the recommended blood and kidney checks and report a marked increase in thirst or urination.

Treating high calcium, low potassium, kidney problems, or urinary blockage may prevent NDI from worsening. Do not reduce fluid intake to try to control frequent urination.

Living with it and what to expect

Inherited NDI is usually lifelong. Symptoms can often be controlled, but ongoing planning is needed to prevent dehydration. Children require monitoring of growth, nutrition, kidney function, urine output, and urinary tract health.

Acquired NDI may improve when its cause is corrected. Recovery can take time, and kidney resistance to vasopressin may persist, particularly after long-term lithium exposure or lasting kidney injury.

Many people can continue ordinary activities when they have dependable access to water, toilets, medicines, and follow-up care. School, work, travel, exercise, and hot weather may require advance planning.

It can help to carry water, know where toilets are, and tell relevant caregivers or school staff that drinking must not be restricted. A medical identification card or alert may be useful, especially for children or people with severe NDI.

Illness plans are important because vomiting, diarrhea, fever, or reduced consciousness can prevent you from replacing water losses. Ask your care team what to do during illness and when blood tests are needed.

Routine follow-up may include checks of sodium, potassium, calcium, kidney function, blood pressure, growth in children, medicine effects, and urinary tract symptoms.

When to get medical help

Arrange a routine medical appointment if you develop persistent excessive thirst, repeatedly wake to urinate, or pass much more urine than usual. These symptoms need assessment even if you can keep up by drinking.

Children should be assessed promptly for constant thirst, unusually heavy wet diapers, poor feeding, repeated unexplained fever, vomiting, constipation, poor weight gain, or slower growth.

Contact your care team promptly if you have known NDI and develop vomiting, diarrhea, fever, reduced access to water, or a clear change in urine output. You may need changes to your fluid plan, medicines, or monitoring.

Seek emergency help if you or someone with possible NDI:

A person who is confused or unconscious should not be forced to drink because of the risk of choking.

- Cannot drink enough to replace ongoing urine losses
- Becomes confused, very drowsy, or difficult to wake
- Has a seizure or collapses
- Has severe weakness or loss of coordination

- Is an infant with marked sleepiness, poor feeding, or signs of dehydration

Common questions

Is nephrogenic diabetes insipidus the same as diabetes?

No. Diabetes mellitus involves blood sugar and insulin. NDI involves water balance and the kidneys' response to vasopressin. They can both cause thirst and frequent urination, so testing is needed to tell them apart.

Why am I still thirsty after drinking water?

With NDI, the kidneys continue to release large amounts of diluted urine. Thirst is the body's way of encouraging you to replace that water. Persistent thirst should be medically assessed rather than managed by restricting fluids.

Can nephrogenic diabetes insipidus go away?

Inherited NDI is generally lifelong. Acquired NDI may improve if the cause is corrected, but improvement is not guaranteed. Some kidney changes, including those associated with long-term lithium use, may persist.

Can I drink too much water with NDI?

Most people with untreated NDI drink in response to genuine water loss. However, fluid needs can change during treatment or illness. Drinking far beyond your losses may disturb sodium levels, so follow an individual fluid plan if your care team has provided one.

Does nephrogenic diabetes insipidus damage the kidneys?

NDI does not always cause progressive kidney damage. Long-term high urine volumes can stretch the bladder and urinary tract, and the condition causing acquired NDI may itself affect kidney function. Follow-up helps monitor these risks.

Can I take lithium if I have NDI?

Lithium can cause or worsen NDI, but decisions about continuing it must balance kidney effects with its mental health benefits. Do not stop it suddenly. The clinicians managing your lithium and kidney health can review alternatives, monitoring, and treatments that may reduce urine output.

Sources

- National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes Insipidus . U.S. National Institutes of Health
- Bichet DG. Hereditary Nephrogenic Diabetes Insipidus . GeneReviews, University of Washington, Seattle
- Christ-Crain M, Bichet DG, Fenske WK, et al. Diabetes insipidus . Nature Reviews Disease Primers . 2019;5:54
- Moeller HB, Rittig S, Fenton RA. Nephrogenic diabetes insipidus: essential insights into the molecular background and potential therapies for treatment . Endocrine Reviews . 2013;34(2):278-301
- Gubbi S, Hannah-Shmouni F, Koch CA, Verbalis JG. Diagnostic Tests for Diabetes Insipidus . Endotext , NCBI Bookshelf