CONDITION

Congenital nephrotic syndrome

Congenital nephrotic syndrome is a serious early-life kidney condition that causes large amounts of protein to leak into urine.

WHAT IT IS
Severe protein leakage from the kidneys beginning in early infancy

BODY SYSTEM
Kidneys and urinary system

MAIN SYMPTOMS
Swelling, poor growth, reduced urine, frequent infections

WHAT CAUSES IT
Usually inherited gene changes; sometimes congenital infection

HOW IT IS DIAGNOSED
Urine, blood, genetic, and infection tests

MAIN TREATMENT
Albumin replacement, nutrition, complication control, dialysis, and transplantation

CAN IT BE CURED?
Sometimes - transplant ends kidney protein loss

IS IT AN EMERGENCY?
Sometimes - breathing trouble or suspected blood clot

LONG-TERM OUTLOOK
Serious infancy condition; transplantation can support good long-term health

Overview

Congenital nephrotic syndrome is a kidney condition that begins during pregnancy or within the first 3 months after birth. "Congenital" means present from birth. "Nephrotic syndrome" describes heavy protein loss through the kidneys.

Healthy kidneys filter waste and extra water while keeping important proteins in the blood. In congenital nephrotic syndrome, the kidney filters do not hold protein properly. Large amounts of a blood protein called albumin pass into the urine.

Low albumin allows fluid to move out of blood vessels and into body tissues. This causes swelling, also called oedema. The loss of protein can also affect growth, nutrition, infection defences, thyroid function, and the blood's ability to clot normally.

Most cases are caused by an inherited change in a gene involved in kidney development or filtration. Less often, the condition results from an infection acquired before birth.

This is a serious condition requiring care from a specialist children's kidney team. Treatment aims to replace lost protein, support growth, prevent complications, and plan longer-term kidney care. Some children eventually need dialysis and a kidney transplant.

Symptoms

Symptoms often appear at birth or during the first weeks of life. A baby may initially look well, even when urine tests already show heavy protein loss.

Possible signs include:

Some affected babies are born early. The placenta may have been unusually large, although this finding alone does not confirm the condition.

Swelling can change from day to day. It may improve after treatment and then return as more protein is lost. Because infants cannot describe how they feel, changes in feeding, breathing, alertness, weight, and wet nappies are important.

- Swelling around the eyes, abdomen, genitals, hands, or feet
- Poor feeding or difficulty gaining weight
- Reduced urine or fewer wet nappies
- Tiredness, irritability, or reduced alertness
- Frequent or severe infections
- Breathing difficulty if fluid collects around the lungs
- Pale skin or other signs of poor nutrition

Causes and risk factors

Most congenital nephrotic syndrome is caused by a gene change affecting the kidney's filtration barrier. This barrier contains specialised cells and proteins that stop albumin from escaping into urine.

Changes in the NPHS1 gene are a well-known cause. This gene provides instructions for making nephrin, an important part of the kidney filter. Congenital nephrotic syndrome caused by NPHS1 changes is sometimes called Finnish-type congenital nephrotic syndrome.

Changes in other genes can also cause the condition. Examples include NPHS2 , WT1 , and

LAMB2 . Some gene changes affect only the kidneys. Others are part of a syndrome that can also affect the eyes, nervous system, reproductive organs, or risk of certain tumours.

Many inherited forms follow an autosomal recessive pattern. This usually means both parents carry one altered copy of the same gene but do not have the condition themselves. Each pregnancy may then have a chance of being affected. Other forms follow different inheritance patterns or result from a new gene change.

A family history or parents who are closely related by blood can increase the chance of some inherited forms. However, congenital nephrotic syndrome can occur without either factor.

Less often, an infection during pregnancy damages the developing kidneys. Possible causes include congenital syphilis, toxoplasmosis, and cytomegalovirus. The cause is not always found, even after detailed testing.

Nothing a parent did during routine pregnancy or infant care causes an inherited form of this condition.

Diagnosis

Doctors consider congenital nephrotic syndrome when a young baby has swelling, poor growth, or unexpectedly high protein levels in urine.

Urine testing shows how much protein is being lost. Blood tests commonly show a low albumin level. They can also assess kidney function, salts and minerals, cholesterol, blood counts, thyroid function, and signs of infection.

Genetic testing is an important part of diagnosis. It may identify the cause, show whether other organs need monitoring, guide treatment decisions, and provide information about future pregnancies. Testing may involve a panel of kidney-related genes or a broader genetic test.

Blood, urine, or other samples may be tested for infections acquired before birth. The tests chosen depend on the pregnancy history, the baby's examination, and local patterns of infection.

A kidney ultrasound shows the size and structure of the kidneys. It can also help rule out other urinary problems. A kidney biopsy, in which a small tissue sample is examined under a microscope, is not always needed when genetic testing has found a clear cause. It may be considered when the diagnosis remains uncertain.

High alpha-fetoprotein levels during pregnancy can occur with congenital nephrotic syndrome, but this finding has other causes. It cannot confirm the condition by itself.

Treatment and management

Treatment is coordinated by a specialist paediatric kidney team. Care is tailored to the amount of protein loss, the baby's growth, kidney function, genetic findings, and any complications.

Albumin may be given into a vein to replace protein lost in urine. A diuretic, sometimes called a water tablet like furosemide or hydrochlorothiazide , may be used with albumin to help the kidneys remove extra fluid. Babies with severe ongoing protein loss may need frequent albumin infusions.

Good nutrition is central to treatment. Protein and calories are lost at a time when the body is growing quickly. A specialist dietitian may recommend higher-energy feeding, additional protein, or tube feeding. Salt and fluid advice must be individualised because both dehydration and fluid overload can be harmful.

Some medicines can reduce the amount of protein passing into urine. These may include medicines that affect blood pressure within the kidney or, in selected cases, an anti-inflammatory medicine. They require close monitoring because they can affect kidney function, circulation, and body salts.

Other care may include:

Steroids and other immune-suppressing medicines used for common childhood nephrotic syndrome usually do not correct an inherited kidney-filter problem. They may be considered only when testing suggests an immune-related cause rather than a structural genetic form.

If protein loss remains severe, removing one or both kidneys may be discussed. Removing both kidneys stops urinary protein loss but also stops kidney function. Dialysis is then needed to remove waste and excess water until transplantation is possible.

A kidney transplant provides a new kidney with a working filtration barrier. It is often the most effective long-term treatment for severe genetic congenital nephrotic syndrome. Lifelong anti-rejection medicine and transplant follow-up are still required.

- Thyroid hormone or vitamin and mineral replacement when blood levels are low
- Treatment for confirmed congenital infection
- Vaccination and plans to reduce infection risk
- Monitoring or treatment for abnormal blood clotting
- Care of any long-term intravenous line used for albumin infusions
- Growth, developmental, eye, or tumour monitoring when required by the genetic cause

Complications

Heavy protein loss affects more than fluid balance. Possible complications include poor growth, muscle loss, low thyroid hormone levels, vitamin deficiencies, and weakened bones.

Children may be more vulnerable to serious infection because protective antibodies and other immune proteins are lost in urine. Intravenous lines can also become infected.

Nephrotic syndrome increases the risk of blood clots, including clots in the legs, lungs, or blood vessels supplying the kidneys. At the same time, very young or unwell babies may also have a risk of bleeding. Decisions about blood-thinning medicine therefore need specialist assessment.

Fluid can collect in the abdomen or around the lungs. Severe swelling can make feeding, movement, and breathing harder.

Kidney function may worsen because of dehydration, infection, reduced blood flow, medicines, or the underlying kidney problem. Some children develop long-term kidney failure and need dialysis or transplantation.

Prevention

Inherited congenital nephrotic syndrome usually cannot be prevented. It is not caused by feeding choices, ordinary activities during pregnancy, or something a parent failed to do.

When a gene change has been identified, a genetics professional can explain the inheritance pattern and the chance of the condition affecting another pregnancy. Options may include testing during pregnancy or testing embryos created through in vitro fertilisation. These are personal choices, not requirements.

Some infection-related cases may be reduced through routine pregnancy screening and prevention or early treatment of certain infections. This does not prevent genetic forms of the condition.

Living with it and what to expect

The first months may involve frequent hospital visits, blood and urine tests, albumin infusions, medicine adjustments, and close nutrition support. Some babies need long admissions, while others can receive parts of their care at home through a specialist programme.

Families may be asked to record weight, feeding, swelling, urine output, or concerns about an

intravenous line. Weight changes can reflect fluid movement rather than true growth, so the care team will also follow length, head growth, muscle development, and feeding progress.

The course over time is linked to the underlying cause and how well protein loss can be controlled. Some infection-related cases improve when the infection is treated. Severe genetic forms usually continue to leak protein until the affected kidneys are removed or replaced by a transplant.

Dialysis may be needed while a child grows large enough and becomes medically ready for transplantation. After a successful transplant, the heavy protein loss usually stops. Nutrition, energy, and growth may then improve, although progress is not immediate or guaranteed.

The gene change remains present after transplantation. Features affecting organs other than the kidneys may still need care. Transplant recipients also need ongoing anti-rejection medicine, regular blood tests, and monitoring for infection and medication effects.

Congenital nephrotic syndrome can place significant practical and emotional demands on a family. Kidney nurses, dietitians, pharmacists, social workers, psychologists, genetics professionals, and transplant teams may all be involved. Many children can take part in family, school, and social life after effective long-term treatment, but continuing medical follow-up remains important.

When to get medical help

Seek emergency help if a baby or child with congenital nephrotic syndrome:

Fever in a young infant needs prompt medical assessment. A fever, shaking, marked sleepiness, or redness and discharge around an intravenous line may indicate a serious infection. Follow the child's specialist emergency plan or seek urgent medical care.

Contact the kidney team promptly about clearly reduced urine, repeated vomiting or diarrhoea, worsening swelling, rapid weight change, poor feeding, or problems with a dialysis catheter or intravenous line. These changes can upset fluid balance quickly.

Routine appointments remain important even when the child seems well. They are used to monitor growth, nutrition, thyroid levels, kidney function, clotting risk, medicines, development, and preparation for dialysis or transplantation when needed.

- Is struggling to breathe, breathing very quickly, or turning blue or grey
- Is unusually difficult to wake, has a seizure, or becomes unresponsive
- Develops sudden chest pain, coughs blood, or has unexplained severe breathlessness

- Has sudden painful swelling, colour change, or coolness in one arm or leg

Common questions

Is congenital nephrotic syndrome curable?

Some infection-related cases may improve when the infection is treated. In severe inherited forms, medicines usually cannot repair the kidney filter. A kidney transplant can stop the nephrotic protein loss, but it requires lifelong follow-up and anti-rejection treatment.

Is congenital nephrotic syndrome always genetic?

No. Most cases are linked to gene changes, but infections acquired before birth and other uncommon causes are possible. Genetic and infection testing helps clarify the cause.

Will my baby need a kidney transplant?

Many children with severe, continuing protein loss eventually need a transplant. Others may have a less severe course or an infection-related form that improves. The decision is based on protein loss, growth, complications, kidney function, and the identified cause.

Do steroids like prednisone or hydrocortisone work for congenital nephrotic syndrome?

Steroids usually do not help when the condition is caused by an inherited structural problem in the kidney filter. This differs from many cases of nephrotic syndrome beginning later in childhood, which often respond to steroids.

Can congenital nephrotic syndrome happen again in another pregnancy?

It can. The chance depends on the gene involved and its inheritance pattern. If both parents carry a recessive change in the same gene, each pregnancy has the same inherited risk. Genetic counselling can provide information specific to the family's test results.

Can nephrotic syndrome return after a transplant?

The original structural kidney problem usually does not affect the transplanted kidney. Recurrence can occur in uncommon circumstances, including some immune reactions involving nephrin. The transplant team monitors urine protein and kidney function closely.

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