



NEPHROLOGY

Nephrotic Syndrome

Information for parents and carers



Contact information

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What is nephrotic syndrome?

Nephrotic syndrome is a kidney disorder which causes large amounts of protein to be lost in the wee (urine) leading to low levels of protein in the blood.

Normally, protein in the blood stops water from leaking out of the blood vessels into the tissues of the body.

In nephrotic syndrome, low blood protein levels allows water to leak into the tissues of the body which become swollen. This swelling is called oedema. All body tissues swell but the most obvious sites are the tummy, legs, face, and the penis and scrotum.

What is the cause of nephrotic syndrome?

The most common form of nephrotic syndrome is called steroid sensitive nephrotic syndrome. The cause is unknown. The long term outcome for kidney function is excellent and most cases are cured before adulthood. This form, as the name implies, responds to steroid (e.g. prednisolone) medication. Nephrotic syndrome is most common in two to three year old children, but all ages can be affected. Many children with nephrotic syndrome also have illnesses caused by an allergy (e.g. asthma, eczema, hay fever) but no particular allergic factor has been identified in children with nephrotic syndrome.

There are other forms of nephrotic syndrome, often grouped under the name steroid resistant nephrotic syndrome. These cases need different treatment and have a different outlook. This booklet provides information regarding steroid sensitive nephrotic syndrome only.

What is the main treatment of nephrotic syndrome?

A steroid drug called prednisolone is given to all children diagnosed with nephrotic syndrome. In 90 per cent of cases it causes a complete remission of the condition meaning the protein in the urine (proteinuria) and the oedema disappear. These children have steroid sensitive nephrotic syndrome.

Induction of remission of nephrotic syndrome requires fairly high daily doses of prednisolone for approximately four weeks. These large doses are generally well tolerated however you may notice some roundness of your child's face, and they may have an increased appetite while on the steroids. They may also upset your child's mood or behaviour, sometimes making them more emotional during this time.

In addition, children may be given an antibiotic (commonly penicillin) to prevent infection and an acid suppressing medicine (commonly omeprazole) to prevent gastritis. These medicines are stopped when a child is in remission.

You will be taught how to test your child's urine for protein every morning with a plastic test strip. The stick remains yellow if there is no protein present and turns a different shade of green depending on the level of protein present. If needed, you will be given advice about how much liquid they can drink.

If severe oedema occurs, some nephrotic children need protein given by drip infusion into a vein. The protein given is human albumin, the main part of protein in the blood. This protein is likely to be needed if there is more than a three to four kilo weight gain during a relapse, oedema of the penis or scrotum occurs, or if your child develops cold hands and feet due to poor circulation. Protein infusion causes a reduction of oedema but does not improve the proteinuria which must be cleared with prednisolone. Protein infusions may need to be repeated until remission occurs. When a child has oedema, salty foods and excessive drinking should be avoided.

Special diets are not useful in producing remission or preventing relapse. During relapse, very salty foods should be avoided as salt makes the oedema worse. After remission, normal salt intake is allowed. High protein diets, to replace the lost urinary protein, are to be avoided as they generally are not tolerated by nephrotic children and also contain too much salt.

What are the signs that remission is occurring?

You will be asked to test your child's urine daily to check the level of proteinuria. Once your child is classed as in remission, the urine test strip will become negative for protein over one or two days. Your child will pass large amounts of urine and the oedema will disappear.

Go to www.rch.org.au/nephrology/nephrotic_syndrome to see a video on how to test urine for protein.

When does remission usually occur?

Usually remission occurs in the second week after starting a high dose of prednisolone. Only a small number (10 per cent) of children with nephrotic syndrome remit in the first week with 80 per cent of children in remission by the end of the second week and 90 percent by the end of the third week.

There are generally no signs of improvement after starting prednisolone until the day of remission. While waiting for remission, many patients get more swollen because of the continuing proteinuria and consequent retention of salt and water in the body.

After remission, what happens?

Children with nephrotic syndrome in remission have no signs of their disease. The dose of prednisolone is gradually reduced over the next three months. The doses to be taken will be indicated by your doctor.

You will be asked to continue to test your child's urine every morning and to record the level of proteinuria, as a rising level could indicate a relapse. The results of the test should be recorded in this book.

What is a relapse of nephrotic syndrome?

A relapse is reappearance of heavy proteinuria for at least four days. If not treated, oedema appears within a week or two. By testing every day, nephrotic relapses may be detected with dip strips before oedema develops.

Any child can develop proteinuria for two to three days during a cold or any feverish illness. However, this proteinuria clears quickly in normal children. In a relapse of nephrotic syndrome, the proteinuria persists for longer than three days. Many relapses appear to start with a cold, the proteinuria persisting after the cold has passed.

Relapses occur in most (75 per cent) children with nephrotic syndrome, particularly during the first two years after diagnosis, and up to half of children will experience multiple relapses. Relapses become less frequent as the child grows older and are rare in adulthood. Relapses generally occur when the dose of prednisolone is low or the treatment has been stopped. Relapses rarely occur on high dosages.

What should be done if the urine drip shows protein?

Nothing needs be done immediately provided the child is well and shows no oedema. Continue to test daily and record the results. If proteinuria disappears in a few days, no action is needed. Seek medical advice if heavy proteinuria lasts for four days.

What is the treatment of a relapse of nephrotic syndrome?

Prednisolone is given again in the high dose used to treat the first episode. By starting prednisolone after four days of heavy proteinuria, most relapses of nephrotic syndrome can be cleared before much oedema develops. Early treatment ensures that most relapses are minor and very few require hospitalisation. Most can be managed by telephone consultation alone.

Can you prevent a relapse?

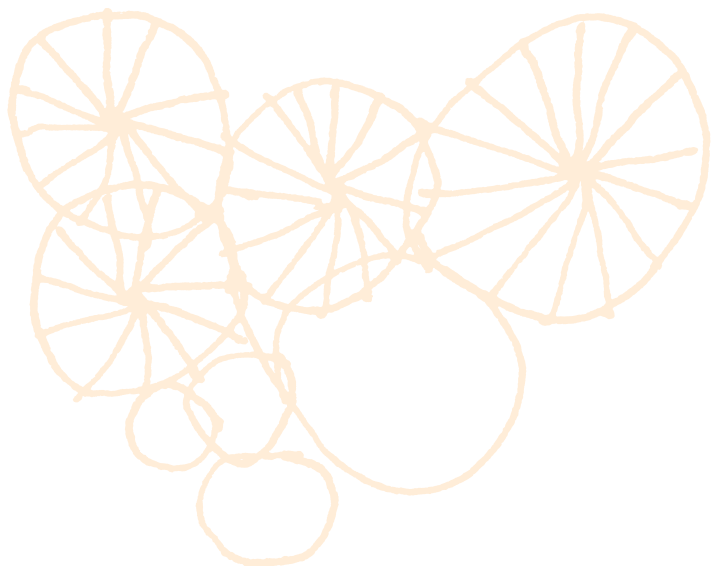
A relapse is often triggered by a respiratory infection and not often preventable. Your doctor may start a short course of steroids at the onset of infection, referred to as a sick day plan, in an attempt to reduce the risk of relapse. It is important to monitor for protein in the urine carefully at times of illness and to have an annual influenza vaccine every year.

Vaccination and nephrotic syndrome

Live virus vaccines including MMR (measles, mumps, rubella), oral polio vaccine, varicella—zoster (chicken pox) and BCG (tuberculosis) can cause problems if your child is on high dose daily steroid like prednisolone. Your child's doctor will generally advise that your child has such immunisations when they are off this medication.

Inactive vaccines including diphtheria, pertussis, tetanus (DPT), salk polio vaccine, hepatitis B, Hib (hemophilus influenza), influenza vaccine, meningococcal vaccine, pneumococcal vaccine do not cause problems when your child is on prednisolone, but the vaccine may not work as effectively. Generally, immunisation for pneumococcal disease and yearly influenza vaccination will be encouraged.

Immunisation does not generally cause a relapse.



Won't large doses of Prednisolone cause side effects?

The reduction in the high daily dose of prednisolone that your child is treated with in the second and subsequent months together with the change to alternate day dosing in the second month results in few children showing side effects by the end of 3 months. Some common reactions to the medication include an increased appetite and mood changes. These changes get better when the prednisolone dose is reduced. If you find any changes in your child that concern you, bring them to the attention of your doctor.

Any other doctor who treats your child should be told they have been taking prednisolone as many illnesses are treated differently if the patient is on this sort of medication.

Treatment with prednisolone must never be stopped suddenly as steroid drugs replace the body's own cortisone production by the adrenal glands, this may take some time to recover after being on steroids. If your child has any serious illness or requires an anaesthetic within two years of receiving prednisolone further steroid therapy may be required as the adrenal glands may be unable to provide the extra cortisone needed to cope with the stress of the illness.

A proportion of children with nephrotic syndrome have frequent relapses, each relapse requiring another treatment course of high dose prednisolone. If four or more relapses occur in one year the frequent large doses of prednisolone may stunt growth, weaken bones or lead to rounding of the face and obesity.

Are there any other treatments for nephrotic syndrome?

If prednisolone causes concerning side effects or if your child suffers from frequent relapses (four relapses per year) your doctor may discuss the introduction of an alternative treatment referred to as a steroid sparing agent. These include tacrolimus, cyclosporin, mycophenolate mofetil, levamisole and rituximab. These medications all work via different mechanisms and help to prevent relapses and/or induce remission in nephrotic syndrome.

The aim of these treatments is to reduce the amount of prednisolone your child will need to take in the future.

These medications generally work by lowering the body's natural immune system function. The immune system is important for the body's response to infection, so extra care has to be taken if your child has a fever or is unwell whilst on these medications.

Additionally, the immune system is an important mechanism by which the body surveys for cancer, so long-term use of these medications can increase the risk of skin cancers.

Tacrolimus

Tacrolimus is a medication that is taken twice a day and can be given as a syrup or a tablet. We often refer to it as 'tac' or 'tacro'. A few blood tests are required when commencing this medication to check levels in the blood. Once stable levels are achieved, blood tests will be necessary to monitor levels approximately every three months.

It is important that tacrolimus levels are tested immediately before taking the morning dose of the medicine. This may require booking into your local pathology provider for your child's blood test. Tacrolimus levels taken after the morning dose has been taken are not informative.

Tacrolimus is generally tolerated very well by most children. Some possible side effects include headache, abdominal discomfort, tremor and high blood pressure. In the long term, tacrolimus can cause diabetes in a small proportion of patients. Another side effect with very long term use (three to five years) is the development of scarring on the kidneys.

Cyclosporin is a medication that has the same effect as tacrolimus and may be used as an alternative. It also requires blood tests to monitor levels and these blood tests must be performed immediately before or two hours after taking the dose of the medication. Its side effects are similar to tacrolimus but also include excessive hair growth and enlarged gums.

Mycophenolate mofetil (MMF)

MMF is a medication that is taken twice a day and can be given as a syrup or tablet. MMF is well tolerated without significant side effects in the majority of children who take it for nephrotic syndrome. It can be associated with abdominal discomfort, diarrhoea and vomiting. MMF can affect the bone marrow's ability to produce blood cells so intermittent blood tests are required to monitor this. Compared to tacrolimus, MMF works for a smaller proportion of patients with nephrotic syndrome. However, in those patients for whom it works, it can work very well and provide a long term management strategy without significant long-term side effects.

Levamisole

Levamisole is a medication that is usually used to treat parasitic worm infections. It is also effective in some children with nephrotic syndrome. Levamisole is well tolerated by most children however some side effects can be nausea and abdominal cramps. Levamisole can affect the bone marrow's ability to produce white cells so intermittent blood tests are required to monitor this whilst your child is taking this medication.

Rituximab

Rituximab is a medication known as a monoclonal antibody that targets B cells, an important component of the immune system. It is given via an intravenous infusion and requires a day stay hospital admission. Patients require infusions roughly once every three to six months, but this is individualised. The most common side effects are allergic reactions which can often be managed by slowing the infusion down or administering pre-medications to reduce these symptoms. Other side effects are very rare but can be serious and will be discussed in length prior to the commencement of this treatment. In many cases, rituximab is capable of achieving longstanding remission in children who have been unable to achieve stability on other therapies.

What is the outlook for nephrotic children?

Most children with nephrotic syndrome have relapses for a few years but fewer relapses occur as the child gets older. There is no particular age at which relapses stop occurring and relapse in adulthood is rare. Between relapses, a child should be fit and well and lead a normal life without restriction. Provided relapses are detected early with urine dipsticks, most relapses can be treated at home and the child remains well throughout.

The long-term outlook for children with steroid sensitive nephrotic syndrome is excellent with children growing up to become healthy adults.

Are there any unusual varieties of nephrotic syndrome?

A small number of children with nephrotic syndrome (10 per cent) have unusual symptoms such as visible blood in the urine or high blood pressure. Some do not have a typical remission of proteinuria when given prednisolone for at least four weeks. Such cases may need other treatments and have a different course and outlook.

The cause of the disease can be more accurately determined by kidney biopsy. This involves taking a small piece of kidney through a needle for examination under a microscope. A kidney biopsy is not required for management of the common, typical case of nephrotic syndrome.

Managing carer stress

The diagnosis of nephrotic syndrome in a child is often a surprise to parents/carers and commonly associated with appropriate concern and worry. We recommend early engagement with your GP to assist in ongoing reviews of your child in addition to management of any stress associated with the new diagnosis.

We will also introduce you to our social work team at The Royal Children's Hospital to provide additional support.

Summary

Nephrotic syndrome in childhood responds well to treatment with prednisolone in adequate doses. Relapses can be expected in most children and are detected by daily urine dipstick tests done at home.

Call your doctor if proteinuria persists for four days or at lower levels for a week or longer (see below "When to call the doctor"). This enables your doctor to start early treatment with prednisolone and avoids further hospitalisation.

Between relapses the only sign to look for is proteinuria. During relapses, weigh your child frequently as accumulation of oedema leads to rapid weight gain. Particularly report weight gain of three to four kilograms, oedema of the scrotum, cold hands and feet and general tiredness or lack of energy. Used in the doses prescribed, prednisolone does not cause serious side effects unless relapses occur very frequently. Then alternative medications will need consideration. The long-term outlook is excellent for children with nephrotic syndrome which responds to treatment with prednisolone.

When to call the doctor

Call the Nephrology office or the doctor on call if:

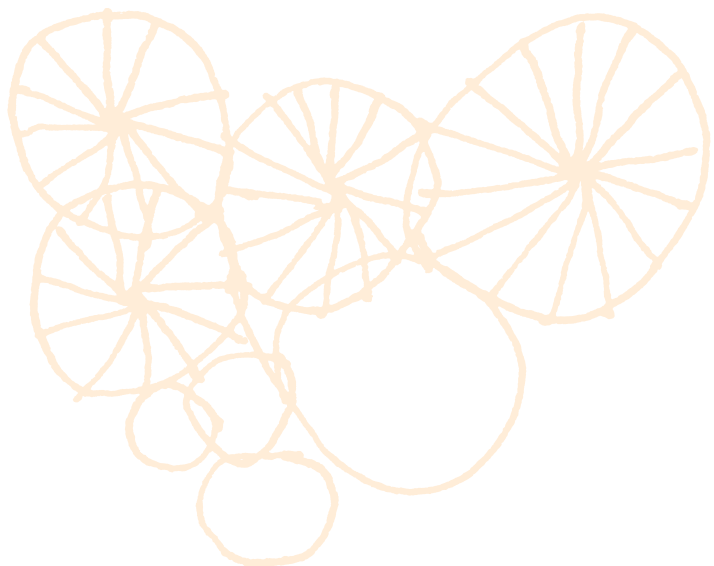
- your child has proteinuria (3+ or 4+ on dipstick) for four consecutive days
- your child has proteinuria (1+-2+ on dipstick) for seven consecutive days
- your child has gained more than 3kg during a relapse
- your child has cold hands and feet, or abdominal pain during a relapse
- your child has fever or vomiting whilst on treatment
- your child has had an exposure to chickenpox whilst on treatment.

Prednisolone course

The first course of prednisolone lasts three months with reductions in medication every few weeks. The change from daily prednisolone therapy to alternate daily therapy is made after the first month. If your child does not enter remission after three to four weeks your doctor may organise other therapy and additional tests.

The treatment of second and subsequent episodes of nephrotic syndrome (relapses) involves two to three months of treatment, with reduction in medication every two weeks. You may also be instructed to give prednisolone to prevent a relapse at the onset of an infection.

Prednisolone is supplied by the chemist on prescription in either 25mg or 5mg tablets or in a suspension (Pred-mix) 5mg/ml.



1st episode

Give	mg daily for	4 weeks
Then	mg every second day for	4 weeks
Then	mg every second day for	10 days
Then	mg every second day for	10 days
Then	mg every second day for	10 days

2nd episode

Give	mg daily until urine trace/neg protein for	days
Then	mg every second day for	days
Then	mg every second day for	days
Then	mg every second day for	days
Then	mg every second day for	days

Alternative regime

Give	mg daily until urine trace/neg protein for	days
Then	mg every second day for	days
Then	mg every second day for	days
Then	mg every second day for	days
Then	mg every second day for	days

Alternative regime

Give	mg daily until urine trace/neg protein for	days
Then	mg every second day for	days
Then	mg every second day for	days
Then	mg every second day for	days
Then	mg every second day for	days

Proteinuria record

Proteinuria record

Proteinuria record

Proteinuria record

Proteinuria record

Proteinuria record

Proteinuria record

Proteinuria record

Proteinuria record

Useful links

How to test your urine for protein (video):
www.rch.org.au/nephrology/Nephrotic_syndrome/

**Nephrotic Syndrome Information book
for parents and carers:**
[www.rch.org.au/uploadedFiles/Main/Content/nephrology/
publication-nephrotic-syndrome-information-and-record-book.
pdf](http://www.rch.org.au/uploadedFiles/Main/Content/nephrology/publication-nephrotic-syndrome-information-and-record-book.pdf)

Nephrotic Syndrome Record book for parents and carers:
[www.rch.org.au/uploadedFiles/Main/Content/nephrology/
publication-nephrotic-syndrome-record-book.pdf](http://www.rch.org.au/uploadedFiles/Main/Content/nephrology/publication-nephrotic-syndrome-record-book.pdf)

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Nephrology

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