The Royal Children's Hospital Melbourne

Nephrology

Nephrotic Syndrome

INFORMATION FOR PARENTS
PREPARED BY THE DEPARTMENT OF NEPHROLOGY

What is nephrotic syndrome?

Nephrotic syndrome is a kidney disorder which causes large amounts of protein to be lost in the urine leading to low levels of protein in the blood. Normally, protein in the blood prevents water from leaking out of the blood vessels into the tissues. In nephrotic syndrome, low blood protein levels allow water to leak into the tissues which become swollen. This swelling is called oedema. All body tissues swell but the most obvious sites are the abdomen, the legs, the face, and the penis and scrotum. Thus, nephrotic syndrome is large amounts of protein in the urine resulting in low level blood protein and oedema.

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 2-3 year old children, but all ages can be affected. Many nephrotic children also have illnesses caused by 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.

What is the main treatment of nephrotic syndrome?

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

Induction of remission of nephrotic syndrome requires fairly high daily doses of Prednisolone for approximately 4 weeks. These large doses are generally well tolerated. 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 behaviour during this time.

In addition patients may be given Penicillin to prevent infection, ranitidine to prevent gastritis and Aspirin or other blood thinners to prevent blood clotting. Nephrotic patients are prone to infection and clotting while oedematous. These medicines are stopped when they are 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 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 constituent of protein in the blood. This intravenous protein is likely to be needed if more than 3-4 kg weight gain occurs during relapse, if oedema of the penis or scrotum occurs, or if the patient develops cold hands and feet due to poor circulation. Protein infusion causes reduction of oedema but does not improve the proteinuria which must be cleared with Prednisolone. Protein infusion often needs to be repeated until remission. When the child has oedema, very salty foods and excessive drinking should be avoided.

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. On remission of the nephrotic episode the test strip will become negative for protein over 1 or 2 days. The child will pass large amounts of urine and the oedema will disappear.

When does remission usually occur?

Usually remission occurs in the second week after starting high does Prednisolone. Only a small number (10%) of nephrotic children remit in the first week but 80% have undergone remission by the end of the second week. 90% have remitted 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?

Nephrotic children in remission have no signs of their disease. The dose of Prednisolone is gradually reduced over the next 5-6 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 relapse of nephrotic syndrome?

Relapse is reappearance of heavy proteinuria for at least 4 days. If not treated, oedema appears a week or two later. By testing every day, nephrotic relapses may be detected with dip strips before oedema develops.

Any child can develop proteinuria for 2-3 days during a cold or any feverish illness, but this clears quickly in normal children. To prevent a relapse while on low dose alternate day prednisolone, your specialist may advise you to give the same dose every day for 3-5 days during such an infection. In a relapse of nephrotic syndrome the proteinuria persists for longer than 4 days. Many relapses appear to start with a cold, the proteinuria persisting after the cold has passed.

Relapses occur in most (75%) children with nephrotic syndrome, particularly during the first 2 years, and up to half the 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.

Vaccination and nephrotic syndrome

Live virus vaccines: These include MMR (measles, mumps, rubella), oral polio vaccine, varicella – zoster (chicken pox) and BCG (for tuberculosis). These vaccines can cause problems when your child is on high dose daily steroid and your doctor will generally advise that your child have immunization when they are off prednisolone.

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

Immunisation does not generally cause relapse of nephrotic syndrome.

What should be done if albustix test shows protein?

Nothing need 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 taken. Seek medical advice if proteinuria lasts for 4 days.

What is the treatment or relapse of nephrotic syndrome?

Prednisolone is given again in the high dose used to treat the first attack. By starting Prednisolone after 4 days of 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.

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 but almost none of these is significant. 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 you child should be told the child has been taking Prednisolone as many other 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 2 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 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. If Prednisolone causes problematic side-effects, or if your child is a frequent relapser (4 relapses/year) your doctor will discuss with you an alternative treatment drug.

What is Cyclophosphamide?

Cyclophosphamide is a drug which prevents relapses of nephrotic syndrome. Approximately 30% of children who have a course of Cyclophosphamide have no further relapses, i.e. are permanently cured of their nephrotic syndrome. A further 50% have no relapses for at least a year after the cyclophosphamide treatment and most of the other children have fewer relapses and therefore do not develop side effects of prednisolone.

Cyclophosphamide is generally given over an 8 week course to children who have had about four relapses/year, in order to avoid prednisolone side effects. Like prednisolone, it is supplied as tablets.

Cyclophosphamide tends to lower the number of white cells in the blood. These cells are involved in resistance to infection. Therefore, during the course of Cyclophosphamide, a weekly blood test is done to check the white blood cell count and thereby adjust the dosage if necessary. Cyclophosphamide occasionally causes a mild temporary hair loss, but patients do not usually lose sufficient hair to be noticeable. Adults given much longer courses of Cyclophosphamide have been made temporarily or permanently infertile. Sterility does not occur after treatment with up to two 8 week courses of Cyclophosphamide in childhood.

Because possible side effects of Cyclophosphamide are more serious than with Prednisolone, Cyclophosphamide is not given to all children with nephrotic syndrome. Tumours have been reported in some children following prolonged treatment with Cyclophosphamide. This has not occurred in any of several hundred children treated over the last 40 years at The Royal Children's Hospital.

Cyclophosphamide is used where the risks of frequent episodes of nephrotic syndrome or Prednisolone side effects outweigh those possible with Cyclophosphamide. It is a very effective drug for such patients.

Are there any other treatments for nephrotic syndrome?

Cyclosporin is given twice daily. Blood tests are required when commencing this medication to check on the drug levels in the blood. The medication is reduced in dose over a period of months so the need for frequent blood tests diminishes. The medication is generally used for either (i) inducing remission in children who have not responded to prednisolone alone and (ii) as a replacement for prednisolone in children who continue to relapse after having cyclophosphamide. Common side effects include gum overgrowth and increased body hair. A side effect of long term higher dose therapy is kidney injury.

Other drugs are of use in special circumstances. These include levamisole,mycophenolate mofetil,and rituximab medications that affects the immune system. Few other drugs or medication appear to help nephrotic syndrome. In particular, vitamins, natural remedies, homeopathic medicines and herbal medications do not induce remission of nephrotic syndrome, and are to be avoided although most are harmless.

Special diets are not useful in producing remission or preventing relapse. During relapse very salty foods should be avoided as salt aggravates the oedema. After remission free salt intake is allowable. High protein diets, to replace the lost urinary protein, are generally not tolerated by nephrotic children and also contain much salt. Therefore high protein diets are to be avoided.

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 cease occurring although relapse is rare in adulthood. Between relapses the child should be fit and well and should lead a normal life without restriction. Provided relapses are detected early with urine dipstrips, most relapses can be treated at home and the child remains well throughout the relapse.

Before Cortisone was discovered in 1952, most children with nephrotic syndrome died. Now the long-term outlook for children with Prednisolone-responsive nephrotic syndrome is excellent and such children grow up to become normal adults.

Are there any unusual varieties of nephrotic syndrome?

A small number of nephrotic children (10%) have unusual features such as blood in the urine or high blood pressure. Some do not have a typical remission of proteinuria when given Prednisolone for at least 4 weeks. Such cases may need other treatments and have a different course and outlook. Then the cause of the disease can be more accurately determined by kidney biopsy or genetic testing. This involves taking a small piece of kidney through a needle for examination under a microscope. Kidney biopsy is not required for management of the common, typical case of nephrotic syndrome.

Summary

Nephrotic syndrome in childhood responds well to treatment with Prednisolone in adequate dose. Relapses can be expected in most children and are detected by daily urine dipstrips tests done at home. Call your doctor if proteinuria persists for 4 days. 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 3-4kg, oedema of the scrotum, cold hands and feet and general lethargy. 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 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 4 consecutive days
- If your child has gained more than 1kg during a relapse
- If they have cold hands and feet, or abdominal pain during a relapse
- If they have fever or vomiting whilst on treatment
- If they have an exposure to chickenpox whilst on treatment.

Prednisolone course

The 1st course for nephrotic syndrome lasts 6 months with reductions in medication every few weeks. The change from daily prednisolone therapy to alternate daily therapy is made after the 1st month. If remission has not been induced by 3 to 4 weeks your doctor may organize other therapy and additional tests.

The treatment of 2nd and subsequent episodes of nephrotic syndrome (relapses) involves 2-3 months of treatment, with reduction in medication every 2 weeks.

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	one month
Then	mg every second day for	one month
Then	mg every second day for	one month
Then	mg every second day for	one month
Then	mg every second day for	one month
Then	mg every second day for	one month

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

Date	Urine test	Prednisolone dose	Date	Urine test	Prednisolone dose

Proteinuria record

Date	Urine test	Prednisolone dose	Date	Urine test	Prednisolone dose

Proteinuria record

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