Nephrotic syndrome in children

1. Nephrotic syndrome in children

Idiopathic nephrotic syndrome is the most common paediatric glomerular disease, characterised by heavy proteinuria, low plasma albumin (leading to oedema) and increased risk of infection. Treatment is us th oral steroids, and prognosis depends on how well the condition respon eatment. Most children will respond well to steroids, and, as a result, mortality from nephrotic syndrome has significantly reduced. However, long-term impacts are common due to the frequent high doses of oral steroids required.

In primary care, we need to be aware of how the condition might present, but also of the long-term care these children need to help prevent relapses and reduce the risk of serious complications.

This article is largely based on a 2023 Lancet review unless otherwise referenced in the text (Lancet 2023;402:809).

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1.1. What is nephrotic syndrome?

If you are anything like me, the intricacies of renal pathophysiology are tricky to grasp and retain! It might help to think about how we would explain nephrotic syndrome to patients and families, and I have paraphrased the following from the patient information group National Kidney Foundation web page and the NHS UK conditions information page on nephrotic syndrome in children:

Nephrotic syndrome is a collection of symptoms that may occur when the filtering units of the kidney are damaged (for example, by an infection). This damage allows protein normally kept in the plasma to leak into the urine, in large quantities. This reduces the amount of protein in your blood, which in turn means that fluid can leak out of the blood vessels into tissues, causing swelling. This loss of proteins can include antibody proteins and proteins which help prevent blood clotting, meaning children are at greater risk of catching infections or developing blood clots.

The likely underlying cause of nephrotic syndrome in children differs depending on the age at first presentation and the degree of responsiveness to initial steroid treatments. Most children will have 'minimal change disease', meaning that the kidneys appear normal on biopsy. This is also known as idiopathic nephrotic syndrome. Although this is the most common glomerular presentation in children, it remains rare, affecting around 2.9/100 000 children per year.

Genetic factors are responsible for up to 30% of cases of steroid-resistant nephrotic syndrome and most of the cases presenting before 3m of age (the congenital forms). Other causes can include CMV, parvovirus, diabetes, sickle cell disease, HIV, hepatitis B and systemic lupus erythematosus.

Definition	When to suspect
Congenital nephrotic syndrome	Children ≥3 months.
Idiopathic nephrotic syndrome – steroid sensitive	The most common type in children, although still rare. Achieve complete remission within 4 weeks of starting steroid treatment.
Idiopathic nephrotic syndrome – steroid resistant	Failure to achieve remission after 4 weeks of steroid treatment.
Remission	Negative (or trace) urine dipstick for protein for ≥3 consecutive days.
Relapse	At least 3+ protein on urine dipstick for 3 consecutive days +/- oedema.
Frequent relapse	≥2 relapses in the first 6 months after initial diagnosis, OR ≥3 relapses in any 12-month period.
Steroid-dependent nephrotic syndrome	2 relapses while on steroids or alternate-day reducing steroids, or a relapse within 2 weeks of stopping steroids.

1.2. How might we see nephrotic syndrome in primary care?

At first presentation

Nephrotic syndrome typically affects children aged 1–10y. However, it can occur in younger or older patients in atypical presentations. For many children, there will have been a triggering event in the weeks before onset, such as an infection or allergic reaction.

Symptoms and signs

- Oedema: commonly periorbital or affecting the face, hands and feet.
    - In severe cases, there may be ascites or pleural effusion.
- Hypovolaemia.
- Increased weight.
- Signs of infection: fever or lymphadenopathy, chest or urinary symptoms, peritonitis.
- Abdominal discomfort.
- Fatigue, dizziness.
- Frothy urine.
- Thrombosis: consider thrombosis in children with chest pain, headache or neurological signs, haematuria or severe abdominal pain.
- Hypertension: elevated blood pressure is rare and might indicate more severe disease.

All children presenting for the first time with suspected nephrotic syndrome should be discussed with our paediatric colleagues because they will need urgent blood tests.

Testing in hospital

Investigations on admission may include:

- Urine protein:creatinine ratios, urinalysis and investigation for haematuria.
- Bloods, including FBC, renal function and albumin. Also wider immune testing such as complement, ANA, antistreptococcal antibodies and antineutrophil cytoplasmic antibodies.
- Assessment for any dysmorphic features, ambiguous genitalia or family history of kidney disease.
- Examination for any rash or arthritis.
- Kidney ultrasound and biopsy is not routine, but will be considered in atypical presentations or where the nephrotic syndrome does not respond to first-line steroid treatment.
- Genetic screening for congenital nephrotic syndrome or steroid-resistant nephrotic syndrome.

Acute treatment

During the acute episode, secondary care treatment is usually with oral prednisolone:

- 2mg/kg (up to a maximum of 60mg) daily for 4–6 weeks, followed by 1.5mg/kg (up to a maximum of 40mg) alternate days for 4–6 weeks.
- Prophylactic anticoagulation, management of fluid status and any concurrent infections may also be needed (decided in secondary care).

Home monitoring

- Urine dipstick daily until remission.
    - Remission is defined as a negative (or trace) urine dipstick for protein for ≥3 consecutive days.
- Urine dipstick twice weekly long term thereafter.
- Urine dipstick testing daily when unwell or if a dip test returns a protein level ≥1+.

Relapse management

Relapse is defined as at least 3+ of protein on urine dipstick for 3 consecutive days +/- oedema. It is common for children with nephrotic syndrome to have relapses until they reach their teens. It is important that relapses are identified and treated early to reduce the risk of complications such as acute kidney injury, hypovolaemia and thrombosis, which can occur in 1–4% of episodes.

Children need daily urine dipstick testing during subsequent illnesses due to increased risk of relapse.

Treatment of relapse

- There is no specific guidance in the UK as to when a child might need admission to hospital to treat their relapse. We would suggest you discuss each case with your local paediatricians because children who are well may be managed at home under the guidance of their secondary care team.
- Resume prednisolone treatment at the dose advised by secondary care, tapering to stop according to response.
    - As an example regimen, we might see 2mg/kg (up to a maximum of 60mg) daily until urine dipstick tests have been negative for protein for 3–5 days, and then reducing to 1.5mg/kg (up to a maximum of 40mg) alternate daily for 4 weeks.
- During a relapse, blood pressure and weight should be monitored twice weekly.

For children with persistent or recurrent relapses, steroid-sparing drugs such as mycophenolate mofetil, cyclophosphamide or rituximab may be considered in secondary care.

Preventative care

Vaccinations

Live vaccines such as nasal flu, MMR/MMRV and BCG should not be given while on immune-suppressing therapy. Immunisation may need to be completed prior to starting immune suppressants, or be delayed until a gap in treatment.

Due to the increased infection risk, comprehensive vaccination is important for these children. The following UK advice is taken from NHS guidance (NHS – nephrotic syndrome in children) and from the Green Book. Scottish guidance can be found here: NHS Scotland - immunisation guideline for children with chronic kidney disease.

- Pneumococcal vaccine: the Green Book advises that antibody levels decline rapidly in individuals with chronic renal disease; re-immunisation is therefore advised every 5 years (gov.uk – pneumococcal, the Green Book, chapter 25).
- Influenza vaccination: advised annually. If immune compromised, do not use the **live nasal** flu immunisation and instead give the **injection** (gov.uk Publishing Service – influenza, the Green Book, chapter 19).
- Varicella vaccine: may be advised in some children (this is a **live** vaccine).

Steroid safety

Children on prolonged or repeated courses of oral steroids are at risk of steroid complications. This is now the greatest cause of morbidity in children with nephrotic syndrome. Our article on *Safe prescribing of steroids* has detailed advice on the checks we need to consider for safe monitoring in adults, but, in children, secondary care may advise:

- Quarterly: blood pressure, height, weight, BMI.

- Yearly: height velocity, and consider vitamin D testing in patients who received oral steroids for at least 6 months.
- Frequency of ophthalmological assessment and DEXA scan to be established on an individual basis.

Nephrotic syndrome in children

- Idiopathic nephrotic syndrome is the most common paediatric glomerular disease.
- Presents with heavy proteinuria, low plasma albumin, oedema and increased risk of infection.
- Treatment is usually with oral steroids.
- Prognosis depends on how well the condition responds to treatment. Most children will respond well to steroids.
- Long-term impacts are commonly due to frequent, high-dose oral steroids.
- In primary care, we need to be aware of how the condition might present, but also of the long-term care these children need to help prevent relapses and reduce the risk of serious complications.

Useful resources:

Websites (all resources are hyperlinked for ease of use in Red Whale Knowledge)

- Kidney Care UK

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