Nephrotic syndrome (idiopathic)

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Background

Definitions:

Nephrotic Syndrome (NS):

- Proteinuria
- Low plasma albumin (<25 g/l)
- Oedema
- Hyperlipidaemia is typically also present

Remission:

- No proteinuria for 3 consecutive days

Frequently Relapsing:

- 2 or more relapses within 6 months of the initial response, or
- 4 or more relapses within any 12 month period

Relapse:

- Proteinuria 3+ or greater for 3 consecutive days
- Oedema and proteinuria – this may be how a relapse presents if regular urine testing has not been done at home

Steroid Dependent:

- relapsing clinical course whilst on alternate day steroids or clinical relapse within 2-weeks of cessation of steroids

Classification:

Idiopathic (primary) NS:
- Steroid responsive
- Steroid resistant – no remission after 4 weeks of full-dose prednisolone

Secondary NS (post-streptococcal nephritis, HSP, SLE, MPGN)

Congenital NS – presents in first 3 months after birth

Assessment

Clinical Features:

Typical Features	Atypical Features
Age 1-10 years	<1yr, >10years
Normal BP	Elevated BP
Normal Creatinine	Elevated Creatinine
+/- Microscopic haematuria	Macroscopic Haematuria

Children who present with **typical** features are:
- generally responsive to steroids (>90%)
- started on steroids without the need for a renal biopsy

Children with **atypical** features:

- **should be discussed with ELCH nephrology department as soon as possible, before commencing any treatment**
- are more likely to be unresponsive to steroid treatment
- are likely to undergo renal biopsy, when the main histological types are
  - Minimal change
  - Focal segmental glomerulosclerosis (FSGS)
  - Mesangioproliferative glomerulonephritis

Investigations

	At presentation	**During hospital stay**
Height	Yes	
Weight	Yes	Twice daily
BP	Yes	4 hourly
Bloods:	• Renal, liver and bone profile • Full blood count • C3, C4 • Varicella zoster IgG titres • Measles IgG titres • NB if atypical features, discuss with ECH, and other investigations may be requested	• Blood tests do not normally need to be repeated if initially normal. • Albumin level alone does not usually guide treatment, so no need to repeat during initial admission.
Urine tests:	• Dip for protein, blood • Protein:creatinine ratio	Daily Once (initially)

During inpatient stay, **input-output monitoring of fluids and twice daily weights** are *essential.*

Management

When to discuss with or refer to ELCH:

- Atypical presentation
- Low C3 and/or C4
- Albumin infusion considered
- Poor urine output
- Renal dysfunction
- Unusual clinical course e.g. develops hypertension or macroscopic haematuria or complications
- Failure to achieve complete remission within 28 days of prednisolone treatment
- Marked steroid side effects regardless of dose
- Frequently relapsing NS

Which children require admission?

- Consider admission if first presentation
- Always admit if child is hypertensive, oedematous or has raised creatinine.
- Most children who have relapsed can be managed at home unless the above apply. Inform treating consultant that they have attended CED and follow up plans.

Treatment of initial presentation

Prednisolone

60 mg/m^2 orally daily, to a maximum daily dose of 60 mg, for 28 days irrespective of whether the child goes into remission before 28 days

- then **40** mg/m^2 orally on alternate days for 28 days
- then **30** mg/m^2 orally on alternate days for 14 days
- then **20** mg/m^2 orally on alternate days for 14 days
- then **10** mg/m^2 orally on alternate days for 14 days
- then **5** mg/m^2 orally on alternate days for 14 days
- Then stop

To minimise side effects give steroids in the morning.

$$\text{Body Surface Area } (m^2) = \sqrt{\frac{Height\,(cm) \times Weight\,(Kgs)}{3600}}$$

Children who are not in remission after 28 days of treatment with prednisolone 60 mg/m^2, at either initial presentation or after a relapse, should be discussed with ELCH nephrology department

Penicillin

Give whilst the child is nephrotic with oedema and low plasma albumin. Discontinue once in remission

Dose:
- 5 yrs old: 125 mg BD orally
- 5yrs and older: 250 mg BD orally

Ranitidine

Give during prednisolone treatment in order to reduce gastritis related symptoms. It can usually be discontinued once the prednisolone dose has reduced to 10 mg/m^2 on alternate days.

Dose:
- 2 mg/kg per dose BD orally (max dose = 150 mg BD).

Low Salt Diet

To help prevent excess thirst and fluid retention. Fluid restriction is only considered if the child continues to gain weight despite a low salt diet and is clinically euvolaemic.

Relapse management

If the child relapses, parents should inform their GP or RACH consultant.

Come straight to CED if the child:

- becomes unwell e.g. with abdominal pain or fever
- has worsening oedema
- has reduced urine output

Treatment with prednisolone can usually be commenced immediately at home.

NB. Duration of treatment is different from treatment of an initial presentation.

Prednisolone dose: 60 mg/m^2 orally daily, to a max daily dose of 60mg, until remission

- then 40 mg/m^2 orally on alternate days for 1 week
- then 30 mg/m^2 orally on alternate days for 1 week
- then 20 mg/m^2 orally on alternate days for 1 week
- then 10 mg/m^2 orally on alternate days for 1 week
- Then consider stopping steroids or
- continue small dose for longer period for those with frequent relapses

Other treatment:

- Follow initial presentation guidelines with regard to penicillin, ranitidine, low salt diet and hypertension management.

Management of subsequent clinical relapses is usually tailored for the individual child and should be discussed with their RACH Consultant Paediatrician or Consultant Paediatric Nephrologist at ELCH.

If child is discharged, CED treating clinician must notify consultant who is looking after the child that they have attended CED with a relapse and the follow up arrangements.

Steroid Dependent NS:

- Maintenance dose of alternate-day steroids is selected by knowing at what dose the child relapses, and above weaning schedule is stopped at a dose just above that dose.
- Dose required for this maintenance regimen varies patient to patient
- Aim is to keep the child on the lowest dose of maintenance steroids that keeps them relapse free.

20% Albumin infusion

<table>
<tr><td>Precautions:</td><td colspan="2">Use of 20% albumin is based on clinical features, not the level of plasma albumin
When being considered, contact ELCH to discuss.
Usually given in daytime hours only when more staff are available to monitor
Maximal expansion of the intravascular compartment may occur 2-3 hours following cessation of albumin infusion – careful observations need to continue after the end of infusion</td></tr>
<tr><td>Indications:</td><td>Hypovolaemia:
– cool fingers and toes
– poor urine output
– abdominal pain
– raised urea, raised Hb/Hct</td><td>Severe oedema:
– causing immobility
– scrotal swelling and ascites causing discomfort
– skin breakdown</td></tr>
<tr><td>Dose of 20% albumin</td><td colspan="2">Infuse 5ml/kg (1g/kg) over 4-6 hours

Consider furosemide IV at end of infusion, to drive diuresis:
– initial suggested dose 0.5mg/kg
– patients usually have normal renal function and are very sensitive to furosemide</td></tr>
<tr><td>Monitoring during 20% albumin infusion:</td><td colspan="2">Monitor oxygen saturation, pulse, blood pressure, respiratory rate every 30 minutes regularly during and for 2 hours post infusion.
Accurate fluid balance measurement essential
Beware of intravascular fluid overload due to fluid shift:
rising pulse, BP, respiratory rate; visible JVP
development of oxygen requirement
If overload develops:
Stop 20% albumin infusion
consider furosemide</td></tr>
</table>

Management of Nephrotic Syndrome complications

Hypovolaemia

- Common finding – clinical assessment can be very difficult.
- The following are recognised as markers, however the child may still be hypovolaemic in the absence of these:

Symptoms
- Abdominal pain
- Cool peripheries
- Reduced urine output

Signs
- Capillary refill time > 2 seconds
- Toe-core temperature gap >2°C
- Poor urine output
- Hypotension (<5th centile), and paradoxically hypertension (>95th centile) can both be features of hypovolaemia
- Persistent tachycardia

Investigations
- Low urinary sodium (can help to confirm intravascular volume depletion if clinically not obvious. <10mmol/L consistent with volume depletion)

Infections

- Increased risk due to loss of immunoglobulins in urine + treatment with steroids.
- Particularly encapsulated organisms, e.g. Strep. pneumoniae & H. influenzae, hence need for prophylactic penicillin V.
- Low threshold for commencing antibiotics.

Spontaneous bacterial peritonitis (SBP)

- Bacterial infection of ascitic fluid.
- Any child with NS presenting with abdominal pain and tenderness +/- fever should be commenced on IV antibiotics (amoxicillin, gentamicin & metronidazole as per protocol for peritonitis) and discussed with the Paediatric ID team.

Shock

- Uncommon in nephrotic syndrome
- Consider 10ml/kg 4.5% albumin solution as an alternative to 0.9% saline

Hypertension

- Majority of children with NS have normal BP.
- If hypertension present, discuss with ELCH prior to commencing treatment.

Clot Formation

- NS is a pro-coagulant state.
- Risk of spontaneous venous and arterial thromboses.
- Consider intravascular thrombosis as a cause of symptoms such as
  - altered behaviour or headaches / vomiting (intracranial thrombosis)
  - cough and breathlessness (pulmonary thrombo-embolism)
  - peripheral vascular changes suggesting DVT or arterial ischaemia
  - renal vein thrombosis (signs can include macroscopic haematuria, palpable kidney, loin tenderness, raised creatinine, hypertension)

Others:

Chicken pox exposure

- Patients on prednisolone and negative for varicella antibodies should be given VZIG if in contact with chicken pox
- VZIG is recommended if exposure to prednisolone is equal to or exceeds
  - 2mg/kg/day for a minimum of one week or
  - 1mg/kg/day for one month
- VZIG is recommended for lower doses of prednisolone than above if the child is also on other cytotoxic drugs or T-cell suppressants

Vaccination

- Avoid live vaccines whilst on steroids
- Aim to administer vaccine when steroids and/or other immunosuppressive drugs have been stopped for at least 12 weeks
- **Pneumococcal** recommended for all children with NS
  - routine pneumococcal vaccine (Prevnar 13) should be supplemented with Pneumovax 23 for over 2 year olds
- **Varicella** – consider in varicella negative children with frequent relapses.
- **Flu** vaccination – use Injection form, not nasal spray, if on immunosuppressive therapy

Discharge and follow up

Discharge checklist for parents

Ensure carer

- Is able to dip urine daily and record the urine test for protein
- Is able to recognise a relapse and who to contact
- Is provided with advice on steroids plus a steroid card.
- Is provided with advice regarding course of action if in contact with chicken pox or measles

- Understands the vaccine advice above.
- Is provided with adequate information about travelling – to seek advice before flying if in relapse and to take enough medication in case of relapse whilst away.

Further useful information for parents can be found on the Infokid website **www.infokid.org.uk**

Monitoring during follow up

For children on steroids, monitor:-

- BP
- height - including bone age and pubertal stage where appropriate
- weight - dietetic review where appropriate
- for glycosuria / HbA1c
- Ophthalmology review – at the discretion of the managing consultant