Whittington Health NHS

Nephrotic Syndrome in Childhood

Subject:	Childhood Nephrotic Syndrome
Policy Number	N/A
Ratified By:	Clinical Guidelines Committee
Date Ratified:	Original 2007, minor amendments March 2011,Feb 2013 and July 2017
Version:	4.0
Policy Executive Owner:	Clinical Director CYP ICSU
Designation of Author:	Dr M Jaswon, Dr J Stannett
Name of Assurance Committee:	Clinical Guidelines Committee
Date Issued:	August 2017
Review Date:	3 years hence
Target Audience:	Paediatricians
Key Words:	Nephrotic syndrome, Children

Version Control Sheet

Version	Date	Author	Status	Comment
1.0	June 2007	Dr. Mervyn Jaswon	Offline	Reviewed no change
2.0	March 2011	Dr. Mervyn Jaswon	Offline	Due for review. No change
3.0	Feb 2013	Dr. Mervyn Jaswon	Offline	Minor amendments
4.0	July 2017	Dr. Mervyn Jaswon	Current	Minor amendments

➢ Background/ introduction

Idiopathic nephrotic syndrome is the commonest glomerular disorder of childhood, with an incidence of 2 - 4 cases per 100,000 children in the UK. There is a greater prevalence among the Asian populations. The commonest age range for presentation is 1 - 6 years. There are four main types:

- minimal change disease (85%)
- mesangial proliferation (5%)
- focal segmental glomerulosclerosis (10%)
- secondary nephrotic syndrome (HSP, SLE)

Approximately 80% of cases respond to oral corticosteroid therapy ('steroid sensitive'). It is now accepted that this is the most important factor in determining future management and prognosis. 75-85% of these children will experience relapse and many will have frequent relapses. It has been shown that for an initial presentation of nephrotic syndrome, a more intense treatment regime produces fewer relapses. This guideline covers initial management of nephritic syndrome and also management of relapses.

➢ Definition of Nephrotic Syndrome

- Proteinuria ≥ 2+ on dipstick for three consecutive days or urine
- protein/creatinine ratio > 0.4g/mmol (normal range < 0.023)*
- Plasma Albumin < 25g/l
- Peripheral oedema
- +/- Hyperlipidaemia

***Some hospitals use urine albumin/creatinine ratio of >200mg/mmol.**

REMISSION:

- Proteinuria dipstick 1 + or less for three consecutive days (irrespective of loss of oedema)

RELAPSE:

- Having previously been in remission
- 2+ or more proteinuria for 3 consecutive days

➢ Initial Management

Examination

- Measure height, weight and blood pressure (BP). Calculate surface area.
- Admit all newly diagnosed cases of acute nephrotic syndrome.
- Daily weights and 4-hourly observations including blood pressure.
- Examine for signs of hypovolaemia (cap refill), infection, sites of oedema including pleural effusions & ascites.

Investigations

- Urinalysis/dipstick
- Urine for microscopy (looking for granular casts) and culture (microscopic haematuria in 20% of minimal change nephrotic syndrome)
- Spot urine protein: creatinine ratio > 0.4g/mmol
- Full blood count, urea & electrolytes, liver function tests
- Serum cholesterol and triglyceride levels (generally elevated)
- Complement levels (C3 & C4)
- Measles and varicella-zoster virus antibodies
- Blood cultures (if febrile)
- Antinuclear factor, anti-streptolysin O titres.

N.B Renal biopsy is not required for diagnosis in most children.

When to consider a renal biopsy:

- Onset < 1year or > 8years age
- Steroid resistance (failure to respond after 1 month of treatment)
- Persistent hypertension, macroscopic haematuria or low plasma C3
- Renal failure – persistent and not attributable to hypovolaemia
- Clinical evidence of systemic disease

➢ Clinical management

INITIAL EPISODE:

General Management:

- Place child on strict fluid intake/output chart.
- Low salt & high protein diet.

Complications & their management:

Hypovolaemia

- Non-specific symptoms including abdominal pain and vomiting. (they may not look dehydrated due to being oedematous).
- Check haematocrit (>0.45) and capillary refill (>2sec)
- Give 4.5% Human albumin 10-20ml/kg IV over 1 hour.
- Monitor urine output.
- If poor urine output, may need to repeat albumin infusion with use of frusemide.
- Check urinary sodium

Diuretics

- May be used in the following situations
- If oedema is symptomatic eg painful scrotal swelling and of moderate degree then oral frusemide may be given (1-2mg/kg), having ascertained that child is not hypovolaemic (see previous paragraph)
- Following albumin infusion for hypovolaemia (4.5%) or during infusion of 20% albumin for intractable oedema

Sepsis

- At risk of pneumococcal sepsis
- Penicillin V (or clarithromycin if allergic)

Severe oedema & ascites

- Administration of 20% human albumin 5ml/kg over 4 hours, with frusemide 1 mg/kg half way through, in normovolaemic state.

Thrombosis

Specific Management:

- Prednisolone* (single morning dose) 60mg/m2/day (equivalent dose 2mg/kg/day with max daily dose 80mg) for 4 weeks followed by (if in remission) prolonged tapering (see below)**
- IV Methylpred' if unable to tolerate oral medication give iv methylpred', once daily, at 4/5th oral prednisolone dose

  i.e. methylpred' 4mg = prednisolone 5mg

  methylpred' 28mg = prednisolone 35mg
- Penicillin V (or clarithromycin if allergic) e.g. 1 - 6 years age 125mg BD or >6years 250mg BD until remission.

*** Give ranitidine if on high dose steroids**

****Calculations based on pre-morbid weight if known or 'ideal weight for height'.**

Table 1: Reducing regimen at presentation

Surface Area/ m2	**0.4 - 0.45**	**0.46 - 0.54**	**0.55 - 0.62**	**0.63 - 0.7**	**0.71 - 0.79**	**0.8 - 0.87**	**0.88 - 0.95**	**>0.96**
Week 1- 4 (60mg/m2/day)	25	30	35	40	45	50	55	60
Week 5 - 6 (60mg/m2/alt days)	25	30	35	40	45	50	55	60
Week 7 - 8 (50mg/m2/alt days)	20	25	30	35	40	40	45	50
Week 9 - 10 (40mg/m2/alt days)	15	20	25	25	30	35	35	40

Week 11 - 12 (30mg/m2/alt days)	12.5	15	20	20	25	25	30	30
Week 13 - 14 (20mg/m2/alt days)	10	10	12.5	15	15	15	20	20
Week 15 -16	5	5	7.5	7.5	10	10	10	10
Week 17 (discontinue)	0	0	0	0	0	0	0	0

RELAPSE:

- Give prednisolone & penicillin V if peripheral oedema only (same dosages as for initial management)
- Once achieved remission (i.e. 3 days of < 2+ proteinuria), use following tapering regimen:

Table 2 - Relapse Regimen for first 2 relapses

Surface Area	**0.4-0.45**	**046-0.54**	**0.55-0.62**	**0.63-0.7**	**0.71-0.79**	**0.8-0.87**	**0.88-0.95**	**>0.96**
Initial Dose (60mg/m2/day)	25	30	35	40	45	50	55	60
Remission Week 1 (50mg/m2/day)	22.5	25	30	35	40	45	50	50
Week 2 (40mg/m2/day)	20	20	25	30	30	35	40	40
Week 3 (30mg/m2/day)	15	15	20	20	25	25	30	30
Week 4 (20mg/m2/day)	10	10	12.5	15	15	17.5	20	20
Week 5 (1 0mg/m2/day)	5	5	5	7.5	7.5	7.5	10	10

Week 6 **(5mg/m2/day)**	2.5	2.5	2.5	5	5	5	5	5

FREQUENT RELAPSES:

- Responds to prednisolone but has had 2 relapses within 6 months of the initial response OR 4 or more relapses in a 12-month period.
- Give prednisolone 60mg/m2/day (max daily dose 60mg) until remission followed by tapering (same as above relapse regimen until week 5)
- Week 6 onwards – maintenance dose of 10-30mg/m2 alternate days.
- Remain on maintenance dose for at least 3 - 6 months before tapering or discontinuing.

STEROID DEPENDENCE:

Defined as two consecutive relapses during prednisolone therapy or within 14 days of completing therapy.

Before commencing any further treatment:

- Attempt to achieve remission with prednisolone

Second Line Treatment

- Levamizole 2.5mg/kg/alt day initially for 12 months with prolonged tapering of Prednisolone (Table 1).

-Must check full blood count 2 weeks after treatment, then monthly for next 3 months and thereafter 3 - monthly.

- Discontinue if leucopenia or rash develops.

- If failed levamizole treatment consider cyclophosphamide.
- If steroid dependency following cyclophosphamide treatment then consider ciclosporin (outside the scope of this guideline)

➢ Contacts

- Dr Mervyn Jaswon ext 5315/ via switchboard
- SpR/Consultant on-call (out of hours)

➢ References (evidence upon which the guideline is based)

1. Childhood Nephrotic Syndrome Guidelines GOSH; Dec 2005
2. Behrman, Kliegman, Jenson (2004) Nelson Textbook of Paediatrics 17th ed; 1753-1 757
3. British Medical Association & Royal Pharmaceutical Society of Great Britain (2005) British National Formulary for Children; pp404
4. Abeyagunawardena et al (2002) Immunosuppressive therapy of Childhood Idiopathic Nephrotic Syndrome, Expert Opinion Pharmacotherapy; 3(5): 513-519
5. Levamizole for corticosteroid dependent nephritic syndrome in children. (1991). The Lancet. 1555-1 556.

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	

		Yes/No	Comments
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	**Yes/No**	**Comments**
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	

	Title of document being reviewed:	Yes/No	Comments
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and Effectiveness**		
	Are there measurable standards or KPIs to support the monitoring of compliance with and effectiveness of the document?	Yes	
	Is there a plan to review or audit compliance with the document?	Yes	
10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			
Relevant Committee Approval			

The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name		Date	
Name of Committee		Name & role of Committee Chair	
Signature			

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	Who will lead on this aspect of monitoring? Name the lead and what is the role of the multidisciplinary team or others if any.	What tool will be used to monitor/check/observe/Asses s/inspect/ authenticate that everything is working according to this key element from the approved policy?	How often is the need to monitor each element? How often is the need complete a report ? How often is the need to share the report?	What committee will the completed report go to?
Element to be monitored	**Lead**	**Tool**	**Frequency**	**Reporting arrangements**