

EVALUATION & MANAGEMENT OF PROTEINURIA AND NEPHROTIC SYNDROME IN CHILDREN

BY:

PROF. ABDULLAH AL SALLOUM

Consultant Paediatric Nephrologist

Paediatric Department

Proteinuria

- Associated with progressive renal disease
- Involved in the mechanism of renal injury

Clinical Testing for Proteinuria

- Urinary dipstick
 - Screening test
 - Color reaction between urinary albumin and tetrabromophenol blue
 - Trace \cong 15 mg/dl
 - 1 + \cong 30 mg/dl
 - 2 + \cong 100 mg/dl
 - 3 + \cong 300 mg/dl
 - 4 + \geq 2000 mg/dl

Urinary dipstick

False-negative

Diluted urine

False-positive

Alkaline urine (PH>8.0)

Concentrated urine (sp.gravity>1:025)

Antiseptic contamination

(Chlorhexidine, benzalkonium chloride)

After intravenous radiograph contrast

Quantitative estimate of proteinuria

- 24-hour urine collections
- Urinary protein/creatinine (pr/cr) ratio
 - Spot urine specimen
 - First morning specimen
 - Normal values
 - <0.2 mg protein/mg creatinine
in children > 2 years
 - <0.5 mg protein/1 mg creatinine
in children 6-24 months old

Protein Handling by the Kidneys in Normal Children

- Normal rate of protein excretion

<4mg/m²/hr

<100mg/m²/day

- 50% Tamm-Horsfall protein
- 30% Albumin
- 20% other protein

- Restricted filtration of large Proteins (albumin & Immunoglobulin)

Proximal tubules reabsorb most of LMW protein (insulin, B2 microglobulin)

Protein Handling in Renal Disorders

Excess urinary protein losses

1. Increase permeability of the glomeruli (glomerular)
2. Decrease reabsorption of LMW proteins by the renal tubules (tubular)

Types of proteinuria

1. Transient

- Fever
- Stress
- Dehydration
- Exercise

2. Orthostatic proteinuria

- Excess urine protein in upright position but normal during recumbency
- School age
- $<1 \text{ gm/m}^2/\text{day}$

3. Persistent proteinuria:

Proteinuria of ≥ 1 + by dipstick in multiple occasions

Association Between Proteinuria and Progressive Renal Damage

- Persistent proteinuria should be viewed as a marker of renal disease and also as a cause of progressive renal injury.

Evaluating Children with Proteinuria

[A] First stage

- Complete history and physical examination (BP)
- Complete urinalysis
- Urindipstick before going to bed and after arise
- Blood level of Albumin, creatinine, cholesterol, electrolyte

[B] Second stage

- Renal ultrasonography
- Measurement of serum C3, C4, complement
- Antinuclear antibody
- Serology for hepatitis B, C, \pm HIV

Evaluation and Treatment of Patients with NS

- Definition
- Heavy proteinuria, hypoalbuminemia
Hypercholesterolemia and edema
- Prevalence 2-3 cases per 100,000 children
- The majority will have steroid responsive
MCNS

Pretreatment Renal Biopsy in NS

- Infantile NS
- Adolescence
- Persistent hematuria
- Hypertension
- Depressed serum complement
- Reduced renal function

Clinical Problems Associated with Children NS

[A] Edema

- Gravity dependent
- Periorbital in the early morning hours then generalized
- Severe edema present as ascites, pleural effusions, scrotal or vulvar edema, skin breakdown.



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[C] Infections

1. Varicella

- Varicella antibody should be obtained
- Varicella – zoster immunoglobulin within 72 hours of exposure
- Steroid should be tapered to 1 mg/kg/day
- Acyclovir or valacyclovir if varicella does develop

2. Other infection

- Cellulitis
- 1° peritonitis
- The organisms usually
 - Pneumococcus
 - E-coli

Immunization in N.S.

- Live viral vaccines should not be given if patient on high dose of steroids
- Pneumococcal vaccine is recommended to all NS (off steroids)
- Varicella vaccine (varivax) in 2 doses regimen is safe and efficacious
- Antibodies to vaccines may fall during relapses (still contravesial)

[D] Hyperlipidemia

- Transient and severe hypercholesterolemia during relapses
- Persist in treatment-resistant NS
- Atherosclerosis in young NS
- Dietary modification : limited benefit
- Cholestyramine is approved in NS

Approaches to treatment of NS

[A] Prednisone/prednisolone

Mainstay of treatment of NS

Typical protocol:

- 2 mg/kg/day (60mg/m²/day)
- (4+4 wks treatment)
- 4 wks daily steroid
- 4 wks every other day
- Recently: 6+6 weeks induce a higher rate of long remissions than the standard (4+4)

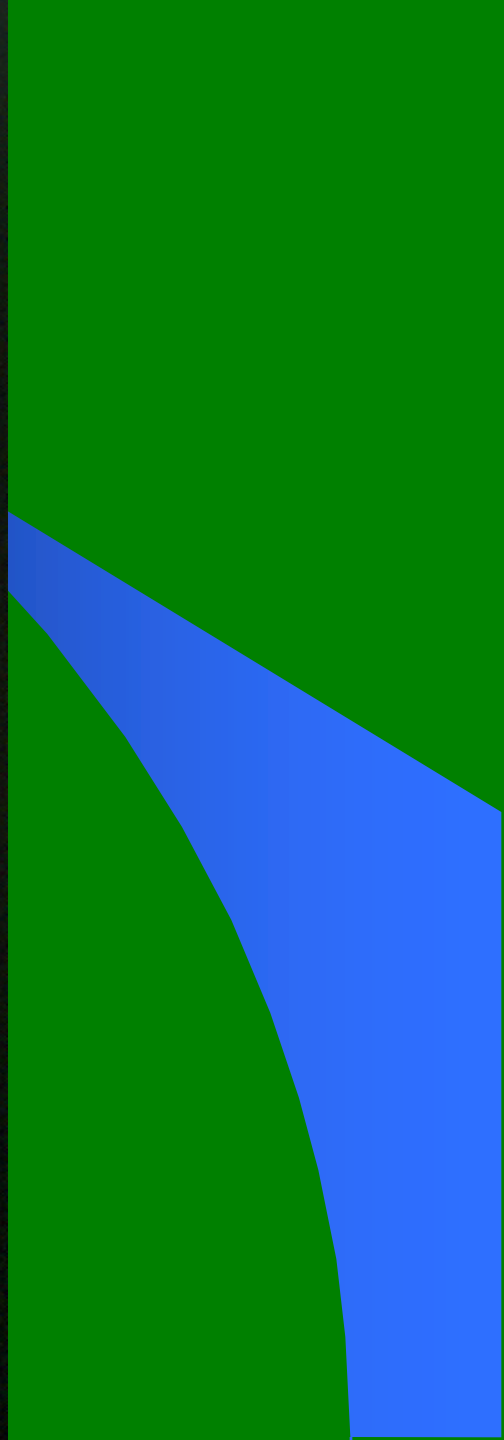
Treatment of Relapses of NS

- 60-80% of patients will relapse
- Prednisolone 2mg/kg/day until the patient is free of proteinuria for 3 days then 4-6 wks of every other day treatment.

Side effects of Glucocorticoids

(Must be discussed with the family)

- Cushingoid habitus
- Ravenous appetite
- Behavioral and psychological changes (mood liability)
- Gastric irritation (including ulcer)
- Fluid retention
- Hypertension
- Steroid-induced bone disease
- (avascular necrosis, bone demineralization)
- Decreased immune function
- Growth retardation
- Night sweats
- Cataracts
- Pseudotumor cerebri
- Steroid-related diabetes





[B] IV Pulse Steroids

- May give success in steroid-resistant NS
- High dose IV methylprednisolone
30 mg/kg (max 1gm)
- To be given every other day for 6 doses
- To continue in tapering regiment for period up to 18 months.
- Side Effects
 - Hypertension
 - Arrhythmias

[C] Cytotoxic Drugs

1. Cyclophosphamide

Over 12 weeks

Total cumulative dose 170 mg/kg

Side Effects

Bone marrow suppressions

Oligospermia, azoospermia and ovarium fibrosis

(If given close to puberty)

Hemorrhagic cystitis

Risk of malignancy

2. Chlorambucil

May cause seizure

[D] Cyclosporin A

- Steroid dependent or resistant NS
- To be given after renal biopsy
- Relapses high after withdrawal
- Side Effects
 - Hypertension
 - Nephrotoxicity
 - Hyperkalemia
 - Hypomagnesemia
 - Hypertrichosis
 - Gingival hyperplasia

[E] Levamisole

- Weak steroid sparing drug
- Long term use
- Side Effects

Neutropenia

Rash

Gastrointestinal disturbances

Seizures

Other Practical Aspects of the Management of NS

- Fluid intake should be limited to double of insensible water loss in severely edematous NS
- Combined diuretics and IV albumin can be given in severe edema
- Diuretics should not be given in mild edema
- ACE: should not be given in the initial course of prednisolone because of the risk of hypotension and thrombosis in the diuretic phase
- ACE: can be given to steroid-resistant NS
- Schooling, activities, diet should be individualized

