Pediatric Nephrotic Syndrome

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National Kidney Foundation

Pediatric Nephrotic Syndrome: Basic Information

- Nephrotic syndrome (NS) reflects glomerular dysfunction causing proteinuria without compromising GFR
- Occurs at all ages but is most prevalent in children between the ages 1.5-6 years
- It affects more boys than girls, 2:1 ratio
- Most studies put the incidence at 2-7 per 100,000 population

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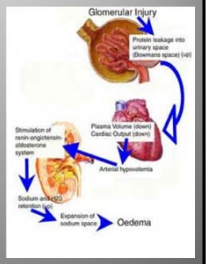
Signs and Symptoms

- Proteinuria
  - Up/c > 2 (g/g) in first morning urine
  - >1g/m^2 per 24 hours in time collection
- Hypoalbuminemia: <3 g/dL
- Hypercholesterolemia
- Edema (underfill [figure] vs. overfill)
- Hypercoagulable state
  - Thromboembolic events occur at most 10% of the rate in adults with NS



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Primary NS: Differential Diagnosis

- Minimal Change Nephrotic Syndrome (MCNS)
- Focal Segmental Glomerulosclerosis (FSGS)
- Membranoproliferative Glomerulonephritis (MGPN)
- Congenital nephrotic syndrome (Cong NS)

Membranous nephropathy, both primary and secondary, is very rare in pediatric patients, i.e. <2% of biopsies for proteinuria/NS (Chen A et al 2007)

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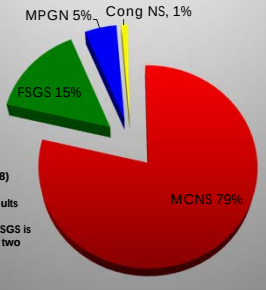
Primary NS: Percentage of underlying diseases



Adolescents (13-18) have disease comparable to adults

The incidence of FSGS is rising over the last two decades

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Secondary Causes

- SLE
- Infection
  - HIV
  - Hepatitis B and C
  - Malaria
  - Syphilis
- Obesity – generally lower proteinuria and less edema
- Drug exposure
  - NSAID
- Henoch Schonlein Purpura
- Malignancy (Rare in children)

***Diabetes* is not a cause of NS in children due to long latency**

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MCNS *versus* FSGS: Diagnosis

	Potential biomarkers					
	Kidney Biopsy		Serum	Urine		
	Galectin 1	Synaptopodin	IGFBP-1	NGAL	Nitrite	CD80
MCNS	↓	Normal	↓	Normal	↑	↑
FSGS	↑	↓	↑	↓	Normal	Normal

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MCNS *versus* FSGS: Clinical aspects

	Therapy		Prognosis
	Steroid Responsive	CNI Responsive	
MCNS	>90%	>85% Frequent relapses when discontinued	Usually resolves by puberty Persists into young adulthood in up to 20% of cases High risk of osteoporosis, hypertension, cataracts, and sperm abnormalities in pts with FR/SD or persistent disease
FSGS	25-30%	40%	1/3 of patients achieve complete remission 1/3 will have persistent proteinuria. 1/3 progress to ESKD over 5-10 yr

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Genetic causes of FSGS

Gene	Discovered	Recessive (R)/Dominant (D)	Pediatric (P)/ Adult (A)
Nephrin	1998	R	P
LMX1B	1998	D	A
WT-1	1999	D	P
Podocin	2000	R	P
ACTN4	2000	D	A
CD2AP	2000	R	P
TRPC6	2005	D	A
PLCE1	2006	R	P
INF	2010	D	A
COQ6	2011	R	P
MYO1E	2011	R	P
ARHGAP24	2011	D	A

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Laboratory Assessment

- Urinalysis: High levels of protein will be found in the urine
  - Quantitative for initial evaluation
  - Dipstick for extended monitoring
- Blood tests
  - Comprehensive metabolic profile
  - C_3
  - All other tests contingent on clinical scenario
- Kidney Biopsy
  - Congenital NS: may be supplanted by genetics
    - Over 80% of cases of NS in first yr of life have genetic mutation
  - Low C_3
  - Atypical clinical features
  - Failure to respond to steroids

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General Management

- Edema
  - Salt Restriction
  - Diuretics
- Proteinuria
  - ACEI/ARB
  - No benefit of protein restriction in children
- Infection: Peritonitis is most common life threatening serious bacterial infection
  - Immunization: Pneumococcal vaccine (Prevnar®, Pneumovax®), Flu Vaccine
  - Prophylactic antibiotics
- Hyperlipidemia
  - Statins
- Bone
  - Calcium
  - Vitamin D, if prolonged steroid usage

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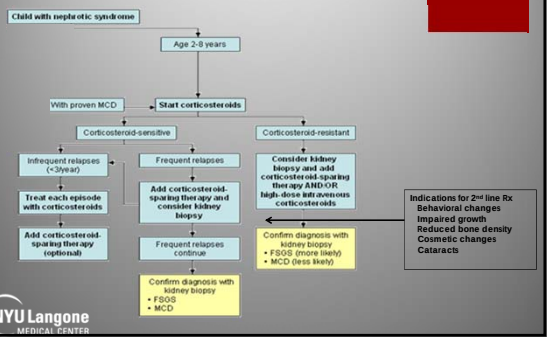
MCNS



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FSGS

- Prednisone
- Cytotoxic agents ineffective
- Calcineurin Inhibitors only agents evaluated in controlled trials
- No benefit of mycophenolate mofetil combined with dexamethasone (FSGS CT, KI 2011)
- Need for novel approaches

MPGN

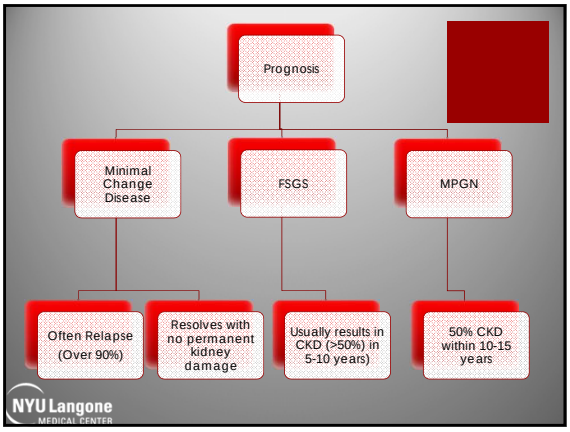
- Alternate day steroids
- MMF
- Eculizumab
  - Under study
  - Impact of serological markers of activation of the alternative pathway of complement

Congenital NS

- Intensive medical management
- Immunosuppressive generally ineffective
- Specific therapy in select genetic causes, e.g. CNI in PLCE1, CoQ treatment
- Bilateral Nephrectomy
- Transplant is usually required

Management of Secondary NS

- SLE: Collaboration with rheumatology
- Infectious:
  - Antibiotics
  - Antivirals for Hepatitis B and C
  - Anti-retroviral therapy for HIV
- Weight reduction if appropriate
- Drugs:
  - Discontinue
- HSP:
  - Steroids plus MMF



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