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.

Signs and Symptoms

- Proteinuria:
  - Up/c > 2 (g/g) in first morning urine
  - >3g/m² per 24 hours in time collection
- Hypoalbuminemia: <3 g/dL
- Hypercholesterolemia
- Edema (underfill vs. overfill)
- Hypercoagulable state
- Thromboembolic events occur at most 10% of the rate in adults with NS.

Primary NS: Differential Diagnosis

- Minimal Change Nephrotic Syndrome (MCNS)
- Focal Segmental Glomerulosclerosis (FSGS)
- Membranoproliferative Glomerulonephritis (MGN)
- 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).

Primary NS: Percentage of underlying diseases

- MCNS 79%
- FSGS 15%
- MGN 5%
- Cong NS, 1%

Secondary Causes

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

Diabetes is not a cause of NS in children due to long latency.
**MCNS versus FSGS: Diagnosis**

<table>
<thead>
<tr>
<th>Kidney Biopsy</th>
<th>Serum</th>
<th>NGAL</th>
<th>Nitrite</th>
<th>CD80</th>
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<tbody>
<tr>
<td>MCNS</td>
<td>Normal</td>
<td>Normal</td>
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<td>Normal</td>
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<tr>
<td>FSGS</td>
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</tbody>
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**Potential Biomarkers**
- Galectin 1
- Synaptopodin
- IGFBP-1
- NGAL
- Nitrite
- CD80

**Genetic causes of FSGS**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Discovered</th>
<th>Recurrent (R)/Dominant (D)</th>
<th>Pedigree (P)/Adult (A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephrin</td>
<td>1998</td>
<td>R</td>
<td>P</td>
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<tr>
<td>LMX1B</td>
<td>1998</td>
<td>D</td>
<td>A</td>
</tr>
<tr>
<td>WT-1</td>
<td>1999</td>
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<tr>
<td>Podocin</td>
<td>2000</td>
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<td>ACRB4</td>
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<td>P</td>
</tr>
<tr>
<td>TRPC-6</td>
<td>2005</td>
<td>D</td>
<td>A</td>
</tr>
<tr>
<td>PLCe1</td>
<td>2006</td>
<td>R</td>
<td>P</td>
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<tr>
<td>INF</td>
<td>2010</td>
<td>D</td>
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<tr>
<td>COQ6</td>
<td>2011</td>
<td>R</td>
<td>P</td>
</tr>
<tr>
<td>MYO1E</td>
<td>2011</td>
<td>R</td>
<td>P</td>
</tr>
<tr>
<td>ARKGAP24</td>
<td>2011</td>
<td>D</td>
<td>A</td>
</tr>
</tbody>
</table>

**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
- C3
- 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 C3
- Atypical clinical features
- Failure to respond to steroids
- Nephrotic syndrome
- ACEI/ARB
- No benefit of protein restriction in children
- Infection: Peritonitis is most common life-threatening serious bacterial infection
- Immunosuppression: Pneumococcal vaccine (Prevnar®, Pneumovax®), Flu Vaccine
- Antihypertensive: ACEI/ARB
- Hyperlipidemia: Statins
- Bone: Calcium, Vitamin D, if prolonged steroid usage

**MCNS**

**Indications for 2nd line Rx**
- Behavioral changes
- Impaired growth
- Reduced bone density
- Cosmetic changes
- Cataracts
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 PKD, CoQ treatment
- Bilateral Nephrectomy
- Transplant is usually required

Management of Secondary NS
- SLE: Collaboration with rheumatology
- Infectious:
  - Antibiotics
  - Antivirals for Hepatitis B and C
  - Antiretroviral therapy for HIV
  - Weight reduction if appropriate
- Drugs:
  - Discontinue
  - HSP: Steroids plus MMF

Prognosis
- Minimal Change Disease
  - Often Relapse (Over 90%)
  - Resolves with no permanent kidney damage
  - Usually results in CKD (50%) in 5-20 years
  - 50% CKD within 10-15 years

- FSGS
- MPGN

References