Evaluation of proteinuria in a child

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LEARNING OBJECTIVES:
∙ Define proteinuria.
∙ Classify proteinuria.
∙ Define nephrotic syndrome.
∙ Recognize the clinical presentation.
∙ Discuss the Causes.
∙ Discuss the investigation.
∙ List the complications.
Proteinuria

- **Normal range**: $\Rightarrow 100 \text{mg/m}^2/\text{day}$ ($150 \text{mg/day}$), $< 4 \text{mg/m}^2/\text{hour}$
- **Proteinuria**: $> 4 \text{mg/m}^2/\text{hour}$

- **Nephrotic range**: $\Rightarrow > 1 \text{gm/m}^2/\text{day}$
  - $> 40 \text{mg/m}^2/\text{hour}$

- **Spot urine for albumin/creatinine ratio (mg:mg)**
  - **Normal**: $< 0.2$ ($0.5$ if $< 2\text{yr}$) g/g
  - **Nephrotic**: $\Rightarrow 2 \text{g/g}$
Proteinuria

- Dipstick test:
  - negative, trace
  - 1+ (closest to 30 mg/dL)
  - 2+ (closest to 100 mg/dL)
  - 3+ (closest to 300 mg/dL)
  - 4+ (greater than 2,000 mg/dL)
Conditions Particularly Associated with Proteinuria

- NON-PATHOLOGIC PROTEINURIA
- PATHOLOGIC PROTEINURIA
NON-PATHOLOGIC PROTEINURIA

- Excessive protein excretion, not as result of a disease state
- Generally less than 1,000 mg/24 hr (1.00 g/24 hr) and is never associated with edema.

Postural (Orthostatic) Proteinuria: Children with this disorder excrete normal or slightly increased amounts of protein in the supine position. In the upright position, the amount of protein in the urine may increase 10-fold or more

Febrile Proteinuria: does not exceed +2 on the dipstick

Exercise Proteinuria: does not exceed +2 on the dipstick
PATHOLOGIC PROTEINURIA

Tubular Proteinuria:

- Injury to the proximal tubules results in diminished re-absorptive capacity and the loss of these low molecular weight proteins in the urine; rarely exceeds 1 g/24 hr; not associated with edema.

- May be associated with other defects of proximal tubular function, such as glucosuria, phosphaturia, bicarbonate wasting, and aminoaciduria (FANCONI)
Glomerular Proteinuria

- Increased permeability of the glomerular capillary wall
- **Selective** (loss of plasma proteins of low molecular weight protein including albumin), primarily in minimal-change nephrosis, or **nonselective** (loss of albumin and of larger molecular weight proteins such as IgG)
- Nephrotic range (40mg/m²/hour), non-nephrotic range (4mg/kg/hour)
PERSISTENT ASYMPTOMATIC PROTEINURIA

- Persists for 3 mo
- The amount less than 2 g/24 hr; it is never associated with edema.
- **Causes**: postural proteinuria, membranous and membrano-proliferative glomerulonephritis, pyelonephritis, hereditary nephritis, developmental anomalies, and "benign" proteinuria.
- **Investigation**: urine culture; measurement of creatinine clearance, 24-hr protein excretion, serum albumin, C3 complement levels, and renal ultrasound
Indications for Renal Biopsy

Persistent asymptomatic proteinuria in excess of 1,000 mg/24 hr (1 g/24 hr) or the development of hematuria, hypertension, or diminished renal function.
Approach to proteinuria

- History and examination
- Confirm persistent proteinuria
- 24 hours for protein
- Fractional urine collection (orthostatic test)
- U/E, creatinine clearance (GFR), serum protein and albumin
- Strept. Serology, C3, ANA
- US and further imaging
- ? Renal biopsy
Nephrotic syndrome

Definition

It is a clinical and laboratory syndrome characterized by massive proteinuria, which lead to hypoproteinemia (hypo-albuminemia), hyperlipidemia and pitting edema.
Nephrotic Criteria:

* Massive proteinuria:
  - qualitative proteinuria: 3+ or 4+,
  - quantitative proteinuria: more than 40 mg/m2/hr in children (selective).

* Hypo-proteinemia:
  - total plasma proteins < 5.5g/dl and serum albumin: < 2.5g/dl.

* Hyperlipidemia:
  - serum cholesterol: > 5.7mmol/L 250mg/dl

* Edema: pitting edema in different degree
Types

Idiopathic 90%

- Minimal change (85%)
- Mesangial proliferation (5%) and membranous nephropathy.
- Focal segmental glomerulosclerosis (10%) – Secondary 10%
  - NS resulted from systemic diseases, such as anaphylactoid purpura, systemic lupus erythematosus, HBV infection.
Nephrotic Syndrome
Minimal Change NS

- More common in boys
- 2-10 years old
- Oedema "pitting"
- Weight gain
- Ascites and/or pleural effusions
- Declining urine output
Pathophysiology

- ↑ glomerular permeability to protein
- Edema
- ↑ lipids
How many pathological types causes nephrotic syndrome?

Figure 35-10 Pathophysiology of the nephrotic syndrome.
Diagnosis

- Urine analysis…protein > 2+
- 24 hours protein excretion >40mg/m2/day
- Urine albumin/creatinine (>2 g/g)
- Serum Albumin < 25 gm/l 2.5g/dl
- Increased cholesterol and triglycerides
- Other investigations: complements (C3 &C4), U&E, lipids, HepBSAg, ANA & ASO titer.
Nephritis
- Frank haematuria
- Hypertension
- Low complement
- Non-nephrotic range proteinuria

Nephrotic
- None or microscopic haematuria (20%)
- Normal BP
- Normal complement
- Nephrotic range proteinuria
Complications

- Hypovolaemia
- Infection: peritonitis (pneumococci)
- Thrombosis
Management

- Edema ⇒ no added salt diet, IV albumin and diuretics if severe (physical discomfort)
- Hypovolaemia ⇒ IV albumin
- **STEROID:** Prednisolone 60mg/m²/day (Max. 60 mg) or 2mg/kg/day (divided doses) for 6 weeks followed by 40mg/m² (max. 40 mg) on alternate days for 6 weeks. Then taper the dose by 10 mg/m² on alternate days every 8 days.
- Excellent prognosis → 90% response to steroid
- If no response after 4 weeks → biopsy
Management

- If frequent relapsers (2 or more in 6 months) or steroid dependent... consider:
  - Levamisole
  - Cyclophosphamide
  - Cyclosporin / Tacrolimus

- If steroid resistant → biopsy and referral to pediatric nephrology
What is diagnosis
THANK YOU