Case 1: a 3 years old boy presents with puffy eyes (not responding to anti-histamine), abdominal swelling and urine dipstick shows (+++) protein.

- What is your diagnosis?
  ✓ **Nephrotic syndrome.** The criteria which are needed to diagnose nephrotic syndrome are:
    - Heavy proteinuria (++) on dipstick or protein:creatinine ratio > 200 mg/mmol.
    - Hypoalbuminemia < 25 g/L
    - Edema (especially peri-orbital).
    - Hypercholesterolemia.

- What is the pathophysiology?
  ✓ The basic physiologic defect is a loss of the normal charge and size selective glomerular barrier to the filtration of plasma proteins.
  ✓ Excessive urinary protein losses lead to the hypoalbuminemia of nephrotic syndrome.
  ✓ Hypercholesterolemia is a consequence of hypoalbuminemia.

- Epidemiology:
  ✓ Male:female ratio is 2:1
  ✓ Commonly between ages of 2-5 years.
  ✓ More common in southeast Asia and among Arabs.

- Causes:
  ✓ **Primary nephrotic syndrome:** minimal change disease (90% of all childhood cases), Focal Segmental Glomerulosclerosis (FSGS), Membranoproliferative Glomerulonephritis (MPGN) and membranous nephropathy.
  ✓ **Secondary nephrotic syndrome:** SLE, infections, obesity, drug exposure, Henoch-Schonlein purpura and malignancy (which is rare in children).

- Investigations which you must order are:
  ✓ CBC.
  ✓ Renal function test (urea and creatinine).
  ✓ Liver Function Test (for albumin).
  ✓ Serum electrolytes.
  ✓ Urinalysis and protein:creatinine ratio (done in the morning).
  ✓ Complement C3 and C4.
  ✓ ANA and anti-dsDNA
  ✓ HBV, HCV
**Treatment:**
- **Corticosteroids** (e.g. prednisolone). Adverse effects of steroids include: osteoporosis and growth retardation, immunosupression, diabetes mellitus, hypertension, cushingoid appearance, abdominal striae, acne and hirsutism.
  - *When do you expect to see a response?*
    - Within 2 weeks there will be negative proteinuria.
    - If there is no response after 1 month of treatment, 3 daily pulses of IV methylprednisolone will be given.
    - If still there is no response, a biopsy is indicated.
  - *Steroid-dependent nephrotic syndrome:* means that patients relapse whenever steroids are stopped.
- **Salt restriction.**
- **Gentle fluid restriction.**
- **Diuretics** (if severe edema is present).

**Complications of nephrotic syndrome:**
- Hypovolemia (due to shifting of fluids).
- Immunodeficiency.
- Pro-thrombotic state (due to loss of antithrombin III in the urine).

- **Acute glomerulonephritis:**
  - **It is characterized by:** hematuria, proteinuria, hypertension and renal impairment (↑ urea and creatinine).
  - **Etiology:** deposition of immune-complexes in glomeruli.
  - **Clinical classification:**
    - Acute and sudden.
    - Chronic.
    - Recurrent.
    - Rapidly progressive.
  - **Histopathology classification:**
    - Post-streptococcal glomerulonephritis (representing 80% of cases in childhood):
      - Commonly preceded by pharyngitis or skin infection with group A β-hemolytic streptococci 1-2 weeks before.
      - Clinical manifestations: cola-colored urine, oliguria, proteinuria, hypertension and edema.
      - Investigations: ↑ASO titer, ↑ blood pressure, urinalysis showing RBC casts, throat swab is obtained for culture, ↓C3 (which will return to normal value after 6-8 weeks; if it remains decreased → your differential diagnosis is SLE or MPGN).
      - Treatment: diuretics, salt and water restriction and antibiotics (controversial).
    - Alport syndrome.
    - IgA nephropathy (more common in adolescents).
  - **Indications for biopsy for any glomerulonephritis:**
    - Rapidly Progressive Glomerulonephritis (RPGN).
    - Abnormal creatinine at 6 weeks.
    - ↓C3 for more than 3 months.
    - Proteinuria for more than 6 months.