- **What are the characteristics of nephrotic syndrome?**
  - Proteinuria (> 3.5 g/day, frothy urine).
  - Hypoproteinemia (< 3 g/dL).
  - Edema.
  - Fatty casts in the urine (image-1)
  - Hypelipidemia.
  Notice that nephritic syndrome is also associated with increased risk of infection and a hypercoagulable state (due to AT III loss in urine).

- **What are the causes of nephrotic syndrome?**
  - **Primary causes:**
    - Focal segmental glomerulosclerosis.
    - Membranous nephropathy.
    - Minimal change disease.
    - Membranoproliferative glomerulonephritis.
  - **Secondary causes:**
    - Diabetes mellitus.
    - Systemic Lupus Erythematosus (SLE).
    - Amyloidosis.

- **What are the glomerular barriers which do not allow blood proteins to enter urine (image-2)?**
  - Endothelial cells with fenestrations.
  - Glomerular Basement Membrane (GBM).
  - Podocytes foot processes.

- **Minimal change disease (lipoid nephrosis):**
  - It is the major cause of nephritic syndrome in children.
  - **Light microscopy:** normal glomeruli – image (3) (lipid may be seen in PCT cells).
  - **Immunofluorescence:** negative.
  - **Electron microscopy:** effacement of foot processes (image-4).

  - **This condition is triggered by:**
    - Recent infection.
    - Immunization.
    - Immune stimulus.

  - It is associated with Hodgkin lymphoma.
  - Excellent response to corticosteroids.
Membranous nephropathy:
- It is the most common cause of primary nephritic syndrome in 
  **Caucasian adults**.
- **It is characterized by the following:**
  - Non-selective proteinuria.
  - Microscopic hematuria.
  - Hypertension.
- **Light microscopy**: diffuse capillary and GBM thickening (image-5).
- **Immunofluorescence**: granular as a result of immune complex deposition (composed of IgG and C3) – image (6).
- **Electron microscopy**: “spike and dome” appearance with subepithelial deposits (image-7).
- Usually this condition is idiopathic but it can be associated with:
  - Drugs (NSAIDs).
  - Infections (HBV, HCV).
  - SLE.
- **Poor response to steroid therapy** (may progress to chronic renal disease).

Focal Segmental Glomerulo-Sclerosis (FSGS):
- **Definition**: sclerosis of some but not all glomeruli (<50%) and involving only a part of the affected glomeruli (segmental).
- It is the most common cause of nephritic syndrome in **African Americans and Hispanics**.
- **It can be idiopathic or associated with**:
  - HIV infection.
  - Sickle cell disease.
  - Heroin abuse.
  - Massive obesity.
- **Light microscopy**: segmental sclerosis and hyalinosis (image-8).
- **Immunofluorescence**: non-specific trapping of serum proteins in the sclerosed area (image-9).
- **Electron microscopy**: effacement of foot processes similar to minimal change disease.
- **Inconsistent response to steroid therapy** (استجابة غير متناسقة).
- May progress to chronic renal disease.
Membranoproliferative glomerulonephritis (image-10):

- It is a nephritic syndrome that can also present with nephritic syndrome.
- **There are two types:**
  - **Type-I:**
    - It is associated with: HBV, HCV. It may also be idiopathic.
    - It is characterized by subendothelial immune complex (IC) deposits with granular immunofluorescence; “tram-track” appearance due to GBM splitting caused by mesangial ingrowth.
  - **Type-II:**
    - It is associated with C3 nephritic factor (↓ serum C3 levels).
    - It is characterized by intramembranous (IC) deposits.