## Urinary outflow obstruction:

## Urolithiasis (stone formation).

- **Most common location of stones:**
  Kidney

- **Can be:**
  - Symptomatic: More common in men
  - Asymptomatic

- Familial tendency towards stone formation.

- 80% unilateral

- **Size:**
  Variable

- **Components**:
  Inorganic salt + organic matrix

- **Types of stones:** (most to least common)
  1. Calcium stones:
     Calcium oxadate + Calcium phosphate
  2. Struvite:
     Magnesium ammonium phosphate
  3. Uric Acid
  4. Cystine stones

- **Causes of Renal Stones:**
  1. **Supersaturation**: Increased urine concentration of stones constituents (exceeding solubility in urine)

     Ex: 50% of pts with calcium stones → Hypercalciuria without hypercalcemia

     5-10% → Hypercalciuria AND Hypercalcemia

  2. **Presence of a nidus** (Central part of the stone made up of organic material).
     a) Urates (nidus for calcium deposition)
     b) Bacterial colonies
     c) Desquamated epithelial cells

  3. **Urine pH**
     a) Acidic → Uric acid stones
     b) UTI → Alkaline → Struvite stones

  4. **Infections:**
     Urea splitting bacteria:
     a) Staph aureus
     b) Proteus Vulgaris

## Hydronephrosis:

- Dilation of the renal pelvis
- Dilation of the renal Calyces
- Thinning of the renal parenchyma (cortex)

- **Occurs due to:**

Obstruction of a more distal area/structure.

- **Dilation location:**

Proximal to the obstructed area.

- **Hydroureter:**

Dilation of the ureter due to distal obstruction at the level of the urinary bladder.

- **Onset**:

Sudden or insidious.

- **Obstruction location:**

Any level from urethra-renal pelvis.

**Causes**:

1. **Congenital**

- Artesia of urethra
- Valve formation in ureter/urethra
- Compression of the ureter by aberrant renal artery
- Renal ptosis with torsion/kinking of ureter

2. **Acquired**

- Foreign bodies
- Tumors
- Inflammation
- Neurogenic

## Tubulointerstitial Nephritis:

- Tubulointerstitial: Involves the tubules and interstitium
- -itis: Inflammation

- Microscopic appearance:
  - Inflammatory cells (Leukocytes): Macrophages, Neutrophils, Eosinophils, Lymphocytes.

- **Causes**:

1. Bacterial infection
2. **Drugs**
3. Metabolic disorders
4. Immune reactions
5. Physical injury (Irradiation)

Drug-Induced Interstitial Nephritis:

**Types**:

a) **Acute drug-induced interstitial nephritis**
   - Most common cause:
     - **Synthetic Penicillin (ampicillin, methicillin)**
   - Other drugs:
     - Synthetic antibiotics
     - Diuretics
     - NSAIDs

- Pathogenesis of acute IN:
  1. Immune mechanism
  2. Type 1 hypersensitivity
  3. T cell mediated (type 4) hypersensitivity

- **Morphology**:
  - Glomeruli: normal
  - Interstitium: lymphocytes, macrophages, eosinophils, neutrophils.

- **Clinical course:**
  - 2-40 days after drug exposure.
  1. Fever
  2. Eosinophilia (eosinophils in the interstitium)
  3. Rash
  4. Renal abnormalities:
     - Hematuria
     - Leukocyturia
     - Minimal/no proteinuria

b) **Chronic drug induced (analgesic) Nephropathy:**

- Cause: Prolonged consumption of large quantities of analgesics.

  - **Acetaminophen**
  - **Aspirin**

- **Pathogenesis**:
  1. Covalent binding and oxidative damage
  2. **MAJOR**: Inhibition of Prostaglandin synthesis (causes vasoconstriction and increase ROS)

  Both lead to papillary necrosis and interstitial fibrosis.

- **Clinical course:**
  - Progressive renal impairment → **Chronic renal failure, hypertension**

- **Complications**:
  - **Transitional-cell carcinoma**

## Acute Tubular necrosis/ Injury (ATN/ATI):

- **Morphology**: **Damaged tubular epithelial cells.**

- **Clinically**: Acute renal function suppression.

- **Most common cause of ACUTE renal failure.**

- **Clinical manifestations:**
  1. Electrolyte abnormality
  2. Signs of fluid overload
  3. Uremia
  4. Acidosis
  5. Oliguria

- **Proximal tubules are particularly sensitive.**

- **Factors (2):**
  1. Toxic Injury
  2. Ischemia

- **Toxic injury → Tubular injury → Damage of tubular epithelial cells:**
  - Sloughed cells
    - Leads to obstruction of the lumen.
  - Interstitial inflammation
    - Leads to decreased GFR
  - Tubular backleak: occurs due to lack of Basement membrane, as tubular cells detach from it.
    - Leads to Decreased Urine output.
- Ischemia → Vasoconstriction → tubular injury → etc.

- **Overall outcome/effect of both factors:**
  1. **Decreased urine output**
  2. **Decreased GFR**

- **ATI types:**
  1. Ischemic ATN: associated with shock.
  2. Nephrotoxic ATN:
     Causes: Poisons, organic solvents, drugs

- **ATI Management:**
  - Tubular regeneration → Gradual improvement
  - Supportive care → chance of complete recovery
  - Patients with preexisting chronic kidney disease → low chance of complete recovery