KIDNEY DISORDERS
PART 2

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Functions:
- Excretion of waste products
- Regulation of water and salt
- Maintenance of acid balance
- Secretion of hormones and by-products

 Syndromes:
- Acute Nephritic syndrome
- Nephrotic syndrome
- Asymptomatic hematuria
- Asymptomatic proteinuria
- Acute renal failure
- Chronic renal failure
- Urinary tract infection (UTI)
- Nephrolitiasis
- Tumors

Kidney disorders – according to locus
1. Glomerulopathies
2. Tubulopathies
3. Tubulointerstitial disorders
4. Renovascular vasculopathies
5. Destructive lesions

Glomerulopathies
**Glomerulopathies - Forms**

**Primary Glomerulonephritis**
- Acute diffuse proliferative GN
- Rapidly progressive GN
- Membranous GN
- Lipoid nephrosis (minimal change disease)
- Focal segmental glomerulosclerosis
- Membranoproliferative GN
- IgA Nephropathy
- Chronic GN

**Secondary (Systemic) Diseases**
- Systemic lupus erythematosus
- Diabetes mellitus
- Amyloidosis
- Goodpasture’s syndrome
- Polyarteritis nodosa
- Wagener’s granulomatosis
- Henoch-Schönlein purpura
- Bacterial endocarditis

**Hereditary Disorders**
- Alport’s syndrome
- Fabry’s disease

**Glomerulopathies - Manifestations**

1. asymptomatic proteinuria
2. nephrotic syndrome
   (proteinuria, hypoproteinemia, hyperlipidemia, edema)
3. asymptomatic hematuria
4. glomerulonephritis
   (hematuria, proteinuria, hypertension, renal failure)
5. acute glomerulonephritis
   (nephritis with short term renal failure)
6. crescentic glomerulonephritis
   (nephritis with rapidly progressive renal failure)
7. chronic glomerulonephritis
   (chronic progression of renal failure)
8. End Stage Renal Disease
   (irreversible renal failure)
1. Nefritic syndrome

**Definition:** finding and laboratory data indicating glomerular damage in kidney; mainly **haematuria + hypertension**

**Symptoms:**
- **haematuria** – failure of barrier; casts of haemolyzed erythrocytes (erythrocyturia), or haemoglobin, or hem (hemoglobinuria) → often precipitates and plugs tubuli → loss of filtration pressure, anuria
- **proteinuria** (mild to moderate) – both low-molecular and high molecular proteins are lost
- **oliguria** – decrease of water filtration → cumulation of water in vessels
- **hypervolemia – hypertension** – due to decreased GFR; if loss of solutes is normal → **hypoosmolalitay** in plasma develops

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**Mediators of immune glomerular injury.**

- Oxidants
- Proteases
- Eicosanoids
- Cytokines
- Growth Factors
- Nitric Oxide
- Others

(A) Circulating Ab-Ag complexes, (C) Ab-Ag complexes created in situ
(B) Antibodies against basement membrane
Membranoproliferative Glomerulonephritis

Mesangial proliferation, basement membrane thickening, leukocyte infiltration and accentuation of lobular architecture. Type I and Type II MGN.

2. Nephrotic syndrome (Nephrosis)

**Definition:** manifestations and lab. findings evidences for heavy damage in glomerular filtration barrier; main features: proteinuria + edemas

**Symptoms:**
- heavy proteinuria (> 3.5 g/d) foamy urine; selective proteinuria (low-molecular – loss of Albumin) or non-selective
- hypoalbuminemia (< 3 g/d) → ↓ oncotic blood pressure → leak of liquid into interstitium → hypovolemia → hyperaldosteronism → reabsorption of NaCl + water
- generalized edemas – face, periorbit, ev. ascites (kids, young adults), ankle swelling (adults)
- hyperlipidemia – liver compensated losses of proteins by overproduction; they are mostly lost in urine except lipoprotein particles leading to relative abundance of LDL → atherosclerosis
- recurrent infections – are due to losses of immunoglobulins (Ig) and complement in urine
- oliguria (rarely anuria) – is due to capillary and basement membrane thickening
Nephrotic syndrome - Causes

Primary Glomerular Disease

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membranous glomerulonephritis (GN)</td>
<td>5</td>
<td>60%</td>
</tr>
<tr>
<td>Minimal change disease</td>
<td>65</td>
<td>10%</td>
</tr>
<tr>
<td>Focal segmental glomerulosclerosis</td>
<td>10</td>
<td>15%</td>
</tr>
<tr>
<td>Membranoproliferative glomerulonephritisides</td>
<td>10</td>
<td>7%</td>
</tr>
<tr>
<td>Other proliferative glomerulonephritis (focal, &quot;pure mesangial,&quot; IgA nephropathy)</td>
<td>10</td>
<td>15-25%</td>
</tr>
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</table>

Miscellaneous (bee-sting allergy, hereditary nephritis)

Infections (malaria, syphilis, hepatitis B and C, acquired immunodeficiency syndrome)

5%

Malignant disease (carcinoma, lymphoma)

35%

Drugs (nonsteroidal anti-inflammatory, penicillamine, "street heroin")

35%

Diabetes mellitus, Amyloidosis, Systemic lupus erythematosus

35%

Other proliferative glomerulonephritis (focal, "pure mesangial," IgA nephropathy)

5%

Systemic Diseases

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Normally, the base-ment cell membrane does not filter large molecules such as albumin (70,000 kD).

Diabetic Glomerulosclerosis

- Thickening of the basement membrane; nodules of scars (sclerosis) in the glomeruli
- Sclerosis in the walls of arteries (arteriosclerosis) and arterioles (arteriolosclerosis) in the kidneys and other tissues
Tubulointerstitial disorders

Tubulointerstitial Nephritis
- Acute pyelonephritis
- Chronic pyelonephritis
- Drug-Induced interstitial nephritis
- Acute tubular necrosis

Tubulointerstitial disorders - Causes

Infections
- Acute bacterial pyelonephritis
- Chronic pyelonephritis (including reflux nephropathy)
- Other infections (e.g., viruses, parasites)

Toxins
- Drugs, Analgesics
- Acute hypersensitivity interstitial nephritis
- Heavy metals: Lead, cadmium

Metabolic Diseases
- Urate nephropathy
- Nephrocalcinosis (hypercalcemic nephropathy)
- Hypokalemic nephropathy
- Oxalate nephropathy

Physical Factors
- Chronic urinary tract obstruction
- Radiation nephropathy

Neoplasms
- Multiple myeloma (cast nephropathy)

Acute interstitial nephritis (AIN)

Mechanisms
- Renal interstitial inflammation
- T-Cell mediated Hypersensitivity Reaction

Causes

Infection
- Diphtheria (classic), Group A beta hemolytic Streptococcus (classic)
- Legionella Yersinia
- Staphylococcus or Streptococcus infection
- Mycobacterium, Toxoplasmosis, Mycoplasma Leptospira, Rickettsia Syphilis
- Herpes viruses (e.g. CMV, EBV, HSV), Human Immuno-deficiency Virus (HIV), Hantavirus

Medications
- (AIN occurs >2 weeks after drug started)
  - Penicillins, Cephalosporins, Sulfonamides, Vasculitis reaction
  - NSAIDs Nephrotic Syndrome type reaction
  - Rifampin Diuretics, Allopurinol
  - Other medications have caused AIN to a lesser extent

Miscellaneous conditions
- Glomerulonephritis
- Necrotizing Vasculitis
- Systemic Lupus Erythematosus
- Acute kidney transplant rejection

Spread of infection

Chronic pyelonephritis
Hydronephrosis and chronic obstructive pyelonephritis
**Acute interstitial nephritis (AIN)**

**Symptoms and Signs**
- Classic triad
  - Low grade fever (>70% of cases)
  - Rash (>30% of cases)
  - Arthralgia (>15% of cases)
- Acute renal failure (15% of cases)
- Oliguria, Malaise, vomiting
- Recovery in weeks if cause eliminated within 2 weeks
- Poor prognosis in interstitial fibrosis

**Laboratory findings**
- Urine
  - Eosinophiluria, Proteinuria,
  - Creatinine increased
  - Uremia
  - Hyperchloremic metabolic acidosis

**Renal biopsy**
- Inflammation of renal interstitium
  - Mononuclears, T-Lymphocytes
- Glomerular and vascular sparing

**Management**
- Corticosteroids Prednisone 1 mg/kg/day for 2 weeks, Cyclophosphamide in steroid non-responders
- Optimization of fluid status, electrolyte abnormalities and hyperkalaemia
- Symptomatic relief of fever and arthralgias

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**Acute Tubular Necrosis**

**Characterisation:**
- Destruction of epithelial tubular cells, cells “slough off” from the BM; casts plug the tubules; BM may be destroyed too
- Fail to excrete urine even when renal blood flow is restored
- If the BM remains intact, new epithelia grow along BM within 10 to 20 days.

**Causes:**
- Severe ischemia (shock kidney)
  - Circulatory shock - inadequate supply of oxygen and nutrients to the tubular epithel
- Renal poisons - specific toxins to epithel
  - Carbon tetrachloride, Hg, Cd, Pb, ethylene glycol (antifreeze), insecticides, medications (tetracyclines), cis-platinum

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**Renovascular disorders**

- Benign nephrosclerosis
- Malignant hypertension
- Malignant nephrosclerosis
- Thrombotic microangiopathies
Acute Renal Infarction

Malignant hypertension → fibrinoid necrosis of small arteries = formation of pink fibrin

Thickening of arterial wall with hyperplastic arteriolitis "onion skin" appearance

Cystic Diseases of the Kidney

Definition:
- heterogeneous group comprising hereditary, developmental but nonhereditary, and acquired disorders.
- common and often represent diagnostic problems for clinicians, radiologists, and pathologists.
- some forms, such as adult polycystic disease, are major causes of chronic renal failure
- can occasionally be confused with malignant tumors

Classification
1. Cystic renal dysplasia
2. Polycystic kidney disease
   a. Autosomal-dominant (adult) polycystic disease
   b. Autosomal-recessive (childhood) polycystic disease
3. Medullary cystic disease
   a. Medullary sponge kidney
   b. Nephronophthisis
4. Acquired (dialysis-associated) cystic disease
5. Localized (simple) renal cysts
6. Renal cysts in hereditary malformation syndromes (e.g., tuberous sclerosis)
7. Glomerulocystic disease
8. Extraparenchymal renal cysts (pyelocalyceal cysts, hilar lymphangitic cysts)

Cystic diseases of kidney
Autosomal Dominant Polycystic Kidney Disease (ADPKD)
- mutation in one of two kidney building block proteins - polycystin 1 and polycystin 2 (genes PKD1 and PKD2).
- Children can be born with severely enlarged kidneys (the size of normal adult kidneys) and can have immediate kidney failure at birth.

Autosomal Recessive Polycystic Kidney Disease (ARPKD)
- mutation in a kidney building block protein called fibrocystin (gene PKHD1) found in up to 90% of people.
- born with severely enlarged kidneys, high blood pressure, cysts and scarring of the liver.

Cystic Renal Dysplasia
- Occur unilaterally or bilaterally; kidney is usually enlarged, extremely irregular, and multicystic cysts vary microscopic several centimeter.
- Abnormal lobar organization, immature collecting ductules, islands of undifferentiated mesenchyme, often with cartilage.
- Most cases are associated with ureteropelvic obstruction, ureteral agenesis or atresia, and other anomalies of the lower urinary tract.

Possible mechanisms of cyst formation in polycystic kidney disease

Kidney stones

<table>
<thead>
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<th>Types</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Calcium oxalate (or phosphate)</td>
<td>75%</td>
</tr>
<tr>
<td>Magnesium ammonium phosphate</td>
<td>12%</td>
</tr>
<tr>
<td>(struvite, or &quot;triple phosphate&quot;)</td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>6%</td>
</tr>
<tr>
<td>Cystine</td>
<td>1%</td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
</tr>
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</table>
Nephrolithiasis ("staghorn" calculus )
Chronic Obstructive Pyelonephritis