Diseases of urinary system
Diseases of the kidney

Congenital anomalies:

- Agenesis: the absence of both kidneys is not compatible with life.

With agenesis (absence) of one kidney, the single kidney present enlarges sufficiently to maintain normal function (compensatory hypertrophy).

- Hypoplasia: failure of the kidneys to develop to a normal size. It may occur bilaterally, resulting in renal failure in early childhood, but more commonly it is encountered as a unilateral defect.
- Displacement of the kidney (ectopic kidney): results from failure of ascent of one or both kidneys from the pelvis to the loin during embryonic development. The attached ureter may be kinked, thus predisposing to hydronephrosis.
- Horse-shoe kidney: the two kidneys are united together, usually at their lower poles by renal or fibrous tissue.
- Aberrant renal artery: the renal artery enters the kidney at one pole crossing the pelviureteric junction on its way. It may predispose to hydronephrosis and renal hypertension.
- Double ureter with single or double pelvis.
- Congenital stricture of the ureter.
- Congenital cysts:

1-Solitary cyst.

2-Congenital polycystic kidney:

A- Adult type

Presentation:

- Autosomal dominant polycystic kidney disease (ADPCKD).
- Patients usually present in their 40s with flank pain, intermittent hematuria, a palpable abdominal/ flank mass, hypertension, and a positive family history of kidney disease.
- It is characterized by large number of cysts in the renal cortex, compress the renal parenchyma as they enlarge resulting in progressive atrophy and fibrosis.
- The cysts are rounded or oval, mms-5 cm, have smooth lining, filled with serous or haemorrhagic fluid, communicate to each other but not with the renal pelvis.

Aetiology: There is most frequently a mutation of the PKD1 gene on chromosome 16 which produces a transmembrane protein called polycystin1. Other mutations involve PKD2 and polycystin 2.

Diagnosis: A positive family history and bilateral kidney cysts detected by ultrasound. Liver cysts may also be present.

Prognosis:CRF begins at age 40–60 and is the most common cause of death.

Complications:

- include refractory hypertension and urinary infection.
- There is an association with **saccular aneurysms** affecting the circle of Willis, leading to a high incidence of **subarachnoid hemorrhage.**

B- Infantile type

- Inherited as an autosomal recessive trait.
- Rare disease, death shortly after birth.
- Multiple cysts, kidney looks spongy and enlarged.
- Cystic changes from medulla to cortex.
- Patients die from renal failure.

Etiology: A mutation in the PKHD1 gene is implicated.

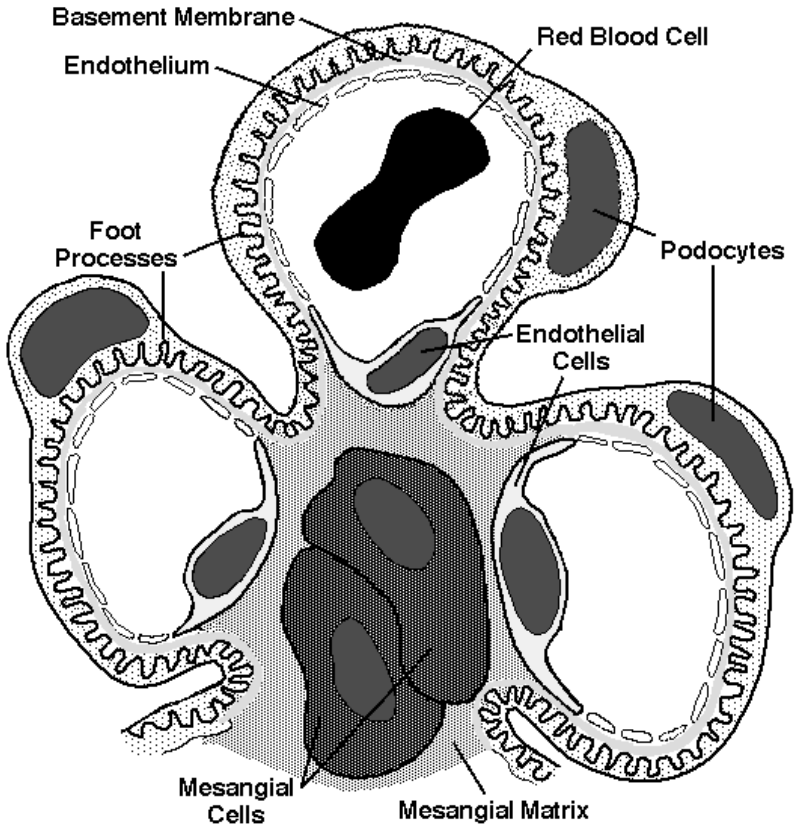
Associated lesions:

- Cysts in liver and pancreas.

- Cerebral aneurysms; it causes subarachnoid Hge in 15% of pt.

Normal structure of the glomerulus:

- Epithelial cells; podocytes (foot processes).
- Basement membrane; formed of lamina rara interna, lamina densa and lamina raraexterna.
- Endothelial cells.
- Mesangial cells and matrix:
  Support.Contractile action.
  Phagocytic activity.
  Secretes mesangial matrix.



Response of the glomerulous to glomerular injury:

1-Cellular proliferation (hypercellularity): due to proliferation of endothelial and mesangial cells.
2-Leucocytic infiltration (neutrophils and monocytes) often accompanied by cellular proliferation.
3-Capillary wall thickening:
a- Thickening of glomerular basement membrane (BM).
b- Addition to the BM of materials like Immune complexes (IC) or extension from the cytoplasm of mesangial cells.
4-Crescent formation; due to proliferation of parietal epithelial cells of Bowman's capsule (BC).
5- Sclerosis & hyalinosis.

The above changes may be:

- Diffuse: affecting all glomeruli.
- Global: affecting the entire glomerulus. **Or**
- Focal: affecting only some glomeruli (<50% of glomeruli).

- Segmental: affecting part or segment of the Glomerular tuft.

Immunologic mechanisms of glomerular diseases:

1-Immune complex disease. (Type III hypersensitivity)
2-Antiglomerular basement membrane disease (Good Pasture disease). (type II hypersensitivity)

Glomerulonephritis

Definition: A group of renal diseases in which the primary lesion is glomerular and, in most cases immunologically mediated.

Classification (clinical presentation):

1-Nephrotic syndrome:	**2**- Nephritic syndrome:
Heavy proteinuria.	Mild hypertension.
Hypoproteinaemia.	Haematuria.
Generalised oedema.	Uremia.
Hypercholesterolaemia.	Oliguria (decreased GFR).
	Mild proteinuria.

Classification (morphologic types):

1- Acute diffuse proliferative GN (post streptococcal, post infective).
2- Rapidly progressive (Crescentic) GN.
3- Focal proliferative GN.
4- Minimal change GN (lipoid nephrosis, Light negative GN, Foot process disease).
5- Focal segmental glomerulosclerosis.
6- Membranous GN.
7- Membranoproliferative GN.
8- Chronic GN.

General Division of Glomerular Diseases

CONDITIONS THAT MANIFEST WITH NEPHROTIC SYNDROME (INCREASED FILTRATION BARRIER PERMEABILITY)	**CONDITIONS THAT MANIFEST WITH NEPHRITIC SYNDROME (INFLAMMATORY DAMAGE TO THE GLOMERULI)**
Minimal change disease	Acute proliferative glomerulonephritis (poststreptoccocal/infectious)
Focal segmental glomerulosclerosis	Rapidly progressive glomerulonephritis (crescentic)
Membranous glomerulopathy	Anti-GBM disease (Goodpasture syndrome)
Membranoproliferative glomerulonephritis (MPGNa)	MPGNa
Diabetic nephropathy associated with systemic disease	IgA nephropathy (Berger disease)
Renal amyloidosis associated with systemic disease	Hereditary nephritis (Alport syndrome)
Lupus nephritisa	Lupus nephritisa

aMPGN and lupus nephritis can present as either nephrotic or nephritic syndrome.
GBM, glomerular basement membrane.

Nephritic Syndrome:

The pathology of this condition is the result of **inflammation of the glomerulus** and **neutrophil-related injury.** Nephritic syndrome is characterized by a distinct set of symptoms:

■**Hematuria** secondary to destruction of glomerular capillaries and loss of RBCs into the Bowman space, resulting in dysmorphic RBCs and RBC casts on urinalysis.

■**Oliguria** and **azotemia** (increased blood urea nitrogen and creatinine) secondary to glomerular injury as a result of infiltration of inflammatory cells and immune complex deposition. This infiltration leads to obstruction of the glomerular capillary lumen, thereby decreasing the GFR.

■**Hypertension** secondary to the increased fluid retention by the kidney due to the decreased GFR.

■**Mild proteinuria** may be observed as a result of the glomerular capillary injury.

Acute Diffuse Proliferative Glomerulonephritis (ADPGN)

Incidence:

- Mostly in children.
- Males > females.
- Usually develops 1- 4 wks. following infection of upper respiratory tract by group A β-haemolytic Streptococci.
- May follow infection by Staph. aureus, viruses, or Falciparum malaria.

Clinically:

-Sudden onset of fever & malaise.
- Mild oedema especially periorbital.
- Mild to moderate hypertension.
- Urine: Haematuria (smoky urine), oliguria & mild proteinuria.

Pathogenesis:

Pathogenesis is secondary to immune-complex deposition in the glomerulus with resulting complement activation and inflammation.

Evidences:

- No organism in kidney, blood or urine.
- ↑ASOT.
- ↓ in serum complement level (hypocomplementaemia).
- Presence of IC deposits on the kidney tissue.

Pathology:

Grossly:

- Size: both kidneys are slightly enlarged.
- Outer surface: smooth, pale grey in colour with red spots due to capsular haemorrhage.
- Capsule: strips easily.
- Cut section: Cortex is pale, slightly thickened and easily demarcated from medulla.

Microscopically:

- Glomeruli: - Swollen & hypercellular (proliferation of endothelial & mesangial cells and infiltration by polymorphs.
- Narrowing of glomerular capillary lumen (bloodless tuft).
- Fibrin and RBCs in the subcapsular space.

- Crescents may appear in some glomeruli.
- Tubules: Cloudy swelling + RBCs & blood casts.
- Interstitial tissue: Oedema + mild inflammatory cell infiltrate.
- Blood vessels: no change.
- **EM.:** Discrete subepithelial electron dense deposits (humps).
- **Immunological:** Granular deposits; IgG, C3 & fibrin.

Biochemical changes:
*Urine: - Oliguria or anuria due to ↓GFR.
- Haematuria: smoky urine.
- Mild proteinuria.
- ↑ Specific gravity (SG) >1018.
- Casts: hyaline, granular, epithelial &**blood casts**.
- Urine is negative for organisms.

*Blood: - Mild ↑in blood urea, creatinine & non protein nitrogen.

Coarse and fate of disease:
- Complete recovery in 95% in children.
- 60-70 % in adults.
- Death in acute stage from acute RF or HF.
- May progress to rapidly progressive GN.
- May progress to chronic GN →chronic RF.
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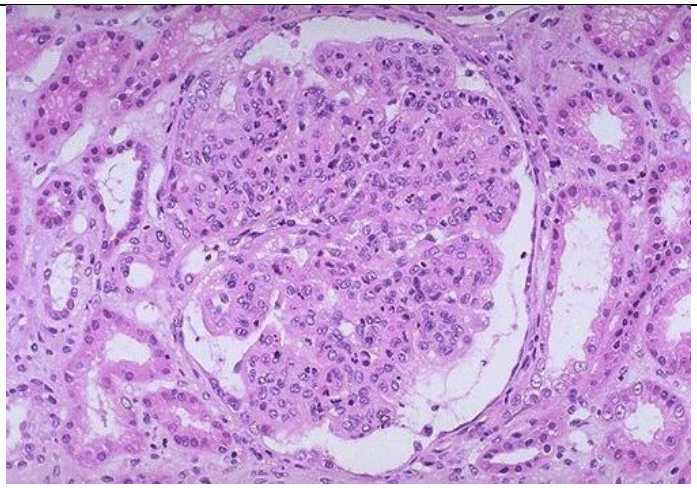
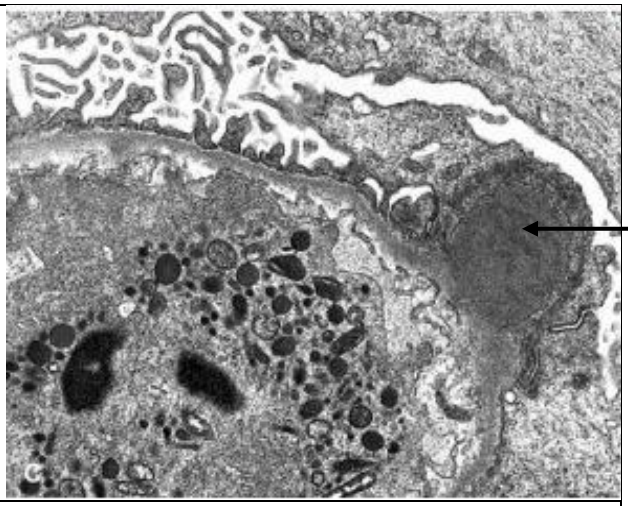
	
Light microscopy of ADPGN shows enlarged, hypercellular glomerulus (caused by proliferation of mesangial cells, endothelial cells, and global leukocytic infiltration in all lobules of the glomerulus) Several tubules contain red cells due to cloudy swelling. Mild interstitial edema is also evident.	Sub epithelial electrom-dense deposit (arrow)

Rapidly progressive Glomerulonephritis (RPGN or Crescentic GN)

- Rapidly progressive glomerulonephritis (crescentic GN) is not a disease, per se, but rather is an aggressive form of nephritic syndrome in which progressive loss of kidneyfunction occurs within weeks or months following the primary insult.
-It is most common in adults aged 30–60 years and is slightly more common in men.

■**Presentation**
Classic nephritic syndrome; varies based on the underlying cause.
(As ADPGN but progressively more severe) (more severe oliguria and more elevated hypertension).

■**Etiology:**
There are three distinct types of RPGN(table)

TYPE	**DISEASES**	**IMMUNOFLUORESCENCE FINDINGS**
I	Goodpasture syndrome	ANCA-negative, linear IgG and C3 deposits along the GBM (anti GBM Ab)
II	Poststreptoccocal GN, SLE, IgA nephropathy, Henoch-Schonlein purpura	ANCA-negative, granular "lumpy-bumpy" deposit
III	Granulomatosis with polyangiitis or idiopathic	ANCA-positive, no deposits on the GBM

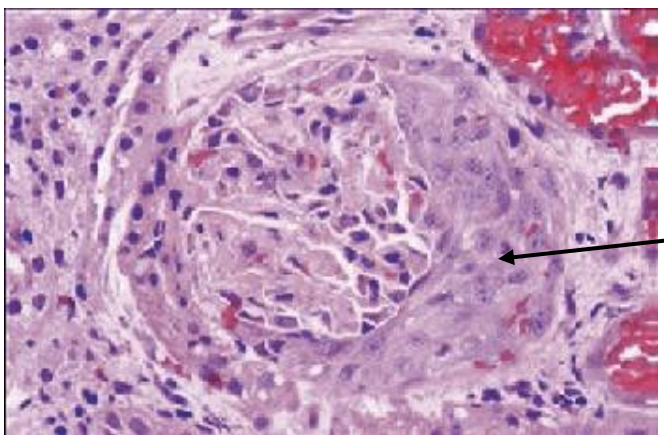
ANCA, antineutrophil cytoplasmic antibody; GBM, glomerular basement membrane; GN, glomerulonephritis; SLE, systemic lupus erythematosus.

■**Diagnosis**
Effective diagnosis can be made based on history and histologic findings.
■**Serum chemistry:**
- UN and creatinine may rise rapidly.
- Anti-GBM-antibody positive in association with Goodpasture syndrome.
- ANCA presence varies based on the underlying cause.
- Complement levels may be decreased in some cases.

■**Urinalysis:** Blood (RBCs), protein, WBC (monocytes), and casts.

■**Pathology:**
Grossly: more petichealHge. in the cortex.
Microscopically: Like ADPGN, but:
- Crescents are found in > 50% of the glomeruli.
- Crescents largely consist of proliferated glomerular parietal cells; Bowman space is filled with monocytesand macrophages. Large amounts of **fibrin** accumulate within the cellular layers ofthe crescents.
- Hge and necrosis of glomerular capillary wall.
- Immunofluorescence: granular or linear fluorescence according to etiology.
- EM: according to etiology.

■ **Prognosis:** Bad. Death occurs within weeks to a year due to ARF or HF.



Light microscopy of RPGN showing cellular crescent (arrow)

Antiglomerular Basement Membrane Disease (Goodpasture Syndrome)

Disease characterized by **antibodies against proteins in the GBM.** Symptoms can be isolated to the kidney or may also be seen in the lung due to cross-reactivity of antigens (eg, **α3 chain of collagen type IV**) that are common to both alveolar and GBMs. The underlying pathogenesis is based on a type II hypersensitivity reaction. This disease accounts for < 1% of glomerulopathies.

■**Goodpasture syndrome**: Both alveolar and glomerular symptoms occur.

■**Idiopathic anti-GBM disease:** Symptoms are isolated to the kidney.

Presentation:

Hematuria and other nephritic symptoms, subnephrotic range proteinuria, and RPGN over the course of a few weeks is common. Pulmonary hemorrhage presenting with hemoptysis and dyspnea occurs in those patients with both glomerular and alveolar injury.

■**Diagnosis:**

- Gold standard is renal biopsy with immunofluorescence. Chest plain film shows bibasilar shadows in cases with pulmonary involvement.