Renal pathology

By

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Histology of glomerulus

The glomerulus has two poles:

- **The vascular pole**, It is the entrance of the afferent arteriole and exit of efferent arteriole.

- **The urinary pole** It is the beginning of the proximal convoluted tubule.

The afferent arteriole divides into capillary branches. Each of these branches gives rise to a capillary network (glomerular tuft) which runs toward the urinary pole, turns back towards the vascular pole and form the efferent arteriole.

- **The basement membrane** extends to cover all the nephron in continuity with that of the Bowman’s capsule and extends till the vascular pole where the basement membrane is reflected over the capillary tuft. The basement membrane is lined by epithelial cells through all its extent. The nature of epithelial cells varies according to the site of the nephron. At the proximal tubules the epithelial cells are voluminous with eosinophilic cytoplasm and have a brush border.

At the Bowman’s capsule, the basement membrane is lined by flat simple squamous epithelial cells forming the parietal layer then extends till the vascular pole where the basement membrane with its epithelial lining is reflected over the capillary tuft forming the visceral layer of Bowman’s capsule or the capillary basement membrane. The morphology of the epithelial lining with this reflection changes from the flat parietal epithelial cells to form visceral epithelial cells (podocytes).

The space between the two layers of Bowman’s capsule is the urinary space.

Thus the glomerular capillary wall is made essentially by the basement membrane. At the Outer side of the basement membrane (towards the Bowman’s space the visceral epithelial cells are situated with their foot processes interdigitating with foot processes from other podocytes). The inner side of the basement membrane is lined by the endothelial cells.

The main bulk of the endothelial cell with its nucleus is situated at the mesangial side.

A thin sheet of fenestrated endothelial cell cytoplasm extends to line the inner capillary circumference. One endothelial nucleus appears per cro
The basement membrane (arrows) extends to cover all the nephron in continuity with that of the Bowman’s capsule and extends till the vascular pole where the basement membrane is reflected over the capillary tuft. The basement membrane is lined by epithelial cells through all its extent.

Electron micrograph. Podocyte foot processes cover the outer surface of basement membrane. A thin sheet of fenestrated endothelial cell cytoplasm extends to line the inner capillary circumference.

A diagram showing the glomerular structure. The basement membrane is reflected over the capillaries. With this reflection the epithelial lining changes from the flat parietal epithelial cells to form visceral epithelial cells (podocytes).
Diagram of glomerular capillary

Electron micrograph of part of capillary wall.
CL=capillary lumen. BS= Bowman's space
## Hereditary cystic diseases of the kidney

They are heterogeneous groups including many types. Two important types will be discussed:

1. Adult polycystic kidney disease (autosomal dominant).
2. Childhood polycystic kidney disease (autosomal recessive).

<table>
<thead>
<tr>
<th></th>
<th>Adult Polycystic kidney disease</th>
<th>Childhood polycystic kidney disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>More common</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Inheritance</strong></td>
<td>Autosomal dominant</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td><strong>Symptomatic</strong></td>
<td>Late in adult life</td>
<td>Early in life. It may present neonatal, postnatal or juvenile.</td>
</tr>
<tr>
<td><strong>N/E</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Outer surface</td>
<td>Multiple variable sized cysts.</td>
<td>Outer surface is smooth.</td>
</tr>
<tr>
<td></td>
<td>Translucent of variable colors: Clear, hemorrhagic or brown.</td>
<td></td>
</tr>
<tr>
<td>• Cut surface</td>
<td>Rounded and oval thin walled cysts, which may communicate with each other but not with the renal pelvis.</td>
<td>Dilated elongated channels perpendicular to the cortex and present in both the cortex and medulla</td>
</tr>
<tr>
<td><strong>M/E</strong></td>
<td>Some nephrons are involved. Others are preserved.</td>
<td>Cysts affect only the collecting tubules and are lined by its type of epithelium i.e. cuboidal epithelium</td>
</tr>
<tr>
<td></td>
<td>Cysts affect any part of the nephron even the glomeruli. So the lining is variable according to the segment of the nephron affected.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>In between the cysts there is atrophic and compressed renal tissue.</td>
<td></td>
</tr>
<tr>
<td><strong>Associated Conditions</strong></td>
<td>Cysts of the liver and Berry aneurysms.</td>
<td>Cysts of the liver, periportal fibrosis and portal hypertension.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic renal failure early in life.</td>
</tr>
</tbody>
</table>

Renal pathology
Adult Polycystic kidney disease. Outer surface shows multiple variable sized cysts.

Infantile Polycystic kidney disease. Outer surface is smooth. Cut section shows dilated elongated channels perpendicular to the cortex and present in both the cortex and medulla.

Adult Polycystic kidney disease. Rounded and oval thin walled cysts, which may communicate with each other but not with the renal pelvis.
CLINICAL RENAL SYNDROMES.

- Nephrotic syndrome.
- Nephritic syndrome
- Rapidly progressive Glomerulonephritis.
- Chronic renal failure.
- Acute renal failure.

NEPHROTIC SYNDROME.

Clinical picture:
- Proteinuria.
- Hypoproteinemia.
- Hypercholesterolemia.
- Edema: Nephrotic oedema is massive generalized oedema. It may be associated with ascitis and pleural effusion. In such conditions it is called generalized anasarca.

Pathogenesis of nephrotic syndrome

- Vascular functional changes in the glom.cap
- Glom.cap.permeability to proteins
- Prolonged heavy Proteinuria

Urine changes in nephrotic syndrome
- Volume ↓
- Specific gravity ↑
- Albumin and globulin ↑
- Casts ↑
Types of casts in nephrotic syndrome.

- **Hyaline casts**: Transparent and homogeneous casts formed of proteins secreted by tubular epithelium and albumin secreted in urine.
  
  The other types of casts are formed of a core of hyaline cast with other components sticking to the coagulated protein.

- **Fat casts**: Due to leakage of lipoproteins with cholesterol and neutral fat sticking to coagulated protein.

- **Granular casts**: Fragmented cells sticking to coagulated protein.

- **Epithelial casts**: Formed of tubular epithelial cells sticking on the surface of hyaline casts.

**ACUTE NEPHRITIS**

Clinical picture of acute nephritis:

- Oliguria
- Hematuria (smoky urine)
- Hypertension.
- Proteinuria.
- Nephritic edema. It is never massive. It is in the form of morning puffiness and mild oedema of lower limbs.

Pathogenesis of acute nephritis
Renal pathology

Urine changes in acute nephritis:
- Oliguria
- Hematuria
- Mild albuminuria
- Casts:
  - Hyaline
  - Blood (hematuria)
  - Granular
  - Cellular (neutrophils)

Classification of Glomerulonephritis (GN):

I- Primary GN: (Etiology not known. The disease affects the kidney only)
   1. Minimal change
   2. Focal segmental glomerulosclerosis
   3. Proliferative GN.: Focal and diffuse proliferative GN.
   5. Membranoproliferative GN
   6. Crescentic GN.

II- Secondary GN: (known etiology. The disease affects other system in addition to the kidney)

1- Vascular:
   - Wegner’s granulomatosis
   - Microscopic polyarteritis.
   - SLE.
   - Henoch Schoenlein purpura.

2- Infective:
   - Viral (hepatitis)
   - Bacterial (Post streptococcal, Subacute bacterial endocarditis).
   - Parasitic (Bilharzial and malarial).

3- Metabolic:
   - Diabetes mellitus.
   - Amyloidosis.

4- Hereditary:

5- Paraneoplastic syndromes.
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1- Primary Glomerulonephritis

1- Minimal change

Age:
- Mainly in children
- May occur in adults.

Causes:
Idiopathic or secondary e.g. Hodgkin’s lymphoma

Clinical picture: Nephrotic syndrome

Microscopy:
- Light microscopy: Glomeruli, tubules and interstitium show no abnormalities.
- Immunofluorescence: No immune deposits.
- Electron microscopy: The only abnormality seen is fusion of foot processes.

Prognosis:
- Spontaneous remissions and exacerbations.
- Good response to steroids. With increasing age spontaneous cure occurs.

2- Focal segmental glomerulosclerosis

Age: Any age may be affected.

Causes: Idiopathic or secondary (e.g. SLE, Bilharsiasis)

Clinical picture: Nephrotic syndrome, hypertension and hematuria.

Microscopy:
- L/M: Glomeruli: show focal (Some but not all the glomeruli involved)
  and Segmental (a segment of an individual glomerulus is affected) glomerulosclerosis.
- Tubules: Focal tubular atrophy.
- Interstitium: Focal fibrosis.
- I/F: focal immune deposits of Ig M and C 3.
- E/M: fusion of foot processes, increased mesangial matrix and electron dense deposits.

Prognosis: Progression to renal failure.
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Minimal change

Diagram of electron microscopic appearance. The only abnormality seen is fusion of foot processes.

By light microscopy glomeruli appear normal as regards basement membranes, cellularity and mesangium.

Each circle represents a glomerulus.

Focal segmental glomerulosclerosis

One of the glomeruli is segmentally sclerotic (arrow).

Diffuse segmental sclerosis

Focal segmental sclerosis

FSGS Perihilar

Sclerotic segment
3- Membranous Nephropathy

Age: Mainly in adults or older children.

Causes: Idiopathic or secondary (viral infections e.g. hepatitis, paraneoplastic e.g. lymphoma, SLE, Drugs e.g. penicillamin).

Clinical picture: Nephrotic syndrome with or without hypertension.

Microscopy:

- **Light microscopy:** Glomeruli: Diffuse ribbon -like thickening of the basement membranes.
  
  Silver stain that stains only the lamina densa shows spikes projecting from the basement membranes. In advanced stages silver stain shows double contoured appearance of the capillary basement membranes

Tubules and interstitium: They show variable degrees of chronic changes

- **Immunofluorescence:** Diffuse finely granular deposits of IgG and C3 along the basement membranes.

- **Electron microscopy:** Fusion of foot processes. Diffuse regular subepithelial deposits along the basement membranes. With increased size of the deposits they press on the lamina densa which projects in between the deposits forming the spikes seen by the silver stain.
  
  With more increase in size the deposits become surrounded by the lamina densa and the intervening septa disappear. Then the basement membranes show the double contoured appearance by silver stain.

Prognosis: Some cases undergo remission. Others progress to renal failure.

4- Proliferative glomerulonephritis

Age: Any age may be affected.

Causes: Idiopathic and secondary (viral, bacterial (post streptococcal), , subacute bacterial endocarditis, SLE, vasculitis).

Clinical picture: Nephrotic syndrome or nephritis.

Microscopy:

- **Light microscopy:** Glomeruli: Mesangial proliferative focal or diffuse.
  
  Tubules and Interstitium: Variable degrees of tubular atrophy and interstitial fibrosis.

- **Immunofluorescence:** Variable + ve or -ve.

- **Electron microscopy:** Mesangial proliferation focal or diffuse.

Prognosis: Recovery in some mild cases: Others may progress to renal failure.
Diffuse mesangial proliferation

Light microscopy. Diffuse hyaline thickening of basement membranes. No associated hypercellularity.
Acute diffuse proliferative G.N.
(Post streptococcal G.N.)

**Age:** Affects mainly children and young adults.

**Etiology:** It following an acute infection with Group A beta hemolytic streptococci, mostly after tonsillitis, pharyngitis, gastroenteritis and skin infection.

**Pathogenesis:** It is an immune complex disease. Antigens are fixed to glomeruli with subsequent antibodies formation and complement fixation.

The antigen could be one of the following:

1. Glomerular antigen altered by streptococcal enzymes.
2. Specific nephritogenic streptococcal antigen adhere to glomerular basement membranes and acts as planted antigens.
3. Altered autologous IgG: Streptococcal enzymes lead to alteration of autologous IgG. Then antibodies are formed against altered IgG Altered IgG-IgG complex.

**Microscopy:**

- **Light microscopy:**
  - Glomeruli: They are enlarged and hypercellular due to endothelial and mesangial proliferation as well as excess infiltration by neutrophils and macrophages. Capillary lumens are obliterated by the proliferated endothelial cells and neutrophils infiltration.
  - Tubules: Casts: Hyaline, blood and neutrophilic casts.
  - Interstitium: Interstitial inflammatory cellular infiltrate formed of neutrophils, lymphocytes and plasma cells.

- **Immunofluorescence:** Large granular deposits of IgG.

- **Electron microscopy:** The same findings seen by light microscopy and subepithelial immune complex deposits called humps.

**Prognosis:**

- 90% of children and 65% of adults recover.
- Death from heart or renal failure.
- Development of chronic glomerulonephritis.
Acute diffuse proliferative G.N.
*(Post streptococcal G.N.)*

Diagram showing electron microscopic changes of Post streptococcal G.N.

Acute diffuse proliferative G.N.
*(Post streptococcal G.N.)*

Glomerular hypercellularity encroaching on capillary lumens. Frequent neutrophil infiltration.
5- Membranoproliferative Glomerulonephritis

**Age:** Can affect any age.

**Causes:** Idiopathic or Secondary (Viral infection e.g. hepatitis, paraneoplastic syndrome, SLE and drugs).

**Clinical picture:** Nephrotic syndrome and in some cases nephritis.

**Microscopy:**
- **Light microscopy:** Glomeruli: Diffuse thickening of the capillary basement membranes and increased mesangial matrix and cellularity resulting in prominent mesangial lobulation.

  Tubules and interstitium: Variable degrees of chronic changes.

- **Immunofluorescence** Mesangial and capillary deposits of IgM, IgG and C3.

- **Electron microscopy** There are 3 types according to the cause of thickening of basement membrane.
  1. **Type I:** Subendothelial immune complex deposits and mesangial interposition between the basement membrane and endothelial cells.
  2. **Type II:** Dense deposits disease. There is replacement of the lamina densa by electron dense material. Its nature is not exactly known.
  3. **Type III:** Subendothelial and subepithelial deposits.

**Prognosis:** Progression to renal failure.

6- Crescentic Glomerulonephritis

**Age:** Any age may be affected.

**Causes:** Idiopathic and secondary (Post streptococcal, Good Pasture’s syndrome and vasculitis).

**Clinical picture:** Severe form of nephritis, acute renal failure, or nephritic syndrome.

**Microscopy:**
- **Light microscopy:**
  Glomeruli: Epithelial crescents result from: Proliferation of parietal epithelial cells lining the Bowman's capsule, fibroblasts, histocytes and cells of unknown origin.

  Tubules and Interstitium: Variable degrees of tubular atrophy and interstitial fibrosis.

- **Immunofluorescence:** Varies according to the etiology:
  1- Granular Ig deposits if the cause is immune complex.
  2- Negative if the cause is non immunologic
  3- Linear deposits of IgG along the basement membranes in cases of Good Pasture’s syndrome.
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MPGN type: Thickening of basement membrane is due to subendothelial deposits (D) and mesangial interposition (M).

Membranoproliferative glomerulonephritis (MPGN): Thickening of the capillary basement membranes and increased mesangial matrix and cellularity resulting in prominent mesangial lobulation.

Crescentic GN: Epithelial crescents (arrows) result from: Proliferation of parietal epithelial cells lining the Bowman's capsule, fibroblasts, histocytes and cells of unknown origin.
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- **Electron microscopy:** Fusion of foot processes, crescents and immune complex deposits

**Prognosis:** Rapid progression to chronic renal failure.

**Chronic Glomerulonephritis**

**Gross appearance**
- Size: The kidney becomes smaller.
- Consistency: firm.
- Capsule: Adherent with decortications (It strips off with portions of the cortex).
- Outer surface: It is finely granular.
- Cut surface:
  - Cortex and medulla: Narrow with no differentiation between the two.
  - Calyces and pelvis: They are not affected.
  - Large vessels: They show evidence of hypertension i.e. thick and gaping

**Microscopic picture**
- **Glomeruli:** All or most of them are totally sclerotic. Few show the original glomerulopathy. Some show compensatory hypertrophy.
- **Tubules and Interstitium:** Tubular atrophy, interstitial fibrosis and chronic inflammatory cellular infiltrate.
- **Blood vessels:** Hypertensive changes.

**Pyelonephritis**

**Definition:** It is a suppurative bacterial infection of renal pelvis, calyces and interstitium.

**Microorganisms:** Mostly E-coli or mixed with other bacteria.

**Predisposing factors:**
1. Obstruction either incomplete gradual or complete intermittent. Obstruction causes: Stagnation of urine which encourages bacterial proliferation, It decreases vitality of the tissues and leads to upward spread of lower UT infection.
2. Structural abnormalities of urinary tract.
3. Diabetes mellitus.
4. Instrumentation.
5. Sex: Females are more affected than males. That is because: Females have short urethra.

Effect of pregnancy: It leads to ureteric dilatation and urinary stasis due to: a- Mechanical pressure of enlarged uterus leading to obstruction b- relaxing effect of hormones on the smooth muscles.
Chronic Glomerulonephritis
Outer surface: It is finely granular

Causes of urinary tract obstruction
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Mode of infection:
1- Ascending following cystitis: via lumen (in cases of vesicoureteric reflux subepithelially or periureteric lymphatics.
2- Haematogenous.
3- From the neighboring organs through the communicating lymphatics.

N.B. *the presence of pus cells in urine (pyuria) can result from infection anywhere in the urinary tract. However, the presence of neutrophils casts indicates Pyelonephritis. (Casts = tubular origin).

Pyelonephritis is either acute or chronic.

### N/E of Pyelonephritis

<table>
<thead>
<tr>
<th></th>
<th>Acute Pyelonephritis</th>
<th>Chronic pyelonephritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td><strong>Capsule</strong></td>
<td>Strips easily</td>
<td>Adherent with decortication</td>
</tr>
<tr>
<td><strong>Outer</strong></td>
<td>Suppurative patchy foci surrounded by hyperemia.</td>
<td>Irregular coarsely granular (due to underlying coarse irregular scarring).</td>
</tr>
<tr>
<td><strong>Cut surface</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cortex and medulla</td>
<td>Radial lines radiating from tips of papillae pelvis to cortex</td>
<td>Narrow cortex and medulla, opaque scarred areas.</td>
</tr>
<tr>
<td>- Calyces and pelvis</td>
<td>Distorted.</td>
<td>Deformed by scarring</td>
</tr>
<tr>
<td>- out lines</td>
<td>Hyperemic</td>
<td>Rough thick and mildly hyperemic</td>
</tr>
<tr>
<td>- Mucosa</td>
<td>Full of pus</td>
<td>Some pus</td>
</tr>
<tr>
<td>- Contents</td>
<td></td>
<td></td>
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</tbody>
</table>

### M/E of pyelonephritis

<table>
<thead>
<tr>
<th></th>
<th>Acute pyelonephritis</th>
<th>Chronic pyelonephritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glomeruli</strong></td>
<td>--------------</td>
<td>Periglomerular fibrosis. Some totally sclerotic glomeruli.</td>
</tr>
<tr>
<td><strong>Tubules</strong></td>
<td>Neutrophil casts.</td>
<td>Groups of atrophic tubules (thyroidization i.e. dilated and lined by flattened epithelium and contain hyaline casts picture simulating thyroid follicles) Some tubules contain neutrophil casts.</td>
</tr>
<tr>
<td><strong>Intertitium</strong></td>
<td>Focal infiltration with acute inflammatory cells.</td>
<td>Focal fibrosis and chronic suppurative inflammation.</td>
</tr>
<tr>
<td><strong>Blood vessels</strong></td>
<td>--------------</td>
<td>Hypertensive changes</td>
</tr>
</tbody>
</table>
**Chronic pyelonephritis.** Outer surface is irregular coarsely granular (due to underlying coarse irregular scarring).

**Chronic pyelonephritis:** Periglomerular fibrosis. Other glomeruli are totally sclerotic.

**Chronic pyelonephritis:** Groups of atrophic tubules (thyroidization). Some tubules contain neutrophil casts. Interstitium is densely infiltrated by inflammatory cells.
**Fate of pyelonephritis**

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Recovery</td>
<td>- Chronic renal failure</td>
</tr>
<tr>
<td>- Acute renal failure.</td>
<td>- Secondary hypertension</td>
</tr>
<tr>
<td>- Chronic pyelonephritis</td>
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</tbody>
</table>

**Differences between chronic glomerulonephritis and chronic pyelonephritis.**

<table>
<thead>
<tr>
<th></th>
<th>Ch. G.N.</th>
<th>Ch. pyelonephritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size</strong></td>
<td>Decreased</td>
<td></td>
</tr>
<tr>
<td><strong>Consistency</strong></td>
<td>Firm</td>
<td></td>
</tr>
<tr>
<td><strong>Capsule</strong></td>
<td>Adherent with decortications</td>
<td></td>
</tr>
<tr>
<td><strong>Outer surface</strong></td>
<td>Finely granular</td>
<td>Coarsely granular</td>
</tr>
<tr>
<td><strong>Cut surface</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Cortex and medulla</td>
<td>Narrow with no differentiation between cortex and medulla</td>
<td>- Narrow with no differentiation between cortex and medulla.</td>
</tr>
<tr>
<td>* Calyces and pelvis</td>
<td>Not affected</td>
<td>Distorted and deformed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contain pus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rough mucosa</td>
</tr>
<tr>
<td><strong>Large vessels</strong></td>
<td>Thick gaping due to effect of hypertension</td>
<td></td>
</tr>
<tr>
<td><strong>Glomeruli</strong></td>
<td>Most of them are sclerotic. Small No. still shows glomerulopathy.</td>
<td>Some glomeruli are sclerotic. Other show periglomerular fibrosis.</td>
</tr>
<tr>
<td><strong>Tubules</strong></td>
<td>Atrophy, thyrodization and dilatation.</td>
<td>In addition to changes seen in chronic GN. There are neutrophil casts.</td>
</tr>
<tr>
<td><strong>Interstitium</strong></td>
<td>Diffuse fibrosis and focal chronic inflammatory cells.</td>
<td>Focal fibrosis and chronic suppurative inflammatory cells.</td>
</tr>
<tr>
<td><strong>Blood vessels</strong></td>
<td></td>
<td>Hypertensive changes</td>
</tr>
</tbody>
</table>
## Acute Tubular Necrosis (ATN)

It may be toxic or ischemic or combined toxic and ischemic.

<table>
<thead>
<tr>
<th>Causes</th>
<th>Toxic ATN</th>
<th>Ischemic ATN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ingestion or inhalation of toxic substances:</strong></td>
<td>1- Severe renal hypoperfusion: Hypotensive shock, 2- Decreased blood volume (burns, dehydration, ++ hemorrhage).</td>
<td></td>
</tr>
<tr>
<td>1- Drugs: Mercurial diuretics paracetamol</td>
<td>• Proximal convoluted tubule segments (PCT) and straight portions but necrosis of the distal tubule, particularly ascending Henle's loop, also occurs. Extensive necrosis with long continuous segments are involved.</td>
<td>• Straight segments of proximal tubules (PST) and ascending limbs of Henle's loop (HL). • Tubular necrosis is patchy Focal short segments are involved with large skip areas.</td>
</tr>
<tr>
<td>2- Chemicals: Carbon tetrachloride (dry cleaning), ethylene glycol (antifreeze).</td>
<td>3- Poisons: Arsenic, chromium, mercury.</td>
<td></td>
</tr>
<tr>
<td>3- Poisons: Arsenic, chromium, mercury.</td>
<td></td>
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</tr>
</tbody>
</table>

### Sites
- Proximal convoluted tubule segments (PCT) and straight portions but necrosis of the distal tubule, particularly ascending Henle's loop, also occurs. Extensive necrosis with long continuous segments are involved.

### Morphology
- **Glomeruli** are normal.
- **Affected tubules:**
  - Tubular epithelial accompanied by rupture of basement membranes (tubulorrhexis) and occlusion of tubular lumens by casts. Attenuation or loss of proximal tubule brush borders, cell swelling and vacuolization, and sloughing of tubular cells into the tubular lumina.
  - Lumens contain casts (Tamm-Horsfall protein secreted by tubular epithelial cells, HB casts, myoglobin casts according to the etiology).
  - Some tubules show disruption of their basement membranes.
- **Interstitial:** Edema, inflammatory cellular infiltrate and scarring later on.

### Combined toxic and ischemic Acute tubular necrosis:

**Causes:**
- **Hemoglobinuria** (incompatible blood transfusion)
- **Myoglobinuria** (crush injury strenuous exercises).

**Tubular necrosis is due to:**
1- Toxic effect of the nature of the casts on the tubular epithelium.
2- Ischemic effect due to associated hypovolemia and shock.
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Course of acute tubular necrosis

- Severe oliguria due to:
  - Ischemia cause vasoconstriction > decrease in glomerular filtration rate.
  - Complete reabsorption of glomerular filtrate due to denuded tubular basement membranes.
  - Tubular obstruction by Tamm-Horsfall protein

- Diuresis:
  Loss of concentrating capacity of tubules.

- Recovery may occur.

Urinary calculi (Stones)

Pathogenesis: They are formed by the precipitation of the urinary crystalloids and colloids around a nidus.

1- Disturbance of normal crystalloid balance:

- Increased crystalloid concentration e.g. in cases of dehydration.

- Metabolic disorders:
  - Oxaluria (diet containing ++ tomatoes).
  - ++ Uric acid (gout).
  - Cysteinuria (hereditary).

- Hypercalcinuria (e.g. Hyperparathyroidism).

2- Stasis of urine as in cases of obstruction which leads to:

- Concentration of urine.
  - Precipitation of urinary constituents.
  - Predisposes to infection

3- Urinary tract infection:

- Provides a nidus formed of mucus, cells, blood, bacteria.

- Change PH e.g. E-coli → acidic urine which help formation of oxalate and uric acid stones. Pyogenic bacteria → alkaline urine that favors formation of phosphate stones.

- Disturbance of crystalloid balance: Infection provides abnormal colloid as mucus, fibrin.

Types of urinary stones:

1- Primary stones: Formed of one type of crystalloids.
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- **Metabolic stones** Occur in healthy renal pelvis and calyces. PH is acidic.
  - Calcium oxalate stones.
  - Uric acid stones.
  - Cystine stones.

- **Phosphate stones**

2- **Compound stones** They are primary stones as a nucleus and having concentric laminated secondary deposits on the surface

### Type and criteria of urinary stones.

<table>
<thead>
<tr>
<th>Primary stones</th>
<th>Metabolic stones</th>
<th>Phosphate stones</th>
<th>Compound stones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium oxalate stones</td>
<td>Oxaluria</td>
<td>Gout</td>
<td>Cystinuria</td>
</tr>
<tr>
<td>Uric acid stones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystine stones</td>
<td></td>
<td></td>
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</tbody>
</table>

| Etiology | Oxaluria | Gout | Cystinuria | Alkaline urine with infection especially in the presence of hypercalcnuria | Primary stone as a nucleus + secondary deposits. |
| N/E | Rounded | Rounded or oval | Rounded or oval | - Variable: rounded, oval or stag-horn* | - Variable: rounded, oval or stag-horn |
| - Shape | Hard | Moderately hard | Soft | - Friable | - Variable |
| - Consistency | - Spiny | - Smooth | - Smooth | - Smooth | - Smooth |
| - Outer surface | | | | | |
| - Color | - Brownish due to altered blood. | - Light brown | - Yellow | - White chalky | - Different colors according to lamellations |
| Chemical composition | Ca oxalate | Uric acid and urates | Cystein | Triple phosphate with magnesium, ammonium, carbonate and calcium | Primary or secondary deposits. |

When a stone is present in the renal pelvis and calyces it takes the shape of the branches of the calyces and acquire a **stag-horn shape**.

Uric acid stone light brown rounded

Cystein stone yellow rounded to oval

Phosphate stone white shalky

Compound stone with a primary stone as nidus

Stag horn stone
Complications of urinary stone

1- Obstruction
   - Sudden and complete obstruction → acute renal failure.
   - Complete intermittent obstruction or incomplete gradual obstruction → Dilatation of urinary tract above the level of obstruction.

2- Infection.

3- Ulceration, hematuria and perforation.

4- Squamous metaplasia predisposing to carcinoma.

Urinary tract obstruction

Causes

I. Urethral obstruction:
   • Congenital:
     - Phymosis (Congenital stenosis of prepuce opening),
     - Stricture.
     - Mucosal - like folds.
   • Acquired:

I- In the wall: Stricture (post traumatic instrumentation or inflammatory).

2- In the lumen: Calculi.

3- From outside: Enlarged prostate.

II- Urinary bladder obstruction

1- Organic: Stones, tumors obstructing the bladder neck or ureteric orifices. Bladder neck fibrosis e.g. due to fibrosis, prostatic hyperplasia....

2- Functional: Neurogenic disturbances of bladder control due to spinal cord lesion.

III. Ureteric obstruction

1- From outside:
   - Aberrant: vessels crossing in front of ureter or renal pelvis e.g. renal artery or ovarian vein.
   - Tumors, enlarged nodes, hematoma or fibrous bands.
   - Periureteral inflammation e.g. appendicitis.

2- In the wall:
   - Ptosed kidney or floating kidney due to exhaustion of supporting fat → (kink the ureter).
   - Tumors.
Fibrosis.

3- In the lumen: Stones, Ureteritis cystica.

**IV Renal Pelvis obstruction**

Stones and tumors in the renal pelvis.

**Effects of UT obstruction**

- Sudden acute obstruction → reflex anuria.
- Incomplete gradual obstruction or complete intermittent obstruction:

A- Dilatation of UT. Above the obstruction:

- Kidney → hydronephrosis.
- Ureter → hydroureter.
- Bladder → dilatation, hypertrophy and diverticulum formation.

B- Infection:- Pyelonephritis, pyonephrosis, pyoureter and cystitis.

C- Urinary calculi.

**Hydronephrosis**

**Definition:** - It is dilatation of calyces and renal pelvis with pressure atrophy of renal parenchyma due to lower down obstruction.

**Gross appearance**

- **Size** Increased.
- **Outer surface:** Lobulated.
- **Cut section:** Cortex is atrophic it forms thin walled sac also the calyces and both are filled with fluid and communicating with each other and with the renal pelvis.

**Microscopic picture:** Atrophic tubules and glomeruli.

**Complications:** Secondary infection, hypertension and chronic renal failure.
Renal pathology

Pyonephrosis

Definition: It is a chronic suppurative inflammation of the renal pelvis, calyces and interstitium with obstruction. The kidney is converted to a bag of pus.

Causes:

- Pyelonephritis with obstruction.
- Secondary infected hydronephrosis

Gross appearance

- Size: ↑
- Capsule: Thick and adherent with decortication.
- Outer surface: Irregular due to underlying locules of pus.
- Cut surface: Thin atrophic cortex, dilated calyces communicating with each other and with dilated pelvis forming locules of pus.

Pyemic kidney

It is due to systemic arterial pyemia. It results in formation of multiple abscesses in the cortex and medulla. They are related to the distribution of arterioles and capillaries.

Chronic renal failure

Causes: Bilateral chronic renal disease:

1. Polycystic disease of the kidney.
2. Chronic glomerulonephritis.
3. Chronic pyelonephritis.
4. Chronic pyelonephritis.
5. Unresolved acute tubular necrosis.
7. Chronic obstruction with hydronephrosis or pyonephrosis.

Clinical picture chronic renal failure:

1. Anemia: Due to ↓ erythropoietin
2. Nervous system: Due to the effect of uremic toxins > headache drowsiness, insomnia, coma. epileptic fits (due to hypocalcemia) and peripheral neuropathy.
3. Gastrointestinal system:
   - White coated tongue and ammonia breath due to ↑ concentration of ammonia in saliva.
   - Gastritis and erosion due to irritation by ammonia dissolved in gastric juice. It → nausea, vomiting and sometimes hematemesis.
- Colon and rectum: Deposition of urea in submucosa > ulceration and bleeding per rectum and dysentery.

4- Cardiovascular system:
- Hypertension due to high renin and salt and water retention.
- Fibrinous pericarditis and effusion due to urea deposition in the pericardial sac.
  This causes friction between visceral and parietal layers.
- Cardiomyopathy.

5- Lung:
- Pulmonary oedema (fluid overload).
- Recurrent chest infection.
- Pleurisy

6- Renal osteodystrophy:
- Renal rickets (in children).
- Osteomalacia (in adults)

**Laboratory investigations:**

Urine: Fixed specific gravity.

Blood:
- Uemic toxins (e.g Urea and non-protein nitrogenous com-pound).
- Phosphorous and potassium
- Calcium
- Creatinine.

Acidosis (Failure of the kidney to secrete acid load released from protein catabolism).

**Causes of small contracted kidney**

1- Chronic glomerulonephritis.
2- Chronic pyelonephritis.
3- Chronic interstitial nephritis.
4- Nephrosclerosis (Hypertensive kidney)

**Acute renal failure**

Definition: It is a syndrome associated with acute suppression of kidney function.

**Causes:**

I. Renal factors

1- Acute tubular necrosis.
2- Severe glomerular disease as rapidly progressive glomerulonephritis.
3- Massive infection (pyelonephritis).
4- Vascular obstruction
II. Prerenal factors
Acute circulatory failure (shock)

III. Post renal factors
Sudden complete continuous UT obstruction

Tumors of the kidney

Benign tumors:
- Fibroma (in the medulla).
- Adenoma (in the cortex).
- Hemangioma

Malignant tumors:
- Renal adenocarcinoma (Hypernephroma).
- Wilm's Tumor (Nephroblastoma).
- Secondaries.

Hypernephroma (Renal adenocarcinoma)

Origin: Renal tubules.

Age: more than 40 Years.

The tumor may secrete parathormone.

Gross appearance
- Arises from any part of the kidney.
- It is pseudocapsulated.
- Cut surface shows variable colors: Golden yellow due to ++ lipid contents of the cells. Brownish red due to excess vascularity and hemorrhage. Whitish due to bands and patches of fibrous tissue.
- Cysts containing serous, mucinous, Hemorrhagic or necrotic material.

Microscopic picture:
- Cell arrangement: Cells are arranged either in tubules, papillae or papillary cystadenocarcinoma pattern.
- Stroma: Delicate, thin vascular.
- Cells: The cells are either:
  - Clear cells: This is the commonest. They are large, uniform, rounded or polyhedral
Hypernephroma Cells are arranged in cords and tubules. Stroma: is Delicate, thin vascular. The cells have clear abundant cytoplasm, (due to its content of lipids and glycogen). with well defined border. The nucleus is small, rounded and central. This is the commonest cellular pattern.

Hypernephroma. Cut surface shows variable colors: Golden yellow due to excess lipid contents of the cells. Brownish red due to excess vascularity and hemorrhage. Whitish due to bands and patches of fibrous tissue.

Spread of hypernephroma

- Direct
  - Through capsule into perinephric fat
  - Renal pelvis
  - Through Gerota’s fascia
  - Rarely to adjacent organs

- Hematogenous
  - Lung, bone, brain, skin are common sites

- Contiguous venous spread
  - Renal vein
  - Inferior vena cava as solid tumor mass
  - To right atrium

- Lymphatic
  - Renal hilar nodes
  - Para-aortic nodes
  - Cervical nodes (rare)
Renal pathology

with well defined border, clear abundant cytoplasm (due to its content of lipids and glycogen). The nucleus is small, rounded and central.

- **Tall columnar**
- **Cuboidal**: with granular cytoplasm.
- **Spindle cells**

**Spread:**
- **Local**: To the renal pelvis, capsule and surrounding tissue.
- **Blood**: The cells frequently form thrombus-like masses into renal vein tributaries and inferior vena cava.
- **Lymphatics**: To the lumbar and para aortic lymph nodes.

**Nephroblastoma (Wilm’s tumor)**

**Origin**: Embryonic tumor arises from persisting immature cells of kidney rudiments called nephrogenic rests. They are foci of persistent nephrogenic cells resembling those of developing kidney. They are small tubular structures composed of cuboidal epithelium with darkly stained nuclei. Presence of such nephrogenic nests in the other grossly uninvolved kidney is the cause of development of Wilm's tumor later on in this kidney. So the tumor may arise bilaterally in the same time or later on.

**Age**: first four years of life.

**Gross appearance:**
- May be bilateral.  
- It remains enclosed within the kidney capsule.
- It is soft and fleshy.  
- Cut surface is homogeneous grey.

**Microscopic picture**: It is an adeno-sarcoma:
- Sarcomatous elements: Short, spindle or rounded embryonal dark cells, striated muscles, cartilage, bone, myxomatous tissue.
- Carcinomatous elements: Acini, imperfect tubules and glomerulus –like structures.

**Spread:**
- **Local**: To the capsule and surrounding tissues
- **Lymphatics**: To the lumbar and para aortic lymph nodes.
- **Blood**: Rapid spread.
Renal pathology

M/E of Nephroblastoma: is an adeno-sarcoma. Sarcomatous elements: Forms the background. Short, spindle or rounded dark embryonal cells. Carcinomatous elements: Acini, imperfect tubules and glomerulus–like structures.

N/E of Nephroblastoma: Tumour is well defined circumscribed. Cut surface is homogeneous grey.

Diseases of the urinary bladder

- **Cystitis**: Acute and chronic
- **Diverticulae**: Congenital and acquired.
- **Stones**.
- **Tumors**.

**Cystitis**

**Predisposing factors**: Obstruction, diabetes mellitus, local lesions (stones, Bilharsiasis, diverticulum and tumors)

**Organisms**: E-Coli, pyogenic cocci and specific organism as TB.

**Mode of infection**: Ascending, descending, hematogenous, lymphatics or nearby infection.

**N/E**: Thick wall due to inflammation and fibrosis.

**M/E**: 1- Acute inflammation: catarrhal, purulent or membranous.
2- Chronic inflammation: Non specific and specific.

**Complications**: Ascending infection → Ureteritis and Pyelonephritis.
- Local effects: Gangrene, stones and leukoplakia (whitish patches in the mucosa due to squamous metaplasia)
Effects of urinary tract obstruction on the urinary bladder

1- Dilatation.

2- Compensatory hypertrophy of the muscles → thick prominent trabeculae separated by depressions.

3- Herniation of the mucosa over the depressions → false diverticulae.

4- Failure of compensatory mechanisms → huge bladder dilatation with thin wall.

**Bladder diverticulae**

**Definition:** It is local dilatation producing a pouch-like projection.

**Types:**

1- Congenital: True diverticulum. Its wall is formed of the whole thickness of the urinary bladder.

2- Acquired: It is a false diverticulum. Its wall is formed of the mucosa only.

**Pathogenesis of diverticulum formation:** Herniation of the mucosa over depressions between the hypertrophied muscle bundles (trabeculations) resulted due to the effect of obstruction.

**Complications:** Stagnation, infection, stones, ulceration, perforation and malignancy

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**Cross section of bladder wall including muscles & mucosa**

**Trabeculation of bladder wall due to hypertrophied muscle bundles**

**Wall of diverticulum devoid of muscles**

**Hyperplastic prostate**

Bladder diverticulae
Renal pathology

Tumors of the urinary bladder

Benign:

1. **Epithelial** Transitional cell papilloma.
2. **Non epithelial**: Leiomyoma, fibroma, lipoma, hemangioma.

Malignant:

**Predisposing factors:**

1. Urinary Bilharziasis
2. villous papilloma
3. Workers in some industries e.g. aniline dyes, rubber and benzidine.
4. Cigarette smoking
5. Prolonged high doses of analgesics.

**Gross appearance** It may form a fungating mass or malignant ulcer or diffuse infiltrating tumor. In addition, the transitional cell carcinoma may have a papillary villous pattern.

**Histopathological types**

1. **Transitional cell carcinoma:**

**M/E:** The tumour has one of the following patterns:

- **Transitional cell carcinoma in situ:** Replacement of normal urothelium by highly atypical cells having the criteria of malignancy which include: Loss of normal polarity and arrangement of the normal transitional epithelium, pleomorphism, hyperchromatism, frequent mitotic figures and increased nuclear cytoplasmic ratio. There is no invasion of the basement membrane.

- **Papillary transitional cell carcinoma:** The tumour is arranged in papillae with thin vascular cores not infiltrating the muscles or subepithelial tissue.

- **Papillary and infiltrating transitional cell carcinoma:** The tumour forms solid sheets infiltrating the subepithelial tissue with or without invasion of the muscles.

2. **Squamous cell carcinoma**.

It arises on top of squamous metaplasia

**M/E:** Sheets of malignant squamous cells with variables degrees of keratinization and cell nests formation. The more differentiated tumors show more cell nests.

3. **Adenocarcinoma**

It arises on top of glandular metaplasia or remnants of urachus at the apex of urinary bladder.

**M/E:**

- Malignant Glands in different grades of differentiation forming irregular glands sheets infiltrating the subepithelial tissue and surrounded by a fibrous stroma.
The tumour is arranged in papillae with thin vascular cores.
Papillary transitional cell carcinoma. The tumour has villous surface.
Sheets of malignant squamous cells with variable degrees of keratinization and cell nests formation.
Fungating nodular mass.

Stages of bladder tumour infiltration.
Renal pathology

- **Signet ring adenocarcinoma**: the cells may have a signet ring appearance in a background of mucin.

4- **Anaplastic carcinoma**.

Tumour cells Lose any pattern of differentiation

**Bilharzial carcinoma**

Common in Egypt. Males are affected more than females. At younger age.

**M/E**: squamous cell carcinoma mainly and to lesser extent adenocarcinoma.

**Pathogenesis**: Chronic bilharzial cystitis → squamous and glandular metaplasia and predisposes to Gm-ve cystitis. Bacteria break down dietary nitrites and nitrates secreted in urine forming the carcinogenic material nitrosamines which acts as initiator of carcinoma.

**Spread of carcinoma of the urinary bladder**.

**Local**: To the wall of bladder and surroundings

**Lymphatic**: To pelvic lymph nodes.

**Blood**: By the systemic circulation to the lungs then bones and other organs.

**Hematuria**

It is passage of blood with urine.

**Causes**:

I. **Renal Diseases**:

2. Conditions associated with nephritis e.g. poststreptococcal GN. and rapidly progressive GN.
3. Infarction.
4. Acute pyelonephritis
5. Tumors.

II. **Urinary bladder diseases**:

1. Diverticulae.
2. Cystitis especially bilharzial.
3. Tumors.
4. Calculi.

III. **Blood diseases**.

- The renal pelvis and ureter can acquire the same epithelial tumours of the urinary bladder.