

DISEASES OF KIDNEY AND URINARY TRACT

Diseases of the kidney are characterized by the injury basic morphologic components:

- glomeruli,
 - tubules,
 - interstitium, and
 - blood vessels.
- The clinical manifestations of renal diseases can be grouped into reasonably well-defined syndromes.

the major renal syndromes:

Acute nephritic syndrome is

a **glomerular syndrome** dominated by the acute inset of usually grossly visible

- hematuria (red blood cells in urine),
- mild to moderate proteinuria,
- hypertension;

it is the classic presentation of

acute poststreptococcal glomerulonephritis GN).

the major renal syndromes:

The **nephrotic syndrome** is characterized by :

- heavy proteinuria,
- hypoalbuminuria,
- severe edema,
- hyperlipidemia,
- lipiduria.

the major renal syndromes:

subtle or mild glomerular abnormalities

is characterized by :

- Asymptomatic hematuria
- Asymptomatic proteinuria,
- or a combination of them,

the major renal syndromes

Acute renal failure is dominated by:

- oliguria or anuria,
- with recent onset of azotemia.

It can result from:

- glomerular injury,
- interstitial injury,
- acute tubular necrosis.

the major renal syndromes

Chronic renal failure characterized by:

- prolonged symptoms and
- signs of uremia,
- is the final result of all chronic renal diseases.

the major renal syndromes:

Renal tubular defects are dominated by :

- polyuria,
- nocturia,
- electrolyte disorders.
- They are the result of either diseases directly affecting tubular structure or defects in specific tubular infection. The latter may be inherited or acquired.

•**Urinary tract infection** is characterized by bacteriuria and pyuria. The infection may be symptomatic or asymptomatic, and it may affect the kidney or the bladder only.

the major renal syndromes

Nephrolithiasis (renal stone) is manifested by:

- renal colic,
- hematuria,
- recurrent stone formation

Glomerular Diseases

•*Glomerular injury* is a major cause of renal disease and may be primary and secondary.

Primary glomerular diseases are characterized by primary injury of the glomeruli:

- acute and chronic glomerulonephritis (GN),
- lipoid nephrosis, etc.).

In **secondary glomerular diseases** the kidney is one of many organs and systems damaged by a systemic disease :

- Systemic lupus erythematosus,
- diabetes mellitus,
- amyloidosis, etc.)

Pathogenesis of glomerular injury

At glomerular injury is involved :

- endothelial*,
- mesangial*,
- visceral epithelial*,
- and *parietal epithelial cells* .

There are two basic mechanisms of glomerular injury: immune and nonimmune.

•Immune mechanisms

•A. Antibody-mediated glomerular injury

- 1. Immune complex disease.

Pathogenesis of glomerular injury

•Immune complex GN is observed in the following diseases:

•*Primary GN*: acute diffuse proliferative GN, membranous GN, membranoproliferative GN, IgA some nephropathy and cases of rapidly progressive GN and focal GN.

•*Systemic* diseases: glomerular disease in SLE, malaria, syphilis, hepatitis, Henoch-Schonlein purpura and idiopathic mixed cryoglobulinemia.

Pathogenesis of glomerular injury

•2, **Anti- GBM disease**. Less than 5% cases of human GN are associated with anti-GBM antibodies. The component of GBM acting as antigen appears to component of collagen IV of the basement membrane.

•Anti-GBM disease is classically characterized by *homogeneous linear deposits* of anti-GBM antibodies (mostly IgG; rarely IgA and IgM) and complement (mainly C3) along the glomerular basement membrane.

•Anti-GBM disease is characteristically exemplified by glomerular injury in **Goodpasture's syndrome**. About half to two-third of the patients with renal lesions in Goodpasture's syndrome have pulmonary hemorrhage mediated by cross-reacting autoantibodies against alveolar basement membrane.

Pathogenesis of glomerular injury

•**3. Alternative pathway disease.** The complement system, in particular C3, contributes to glomerular injury in the majority of forms of GN.

•Alternate pathway disease occurs in most cases of type II membranoproliferative GN, some patients of rapidly progressive GN, acute diffuse proliferative GN, IgA nephropathy and in SLE.

Pathogenesis of glomerular injury

4. Other mechanisms of antibody-mediated injury.

•*Anti-neutrophil cytoplasmic antibodies (ANCA).*

•*Anti-endothelial cell antibodies (AECA).*

Autoantibodies against endothelial antigens have been detected in circulation are several inflammatory vasculitis and glomerulonephritis.

•**B. Cell-mediated Glomerular Injury**

•**C. Secondary pathogenetic mechanisms**

Secondary pathogenetic mechanisms are a number of mediators of immunologic glomerular injury, such as: neutrophils, mononuclear phagocytes, complement system, platelets, mesangial cells, and coagulation system.

Nonimmune mechanisms

•Though most forms of GN are immunologically mediated, a few examples by non-immunologic mechanisms are found:

•Metabolic glomerular injury, e.g. diabetic nephropathy.

•Hemodynamic glomerular injury, e.g. systemic hypertension.

•Deposition diseases, e.g. cryoglobulinaemia, amyloidosis.

•Infectious diseases, e.g. HBV, HCV, HIV.

•Inherited glomerular diseases, e.g. Alport's syndrome, nail-patella syndrome.

These diseases destroy sufficient functioning nephrons.

•Adaptive changes in glomeruli to the increased workload cause epithelial and endothelial injury and result in proteinuria. The mesangial response, involving mesangial cell proliferation and matrix deposition, and intraglomerular coagulation cause the glomerulosclerosis.

Acute Glomerulonephritis

The first group of glomerular diseases are characterized :

- anatomically by inflammatory alterations in the glomeruli

- clinically by a complex of findings classically referred to as the syndrome of acute nephritis.

It is infectious-allergic or unknown etiology disease with double nonsuppurative glomerulitis.

The nephritic patient usually presents with hematuria, red cell casts in the urine, azotemia, oliguria, and mild to moderate hypertension.

Nonrenal features:

-arterial hypertension,

-hypertrophy of left heart,

-disproteinemia,

-edema,

-hypernitrogenemia

- uremia .

•The patient also commonly has proteinuria and edema

glomerulonephritis classification

•- Glomerulonephritis may be primary or secondary.

•- According to the etiology it may be bacterial, viral, unclear.

- According to the *pathogenesis* there are 2 types of glomerulonephritis: -immuno- associated and non-immunoassociated.
- According to the *course GN* may be classified into acute, sub-acute, chronic.
- In *morphological classification*, topography, character, propagation of pathological process are accounted:
- According to topography: intra- and extracapillary GN.
- According to character of inflammation: nonsuppurative exudative and proliferative.
- According to propagation: diffuse and local.

Acute poststreptococcal glomerulonephritis

- It usually appears 1 to 4 weeks after streptococcal infection of the pharynx or the skin.
- It occurs most frequently in children of six to ten years of age, but adults of any age can be affected.
- Duration of disease may 1,5 to 12 months.

Acute poststreptococcal glomerulonephritis

Gross appearance:

- Kidney enlarged;
- cortex broad, pale, without markings;
- medullary rays congested;
- glomeruli just visible as grey avascular dots.

Acute poststreptococcal glomerulonephritis

- The classic diagnostic picture is one of enlarged, hypercellular, relatively bloodless glomeruli.
- The most often the histological type is intracapillary proliferative GN:
- Proliferation of endothelial and mesangial cells and, in many cases, epithelial cells.
- Infiltration by leukocytes, both neutrophils and monocytes. The proliferation and leukocytes infiltration are diffuse, that is, involving all lobules of all glomeruli.
- There is also swelling of endothelial cells, and the combination of proliferation, swelling, and leukocytic infiltration obliterates the capillary lumen.
-

Acute poststreptococcal glomerulonephritis

- Special stains can demonstrate small deposits of fibrin within capillary lumina and mesangium.
- There may be interstitial edema and inflammation, and the tubules often contain red cell casts and may show evidence of degeneration.
- By immunofluorescence microscopy there are granular deposits of IgG, IgM, and C3 in the mesangium and along the basement membrane. Although present, they are often focal and sparse. The characteristic electron microscopic findings are the discrete, amorphous, electron-dense deposits on the epithelial side of the membrane, often having the appearance of "humps", presumably representing the antigen-antibody complexes at the epithelial cell surface. Subendothelial and intramembranous deposits sometimes seen, and there is often swelling of endothelial and mesangial cells.

proliferative glomerulonephritis

- This glomerulus is hypercellular and capillary loops are poorly defined. This is a type of proliferative glomerulonephritis known as post-streptococcal glomerulonephritis.

post-streptococcal glomerulonephritis

- The hypercellularity of post-streptococcal glomerulonephritis is due to increased numbers of epithelial, endothelial, and mesangial cells as well as neutrophils in and around the capillary loops. This disease may follow several weeks after infection with certain strains of group A beta hemolytic streptococci. Patients typically have an elevated anti-streptolysin O (ASO) titer.

Rapidly progressive (crescentic) glomerulonephritis

It is a syndrome characterized by the accumulation of cells in Bowman's space in the form of "*crescents*" accompanied by:

- a rapid, progressive decline in renal function,
- frequently with severe oliguria or anuria,
- usually resulting in irreversible renal failure in weeks or months.

Rapidly progressive (crescentic) glomerulonephritis

•Morphology

- According to histological picture there is extracapillary proliferative GN.
- The kidneys are enlarged and pale, often with petechial hemorrhages on the cortical surfaces.
- Depending on the underlying cause, the glomeruli may show focal necrosis, diffuse or focal endothelial proliferation.
- The syndrome is characterized histologically by the accumulation of cells in Bowman's space in the form of "crescents".

Rapidly progressive (crescentic) glomerulonephritis

Morphology:

- The histologic picture, however, is dominated by the formation of distinctive crescents, which are formed by proliferation of parietal cells and by migration of monocytes and macrophages into Bowman's space. Neutrophils and lymphocytes can be present.
- The crescents eventually obliterate Bowman's space and compress the glomerular tuft.
- Fibrin strands are prominent between the cellular layers in the crescents.
- Electron microscopy may disclose subepithelial deposits in some cases, but in all cases shows distinct ruptures in the GBM.
- In time, most crescents undergo sclerosis.

Rapidly progressive (crescentic) glomerulonephritis

This syndrome may occur in the course of three broad disease groups:

- Postinfectious rapidly progressive (crescentic) glomerulonephritis, complicating acute GN.
- Systemic diseases (SLE, Goodpasture's syndrome, polyarteritis nodosa, etc).
- Idiopathic.

Nephrotic syndrome

•Membranous glomerulonephritis (MGN)

- It is a major cause of nephrotic syndrome in adults.
- It is characterized by the presence of electron-dense, immunoglobulin-containing deposits along the epithelial side of the basement membrane.
- In situ formation and deposition of circulating immune complexes, involving intrinsic glomerular antigens or endogenous and exogenous or planted antigens, are postulated to account for the subepithelial electron-dense deposits.
- Early in the disease, the glomeruli may appear normal by light microscopy, but well-developed cases show diffuse thickening of the capillary wall.

Membranous glomerulonephritis (MGN)

•Etiology

- Malignant epithelial tumors, particularly carcinoma of the lung and colon and melanoma.
- Systemic lupus erythematosus (SLE).
- Exposure to inorganic salts (gold, mercury).
- Drugs (penicillamine, captopril).

- Infections (chronic hepatitis B, syphilis, schistosomiasis, malaria).
- Metabolic disorders (diabetes mellitus, thyroiditis).
- In about 85% of patients, the condition is truly "idiopathic".

Membranous glomerulonephritis (MGN)

morphology

- By light microscopy, the glomeruli appear normal in the early stages of the disease or exhibit uniform, diffuse thickening of the glomerular capillary wall, hence the term 'membranous'.
- By electron microscopy the apparent thickening is caused by irregular dense deposits between the basement membrane and the overlying epithelial cells, the latter having lost their foot processes.
- Basement membrane material is laid down between these deposits, appearing as irregular spikes protruding from the GBM.
- Immunofluorescence microscopy demonstrates that the granular deposits contain both immunoglobulins and complement.
- Others changes: protein and fatty droplets in the tubular epithelium and stroma. Foamy macrophages and giant cells form granulomas is association with cholesterol deposits.
- With progress of the disease, narrowing of the glomerular capillaries causes ischemic atrophy of the tubules and interstitial fibrosis.

Membranoproliferative glomerulonephritis (MPGN)

- As the term implies, this group of disorders is characterized histologically by alteration in the basement membrane and proliferation of glomerular cells. Because the proliferation is predominant in the mesangium, a frequently used synonym is *mesangiocapillary GN*.
- Like many other GN, histologic MPGN either can be associated with other systemic disorders and known etiologic agents (secondary MPGN) or may be primary, without known cause (idiopathic) in the kidney.
- Patients have hematuria or proteinuria demonstrate a combined nephritic-nephrotic picture.

Membranoproliferative glomerulonephritis (MPGN)

Morphology

- Primary MPGN is divided into two major types on the basis of distinct ultrastructural, immunofluorescent, and probably pathogenic findings.
 - By light microscopy both types are similar.
 - The glomeruli are large and hypercellular.
 - The hypercellularity is produced by proliferation of cells in the mesangium, although infiltrating leukocytes and parietal epithelial crescents are present in many cases.
 - The glomeruli have a "lobular" appearance accentuated by the proliferating mesangial cells and increased mesangial matrix.
 - The GBM is clearly thickened, often focally, most evident in the peripheral capillary loops.
 - The glomerular capillary wall often shows a "double-contour" or "tram-track" appearance, especially evident in silver or PAS stains.
 - This is caused by "splitting" of the basement membrane because of the inclusion within it of processes of mesangial cells extending into the peripheral capillary loops, so-called mesangial interposition.
 - Injury of tubular structures and stroma take place.
- membranous glomerulonephritis
- By electron microscopy in membranous glomerulonephritis, the darker electron dense immune deposits are seen scattered within the thickened basement membrane. The "spikes" seen with the silver stain represent the intervening matrix of basement membrane between the deposits.

Minimal change disease (MCD) (Lipoid nephrosis)

-- Nephrotic syndrome in children can be often; characterized by normal glomeruli on light microscopy but uniform and diffuse effacement of the foot processes of visceral epithelial cells on electronic microscopy.

• **Etiology** is unknown.

-- Immunofluorescence shows no immune deposits.

-- The most characteristic feature of this condition is the good response to corticosteroid therapy.

-- Proteinuria is usually selective and is associated with loss glomerular filtration (negative charges) and a hyperpermeable capillary wall.

• **Morphology**

-- GBM isn't changes.

-- Tubules are dilated; their epithelium is swelling, containing hyaline and fatty droplets.

-- Fatty degeneration, necrobiosis, atrophy, desquamation in tubular epithelium take place.

-- Gross appearances (*big white kidneys*): kidneys enlarged, flabby, yellow color.

Chronic glomerulonephritis (CGN)

•- CGN is the final stage of GN when sclerosis has eliminated many glomeruli and their associated tubules.

•- This is often the late result of membranous or membranoproliferative GN, less commonly postinfectious acute nephritis.

•- At the final stage, it is difficult to determine the etiology of the pathological lesion.

Chronic glomerulonephritis (CGN)

Morphology

•- The kidneys are symmetrically contracted and have diffusely granular, cortical surfaces.

• Pieces of renal tissue adhere to stripped capsule;

• Capsule is adherent and strips with difficult.

• Weight is 50 gm each.

• On section, the cortex is thinned and irregular, pelvis dilated and they're in an increasing peripelvic fat. Such kidneys are called "*secondary shrinkage kidneys*".

Chronic glomerulonephritis (CGN)

Morphology

The glomerular histology depends on the stage of the disease.

- In early cases, the glomeruli may still show evidence of the primary disease.

-- Kidneys from the patients with end-stage disease on long-term dialysis exhibit a variety of so-called "dialysis changes" that are unrelated to the primary disease.

• Histological feature is nephrosclerosis.

-- These include arterial intimal thickening caused by accumulation of smooth muscle-like cells and a loose, proteoglycan-rich stroma;

• calcification, most obvious in glomerular tufts and tubular basement membranes;

• extensive deposition of calcium oxalate crystals in tubules and interstitium;

• acquired cystic disease;

• increased numbers of renal adenomas and borderline adenocarcinomas.

Chronic glomerulonephritis (CGN)

Patients dying with chronic GN also exhibit pathologic changes outside the kidney that are related to the uremic state and are also present in other forms of chronic renal failure.

• Often clinically important, these includes uremic pericarditis, uremic gastroenteritis,

• secondary hyperparathyroidism with nephrocalcinosis and renal osteodystrophy,

• left ventricular hypertrophy due to hypertension,

- pulmonary changes of diffuse alveolar damage often ascribed to uremia (uremic pneumonitis).
- Uremia, hypertensive cardiac failure or cerebral hemorrhage may cause death.

Amyloidosis of the kidney

• Here amyloid deposits are seen in glomeruli at the left and arteries at the right. Amyloidosis may be of the "AL" type in patients with plasma cell dyscrasias (multiple myeloma) in which the amyloid is associated with excess immunoglobulin light chain production, or it may be the "AA" type or "amyloid associated" in which the cause is often chronic inflammatory diseases.

Tubulopathy

• **Acute renal failure (ARF)**

• **acute tubular necrosis**

Acute renal failure (ARF)

• is a syndrome associated with acute suppression of renal function, often accompanied by oliguria, and rarely anuria or polyuria. ARF is caused by:

- Organic vascular obstruction.
- Severe glomerular disease.
- Acute tubulointerstitial nephritis.
- Massive infection.
- Disseminated intravascular renal coagulation.
- Urinary obstructions.
- Acute tubular necrosis.

Acute tubular necrosis (ATN)

ATN is characterized by destruction of renal tubular epithelial cells either from

- -ischemia or
- - nephrotoxins.

Ischemic ATN

• is called tubulorrhectic ATN or shock kidney,

• occurs due to hypoperfusion of the kidneys resulting in focal damage to the tubules.

acute tubular necrosis (ATN),

• The tubular vacuolization and dilation here is a result of ethylene glycol poisoning. This is representative of acute tubular necrosis (ATN), which has many causes. ATN resulting from toxins usually has diffuse tubular involvement, whereas ATN resulting from ischemia (as in profound hypotension from cardiac failure) has patchy tubular involvement.

Ischemic ATN

Etiology.

Ischemia may result from following causes:

- Shock (post-traumatic, surgical, burns, dehydration, obstetrical and septic).
- Crush injuries.
- Non-traumatic rhabdomyolysis induced by alcohol, coma, muscle disease or extreme muscular exertion (myoglobinuria nephrosis).
- Mismatched blood transfusions, black-water fever (hemoglobinuric nephrosis).

Ischemic ATN

The *pathogenetic mechanism* of ischemic ATN is explained on the basis of:

- Arteriolar vasoconstriction induced by renin-angiotensin system.

- Tubular obstruction by casts in the lumina or by interstitial edema.
- Back-leak of tubular fluid into the interstitium.

Ischemic ATN

Morphology

- The kidneys are enlarged and swollen.
- On cut section, the cortex is often widened and pale, while medulla is dark.
- Predominant changes are seen in the tubules, while glomeruli are normal.
- Interstitium shows edema and mild chronic inflammatory cell infiltrate.
- Tubular changes are as follows:
 - Dilatation of the proximal and distal convoluted tubules.
 - Focal tubular necrosis at different points along the nephron.
 - Flattened epithelium lining the tubules.
 - Eosinophilic hyaline casts or pigmented hemoglobin and myoglobin casts in the tubular lumina.
 - Disruption of tubular basement membrane (tubulorrhexis).

Nephrotoxic ATN

occurs as a result of direct damage to tubular cells by ingestion, injection or inhalation of a number of toxic agents.

Etiopathogenesis.

The toxic agents causing toxic ATN are:

- General poisons such as mercuric chloride, carbon tetrachloride, ethylene glycol, mushrooms and insecticides.
- Heavy metals (mercury, lead, arsenic, phosphorus and gold).
- Drugs, such as sulfonamides, certain antibiotics (gentamycin, cephalosporin), anaesthetic agents (methoxyflurane, halothane), barbiturates, salicylates.
- Radiographic contrast material.
- The *pathogenetic mechanism* producing ARF in toxic ATN is in principle similar to that for ischemic ATN.

Nephrotoxic ATN

Morphology

- The kidneys are enlarged and swollen.
- On cut section, the cortex is pale, while the medulla is slightly darker than normal.
- In general it involves the segment of tubule diffusely. In mercuric chloride poisoning, the features are as follows:
 - Epithelial cells of mainly proximal convoluted tubules are necrotic and desquamated into the tubular lumina.
 - The desquamated cells may undergo dystrophic calcification.
 - Tubular basement membrane is generally intact.
 - The regenerating epithelium, which is flat and thin with few mitoses, may be seen lining the tubular basement membrane.

Nephrotoxic ATN

The clinical course of ATN may be divided into stages:

- The **initiating stage (shock)**
- The **maintenance stage (Oliguric phase)**,
- The recovery stage (Polyuric phase)

Nephrotoxic ATN

The clinical course of ATN :

The **initiating stage (shock)**, lasting for about 36 hours, is dominated by the inciting medical, surgical, or obstetric event in the ischemic form of ATN.

- Macroscopically,
- kidneys are diffusely swollen and edematous.

- It is characterized by ischemic cortex and congestion of pyramids.
- Acute renal failure and
- oliguria,
- hyperkalemia and
- fluid overload in patients develop.

Nephrotoxic ATN

The clinical course of ATN

- The **maintenance stage (Oliguric phase)**, 2-9 days) is characterized by sustained decreases in urine output to between 40 to 400 ml per day, with salt and water overload,
- rising blood urea nitrogens,
- hyperkaliemia,
- metabolic acidosis,
- and other manifestations of uremia dominating this phase.
- There is blockage of renal tubules by necrotic cells, and a secondary reduction in glomerular blood flow (caused by arteriolar constriction) reduces glomerular filtration.
- It stage may be fatal.

Nephrotoxic ATN

The clinical course of ATN

- The **recovery stage (Polyuric phase)**, 10-21 days) is ushered by a steady increase in urine volume that may reach up to 3 liters per day.
- Regeneration of renal tubular epithelium takes place, with removal of dead material by phagocytic cells, as well as in the form of casts in urine.
- As tubules open up and glomerular blood flow increases, patients develop polyuria.
- This is because the regenerated tubular cells are undifferentiated and have not developed the specializations necessary for resorption of electrolytes and water. Replacement of fluid and electrolytes is needed to compensate for excessive loss from urine. Hypokalemia, rather than hyperkalemia, becomes a clinical problem The prognosis of ATN depends on the clinical setting surrounding its development

Tubulointerstitial Disease

- The term tubulointerstitial nephritis is used for inflammatory process that predominantly involves the renal interstitial tissue and is usually accompanied by some degree of tubular damage.
- The term *interstitial nephritis* is reserved for those cases where there is no primary involvement of glomeruli, tubules or blood vessels.
- A number of bacterial and non-bacterial, acute and chronic conditions may produce tubulointerstitial nephritis.
- In this case of drug-induced interstitial nephritis, there are some scattered eosinophils, along with neutrophils and mononuclear cells in the inflamed interstitium

Pyelonephritis (PN)

PN is a renal disorder affecting tubules, intrestitium, and renal pelvis and is one of the most common diseases of the kidney.

It occurs in two forms:

- Acute PN is acute pyogenic infection.
- Chronic PN is a more complex disorder:
- bacterial infection plays a dominant role, but other factors (vesicoureteral reflux, obstruction) are involved in its pathogenesis.
- The term urinary tract infection (UTI) implies involvement of either the "bladder (cystitis) or the kidney and their collecting system (pyelonephritis), or both.
- UTIs are extremely common disorders.

Pyelonephritis (PN)

Etiopathogenesis

- The dominant etiologic agents are the gram-negative bacilli that are normal inhabitants of the intestinal tract: E.coli (Proteus, Klebsiella and Enterobacter), Str. fecalis etc. In most patients with UTI, the infecting organisms are derived from the patient's own fecal flora. This is thus a form of endogenous infection.
- There are two routes by which bacteria can reach the kidneys:
- Through the bloodstream (hematogenous).
- From the lower urinary tract (ascending infection).

Although obstruction is an important predisposing factor in the pathogenesis of ascending infection, it is incompetence of the vesicoureteral orifice that allows bacteria to ascend the ureter into the pelvis.

Acute Pyelonephritis

Morphology

- The hallmarks of acute PN are patchy interstitial suppurative inflammation and tubular necrosis.
 - Macroscopically,
 - the kidneys show variable numbers of small, yellowish white cortical abscesses, which are usually spherical, under 2 mm in diameter, and are sometimes surrounded by a zone of hyperemia;
 - the cortical abscesses are often most prominent on the sub-capsular surface, after the capsule has been stripped away.
 - In the medulla the abscesses tend to be in the form of yellowish white linear streaks that converge on the papilla.
 - The pelvicalyceal mucosa is hyperemic or covered with a fibrinopurulent exudate.
 - Histologically:
 - the neutrophilic infiltration is limited to the interstitial tissue.
 - Some tubules destroyed: abscesses formed; other tubules filled by puss cells.
 - Glomeruli usually unaffected.
- pyelonephritis microabscesses
- The cut surface of the kidney reveals many small yellowish microabscesses in both cortex and medulla. This type of pyelonephritis is most typical for hematogenous dissemination of infection to the kidney, rather than the more typical ascending urinary tract infection.

Acute Pyelonephritis

Clinical features.

- Classically, acute pyelonephritis has an acute onset with chills, fever, loin pain, lumbar tenderness, dysuria and frequency of micturition.
- Urine will show bacteria, pus cells and pus cell casts in the urinary sediment.

Acute Pyelonephritis

complications of acute PN

- Papillary necrosis is seen mainly in diabetics and in those with urinary tract obstruction. Papillary necrosis is usually bilateral, but may be unilateral.
- Pyonephrosis is seen when there is total or almost complete obstruction, particularly when it is high in the urinary tract (pelvis filled with puss).
- Perinephric abscess implies extension of suppurative inflammation through the renal capsule into the perinephric tissue.
- At the acute phase of PN, healing occurs. The neutrophilic infiltration is replaced by macrophages, plasma cells, and (later) lymphocytes. The inflammatory foci are eventually replaced by scars. The pyelonephritic scar is almost always associated with inflammation, fibrosis, and deformation of the underlying calyx and pelvis.

•Uncomplicated acute PN usually follows a benign course, and the symptoms disappear within a few days after the institution of appropriate antibiotic therapy. In the presence of unrelieved urinary obstruction, diabetes mellitus acute PN may be more serious, leading to repeated septicemic episodes.

acute pyelonephritis

•This is an ascending bacterial infection leading to acute pyelonephritis. Numerous PMN's are seen filling renal tubules across the center and right of this picture.

acute pyelonephritis

•At high magnification, many neutrophils are seen in the tubules and interstitium in a case of acute pyelonephritis. The neutrophils can collect in the distal tubules and be passed in urine as WBC casts.

papillary necrosis.

•The pale white areas involving some or all of many renal papillae are areas of papillary necrosis. This is an uncommon but severe complication of acute pyelonephritis, particularly in persons with diabetes mellitus. Papillary necrosis may also accompany analgesic nephropathy.

Chronic Pyelonephritis (CPN)

Chronic PN is a chronic tubulointerstitial renal disorder in which chronic tubulointerstitial inflammation and renal scarring are associated with pathologic involvement of the calyces and pelvis.

•*Etiopathogenesis*. Two types of chronic pyelonephritis are described:

•Reflux nephropathy. Reflux of urine from the bladder into one or both the ureters during micturition is the major cause of chronic pyelonephritis.

•*Vesicoureteric reflux* is particularly common in children, especially in girls, due to congenital absence or shortening of intravesical portion of the ureter so that ureteris not compressed during the act of micturition.

Reflux results in increase in pressure in the renal

pelvis so that the urine is forced into renal tubules, which are eventually followed by damage to the kidney and scar formation.

•Obstructive pyelonephritis. Obstruction to the outflow of urine at different levels predisposes the kidney to infection. Recurrent episodes of such obstruction and infection result in renal damage and scarring.

Chronic Pyelonephritis (CPN)

Morphology

• The kidneys are usually small and contracted (weighing less than 100 gra) showing unequal reduction; if bilateral, the involvement is asymmetric.

•The surface of the kidney is irregularly scarred; the capsule can be stripped off with difficulty due to adherence to scars.

•There is generally dilatation of pelvis and blunted calyces.

-The *microscopic changes* involve predominantly tubules and interstitium.

--The tubules show atrophy in some areas and hypertrophy in others, or dilatation. Dilated tubules may be filled with colloid crystals, producing *thyroidisation of tubules (thyroid-like)*.

--Interstitium. There is chronic interstitial inflammatory reaction, chiefly composed of lymphocytes, plasma cells and macrophages with

pronounced interstitial fibrosis.

•Pelvicalyceal system. The renal pelvis and calyces are dilated. And show marked chronic inflammation and fibrosis.

•Blood vessels. Blood vessels entrapped in the scarred areas show obliterative endarteritis.

•Glomeruli. There is often periglomerular fibrosis. In advanced cases, there may be hyalinisation of glomeruli.

chronic pyelonephritis

•The large collection of chronic inflammatory cells here is in a patient with a history of multiple recurrent urinary tract infections.

chronic pyelonephritis.

- Both lymphocytes and plasma cells are seen at high magnification in this case of chronic pyelonephritis. It is not uncommon to see lymphocytes accompany just about any chronic renal disease: glomerulonephritis, nephrosclerosis, pyelonephritis. However, the plasma cells are most characteristic for chronic pyelonephritis.
- chronic renal failure
- The cortex is fibrotic, the glomeruli are sclerotic, there are scattered chronic inflammatory cell infiltrates, and the arteries are thickened. Tubules are often dilated and filled with pink casts and give an appearance of "thyroidization."

Chronic Pyelonephritis (CPN)

Clinical features.

- *Chronic pyelonephritis often has an insidious onset.*
 - *The patients present with clinical picture of chronic renal failure or with symptoms of hypertension.*
 - Chronic obstructive PN* may be insidious in onset or may present the clinical manifestations of acute recurrent PN with back pain, fever, frequent pyuria, and bacteriuria.
- xanthogranulomatous pyelonephritis
- Sometimes long-standing infection may be localized and form a mass-like lesion. This is a disease known as xanthogranulomatous pyelonephritis. It is uncommon, but may mimic a neoplasm.
- xanthogranulomatous pyelonephritis
- The microscopic appearance of xanthogranulomatous pyelonephritis shows many pale to foamy macrophages from breakdown of renal parenchyma with ongoing inflammation.

Urolithiasis

- Urolithiasis or formation of urinary calculi at any level of the urinary tract is a common condition. It is estimated that approximately 2% of the population experiences renal stone disease at sometime in their life with male-female ratio of 2:1.
- Renal calculi are characterized clinically by colicky pain (*renal colic*) as they pass down along the ureter and manifest by hematuria.
- Sites of formation:
- Precipitates form in the collecting tubules and pass into renal pelvis where they enlarge.
- Deposits are formed in the lymphatic vessels of the renal papillae and are extruded into the renal pelvis.

Types of Urinary Calculi

- Calcium stones.* Calcium stones are the most common comprising about 75% of all urinary calculi. They may be pure stones of calcium oxalate (50%) or calcium phosphate (5%), or mixture of calcium oxalate.
- Mixed (Struvite) stones.* About 15% of urinary calculi are made of magnesium-ammonium-calcium phosphate, often called *struvite*. "Staghorn stone which is a large, solitary stone that takes the shape of the renal pelvis where it is often formed is an example of struvite stone.
- Uric acid stones.* Uric acid calculi are radiolucent unlike radio-opaque calcium stones. Uric acid stones are smooth, yellowish-brown, hard and often multiple.
- Cystine stones.* Cystine stones are small, rounded, smooth and often multiple. They are yellowish and waxy. They are seen in heritable tubular transport defects causing cystinuria.

large renal calculus (stone)

- There was a large renal calculus (stone) that obstructed the calyces of the lower pole of this kidney, leading to a focal hydronephrosis (dilation of the collecting system). The stasis from the obstruction and dilation led to infection. The infection with inflammation is characterized by the pale yellowish-tan areas next to the dilated calyces with hyperemic mucosal surfaces. The upper pole is normal and shows good corticomedullary demarcations.

Urolithiasis

Complications:

- pyelonephritis,
- hemorrhage,
- hydronephrosis

"staghorn calculus".

• Sometimes a very large calculus nearly fills the calyceal system, with extensions into calyces that give the appearance of a stag's (deer) horns. Hence, the name "staghorn calculus". Seen here is a horn-like stone extending into a dilated calyx, with nearly unrecognizable overlying renal cortex from severe hydronephrosis and pyelonephritis. Nephrectomy may be performed because the kidney is non-functional and serves only as a source for infection.

Hydronephrosis

• is the term used for dilatation of renal pelvis and calyces due to partial or intermittent obstruction to the outflow of urine.

• Hydroureter nearly always accompanies hydronephrosis

• Hydronephrosis may be *unilateral or bilateral*.

hydronephrosis

• Here is a kidney with much more advanced hydronephrosis in which there is only a thin rim of remaining renal cortex. Such a kidney is non-functional and a source for ongoing infection. If this process is unilateral, then the problem originates from the ureteral orifice up to the pelvis.

Unilateral hydronephrosis

• This occurs due to some form of ureteral obstruction at the level of periureteric junction (PUJ).

• The causes are:

• Intraluminal, e.g. a calculus in the ureter or renal pelvis.

• Intramural, e.g. congenital PUJ obstruction, atresia of ureter, inflammatory stricture, trauma, neoplasm of ureter or bladder.

• Extramural, e.g. obstruction of upper part of ureter by inferior renal artery or vein, pressure on ureter from outside such as carcinoma cervix, prostate, rectum, colon or cecum and retroperitoneal fibrosis.

hydronephrosis

• The arrow points to the culprit in this case of hydronephrosis--a ureteral calculus at the ureteropelvic junction.

This kidney demonstrates marked hydronephrosis with nearly complete loss of cortex.

Bilateral hydronephrosis

• This is generally the result of some form of urethral obstruction but can occur from the various causes listed above if the lesions involve both sides.

• Congenital, e.g. atresia of the urethral meatus, congenital posterior urethral valve.

• Acquired, e.g. bladder tumor involving ureteric orifices, prostatic enlargement, prostatic carcinoma and prostatitis, bladder neck stenosis, inflammatory or traumatic urethral stricture and phimosis.

hydroureter and hydronephrosis

• A long-standing obstruction (probably congenital) at the ureteral orifice through which the metal probe passes led to the marked hydroureter and hydronephrosis seen here.

Hydronephrosis

Morphology

• The kidneys may have moderate to marked enlargement.

• Initially, there is *extrarenal hydronephrosis* characterised by dilatation of renal pelvis medially in the form of a sac.

• Eventually, the dilated pelvi-calyceal system extends deep into the renal cortex so that a thin rim of renal cortex is stretched over the dilated calyces and the external surface assumes tabulated appearance. This advanced stage is called as *intrarenal hydronephrosis*.

• The wall of hydronephrotic sac is thickened due to fibrous scarring and chronic inflammatory cell infiltrate.

Cystic disease of the kidney

- There are several cystic diseases of the kidney, some of which produce renal failure by causing disturbance of renal structure. Importantly, some conditions are heritable.
 - Adult polycystic disease* is inherited in an autosomal dominant trait, generally becoming clinically manifest in adult life. Increasingly, disease is detected in childhood, with family screening and ultrasound examination.
 - -Cysts develop and progressively enlarge over a number of years, but remain asymptomatic until the number and size of the cysts is so great that the patient becomes aware of abdominal masses.
 - At about the same time, the replacement and compression of functioning renal parenchyma by the cysts leads to slowly progressive impairment of renal function, and patients develop chronic renal failure and hypertension.
 - -Patients with adult-type polycystic renal disease may also develop cysts in the liver, lung and pancreas. There is an association with berry aneurysms of the cerebral arteries, which, with development of hypertension, predisposes to intracranial hemorrhage.
- polycystic kidney disease (RPKD).
- Here is the microscopic appearance of recessive polycystic kidney disease (RPKD). Note that the cysts fill most of the parenchyma, and it is hard to find glomeruli. Many of the cysts are elongated and radially arranged from the center of the kidney on the right, much like spokes on a wagon wheel.

Cystic disease of the kidney

- Infantile polycystic disease* is uncommon and is encountered at birth. Children develop severe renal failure, with compression of the lungs due to massive enlargement of the kidneys.
- Simple renal cysts are the most common form of renal cystic disease and must be distinguished from the congenital types discussed above. They are widely held to be acquired abnormalities, incidence increasing with age. They contain clear, watery fluid and have a smooth lining.
- Simple cysts may be single or multiple and vary in size, generally being no larger than 5-6 cm. They have no effect on renal function, but may rarely become infected or develop hemorrhage.
- Acquired cystic disease* is seen in kidneys left *in situ* while patients are treated by dialysis or transplantation for chronic renal failure. The kidney is converted into a mass of large cysts. Hemorrhage into cysts is common, leading to bloodstained contents.

multicystic dysplastic kidney

- This kidney in a patient with DPKD weighed 3 kilograms! This disease is inherited with an autosomal dominant pattern, so the recurrence risk in the family is 50%. The cysts are not usually present at birth, but develop slowly over time, so the onset of renal failure occurs in middle age to later adult life.

multicystic dysplastic kidney

- The microscopic appearance of multicystic dysplastic kidney (cystic renal dysplasia, or Potter's type II) is characterized by large cysts lined by flattened cuboidal epithelium and an intervening parenchyma that is fibrotic with islands of bluish cartilage and rare glomeruli.

multicystic dysplastic kidney

- These kidneys are about normal in size but have a few scattered cysts, none of which is over 2 cm in size. This is cystic change associated with chronic renal dialysis.

Chronic renal failure

- Nephrosclerosis** is morphologic basis of chronic renal failure.
- Uremia is final stage of chronic renal failure
- Uremia is a syndrome encompassing a group of clinical and biochemical signs derived essentially from the retention of waste products and the failure to control fluid and electrolyte balance.

glomerulosclerosis (Kimmelstiel-Wilson disease

- This is a PAS stain of nodular glomerulosclerosis (Kimmelstiel-Wilson disease) in a patient with long-standing diabetes mellitus. Note also the markedly thickened arteriole at the lower right which is typical for the hyaline arteriosclerosis that is seen in diabetic kidneys as well.

diffuse glomerulosclerosis

•This PAS stain demonstrates diffuse glomerulosclerosis associated with long-standing diabetes mellitus. There is an increase in mesangial matrix, a slight increase in mesangial cellularity, and capillary basement membrane thickening. These changes gradually advance until the entire glomerulus is sclerotic.

Chronic renal failure

•**Uremia** is characterised by

•Hypernitrogenemia.

•Metabolic acidosis (accumulation of sulphates, phosphates, and organic acids).

•Hyperkalemia, hypercalcemia.

•Anemia.

•Depression of immunological reaction. Infections are common and will in turn affect renal function.

•Arterial hypertension.

•Hemorrhagic syndrome (petechias, hemorrhagic erosions and ulcer in mucosa).

•Fibrinous inflammation:

•Fibrinous pericarditis ("cor vilosum").

•"Uremic pneumonitis" with pleural exudates,

•Uremic gastritis, enteritis, colitis.

•Edema of lungs.

The prognosis of final stage renal failure has been greatly improved by dialysis, renal transplantation.

thanks