Pathology of The kidney

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DISEASES OF THE KIDNEY:

CONGENITAL ANOMALIES Of THE KIDNEYS

1-Agenesis: Absent kidney

2-Hypoplasia Undersized kidney

3-Ectopic kidney : Pelvic kidney not ascending to its normal position

4-Horse-shoe kidney :Both kidneys are fused at their lower poles.

5-Supernumerary kidneys.

6-Double ureter or double pelvis.

7-Congenital cystic kidneys:

A) Adult Polycystic Disease of the Kidney:

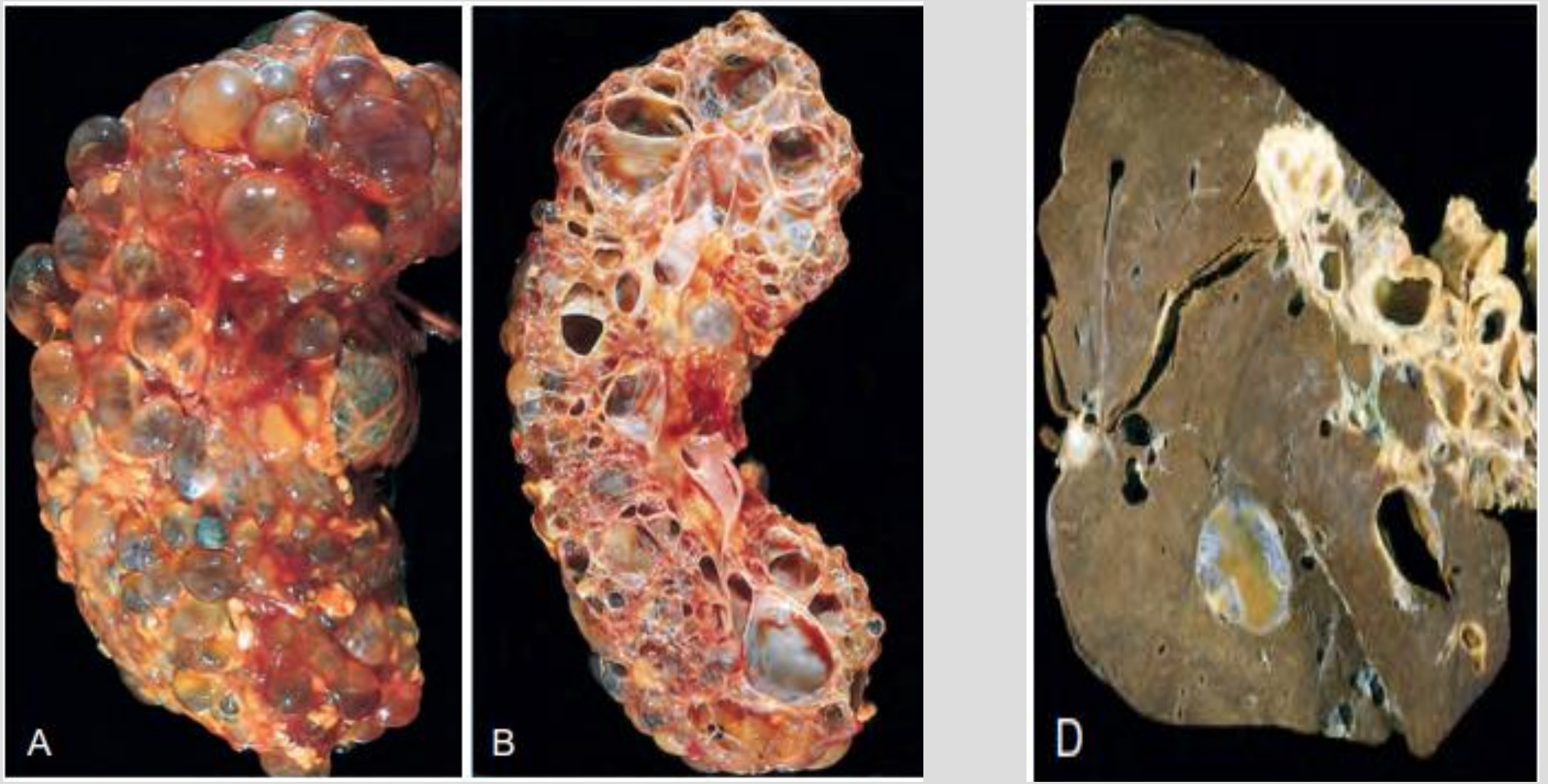
It may be associated with cystic liver & cerebral berry aneurysms.

Pathogenesis: Autosomal dominant inheritance. Renal cysts are believed to be arise to failure of communication between convoluted & collecting tubules.

Gross: Both kidneys are enlarged and show numerous small or large cysts containing clear or hemorrhagic (brownish or bluish) fluid.

Their lining is smooth .The cysts do not communicate with the renal pelvis. As the patient grows the cysts enlarge and cause pressure atrophy of the renal parenchyma.

Microscopy: Cysts are lined by cuboidal or flattened epithelium.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Complications:

a)Hematuria

b)Secondary infection

c)Hypertension

d)Chronic renal failure

B) Infantile/Childhood Polycystic Disease of the Kidney:

A rare condition.

Autosomal recessive inheritance.

Associated with congenital hepatic fibrosis.

Renal cystic affection is much more marked than the adult type.

Death occurs during infancy or childhood due to renal failure

CLINICAL MANIFESTATIONS OF RENAL DISEASES

• Azotemia is a biochemical abnormality that refers to an elevation of blood urea nitrogen (BUN) and creatinine levels, and is related largely to a decreased glomerular filtration rate (GFR). When azotemia leads to clinical signs and symptoms associated with biochemical abnormalities, it is termed uremia.

• Nephritic syndrome is a clinical entity caused by inflammatory glomerular disease and is dominated by the acute onset of either grossly visible hematuria (red blood cells in urine) or microscopic hematuria with dysmorphic red cells and red cell casts on urinalysis diminished GFR, mild to moderate proteinuria, and hypertension. It is the classic presentation of acute poststreptococcal glomerulonephritis. Rapidly progressive glomerulonephritis (RPGN)

• Nephrotic syndrome, also due to glomerular disease, is characterized by heavy proteinuria (more than 3.5 g/day), hypoalbuminemia, severe edema, hyperlipidemia, and lipiduria (lipid in the urine).
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•Acute kidney injury (previously called acute renal failure) is characterized by rapid decline in GFR (within hours to days) with concurrent dysregulation of fluid and electrolyte balance, and retention of metabolic waste products normally excreted by the kidney including urea and creatinine. In its most severe forms, it is manifested by oliguria or anuria (reduced or no urine flow). It can result from glomerular, interstitial, vascular, or acute tubular injury (ATI).
•Chronic kidney disease (previously called chronic renal failure) is defined as the presence of a diminished GFR that is persistently less than 60 mL/min. for at least 3 months, from any cause, and/or persistent albuminuria.

•Renal tubular defects are dominated by polyuria (excessive urine formation), nocturia, and electrolyte disorders (e.g., metabolic acidosis). They are the result of diseases that either directly affect tubular structures.
•Urinary tract obstruction and renal.
•Nephrolithiasis (renal stones) is manifested by spasms of severe pain (renal colic) and hematuria, often with recurrent stone formation.

Systemic Manifestations of Chronic Kidney Disease and Uremia

Fluid and Electrolytes

Dehydration

Edema

Hyperkalemia

Metabolic acidosis

Calcium Phosphate and Bone

Hyperphosphatemia

Hypocalcemia

Secondary hyperparathyroidism

Hematologic

Anemia

Bleeding diathesis

Cardiopulmonary

Hypertension
Congestive heart failure
Cardiomyopathy
Pulmonary edema
Uremic pericarditis

Gastrointestinal

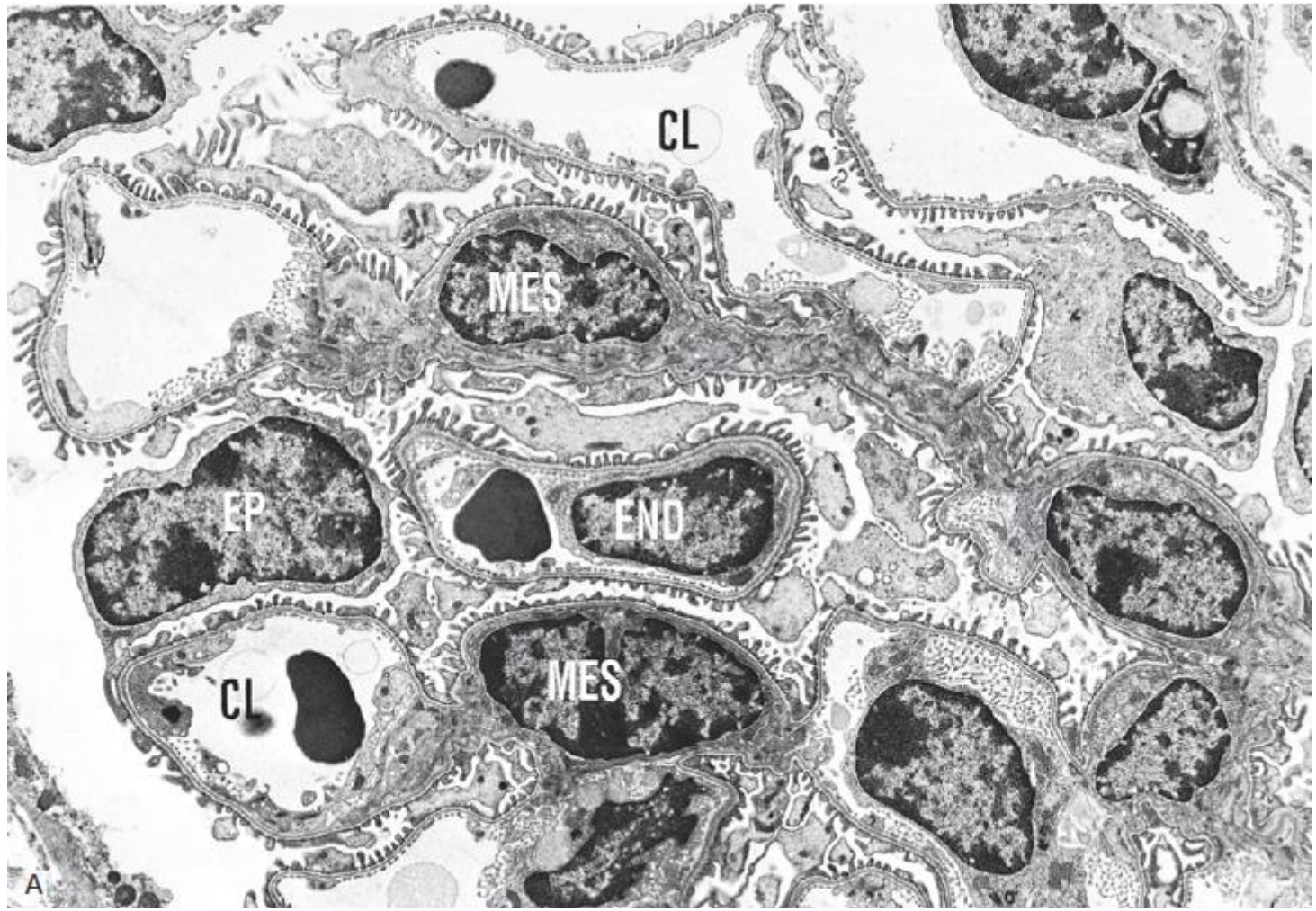
Nausea and vomiting
Bleeding
Esophagitis, gastritis, colitis

Neuromuscular

Myopathy
Peripheral neuropathy
Encephalopathy

Dermatologic

Sallow color
Pruritus
Dermatitis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Pathologic Responses of the Glomerulus to Injury

Various types of glomerulopathies are characterized by one or more of four basic tissue reactions:

Hypercellularity

- Proliferation of mesangial or endothelial cells.
- Infiltration of leukocytes, including neutrophils, monocytes, and, in some diseases, lymphocytes.
- Formation of crescents.

Basement Membrane Thickening

Hyalinosis and Sclerosis

Hyalinosis, as applied to the glomerulus, denotes the accumulation of material that is homogeneous and eosinophilic by light microscopy. Hyalin is an extracellular, amorphous material composed of plasma proteins that have insudated from the circulation into glomerular structures. When extensive, these deposits may obliterate the capillary lumens of the glomerular tuft. Sclerosis is characterized by deposition of

Histological Patterns of Glomerular Affection:

1-Diffuse: All glomeruli are affected. Glomerular affection is almost global.

2-Focal: Some glomeruli are affected (global or segmental), others are intact:

a Global Affection: Whole capillary tuft is affected.

b)Segmental Affection: Only a portion of the capillary tuft is affected.

Types of Glomerulonephritis (GN)

1-Primary GN: The disease mainly affects the kidneys

2-Secondary GN: kidneys are affected as a part of another disease as SLE, hypertension, diabetes mellitus

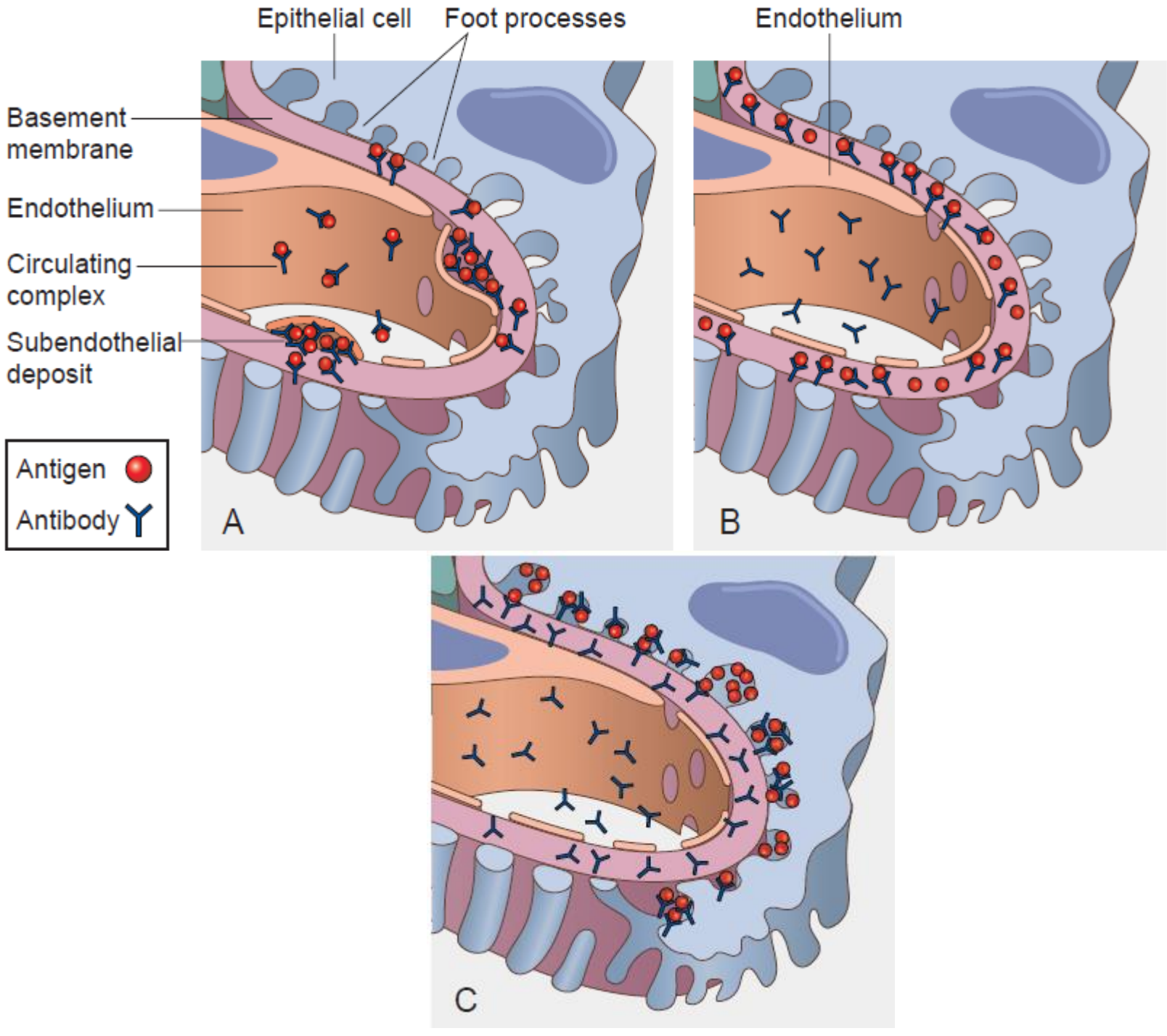
Pathogenesis of Glomerular Injury

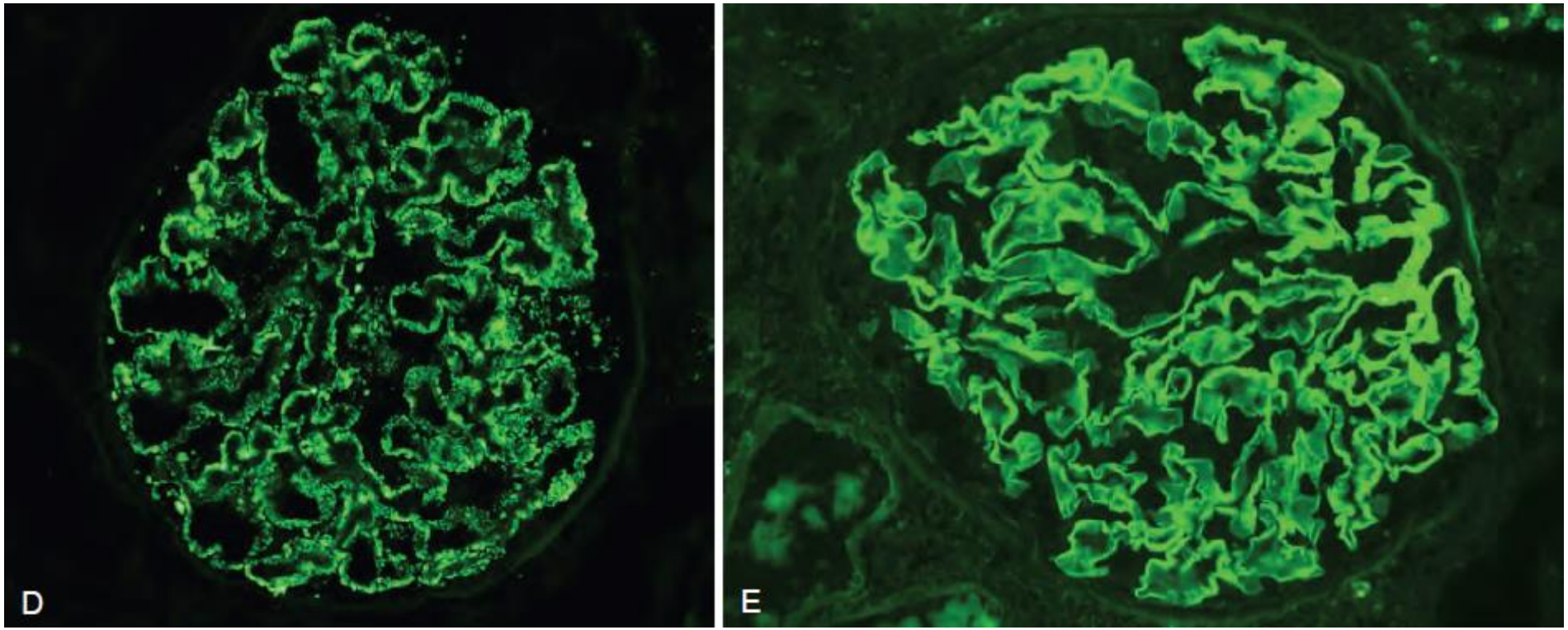
Although much remains unknown about etiologic agents and triggering events, it is clear that immune mechanisms underlie most forms of primary glomerulopathy and many secondary glomerular disorders .Glomerulonephritis can be induced experimentally by antigen-antibody reactions. Furthermore, glomerular deposits of immunoglobulins, often with components of complement, are found in the majority of individuals with glomerulonephritis.

Table 20.4 Immune Mechanisms of Glomerular Injury

Antibody-Mediated Injury
In Situ Immune Complex Deposition
Fixed intrinsic tissue antigens
NC1 domain of type IV collagen antigen (anti-GBM nephritis)
PLA_2R antigen (membranous glomerulopathy)
Mesangial antigens
Others
Planted antigens
Exogenous (infectious agents, drugs)
Endogenous (DNA, nuclear proteins, immunoglobulins, immune complexes, IgA)
Circulating Immune Complex Deposition
Endogenous antigens (e.g., DNA, tumor antigens)
Exogenous antigens (e.g., infectious products)
Cell-Mediated Immune Injury
Activation of Alternative Complement Pathway

GBM, Glomerular basement membrane.


Epithelial cell
Foot processes
Endothelium
Basement membrane
Endothelium
Circulating complex
Subendothelial deposit
Antigen
Antibody
A
B
C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Primary Glomerulopathies

Acute proliferative glomerulonephritis
- Postinfectious
- Other

Rapidly progressive (crescentic) glomerulonephritis
Membranous nephropathy
Minimal change disease
Focal segmental glomerulosclerosis
Membranoproliferative glomerulonephritis
Dense deposit disease
IgA nephropathy

Systemic Diseases With Glomerular Involvement

Systemic lupus erythematosus
Diabetes mellitus
Amyloidosis
Goodpasture syndrome
Microscopic polyarteritis/polyangiitis
Granulomatosis with polyangiitis
Henoch-Schönlein purpura

Hereditary Disorders

Alport syndrome
Thin basement membrane nephropathy
Fabry disease

Nephritic Syndrome

Glomerular diseases presenting with a nephritic syndrome are characterized by inflammation in the glomeruli. The main clinical features of nephritic syndrome include the following:

- Hematuria (red blood cells and red cell casts in urine)
- Proteinuria (usually subnephrotic range) with or without edema
- Azotemia
- Hypertension

Nephritic syndrome is the typical clinical presentation of most proliferative types of GN such as post infectious GN, crescentic GN, and proliferative lupus GN. The lesions that cause the nephritic syndrome have in common proliferation of the cells within the glomeruli, often accompanied by an inflammatory leukocytic infiltrate. This inflammatory reaction severely injures the capillary walls, permitting blood to pass into the urine and inducing hemodynamic changes that lead to a reduction in GFR. The reduced GFR is manifested clinically by oliguria, fluid retention, and azotemia.

Hypertension probably is a result of both the fluid retention and renin release from the ischemic kidneys.

ACUTE DIFFUSE PROLIFERATIVE GLOMERULONEPHRITIS (POST- STREPTOCOCCAL GLOMERULONEPHRITIS)

AETIOLOGY AND PATHOGENESIS:

it is an immune complex disease affecting children and young adults.

It starts as an upper respiratory infection with nephrogenic strains of group A beta hemolytic streptococci.

Within 1-4 weeks antibodies are formed & combine with streptococcal antigens immune complexes. These immune complexes are deposited on the basement membranes of glomerular capillaries → complement activation → destruction of glomerular capillaries by:

a)Lytic effect of the complement

b) Attraction of neutrophils & release of their proteolytic enzymes.

PATHOLOGICAL FEATURES:

Gross: Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages may be seen.

Microscopy:

a)Glomeruli are enlarged and show:

1) Proliferation of epithelial, endothelial and mesangial cells.

2)Several neutrophils in the glomerular capillaries.

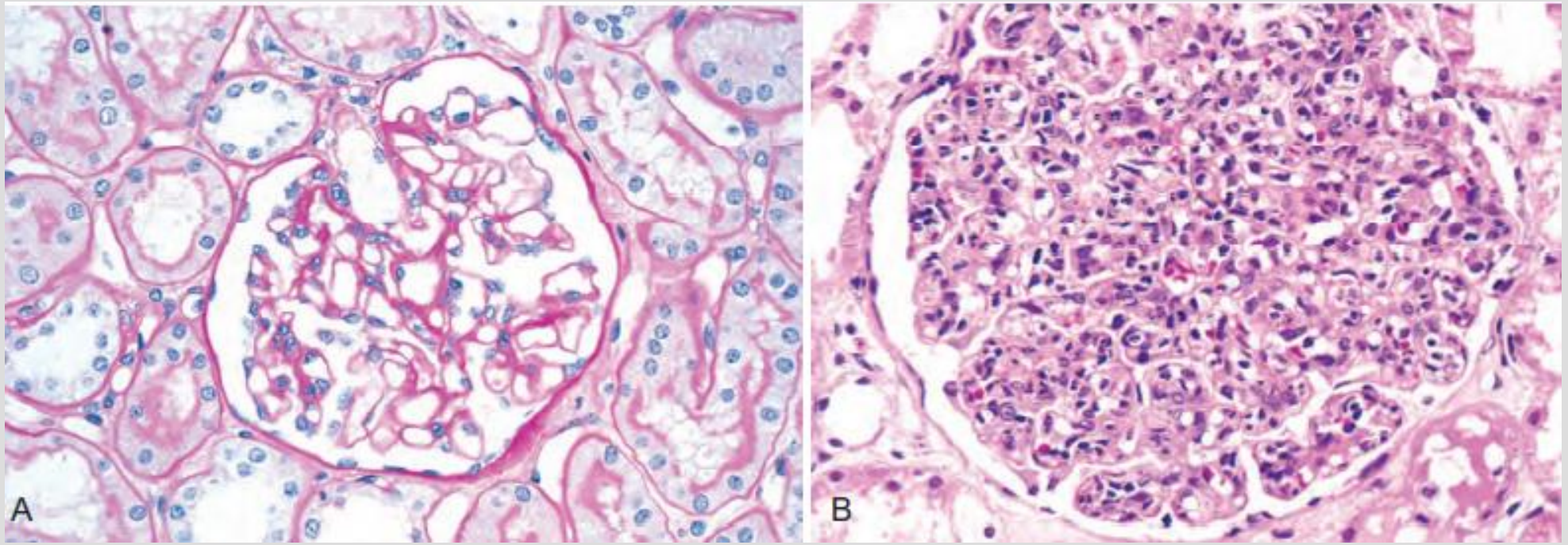
3)Bowman's capsular space shows neutrophils, erythrocytes and some albumin.

b)Tubules show cloudy swelling and casts (mainly blood casts).

c) Interstitium: Edema and neutrophils.

d) Electron Microscopy (E.M): "Humpy-lumpy' immune complex deposits, subepithelial, between podocytes & basement membrane.

e)Immunofluorescence: The deposits consist of IgG, IgM and complement.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Clinical & General Manifestations:

a) Fever & rigors,

b)Nephritic syndrome is the classic presentation. It consists of: Hematuria, oliguria, mild proteinuria, hypertension and:

- Nephritic edema (starts in lids, particularly in the morning then may become generalized).

c) Urine analysis:

-Oliguria

- Hematuria. Urine appears dark (Coca cola like) due to altered blood
- Mild proteinuria
- High specific gravity (1035)
- Contain casts (mainly hyaline & blood casts)

d) Blood analysis: a) Mid rise of urea and creatinine b) Mild anemia

e) Hypertension

Course & Fate:

a-Recovery in more than 95% of children and in two thirds of adults.

b-Development of rapidly progressive GN or chronic GN

C-rarely death from acute renal failure.

REMARK: URINARY CASTS:

These are solid urinary constituents detected in urine as cylindrical bodies :

1-Hyaline casts consist of protein (in cases of proteinuria).

2-Blood casts consist of blood cells (In cases of hematuria).

3-Cellular casts consist of degenerated detached tubular epithelial cells or inflammatory cells.

4-Granular casts consist of debris.

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (CRESCENTIC GLOMERULONEPHRITIS)

A severe type of diffuse GN It is termed rapidly progressive due to rapid progression to renal failure. It is also termed crescentic GN due to a characteristic microscopic development of cellular crescents

AETIOLOGY AND PATHOGENESIS: One of the following possibilities:

a)May follow acute diffuse proliferative G. N.

b)Idiopathic type (unknown pathogenesis).

c)May be a part of Goodpasture's syndrome (Rapidly progressive GN + pulmonary hemorrhages). is an autoimmune disease characterized by glomerular lesions caused by antiglomerular basement membrane antibodies which cross react with alveolar basement membranes causing pulmonary lesions in addition to the glomerular lesions.

d)In association with systemic disease as SLE and Henoch-Shonlein purpura.

PATHOLOGICAL FEATURES:

Gross: Bilateral kidney enlargement with cortical oedema & petechial hemorrhages.

Microscopy:

a) Glomerular enlarged and show:

-Focal necrosis & capillary thrombosis.

-Proliferation of mesangial and endothelial cells.

-Crescents which consist of proliferated parietal epithelial cells, monocytes and fibrin

b) Tubules show cloudy swelling and casts.

c) Interstitial inflammatory cells

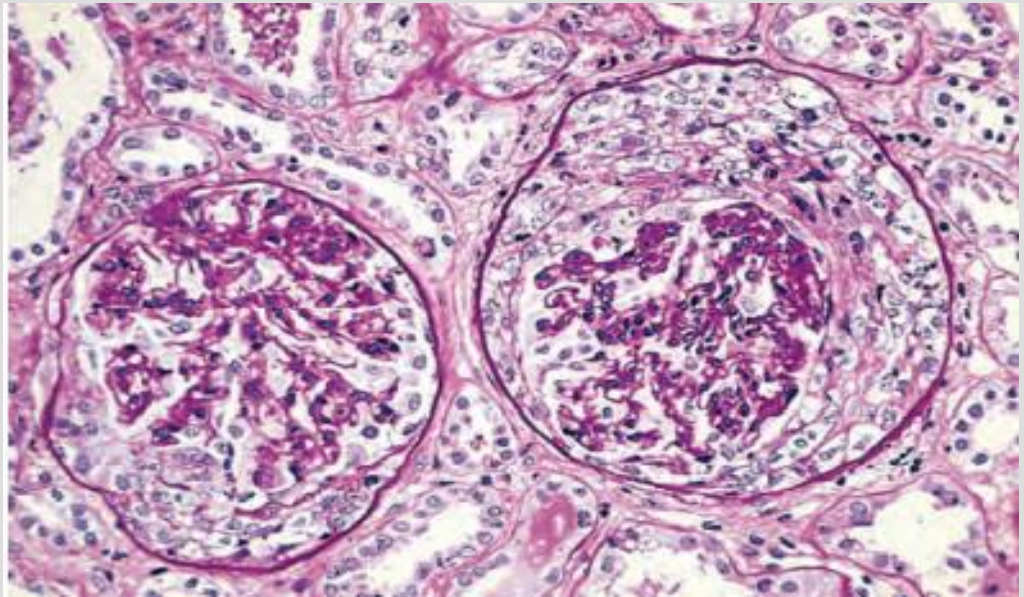
d)EM & Immunofluorescence: Linear deposits of IgG along the glomerular basement membrane (subendothelial)

Clinical manifestations, course and Fate:

a)Nephritic syndrome (hematuria, oliguria, mild proteinuria, hypertension and nephritic edema) of nephrotic syndrome (massive proteinuria, hypoproteinemia, hyperlipemia & generalized edema)

b)Rapid progression to acute renal failure manifested by oliguria, rise of blood urea and creatinine as well as other manifestations

c)Cases that survive longer develop chronic glomerulonephritis.



IgA Nephropathy (Berger Disease)

IgA nephropathy, characterized by the presence of prominent IgA deposits in the mesangial regions and recurrent hematuria, is the most common type of glomerulonephritis worldwide. The disease can be suspected by light microscopic examination, but the diagnosis is made only by the detection of glomerular IgA deposition . Mild proteinuria is usually present, and the nephrotic syndrome may occasionally develop. Rarely, patients may present with crescentic GN.

Morphology:

mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S), tubular atrophy / interstitial fibrosis (T) and crescents (C)

Clinical Features

The disease affects people of any age, most commonly older children and young adults. Many patients present with gross hematuria after an infection of the respiratory or, less commonly, gastrointestinal or urinary tract; 30% to 40% have only microscopic hematuria, with or without proteinuria

Nephrotic Syndrome

Pathophysiology

Nephrotic syndrome is caused by a derangement in glomerular capillary walls resulting in increased permeability to plasma proteins. The manifestations of the syndrome include the following:

- Massive proteinuria, with the daily loss of 3.5 g or more of protein (less in children Hypoalbuminemia, with plasma albumin levels less than 3 g/dL
- Generalized edema
- Hyperlipidemia and lipiduria

MEMBRANOUS GLOMERULONEPHRITIS (MGN)

AETIOLOGY AND PATHOGENESIS: Adults are affected

a- Idiopathic type (85%)

b- Secondary type occurring in association with

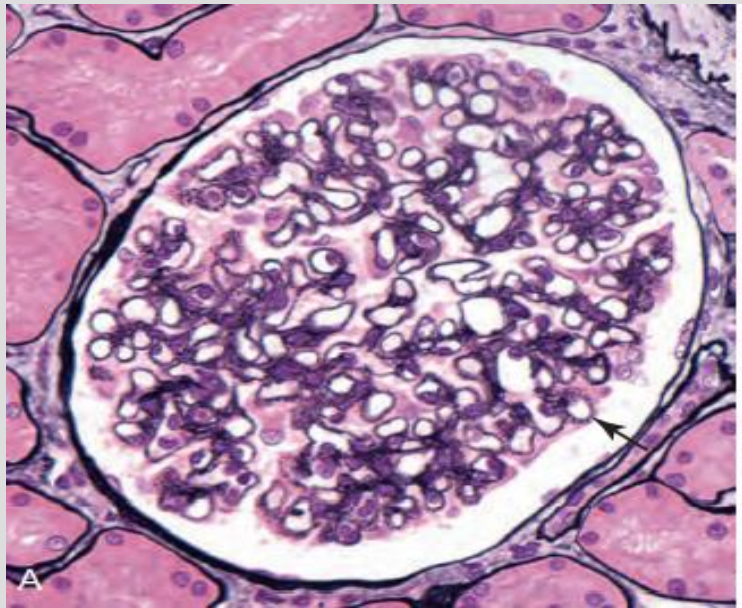
i) Infections as malaria, hepatitis B

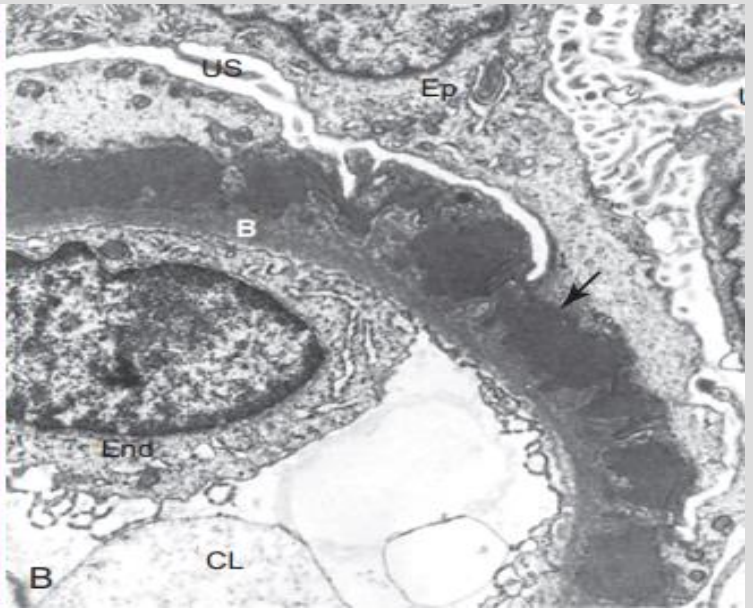
ii) Carcinoma

iii) SLE

iv) some drugs (as mercury gold and penicillamine)

v) Diabetes





PATHOLOGICAL FEATURES:

Gross: Bilaterally enlarged pale kidneys.

Microscopy

a)Glomerular capillary basement membranes are thickened and may exhibit hair comb appearance of the outer part of the membrane due to immunoglobulin deposition

b)E.M and Immunofluorescence: Subepithelial deposits of IgG.

Clinical picture: Nephrotic Syndrome.

Fate: Chronic renal failure develops in 50% of cases of idiopathic MGN within 2 to 20 years.

MINIMAL CHANGE GLOMERULONEPHRITIS (LIPOID NEPHROSIS)

AETIOLOGY AND PATHOGENESIS: Children are affected.

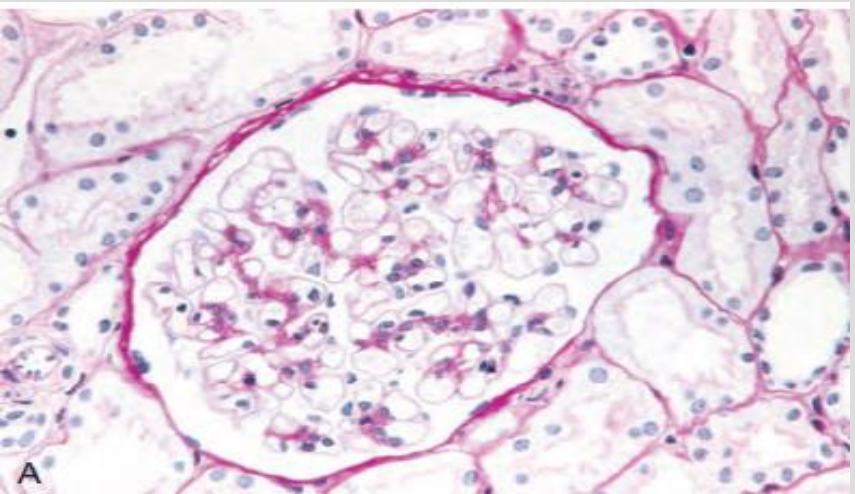
Aetiology is unknown.

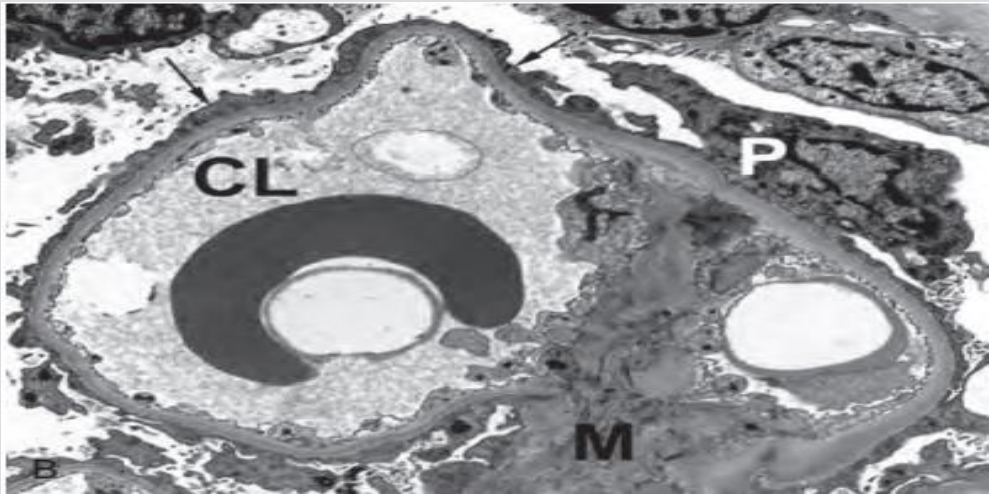
Although antibodies or complement are not detected in the glomeruli, still an immune mechanism is suspected because

a)Many cases follow respiratory infections

b) Excellent response to corticosteroids

c) Association with other atopic disorders (e.g.,eczema, rhinitis)





PATHOLOGICAL FEATURES:

Gross: Unremarkable changes.

Microscopy

a)Unremarkable light microscopic glomerular changes

b)The lining cells of the proximal convoluted tubules may show lipids (due to reabsorption of lipoproteins leaked from the glomeruli)

c)EM and Immunofluorescence:

- Diffuse effacement of the foot processes of the visceral epithelial cells.
- No immunoglobulin deposits

Clinical picture: Nephrotic syndrome (Minimal change GN is the commonest cause of nephrotic syndrome in children).

Fate : The prognosis is usually excellent; most cases are cured by corticosteroid therapy,

FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSG)

AETIOLOGY AND PATHOGENESIS:

1)Idiopathic affecting children 2)Secondary e.g heroin abuse.

PATHOLOGICAL FEATURES:

Gross: Slight renal enlargement.

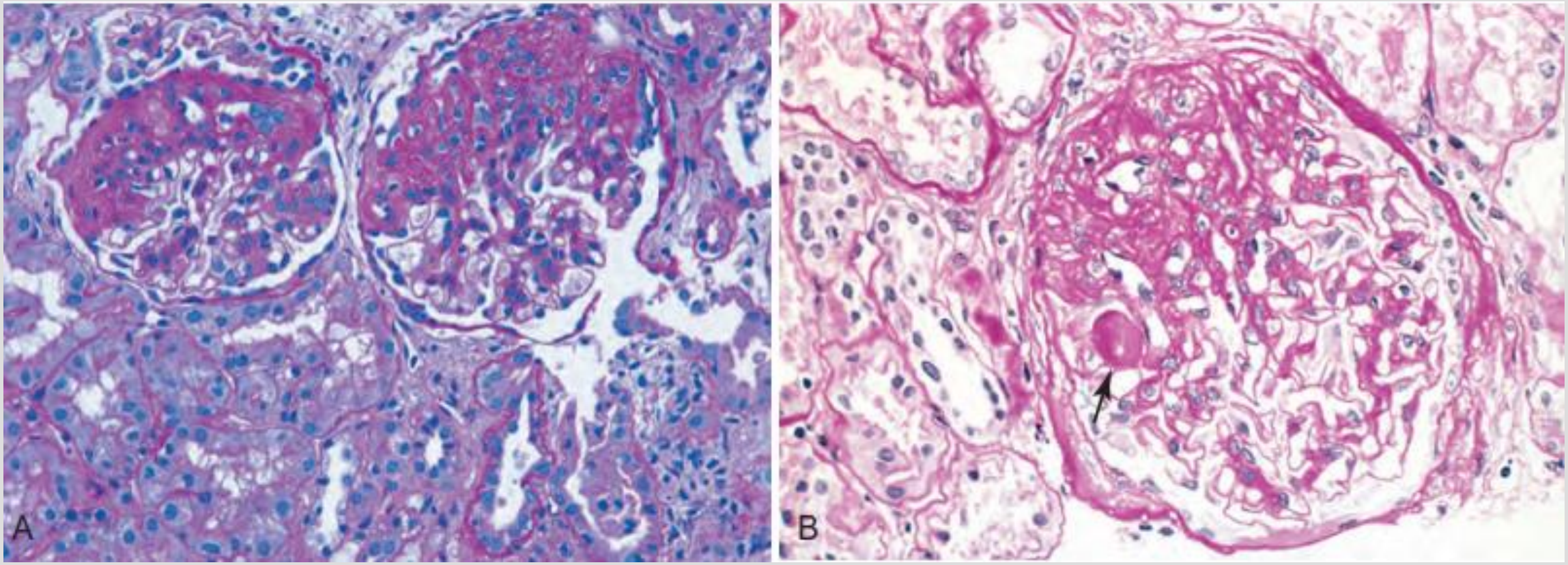
Microscopy:

a) Focal hyalinosis and sclerosis of juxtamedullary glomeruli.

b)E.M and Immunofluorescence: Mesangial deposits of IgM and complement.

Clinical picture: Nephrotic syndrome.

Fate: Chronic renal failure in 50% of cases.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MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN)

AETIOLOGY AND PATHOGENESIS:

Children or adults. Unsettled aetiology. May be post infection.

PATHOLOGICAL FEATURES:

Gross: Bilaterally enlarged and pale kidneys.

Microscopy: Glomeruli are enlarged and show.

a)Proliferation of mesangial cells and increase in mesangial matrix

b) Thickening of capillary basement membranes which appear double contoured 'tram-track appearance

EM and Immunofluorescence:

-Type 1 MPGN: Subendothelial deposits of IgG, M and complement

-Type Il MPGN (Dense Deposits Disease or Alternate Pathway Disease): The glomerular basement membrane shows dense deposits of complement.

Clinical Picture: Nephritic, nephrotic or combined syndromes.

Fate: Unfavorable prognosis; chronic renal failure develops within 10 years in 50% of cases

LUPUS NEPHRITIS

There are five patterns of renal involvement in systemic lupus erythematosus (SLE)

More than one pattern may coexist. These patterns (classes) include:

ClassI: Normal microscopic pattern (rare)

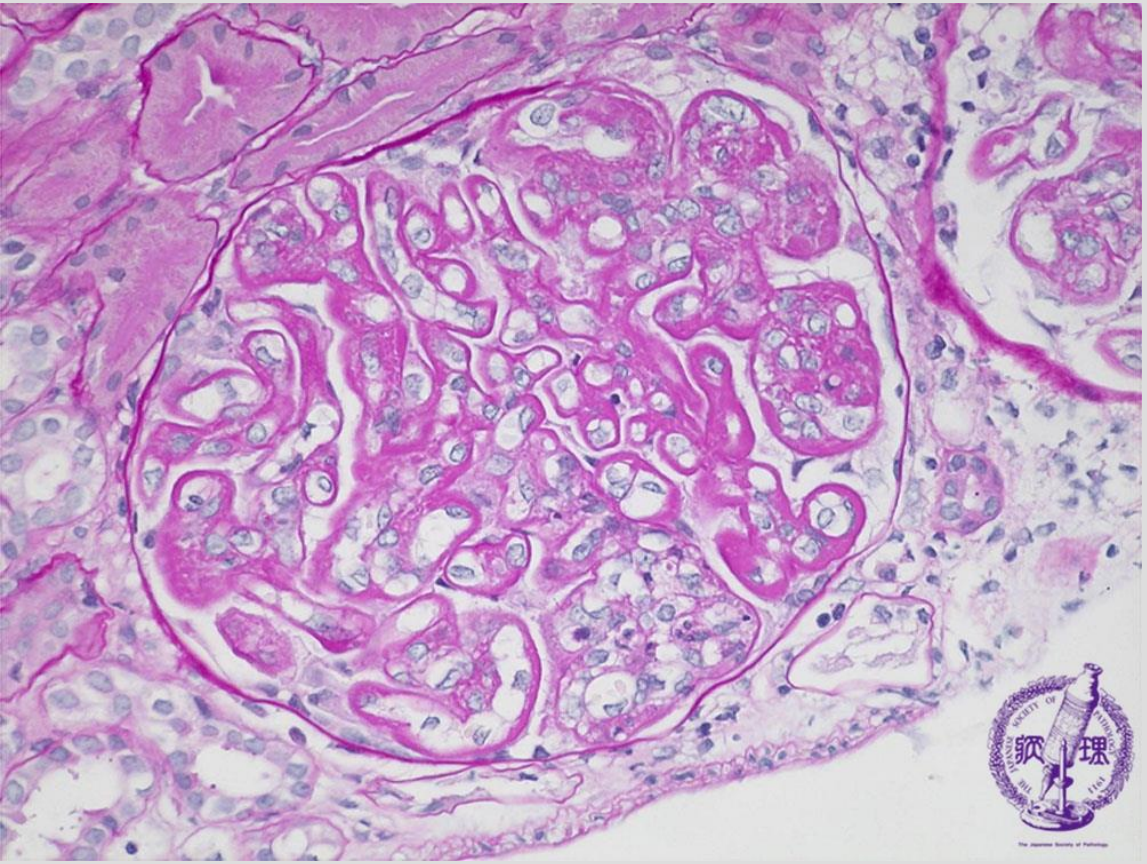
Class II: Mesangial lupus nephritis: Mild increase of mesangial matrix & mesangial cells of the glomeruli

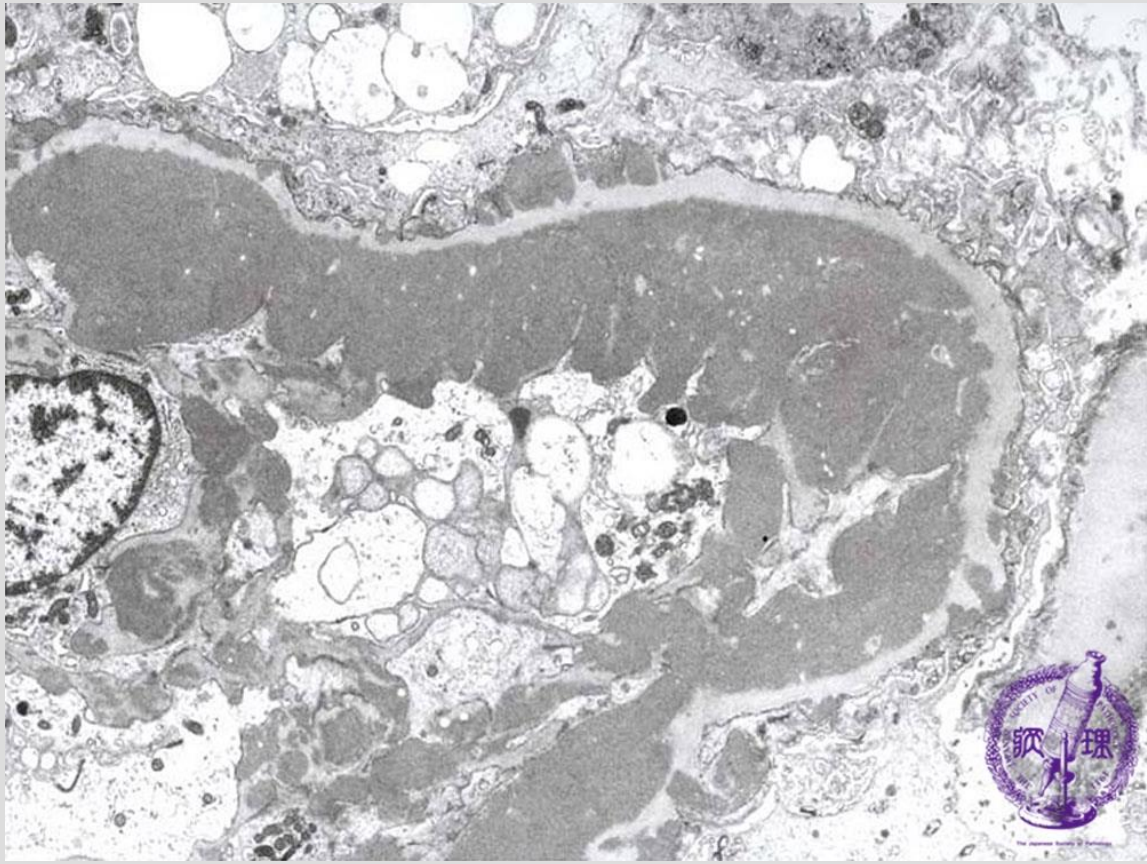
.Mesangial deposits of IgG & C3 are detected. Clinical symptoms are mild.

Class III: Focal proliferative glomerulonephritis. Focal means affection of < 50% of glomeruli (or <50% of the total glomerular capillaries. Clinically: Nephrotic syndrome in 30% of cases

Class IV: Diffuse proliferative glomerulonephritis. Diffuse means affection of > 50% of glomeruli or > 50% of the total glomerular capillaries. This is the most common & most severe form. All glomeruli show diffuse mesangial hypercellularity, commonly with thickening of capillary loops due to fibrinoid necrosis (Wire Loop Lesions). Crescentic lesions may also develop. Clinical effects include nephrotic syndrome (50%). Renal failure ultimately develops.

Class V: Membranous glomerulonephritis characterized by thickening of glomerular capillary basement membranes without cellular proliferation. Clinically, nephrotic syndrome





Diabetic Nephropathy

Class	Description	Inclusion criteria
I	**Mild or nonspecific LM changes and EM-proven GBM thickening**	Biopsy does not meet any of the criteria mentioned below for class II, III or IV
		GBM > 395 nm in female and >430 nm in male individuals over 9 years of age
IIa	**Mild mesangial expansion**	Biopsy does not meet criteria for class III or IV
		Mild mesangial expansion in >25% of the observed mesangium
IIb	**Severe mesangial expansion**	Biopsy does not meet criteria for class III or iv
		Severe mesangial expansion in >25% of the observed mesangium
III	**Nodular sclerosis (Kimmelstiel-Wilson lesion)**	Biopsy does not meet criteria for class IV
		At least one convincing Kimmelstiel-Wilson lesion
IV	**Advanced diabetic glomerulosclerosis**	Global glomerular sclerosis in >50% of glomeruli
		Lesions from classes I through III

Modified from Tervaert et al. (2010)

Alport syndrome:
when fully developed, is manifest by hematuria with progression to chronic renal failure, accompanied by nerve deafness and various eye disorders, including lens dislocation, posterior cataracts, and corneal dystrophy. The disease is inherited as an X-linked trait in approximately 85% of cases. In this X-linked form, males express the full syndrome, and females are carriers in whom manifestations of disease are typically limited to hematuria
Pathogenesis.
The disease manifestations are due to abnormal α3 (COL4A3), α4 (COL4A4), or α5 (COL4A5) chain of type IV collagen.

DISEASES OF TUBULES AND INTERSTITIUM

ACUTE TUBULAR NECROSIS

AETIOLOGY

1- Ischemic necrosis due to:

a) Shock due to severe hemorrhage, incompatible blood transfusion, burns.

b) Rejection after renal transplantation

2-Toxic necrosis caused by carbon tetrachloride, mercury, arsenic.

GROSS: Enlarged kidneys with pale necrotic cortex and congested medulla.

MICROSCOPY

1-Necrosis of tubular epithelium affects the proximal tubules diffusely in case of toxic necrosis. In case of ischemic necrosis, several parts of all tubules are affected associated with basement membrane disruption

2-Occlusion of tubular lumens by granular or epithelial casts.

3-interstitial hyperemia, edema and inflammatory cells

EFFECTS AND FATE

1-Oligo-anuria due to reduced glomerular filtration

Mechanism

a) Decreased glomerular pertusion in case of ischemic necrosis.

b) Vasoconstriction of preglomerular arterioles by chemical substances released due to tubular damage. This results in reduced glomerular filtration

c) Obstruction of tubular lumens by swollen or detached necrotic cells

d) Fluid leakage from the damaged tubules into interstitial tissue

Death is common due to a) acute renal failure b) acute heart failure (due to hyperkalemia)

2-Marked polyuria occurs when glomeruli start to function while the unregenerated tubules are incapable of reabsorbing water and electrolytes. Hypokalemia may be a problem at this phase.

3-Restoration of renal functions occurs after tubular regeneration

PYELONEPHRITIS

DEFINITION: Infection of kidney (interstitial tissue) & renal pelvis.

AETIOLOGY:

Predisposing factors:

1- Low immunity as in cases of

a) Diabetes mellitus

b) AIDS

C) immunosuppressive therapy

2- Urine obstruction (by stones, tumors, strictures...etc)

Stasis of urine favors bacterial growth

3- Females are commonly affected than males because of:

a)Shorter wider urethra (easier infection)

b) Pregnancy, this leads to urinary stasis.

4- Urinary tract instrumentation

Bacteria: E. coli (commonest). Staphylococci. Streptococcal, Pseudomonas, Typhoid bacilli & others.

Routes:

1-Heamatogenous (blood spread from distant infections as those of respiratory tract).

2- Ascending (though periuretric lymphatics or submucosa of ureter).

3- From colon though intercommunicating lymphatics

PATHOLOGY:

Two type. Commonly bilateral

Acute pyelonephritis	Chronic pyelonephritis
Gross pictures	
1-enlarged kidney 2-smooth surface 3-capsule:strips easily 4-Cut section: small cortical abscesses + streaks of pus along medullary rays 5-Pelvis and calyces contain pus	1-Asymmetrical contracted kidneys 2-irregular surface depressions (scars) 3-capsule: adhesion 4-cut section: scarred cortex and medulla demarcated from each other 5-scarred distorted pelvis and calyces
Microscopic features	
1- interstitium of kidney and pelvis : a)Dilated capillaries. b)Neutrophils , pus cells and macrophages (abscesses) c)Oedema 2-Tubules:degeneration , inflammation and leucocytic casts	1- interstitium of kidney and pelvis : a)Endarteritis obliterans b)Lymphocytes , plasma cell and macrophages C)Fibrosis 2-tubules: a)some are fibrotic b)some are cystic c)some contain thyroid like colloid casts
Fate and complications	
1-Mild cases: recovery 2-Severe cases : acute renal failure 3-Some cases develop pyonephrosis or progress to chronic pyelonephritis	1- hypertension 2- chronic renal failure

TYPES OF TUBULO-INTERSTITIAL NEPHRITIS

1-Infective as pyelonephritis, tuberculosis & xanthogranulomatous pyelonephritis.

2-Non-infectious called (interstitial nephritis) e.g. drug induced.

Xanthogranulomatous Pyelonephritis:

Characterized by foam macrophages, giant cells & granulomas.

Often caused by E. coli infection

Acute Drug-Induced Interstitial Nephritis:

This is a well-recognized adverse reaction to a constantly increasing number of drugs. First reported after the use of sulfonamides, acute tubulointerstitial nephritis most frequently occurs with synthetic penicillins (methicillin, ampicillin), other synthetic antibiotics (rifampin), diuretics (thiazides), NSAIDs, and miscellaneous drugs (allopurinol, cimetidine). The disease begins about 15 days (range: 2–40) after exposure to the drug and is characterized by fever, eosinophilia (which may be transient), a rash in about 25% of patients, and renal abnormalities. The latter take the form of hematuria, mild proteinuria, and leukocyturia (often including eosinophils). A rising serum creatinine level or acute renal failure with oliguria develops in about 50% of cases, particularly in older patients.

PYONEPHROSIS

DEFINITION: A chronic condition in which pelvis and calyces are markedly distended with pus atrophy of renal tissue

AETIOLOGY:

1-Pyelonephritis associated with urinary tract obstruction

2-Urinary tract obstruction (hydronephrosis) followed by 2ry infection

PATHOLOGY:

1-Pelvis and calyces are distended with pus.

2-Atrophic renal tissue.

3-Spread of infection to surroundings (perinephritis) fibrosis & fixation of kidney

4-Chronic renal failure in bilateral cases

HYDRONEPHROSIS

DEFINITION: A chronic condition in which pelvis and calyces are markedly distended with urine due to urinary obstruction, followed by pressure atrophy of renal tissue

AETIOLOGY: Incomplete or intermittent urinary tract obstruction This may be due to

1-Urethral Lesions These may be

a) Congenital lesions

- Phimosis (stenosis of opening of the prepuce of penis)
- Stenosis of external urethral meatus
- Prostatic urethral valves

b) Acquired causes

- Posttraumatic or post inflammatory urethral stricture
- Urethral tumors

2.Prostatic Enlargement

a)Senile enlargement and BPH

b) Advance Carcinoma

3-Bladder Neck Obstructions

a)Functional neuromuscular incoordination as in tabes dorsalis

b)Inflammatory stricture

a)Tumors

d)Stone,

4-Ureteric Lesions:

a) Inflammatory stricture.

b) Stone.

c) tumors.

d) Pregnancy.

c) Retroperitoneal fibrosis.

5-Renal Pelvis

a) Stone

b)Tumors

c)Pressure by an aberrant renal artery

d) Kinked pelvis and ureter

PATHOLOGY

Hydronephrosis may be unilateral due to unilateral ureteric or pelvis lesions ,It may be bilateral due to urethral, prostatic or bladder neck lesions),

Bilateral hydronephrosis is associated with

Hypertrophy, dilatation & trabeculation of the bladder

Bladder diverticula may develop due to pouching of the mucosa through muscle detects after marked bladder dilatation

Bilateral hydroureter . Ureters appear hypertrophied, dilated, elongated & tortuous,

Distension of pelvis & calyces with urine → pressure atrophy fattening then cupping of pyramids followed by disappearance of the whole pyramids & progressive atrophy of renal parenchyma

Gross: The affected kidney is enlarged with bossy surface. Cut section reveals a multilocular sac distended with urine.

COMPLICATIONS

1-Secondary infection → pyonephrosis.

2-Hypertension.

3-Stasis. This predisposes to stone formation,

4-Chronic renal failure in bilateral cases,

5-Bladder diverticula may be complicated by secondary infection, stone formation and carcinoma

VASCULAR DISEASES OF THE KIDNEY

1-Infarction

2-Benign and malignant nephrosclerosis (arteriolosclerosis kidney)

3-Senile renal atrophy: Atherosclerotic ischemic atrophy of kidneys in old age.

4-Bilateral cortical necrosis may occur due to severe shock or in cases of toxemia of pregnancy. It is manifested by acute renal failure & is rapidly fatal.

URINARY CALCULI (STONES) (UROLITHIASIS)

They are due to precipitation of urinary crystalloids in renal pelvis or in the bladder.

AETIOLOGY:

1- Disturbances Of Composition of Urine:

a)Decreased water content (concentrated urine) e.g. due to excessive sweating.

b)Increased crystalloids:

- Excess calcium as in hyperparathyroidism.
- Excess uric acid and urates in cases of gout.
- Excess oxalates: 1) hereditary metabolic error 2)excess intake in diet (mango, tomato..).
- Familial Cystinuria.

2 Stasis of Urine due to urinary obstruction:

a Stasis allows easier precipitation of the crystalloids of urine.

b-Stasis predisposes to infection.

3-Urinary Infection: It predisposes to precipitation of urinary crystalloids through:

a)Formation of a nucleus (pus cells, detached necrotic cells):

b)Change of pH of urine:

- Alkalinity (in case of pyogenic bacteria). Precipitation of calcium-magnesium-ammonium
- Phosphate (Triple Phosphate Stone), occurs in alkaline urine.
- Increased Acidity (in case of E. coli). This favors precipitation of oxalates and urates.

TYPES OF STONES:

1-Primery (Metabolic)Stones: Urinary infection is not essential for their formation

a)Calcium Oxalate Stone (60%): It forms in acidic urine. Usually occurs in renal pelvis and are multiple, hard with spiny surface. This leads to injury of urinary mucosa and hemorrhage which leads to dark staining of the stones.

b)Uric Acid and Urate Stones (8%): It forms in acidic urine. Usually occurs in renal pelvis and is single, hard, has a smooth surface and yellowish brown in colour.

c)Cystine Stones (2%): Soft, yellowish green.

2-Secondary (Infected) Stones: Triple Phosphate Stone (30%). It develops in alkaline urine. Usually single, large white and friable with a smooth surface. It commonly forms in urinary bladder but may form in renal pelvis and calyces; casting their shape (Stag Horn Stone).

COMPLICATIONS:

1-Migration from renal pelvis to ureter or bladder: a)Pain (colic) b) Urinary obstruction.

2-Urinary obstruction leading to hydroureter, hydronephrosis and sometimes calculous anuria.

3-Urinary infection (predisposed to by urinary stasis due to obstruction) leading to cystitis, pyelonephritis, pyoureter, pyonephrosis.

4-Injury of urinary mucosa (particularly by oxalate stone). This leads to hematuria.

5-Squamous Metaplasia. Squamous cell carcinoma may occur on top of metaplasia

TUMORS OF KIDNEY & RENAL PELVIS

SECONDARY (METASTATIC) TUMORS:

These are uncommon tumors which may reach the kidney by

1-Blood spread from distant malignant tumors and from myeloma and leukemia

2-Direct or lymphatic spread from adrenal glands, pancreas & colon.

PRIMARY TUMORS :

1-Tumors of Pelvis:

A)Benign Tumors:

a)Villous papilloma & inverted papilloma. May cause hematuria.

b)Hemangioma (capillary or cavernous). May cause hematuria

c)Leiomyoma. , neurofibroma

B)Malignant Tumors:

a) Transitional cell carcinoma

b) Squamous cell carcinoma

2-Tumors of Kidney:

A) Benign Renal Tumors:

a) Cortical Adenoma: It is a benign tumor which appears as a well circumscribed, round, yellowish nodule in the cortex., usually 2 cm or less in diameter. It may change into carcinoma.

b)Oncocytoma: It is a benign tumor derived from proximal tubular cells and may reach a large size. Microscopically, it consists of proliferating epithelial cells having eosinophilic cytoplasm (oncocytes).

c)Angiomyolipoma: A capsular hamartoma which may reach large size, composed of mature adipose tissue, smooth muscle cells and abnormal blood vessels. Usually occurs in association with tuberous sclerosis (epilepsy, mental retardation & sebaceous adenoma of skin).
d) Medullary fibroma.
e)Juxta-glomerular cell tumor: It is a renin secreting tumor leading to hypertension.
f)Others: as hemangioma,, lymphangioma, lipoma ...

B)Malignant Renal Tumors:

a)Wilm's tumor (Nephroblastoma, Embryoma).
b)Renal cell carcinoma (hypernephroma).
c)Sarcomas & lymphoma

RENAL CELL CARCINOMA (HYPERNEPHROMA)

Renal cell carcinoma (RCC) accounts for about 3% of adult malignancy. Men are affected more than women. The peak incidence is in the sixth decade of life.

Etiology

Risk factors: obesity, smoking, hypertension, acquired cystic kidney disease due to end stage renal disease, occupational exposure to trichloroethylene, treated neuroblastoma

Genetic susceptibilities estimated to account for 2 - 4% (WHO 2016)

Usually > 50 years old

Gross appearance:

1-Most tumors arise in pole of the kidney. upper or lower.

2- As the tumor grows it pushes the kidney which may appear crescentic.

3-The tumor finally invades the renal parenchyma and renal pelvis

4-The tumor usually appears defined & eccentrically located

5- Tumor ranges in length between 2 & >30 cm.

6- Cut section is typically bulging and yellowish (due to high lipid & glycogen content of tumor cells). However, the tumor may be whitish or brownish according to microscopic tumor cell type.

7. Variable degrees of cystic changes, hemorrhage & necrosis are common.

Microscopic appearance: Variable:

1- Clear cell type:

This is the most common type.

Tumor cells show vacuolated cytoplasm (due high content of lipids & glycogen)

Cell borders are distinct

Nuclei appear rounded & small (due to abundance of cytoplasm)

The cells are arranged in trabeculae and acini

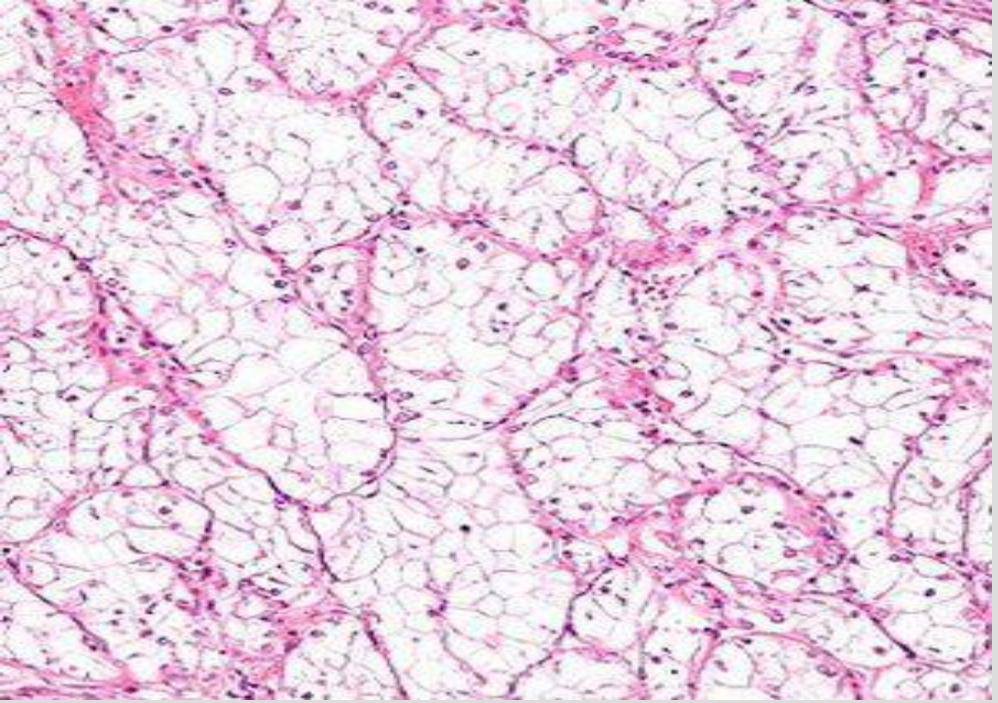
2- Papillary type: Tumor cells are small, cuboidal to low columnar forming papillary projections

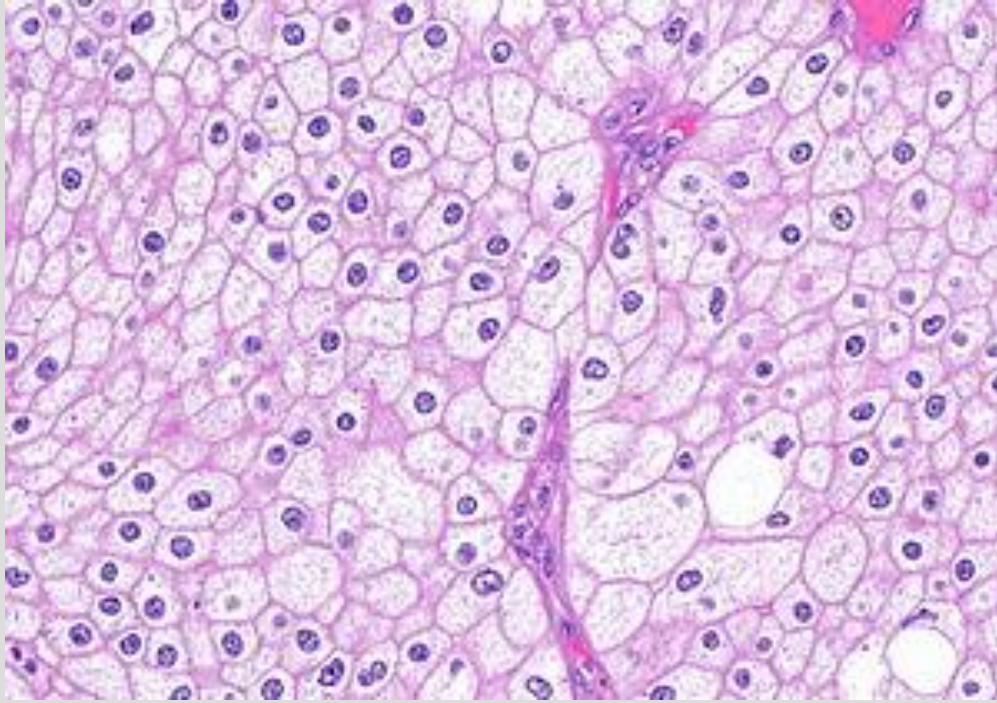
3-Chromophobe cell type: Cells show abundant acidophilic granular cytoplasm.

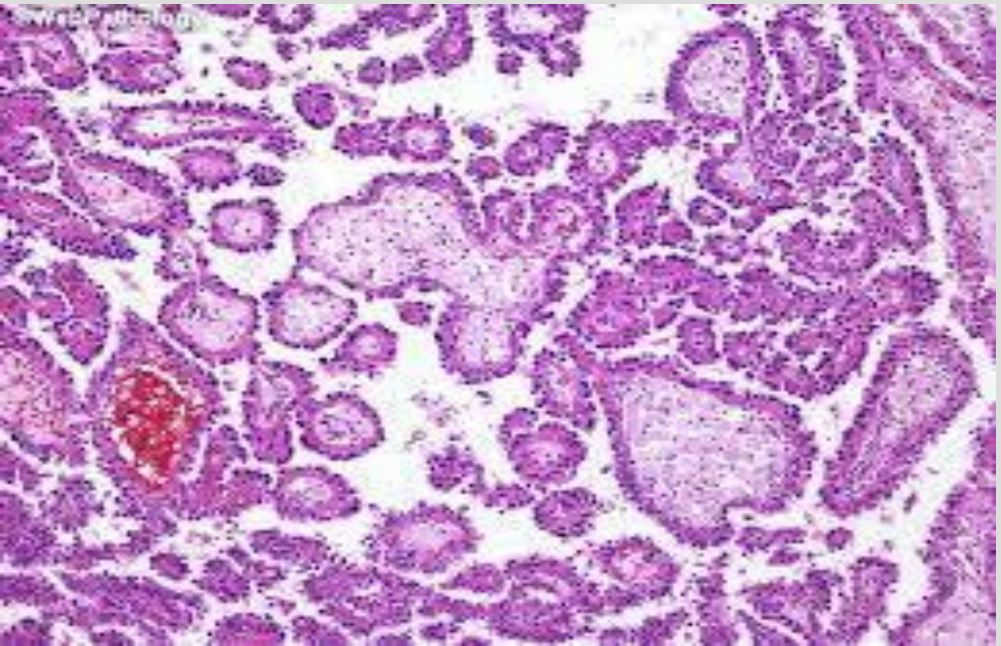
4- Sarcomatoid type: least common variant, formed of undifferentiated spindle epithelial cells thus resembling sarcoma
5-Collecting duct type: Very rare subtype, composed of mixture of dilated tubules & papillae lined by a single layer of cuboidal cells associated with desmoplastic stroma
6-Renal medullary carcinoma: An extremely rare tumor, centered in the renal medulla, arising in young black patients with sickle cell disease

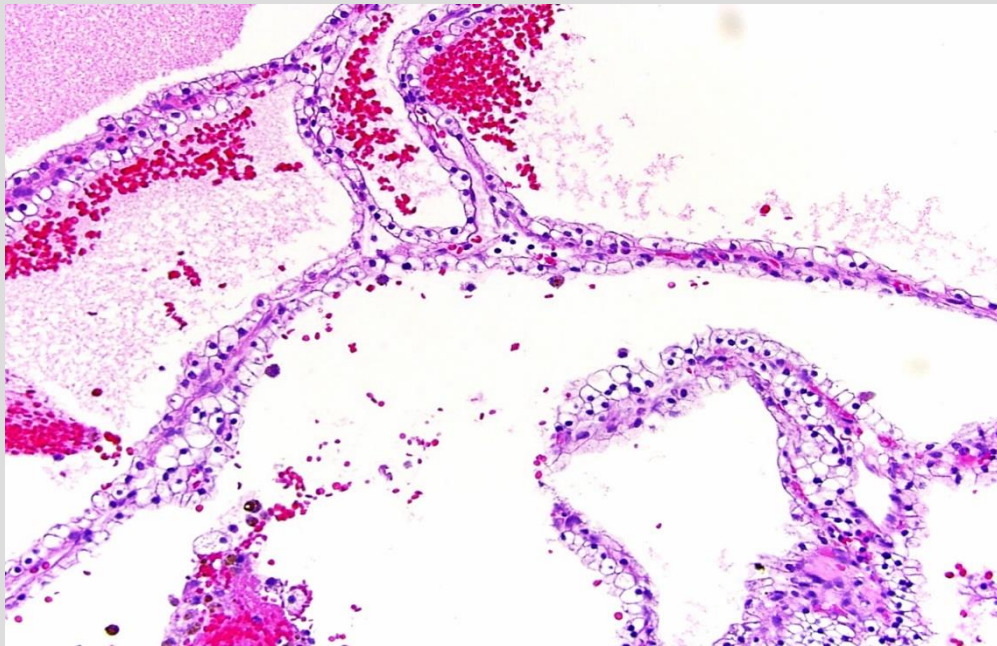
Spread:

1-Direct to renal pelvis, renal vein, perinephric tissue and surrounding structures
2-Lymphatic: Para-aortic nodes
3-Blood: to lungs (commonly causing cannon ball metastases), bones & others









Clinical features:

1-Painless hematuria

2-Loin pain

3-Palpable loin mass

4-Varicocele of left testis in case of left RCC

5-It may remain clinically occult and manifest by metastatic disease

Staging of RCC (TNM Staging):

T1	Tumor limited to kidney < 7 cm
T2	Tumor limited to kidney > 7 cm
T3a	Perinephric or adrenal gland invasion
T3b	Invasion of renal vein or vena cava
T3c	Extension to vena cava above diaphragm
T4	Tumor invades beyond Gerota fascia
N0:	Negative nodes
N1	Single node
N2	2 or more
M0:	No distant metastases
M1	Distant metastases

NEPHROBLASTOMA (WILM'S TUMOR)

The commonest embryonic tumor in infancy and childhood

It accounts for 13-20% of malignant tumors (other than Leukemia's) in children under 15 years of age. In 6% of cases the tumor is bilateral

One third of tumors are hereditary

Etiology

Thought to develop from persistent metanephric tissue or nephrogenic rests

Believed to be due genetic alterations of embryological development of the genitourinary tract

WT1 gene at chromosome 11p13 implicated in tumorigenesis

WT2 gene at chromosome 11p15 (still not isolated) is a second locus

Gross picture:

Most tumors are large

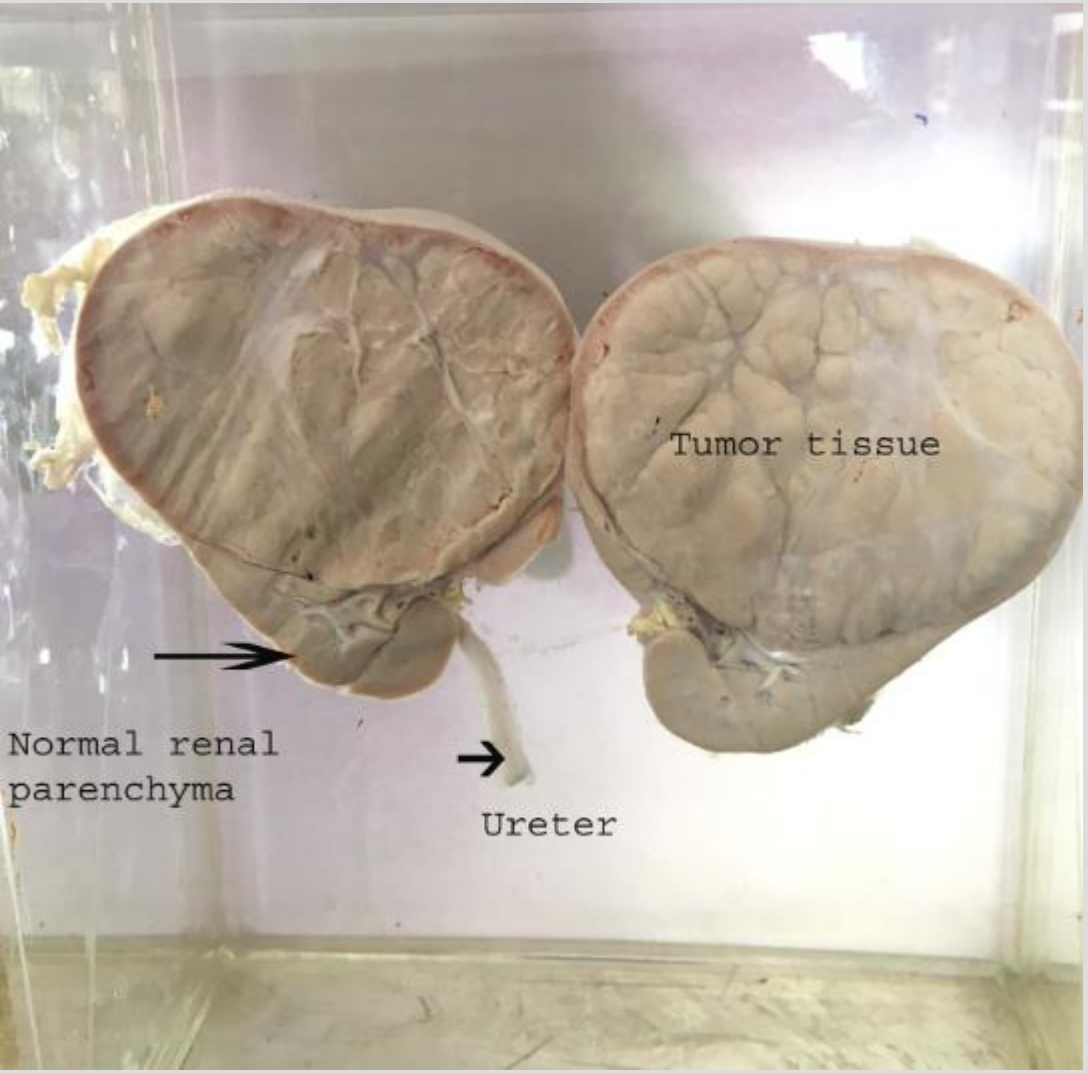
Cut surface is demarcated, noncapsulated, whitish & bulging, giving encephaloid appearance

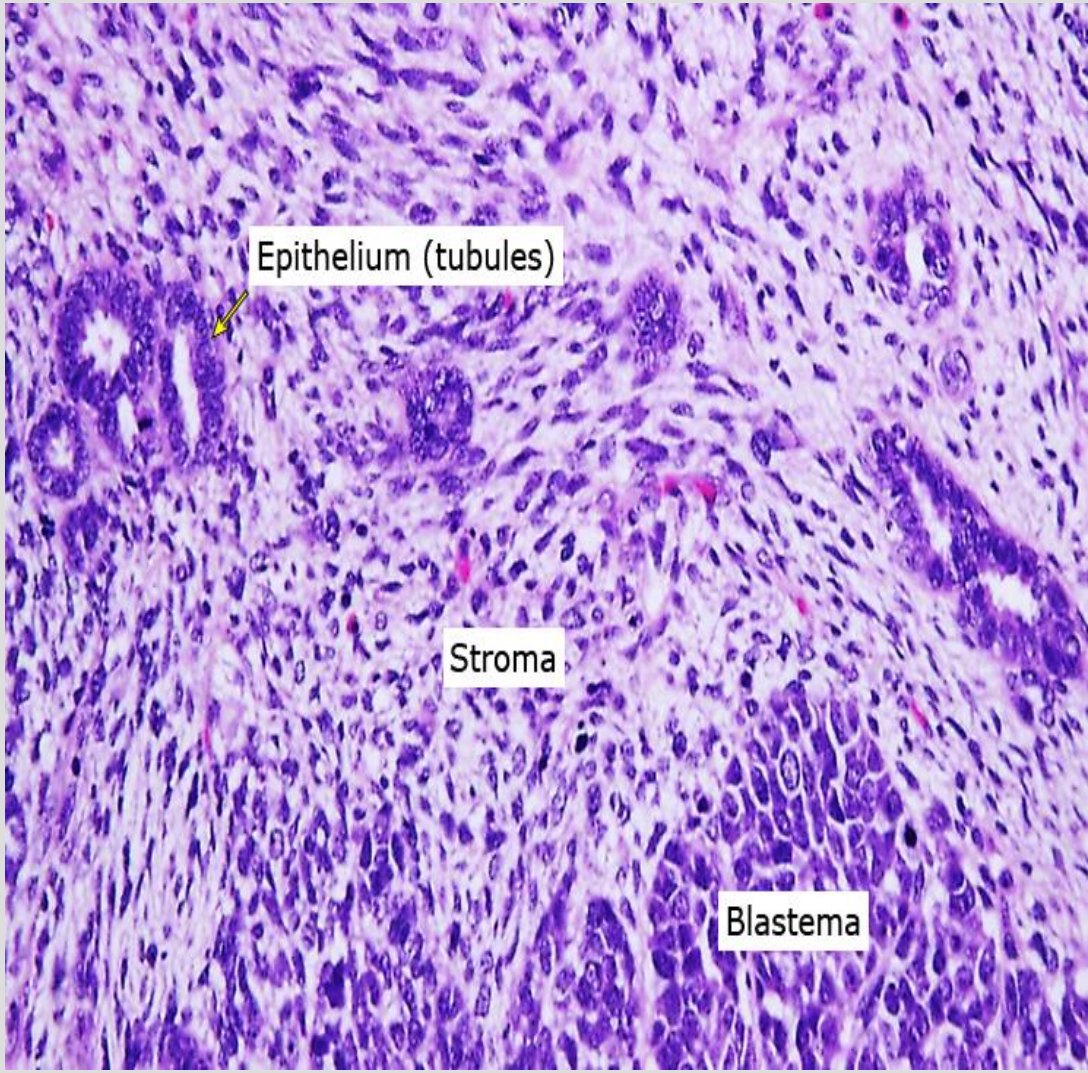
Hemorrhage, cystic changes & necrosis are common

Microscopic picture: Classically the tumor is triphasic & consists of:
Small undifferentiated blastemal cells usually in aggregates
Epithelial cells arranged in ribbons, primitive tubules or glomeruloid structures
Mesenchymal elements which may be undifferentiated or show muscle or cartilaginous differentiation
Poor prognostic histological features in any of the above three elements include 1)marked nuclear enlargement (3 times compared to cells of the same type)
2)marked hyperchromatism 3) multipolar mitoses

Spread:

1-Direct to perinephric tissue and surrounding structures
2-Lymphatic Para-aortic nodes
3-Blood: Lungs, bone, others.


Tumor tissue
Normal renal parenchyma
Ureter


Epithelium (tubules)
Stroma
Blastema

Staging of Wilm's Tumor :

Stage 1: Limited to kidney, completely resected.

Stage II. Invasion beyond kidney, but completely resected

Stage III Residual nonhematogenous tumor confined to abdomen

Stage IV.Hematogenous metastases

Stage V Bilateral renal involvement at diagnosis

Mesoblastic Nephroma

Clinical Features

- Most common congenital renal neoplasm; diagnosis typically made within first 3 months of life
- Uncommon in children older than 1 year old; rarely found in adults
- Almost all infants present with an abdominal mass
- May occasionally recur; rare reports of metastases

Gross Pathology

- Centered in the renal sinus
- Classic mesoblastic nephroma: small with firm, whorled cut surface resembling leiomyoma
- Cellular mesoblastic nephroma: large, frequently soft and cystic with foci of hemorrhage and necrosis

Histopathology

- Classic variant resembling benign fibromatosis; composed of interlacing fascicles of bland fibroblastic cells with infrequent mitoses; locally invasive, extending into adjacent renal fat
- Cellular variant, identical to infantile fibrosarcoma; composed of sheets or ill-defined fascicles of densely packed plump cells with high mitotic activity; less invasive with pushing margins
- Mixed pattern recognized when features of both are present in a single tumor

Clear Cell Sarcoma

- Rare renal tumor; about 5% of all pediatric kidney tumors
- Typically presents between ages 6 months and 5 years
- Presents with an abdominal mass; metastasis often present at time of presentation
- Common sites of metastasis include bone, brain, lung, liver, soft tissue, and lymph nodes

Rhabdoid Tumor

Clinical Features

- About 2% of all pediatric renal neoplasms
- Male-to-female ratio of 1.5:1
- Mean age of 13 months; usually younger than 24 months
- Hematuria, hypercalcemia; 15% associated with posterior fossa primitive neuroectodermal tumor (PNET)

- Highly lethal; 75% of patients die within 1 year of diagnosis
- Widespread hematogenous and lymphatic metastases
- No effective therapy

Gross Pathology

- Moderately circumscribed, nonencapsulated mass
- Necrosis and hemorrhage common

Histopathology

- Sheets of uniform cells with

— Large vesicular nuclei

— Prominent nuclei and cytoplasmic inclusion

Hereditary renal cell tumors

von Hippel-Lindau syndrome

Autosomal dominant, due to germline mutation of VHL gene at chromosome 3p25

Renal lesions: renal cysts and clear cell renal cell carcinoma

Associated with bilateral or multiple renal cell carcinomas in 50%

Other organs: hemangioblastomas of cerebellum and retina, cysts of pancreas, liver and kidney, clear cell tumors of other sites, papillary cystadenoma of epididymis, pheochromocytoma

Hereditary (familial) clear cell carcinoma, without the other manifestations of VHL but with abnormalities involving the same or a related gene, is another familial variant

Hereditary papillary renal cell carcinoma

Due to activating mutation of MET oncogene at chromosome 7q31

Autosomal dominant, late onset bilateral papillary renal tumors

Hereditary leiomyomatosis and renal cell carcinoma
Autosomal dominant, familial
Due to germline fumarate hydratase mutations
Cutaneous or uterine leiomyomas
Renal tumors are often papillary with characteristic large nucleus with a very prominent inclusion-like eosinophilic nucleolus (HLRCC)
Familial papillary thyroid carcinoma
Hyperparathyroidism-jaw tumor syndrome
Tuberous sclerosis
Mutations in TSC1 and TSC2 genes via an alternate pathway not involving VHL mutations
Multiple, bilateral angiomyolipomas or epithelioid angiomyolipoma

Birt-Hogg-Dubé syndrome

Autosomal dominant with incomplete penetrance

Due to germline mutations in BHD gene at chromosome 17p112, which codes for folliculin

Skin lesions: fibrofolliculomas, trichodiscomas, acrochordons

Lung: cysts, spontaneous pneumothorax

Renal tumors variable: oncocytoma, clear cell carcinoma and hybrid oncocytic / chromophobe tumor with areas of clear cells