

RENAL PATHOLOGY

CONGENITAL DISEASES OF THE KIDNEY

- Frequency: 10%
- It includes the following:
 1. Disease related to volume of the renal tissue and differentiation.
 2. Anatomic abnormalities; Vascular and ureteric connection.
 3. Metabolic; enzyme defect affecting tubular transport-----cystinuria and renal tubular acidosis.

Conditions affecting volume of renal tissue:

- A. **Bilateral agenesis;** POTTER'S syndrome, incompatible with life, associated with oligohydramnios due to absence of fetal urine. S&S: Low set ears, receding chin, wide-set eyes, parrot's beak nose
- B. **Unilateral agenesis:** Infrequent. The opposite kidney undergoes hypertrophy. This kidney is prone to infection and trauma. Children with this anomaly won't survive long because of associated congenital abnormalities (spina bifida, meningomyelocele, congenital heart diseases).
- C. **Renal hypoplasia;** prone to infection and stone formation. Disorders of differentiation:
 - Presents with cystic kidney
 - Islands of undifferentiated mesenchyme or cartilage
 - Unilateral or bilateral
 - If nnilateral Good prognosis
 - May be associated with other congenital anomalies
 - May lead to CRF in childhood

Anatomic abnormalities:

- A. **Ectopic kidney-** As pelvic kidney which may be associated with malrotation of the intestine. There is increased risk of infection due to ureteric kinking
- B. **Horse shoe kidney:** Fusion of the 2 poles of the kidney, Majority at lower poles. Renal function is usually normal.
- C. **Reduplication of vessels or ureters** (anomalous polar artery passing anterior to ureters----obstruction)

Metabolic abnormalities:

- A. Cystinuria: Defective tubular reabsorption of several amino acids including cysteine, lysine, ornithine and arginine .
The exact enzyme defect is *UNKNOWN*. It is of *AUTOSOMAL RECESSIVE* inheritance.
- B. Renal tubular acidosis type I: Probably due to defect in enzyme system which enables hydrogen ions to be exchanged for bicarbonate in proximal tubule. Bicarbonate is lost with failure to acidify urine. Such patients are prone to stone formation and infection.
The mode of inheritance is *AUTOSOMAL DOMINANT*. However, such a disease may be *ACQUIRED* due to tubular damage.

Congenital nephrotic syndrome:

First described in Finland, rare, of *AUTOSOMAL RECESSIVE* inheritance. It is due to defect in glycosaminoglycan synthesis leading to abnormal structure of the basement membrane. Such patients are prone to pneumococcal infections. It presents as a cystic lesion.

Alport's syndrome:

1. Nephritis
2. Deafness for high pitch sounds
3. Ocular lesions (in severe cases), discoloration of the lens, cataract, corneal dystrophy.
It is of variable modes of inheritance (50% X-linked); males more affected than females.
4. End with ESRD(end stage renal disease), dialysis and needs renal transplant.

CYSTIC DISEASES OF THE KIDNEY

Could be divided into;

1. Congenital
2. Acquired

Congenital:

1. Autosomal dominant polycystic kidney disease (ADPKD)
2. Autosomal recessive = = (ARPKD)
3. Congenital nephrotic syndrome
4. Uremic medullary cystic disease
5. Medullary sponge kidney

Acquired:

1. Simple renal cyst
2. Renal dialysis associated
3. Hydatid cyst

Acquired cystic disease of the kidney:

- 1. Simple renal cyst:**
 - Common autopsy finding and U\S finding of no significant clinical outcome.
 - Incidence increases with age

- Single or multiple
- Few mm to several cm.
- Smooth lining, clear fluid
- Renal function is not affected, sometimes hemorrhage takes place in the cyst leading to pain.
- **Main importance is to differentiate them from renal tumors.**

2. Dialysis associated cysts:

- Chronic renal failure + dialysis for some years lead to cysts in the cortex and medulla with associated oxalate crystals. Dilatation is due either to fibrosis obstructing the tubular lumens or by the oxalate crystals themselves.
- Numerous cortical & medullary cysts in patients with CRF who have undergone long term dialysis
- Usually asymptomatic but sometimes patients have hematuria
- Main complication is development of renal cell carcinoma in cyst walls (7% over 10 years)

Congenital cystic disease of the kidney:

1. ADPKD:

- Always bilateral
- Kidneys distorted by numerous cysts (few mm to 10 cm) with thin bands of paranchyma stretched between them. Bilateral markedly enlarged kidneys (up to 4 Kg!)
- Cysts contain clear fluid, if brown colored then it is due to old hemorrhages into cysts (hemosiderin)
- All nephrons are affected ;Multiple expanding cysts in both kidneys that eventually destroy intervening parenchyma.
- **Autosomal dominant**
- Presentation; at any age, from childhood to late adult life
- Function is maintained till cysts press on the adjacent structures leading to ischemic changes---hypertension and renal failure
- Other associated congenital abnormalities include Berry aneurysm, hepatic cysts, pancreatic cysts and lung cysts (of no functional significance)
- Types; ADPKD-1 linked to mutation in chromosome 16, the remainder linked to mutation in chromosome 4 (ADPKD-2).Rare cases are of type -3(ADPKD-3).

Clinical features:

- Gradual onset of CRF
- Flank pain or dragging sensation
- Intermittent gross hematuria
- Hypertension (75%) & UTI
- Associated with berry aneurysms in 10-30% & liver cysts in 40%
-

2. ARPKD:

- Rare
- More than one gene affected
- Subgroups include perinatal- 10%
- Either stillborn or the infant dies of renal failure and respiratory distress soon after birth. The kidneys are usually enlarged with characteristic radial pattern of fusiform cysts replacing both cortex and medulla

- and extending to the capsular surface. Smooth kidney surface with numerous small cysts as well as dilated channels perpendicular to surface

The kidneys are usually palpable and thus may impair delivery

- Neonatal, infantile and juvenile subgroups (progressively less severe involvement and a longer survival)
- In both, liver abnormalities (bile duct proliferations, cysts, hepatic fibrosis leading to portal hypertension)

3. Uremic medullary cystic disease complex (UMCD- Nephrophthisis):

- In many, there is family history. The inheritance could be dominant or recessive
- Seen in 20-25% of chronic renal failure patients (children and adolescents). Thus it could also be acquired.
- Histologically, numerous cysts at cortico-medullary junction, interstitial fibrosis, thickened tubular basement membranes.

4. Medullary sponge kidney:

- Results from dilatation of the collecting ducts thus causing cyst formation at the papillae
- Usually bilateral, but could be unilateral
- Function is usually normal, but calculi formation and infection could occur

Hydronephrosis (hydrocalycosis):

It is dilatation of the pelvis and calyces due to partial or intermittent obstruction to the urine outflow.
Types: Unilateral, bilateral.

1. Unilateral hydronephrosis: Causes

- a. Intraluminal: Stone in ureter or pelvis
- b. Intramural: Tumor of the ureter, inflammatory stricture, atresia of the ureter
- c. Extramural: Pressure from outside as in Carcinoma of cervix, prostate, rectum, cecum, retroperitoneal fibrosis or by aberrant renal artery

2. Bilateral hydronephrosis: Causes

- a. As above, if involving both sides
- b. Congenital as atresia of the urethral meatus
- c. Acquired as in prostatic hyperplasia, bladder tumors involving both ureteric orifices, urethral strictures

Pathologic changes:

1. Initially, extra-renal hydronephrosis- dilatation of the renal pelvis medially
2. Intra-renal,- progressive dilatation of the pelvis and calyces----pressure atrophy-----thinning of cortex, surface assumes lobulated pattern(cupping of the calyces).

The question is, how can we differentiate between polycystic kidney disease and hydronephrosis?

Answer: In hydronephrosis there is direct continuity of the dilated cystic spaces (calyces and pelvis).

Histology:

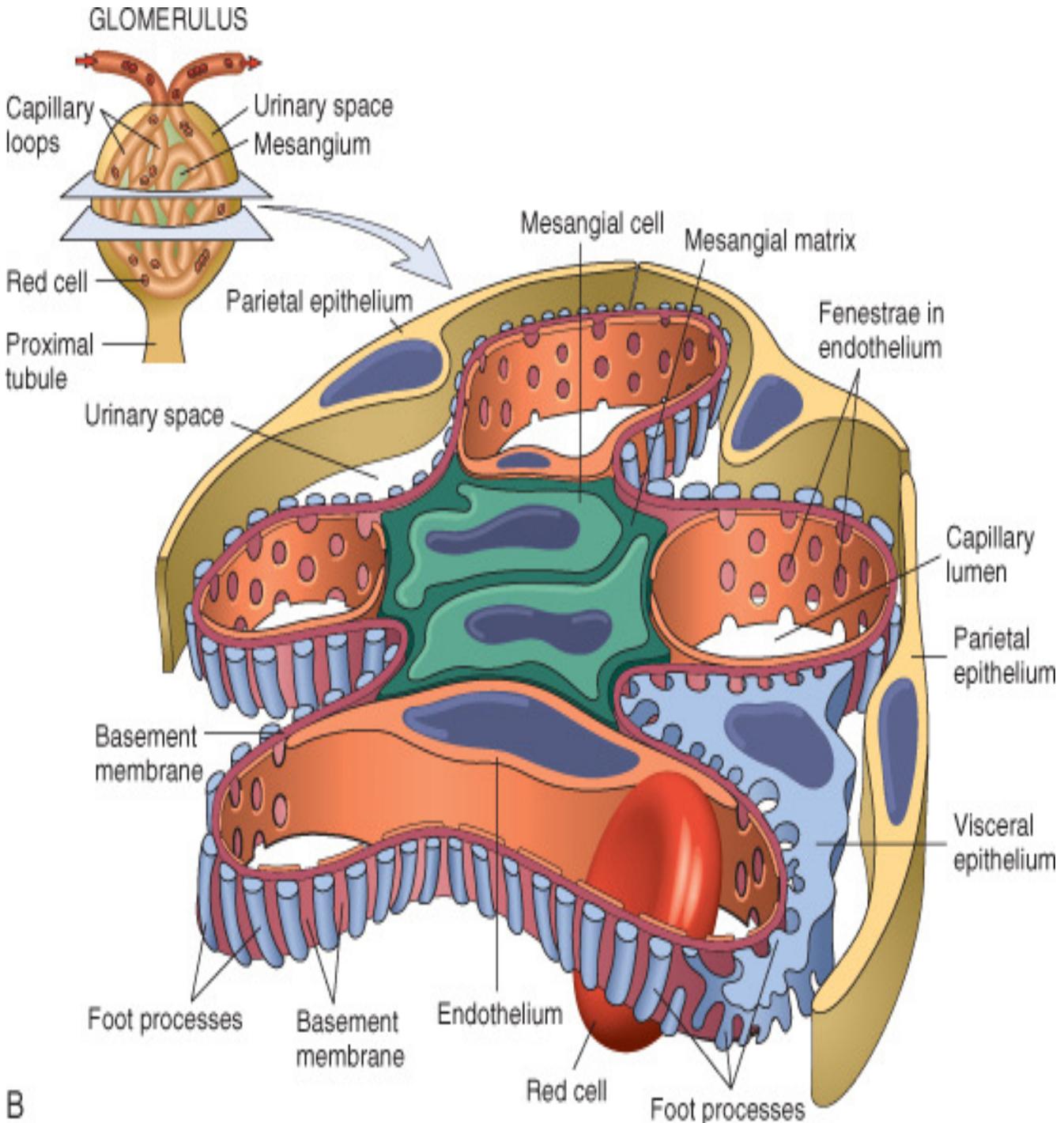
1. Wall of the sac is thickened (fibrosis and chronic inflammatory cells)
2. Progressive atrophy of tubules and glomeruli + interstitial fibrosis
3. Stasis of urine---infections (pyelitis)—pyonephrosis

Glomerular diseases

The glomerulus is an invagination of a specialized capillary network, derived from the afferent arteriole into the Bowman's capsule. It consists of:

1. Endothelium that is fenestrated + B.M. (the B.M. has a strong anionic –negative- charge which repels the major plasma proteins (also anionic).
2. Mesangial cells (two types):
 - a. Contractile smooth muscles which control blood flow.
 - b. Phagocytic (macros)- few in number which ingest proteins and immune complexes.
 - c. Modulation of glomerular filtration.
 - d. Generation of mediators,
3. Epithelial cells: Attached to B.M. by foot processes separated by gaps 30-60 nm and covered by a fine slit of diaphragm. The visceral epith cells are the major glom filter barrier.
4. Glomerular Basement Membrane (GBM) Consists of 3 layers:
 - Lamina densa
 - Lamina rara interna
 - Lamina rara externa
 - Has a strong negative charge
 - It is size and charge selective permeability
 - Main component is type IV collagen

Diagram showing the electronic microscopic features of the glomerulus:



B

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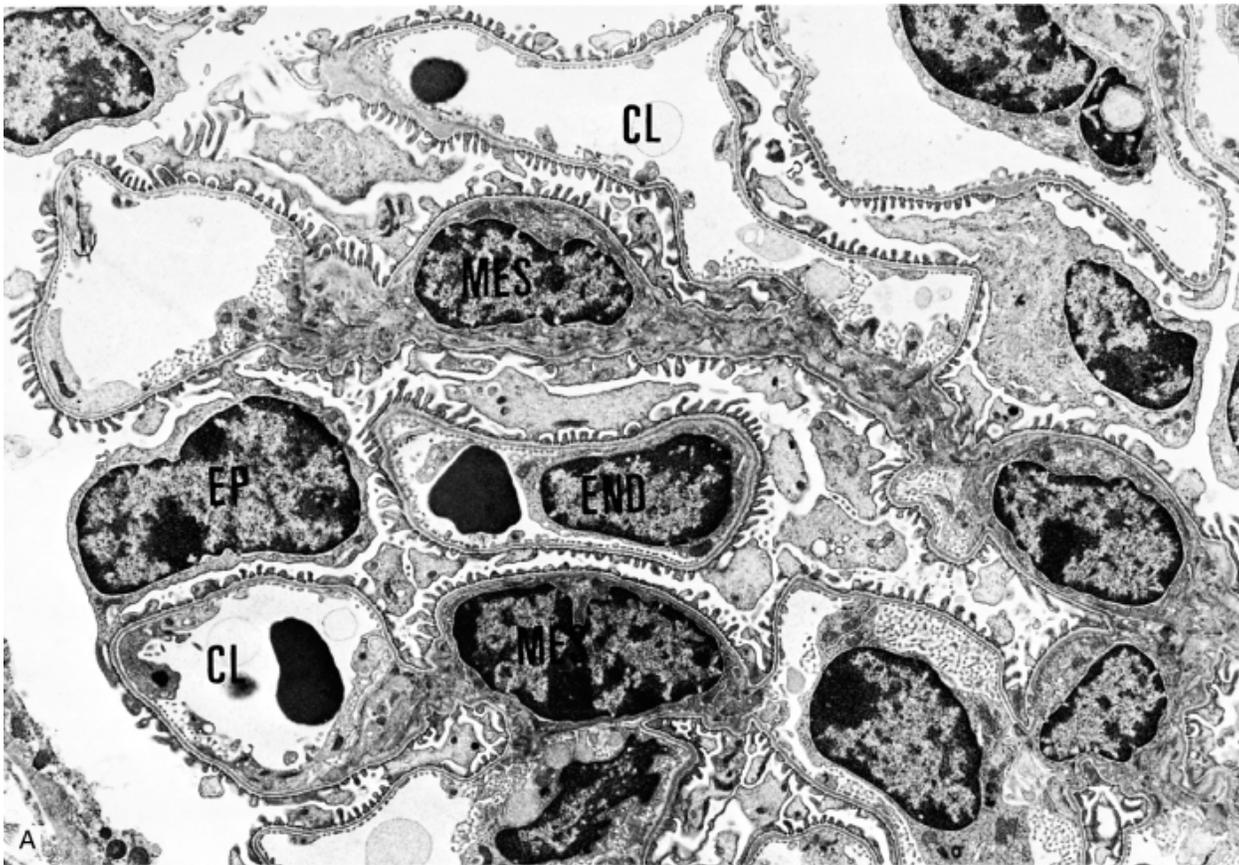
ELECTRON MICROSCOPY OF THE GLOMERULUM

CL=capillary lumen

END=endothelium

EPI=epithelium

MES=mesangium



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Classification of glomerular diseases:

- A heterogeneous group of renal diseases in which the glomeruli are primarily affected. Lesion is bilateral and symmetrical.
- Acute and chronic types
- Primary and secondary types

There are 3 parallel and complementary classifications;

1. Etiological
2. Immunological
3. Morphological

Etiological:

- Primary glomerular lesions- Kidney is the first target
- Secondary glomerular lesions- The kidney is secondary to other events elsewhere

Immunological: reactions involving either;

- Glomerular antigens (anti glomerular basement membrane antibodies)
- Non-glomerular antigens (immune complex deposition)

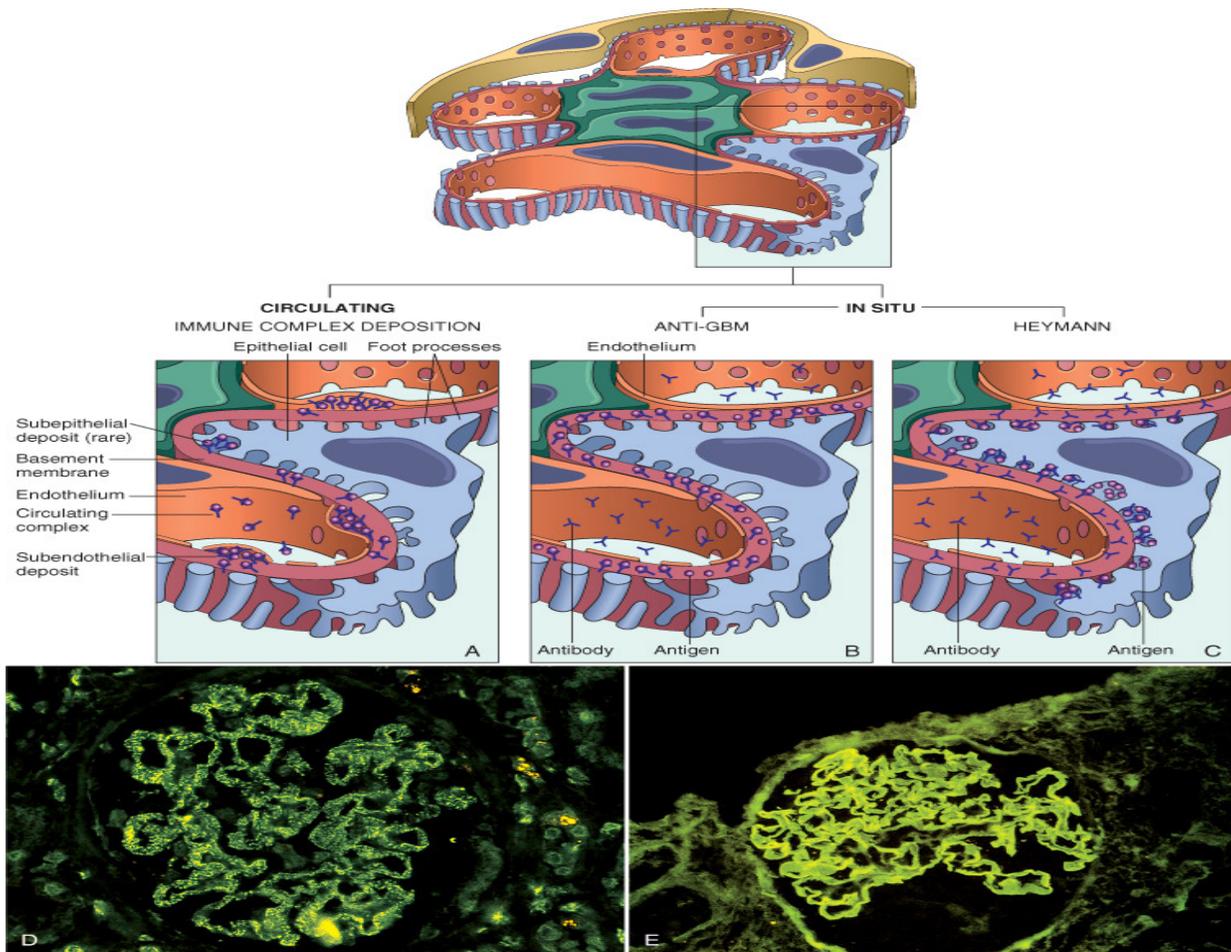
Non-immunological disorders: as in D.M. = secondary glomerular disease

Antibody - mediated injury:

- Circulating immune complex deposition:
 - Endogenous antigens(DNA , tumor antigens)
 - Exogenous antigens (infectious products)
- In situ immune complex deposition:
 - Fixed intrinsic antigens
 - ANTI - GBM NEPHRITIS
 - HEYMANN NEPHRITIS
 - ? IDIOPATHIC HUMAN MEMBRANOUS GN
 - Planted antigens :
 - EXOGENOUS ANTIGENS (drugs ,infectious antigens)
 - ENDOGENOUS ANTIGENS (DNA)

Mediators of immune injury:

- Neutrophils
 - Proteases
 - Oxygen metabolites
 - Arachidonic acid metabolites
- Complement activation C5a , C5b -C 9



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Morphological: Will be discussed later

Nomenclature of glomerular injury:

1. **Diffuse:** Lesion affecting all glomeruli
2. **Focal:** Some glomeruli are affected
3. **Global:** The whole glomerulus is involved
4. **Segmental:** Only part of the glomerulus is involved
5. **Proliferative:** Increase number of cells in the glomerulus + polys and macrophages
6. **Membranous:** Thickened B.M. of the capillary loops
7. **Membrano-proliferative:** Both 5 & 6 with accentuation of the lobular architecture
8. **Crescentic:** Florid proliferation of cells forming crescents in the Bowman's capsule compressing the glomerulus

N.B.: The deposition of immune complexes within the glomeruli leads to inflammation. The inflammatory response may cause proliferation of endothelial, mesangial and epithelial cells and in severe disease, glomerular necrosis.

Two clinical terms to remember:

- Nephritic syndrome; which comprises edema, proteinuria, hypoalbuminemia, hematuria (smoky urine), oliguria and hypertension.
- Nephrotic syndrome; which comprises of albuminuria, hypoalbuminemia, edema, hyperlipidemia, lipiduria.

Causes of nephrotic syndrome:

- Primary Glomerular Disease:
 - Membranous GN
 - Lipoid nephrosis(MGGD)
 - Focal segmental glomerulosclerosis
 - Membranoproliferative GN
 - Other proliferative GN (focal,mesangial,IgA-N)
- Systemic Diseases:
 - DM,SLE,amyloidosis
 - Drugs,malignancy,infections
 - Miscellaneous (hereditary nephritis)

Generalizations about glomerular diseases:

1. A variety of renal morphologic patterns can lead to the same clinical syndrome. Nephritic syndrome and hematuria can be caused by:
 - hereditary nephropathy, MPGN ,IgA-N, acute proliferative GN.
2. One disease may produce different patterns of renal injury (e.g..SLE).
3. One pathologic pattern can be produced by many different diseases (e.g.. MPGN)
4. Renal biopsy is thought to be specific and diagnostic in only few condition (e.g.. Alport 's syndrome).

Immune complex –mediated lesions

1. Proliferative G.N.:

A\ Acute diffuse proliferative G.N. (acute G.N.)

- Follows infection with beta-hemolytic streptococcus (post-streptococcal G.N.); 2-4 weeks after the initial infection.
 - It may follow other causative agents as staph, meningococci, pneumococci, viruses, malaria, toxoplasma, bilharziasis.
- **Histologically;**
1. Glomeruli are distended and hypercellular.
 2. The increased cellularity is due to proliferation and swelling of mesangial, endothelial, epithelial and inflammatory cells as neutros.
 3. The lesion is diffuse.
 4. Stroma is edematous and inflamed.

5. Tubules contain red cell casts, tubular cells show degenerative changes

- Some glomeruli may show proliferation of the lining cells of Bowman's capsule to form crescent. If 80% or more of glomeruli show crescents...therefore it should be considered as rapidly progressive G.N. (Crescentic G.N.) which is of poor prognosis.
- Most patients are children who will recover spontaneously, only 1-2% will progress to chronic G.N.

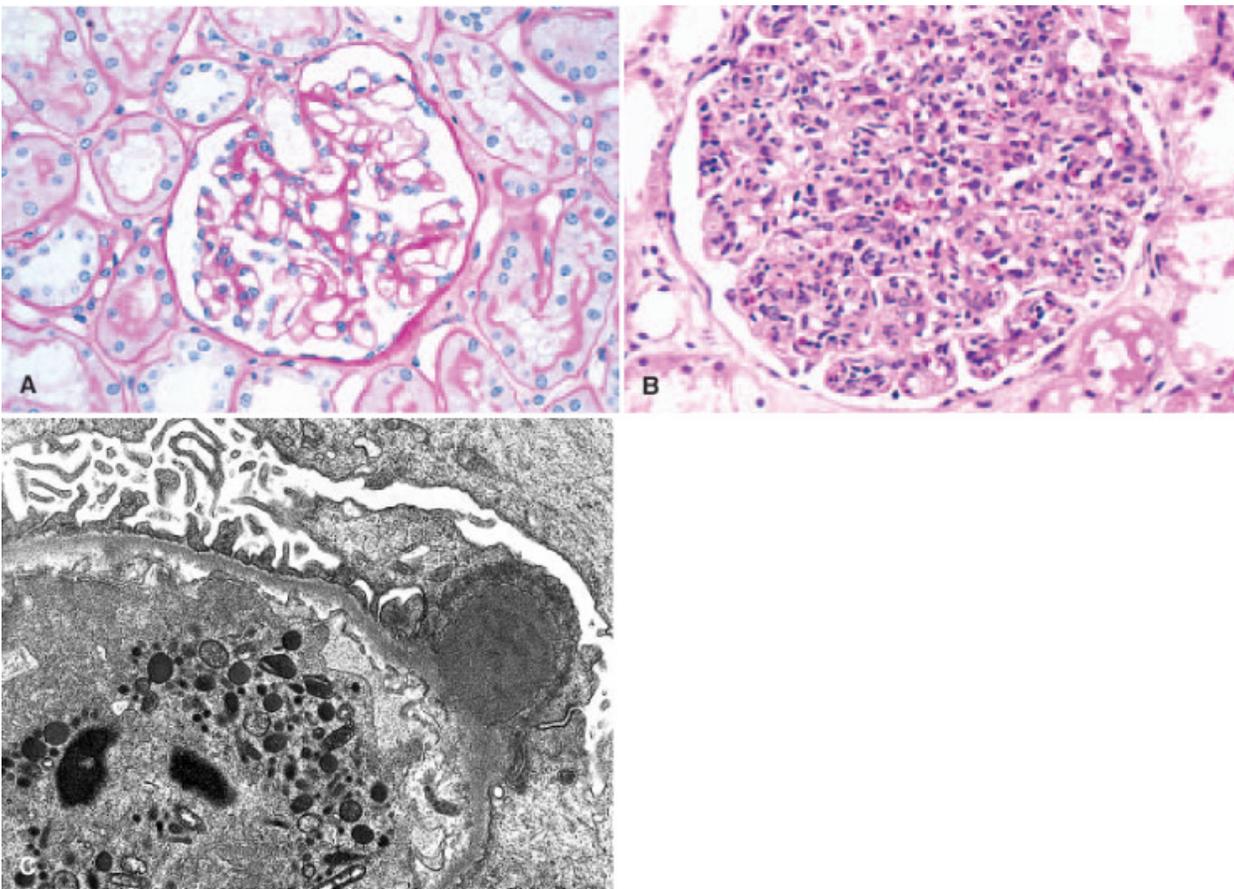
- **Presentation-** Nephritic syndrome.

- **E.M.:** Sub-epithelial immune complex deposits= Immune humps.

● **Prognosis:**

- children >95% recovery ,1% RPGN ,2% CRF
- Adults 15-50% develop ESRD

Poststreptococcus glomerulonephritis(Acute diffuse proliferative glomerulonephritis):



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B\ IgA nephropathy-Berger disease:

- Most common form of G.N. affecting children and young adults
- It may occur after infection, but its real pathogenesis is unknown
- Histologically; focal mesangial cell proliferation and mesangial deposits of IgA complexes (E.M., immunofluorescence)
 - Clinically, variable, from mild hematuria and proteinuria to slowly progressive renal failure (major cause of chronic renal failure)
- Patients do not respond to immunosuppressive drugs or steroids.
- Serum IgA levels increased

C\ Lupus nephritis:

- Seen in 75% of patients with SLE
- Inflammation could be treated by corticosteroids and cyclophosphamide
- 20% of patients may present with membranous nephropathy (resistant to treatment)
- Histologically; Hypercellular glomeruli, wire loop thickening of the B.M.
- E.M., Immunofluorescence----- immune complexes are seen anywhere in the glomerulus
- Presentation; nephritic syndrome of variable severity

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN) or Crescentic GN:

- Clinically - rapid and progressive loss of renal function with severe oliguria and (if not treated) death from renal failure within weeks or months.
- **Histologically-** presence of crescents in most glomeruli.
- RPGN is not a single disease it is a syndrome which could be caused by a number of diseases both primary of kidney and systemic diseases.

CLASSIFICATION AND PATHOGENESIS OF(RPGN) ACCORDING TO IMMUNOFLUORESCENCE FINDINGS :

1- Linear pattern for IgG & C3:

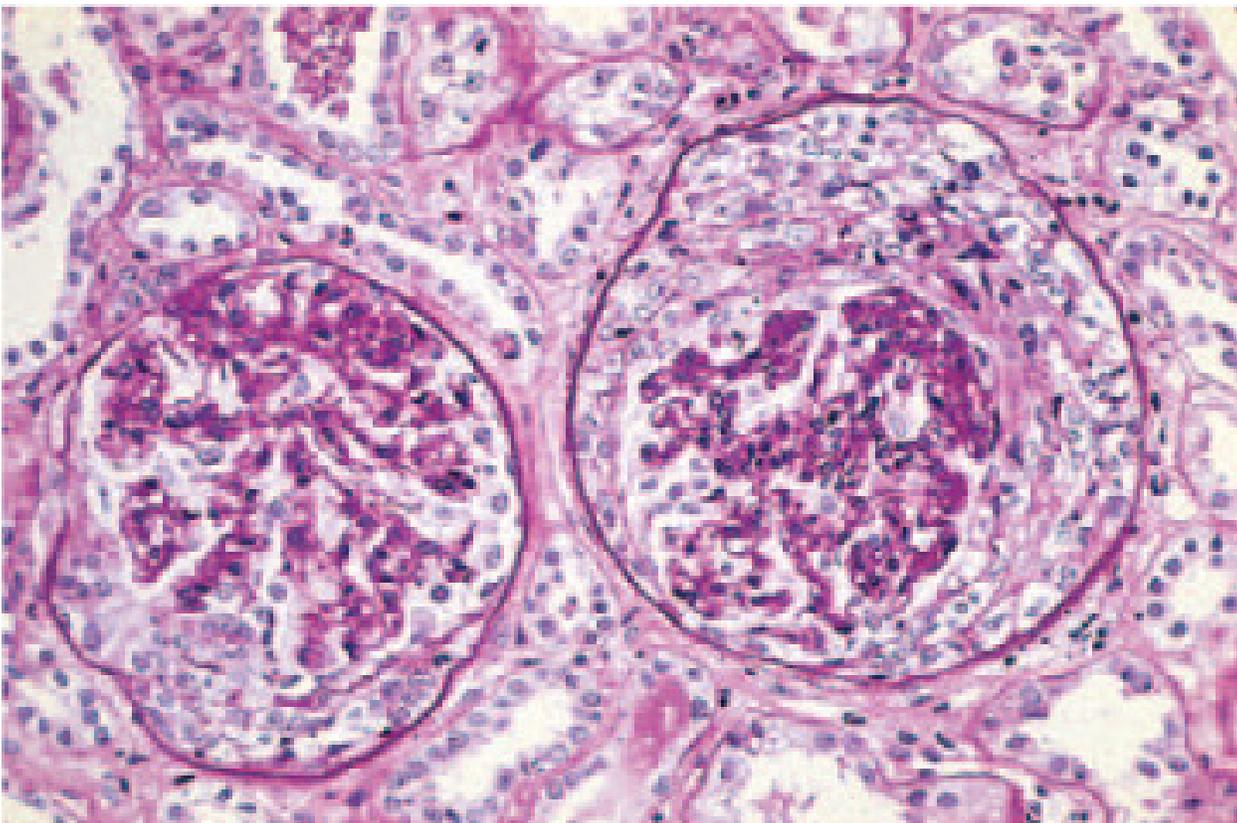
- Anti glomerular basement membrane disease antibodies to G.B.M , could cross react with pulmonary alveolar B.M to produce the clinical syndrome of lung hemorrhage and renal failure (Good Pasture's syndrome).

2- Granular pattern for IgG & C3:

- Immune complex disease
 - post infect., SLE, IgA GN, HSP or idiopathic

MORPHOLOGY OF RPGN:

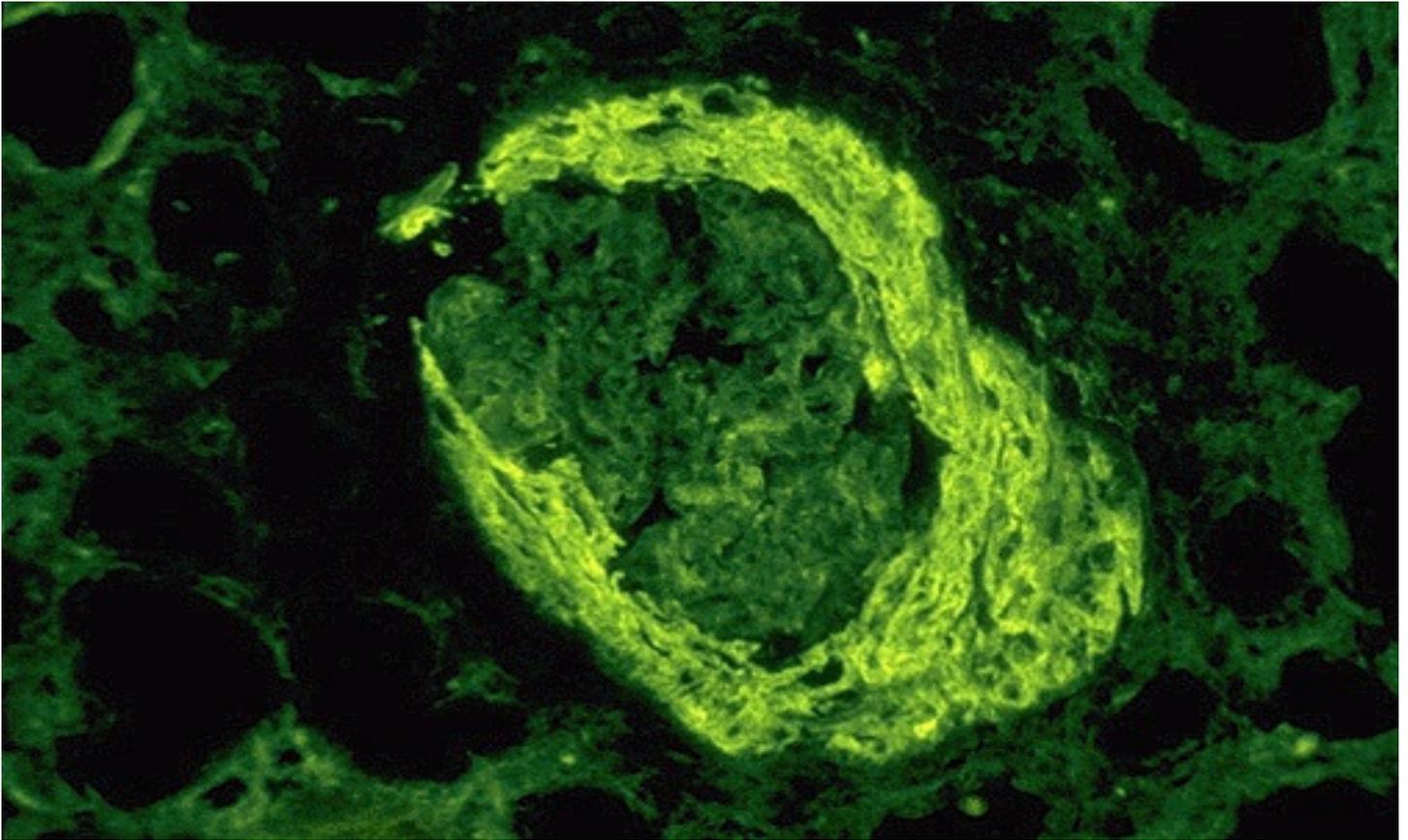
- Light microscopy (CRESCENTIC GN)
 - > 50 - 75% of glomeruli contain crescents obliterating Bowman capsule and compressing the underlying glomeruli which could show normal, focal or proliferative changes.
- EM
 - rupture of GBM only or with electron dense deposits
- IF
 - linear, granular or none.



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Crescentic (rapidly progressive glomerulonephritis)-LIGHT MICROSCOPE

Electron microscopy (Crescentic GN);



Prognosis of (RPGN):

- Milder forms may subside but renal involvement is usually progressive leading to oliguria
- therapy
 - plasma pheresis
 - steroids
 - cytotoxic drugs
- despite therapy patients develop CRF requiring renal transplant or dialysis.

Glomerulopathy:

It is a term applied to diseases that produce signs of glomerular disease but with no inflammation. These diseases cause nephrotic syndrome, which comprises edema, proteinuria, hypoalbuminemia and hyperlipidemia.

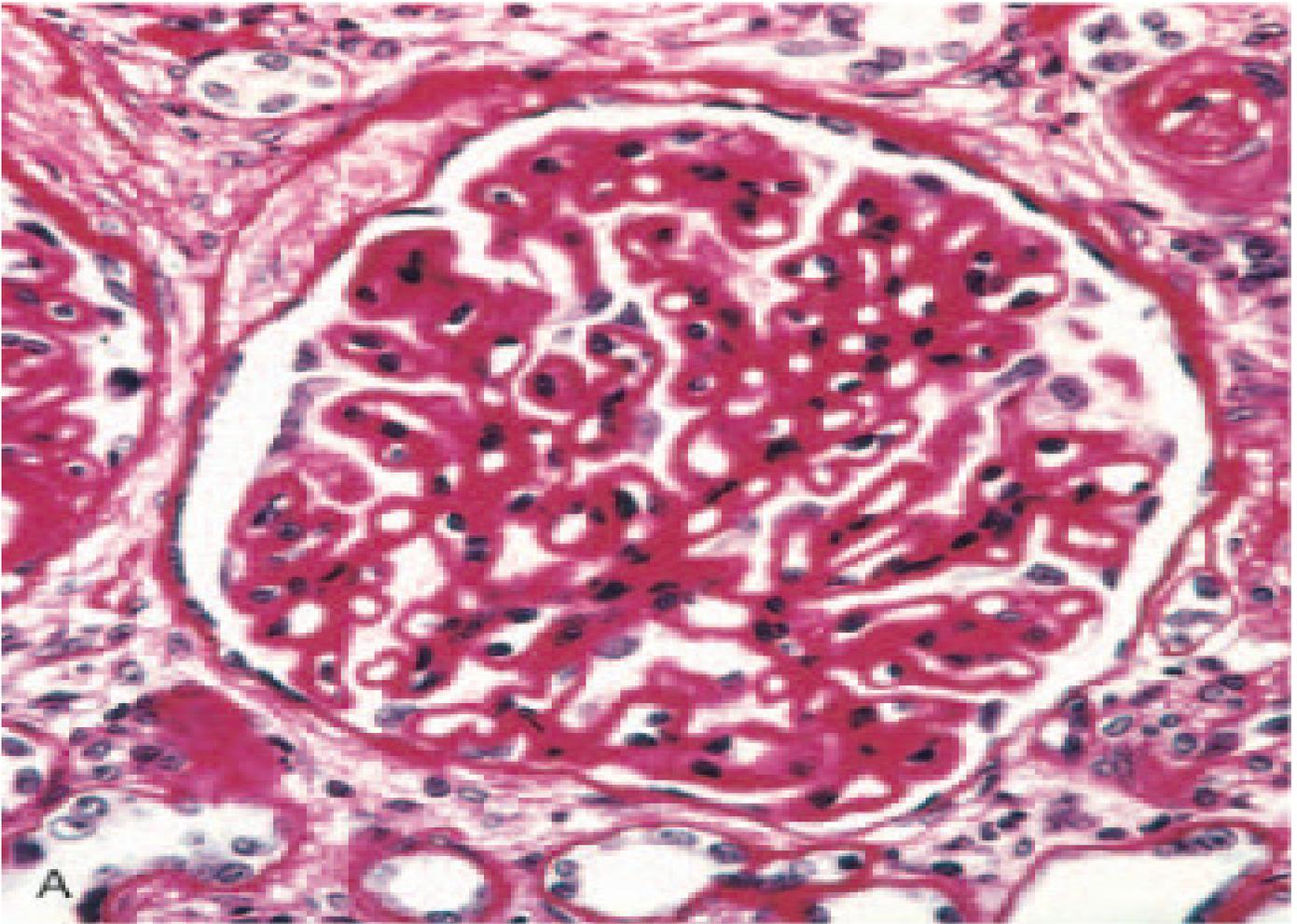
I. Membranous G.N. (glomerulopathy):

- Most common primary renal cause of nephrotic syndrome in adults (85%)
- Two types, primary and secondary

- Primary- idiopathic
- Secondary is due to;
 1. Infections: syphilis, malaria, hepatitis B
 2. Drugs and chemical as gold, mercury, heroin and penicillamine
 3. Tumors as lymphoma, melanoma, bronchogenic carcinoma
 4. SLE-10% of cases
- If we remove the causative agent MGN subsides.

- **Histologically;** B.M. thickening, no cell proliferation or inflammation
- **E.M.:** Diffuse spikes(B.M invaginations between immune deposits) are seen in all glomeruli and noted on the epithelial surface of the B.M. With time, new membrane forms (type IV collagen) encircling the deposits and then these deposits will undergo degradation and lysis.
- **IF:** diffuse, granular or linear dense deposits.
 - **Clinical:**
 - Nephrotic syndrome
 - proteinuria non-selective

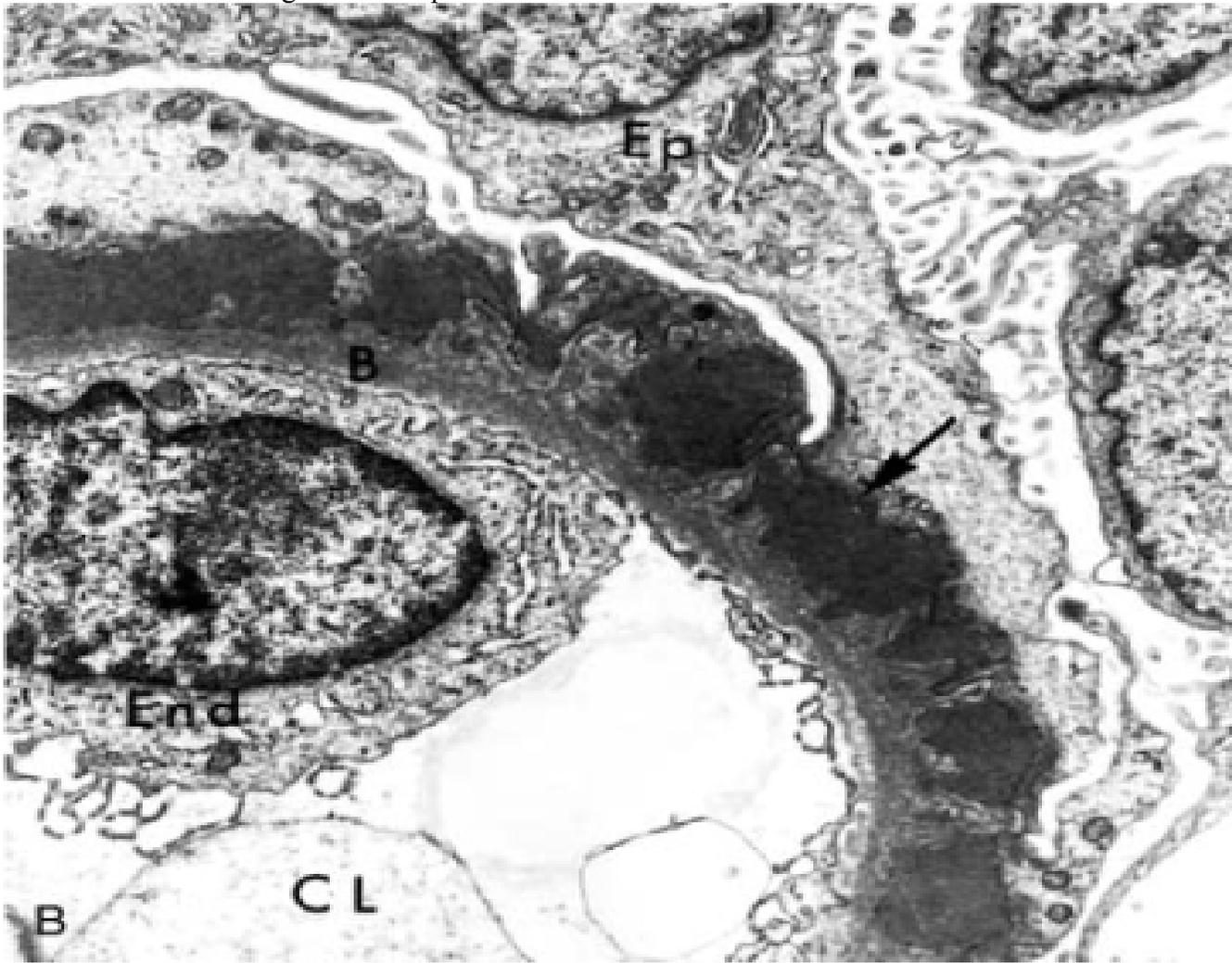
 - **Prognosis**
 - 70--90% proteinuria (irreversible).
 - 50% ---CRF.
 - 10 --30% more benign course.



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Membranous glomerulonephritis

EM: membranous glomerulonephritis



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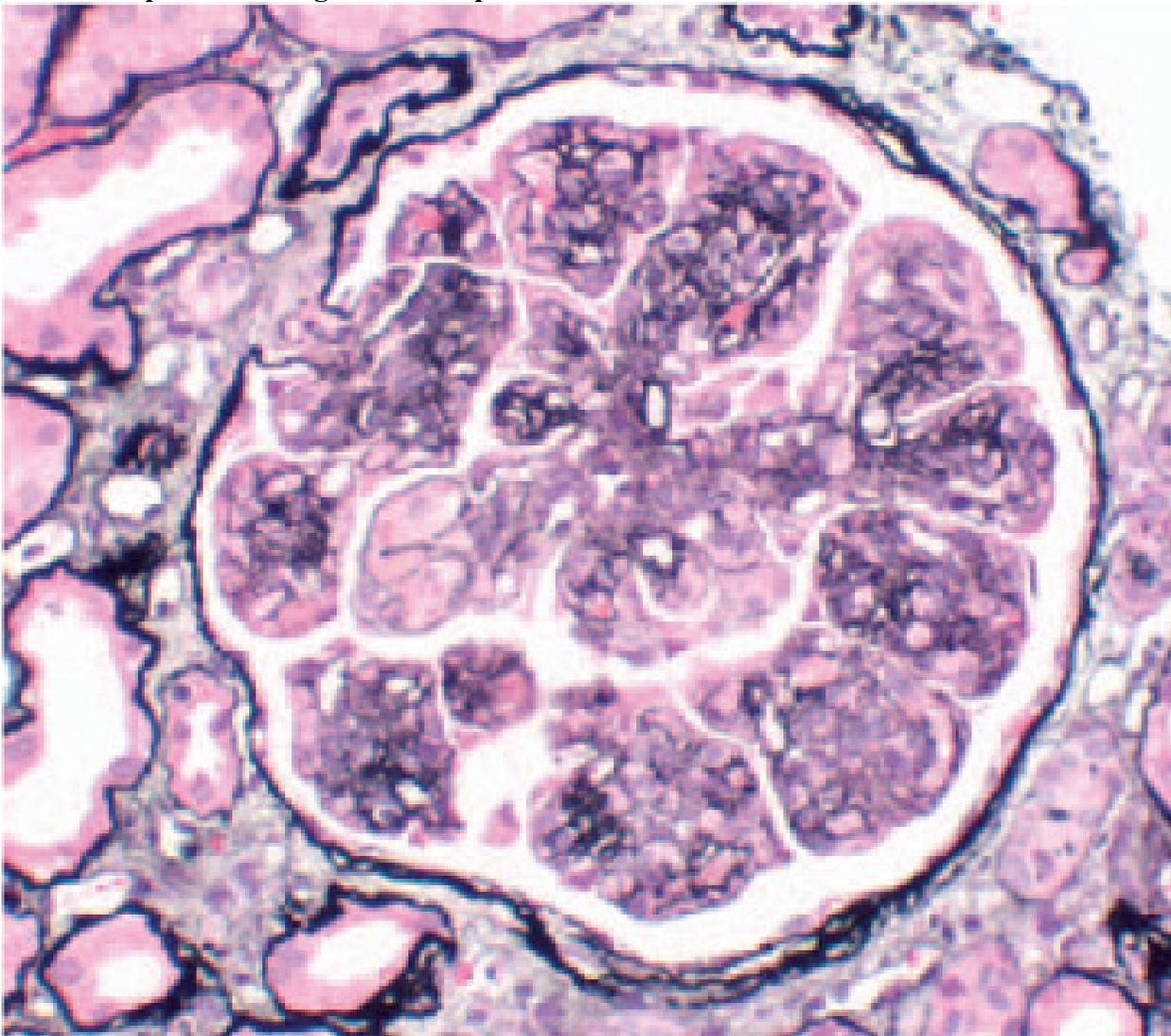
II. Membrano-proliferative (mesangiocapillary):

- **Types:** Type 1: 70% Subendothelial and paramesangial deposits
Type 2: 30% Dense deposits disease (discontinuous linear deposits) in B.M.
Type 3: Rare, deposits seen in B.M., subepithelial, subendothelial aspects of the B.M.
- **Histologically;** glomerulus enlarged, accentuated lobular pattern, and thickened B.M.

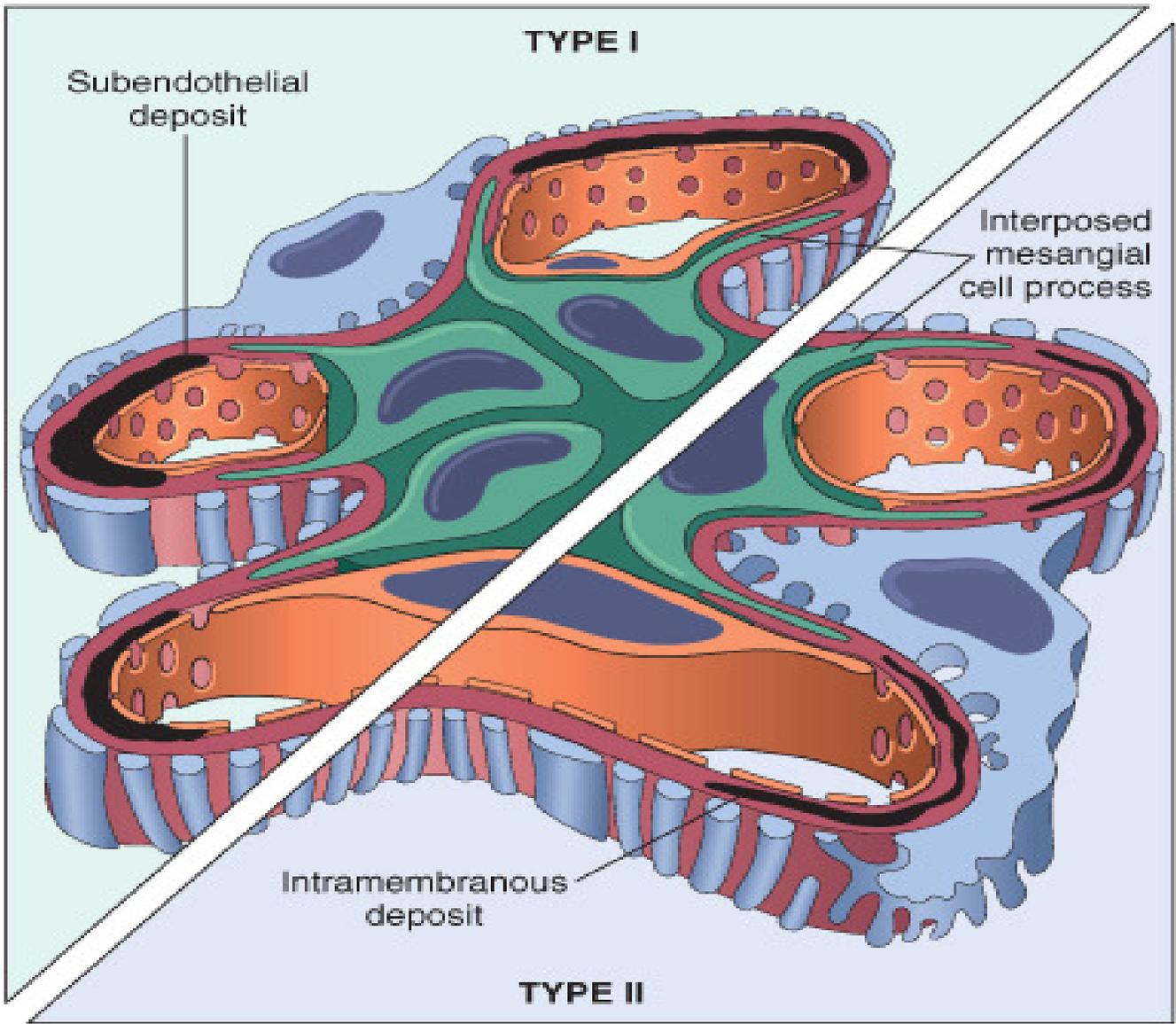
Using special stains as **silver stains** 2 B.Ms are recognized with clear zone in between (**double contour, tram-track B.M.**). The thickening noted is due to subendothelial deposits and ingrowth of the mesangial cytoplasm between the endothelium and B.M.

- **Light mic.:**
 - enlarged glomeruli, proliferation + infiltration of inflammatory cells, lobular accentuation, thickening of capillary walls, "reduplication" of glom cap. "tram-tracking". crescents may be seen. tubulointerstitial changes & vascular changes of HT.
- **EM:** type I
 - sub endothelial deposits, circumferential mesangial interposition. increase of cells & matrix
- **IF:** type I
 - C3, C1q, C4 in granular pattern in mesangial area

Membranoproliferative glomerulonephritis



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- Prognosis
 - 50% ----- CRF in 10 years
 - High recurrence in transplant

III. Minimal change disease (Lipoid nephrosis)

- Affects all age groups, especially children between 2-4 years
- In few patients, it follows upper respiratory tract infection or immunization
- Nephrotic syndrome responding to steroid therapy
- **Histologically- NO FINDING!!**, E.M. = flattening of the foot processes and that's why it is called **foot process disease**.

- **Etiology & Pathogenesis:**

- ? Dysfunction of T-cell function
 - RESPIRATORY INFEC, STEROIDS, ATOPIC DISEASE, HD.

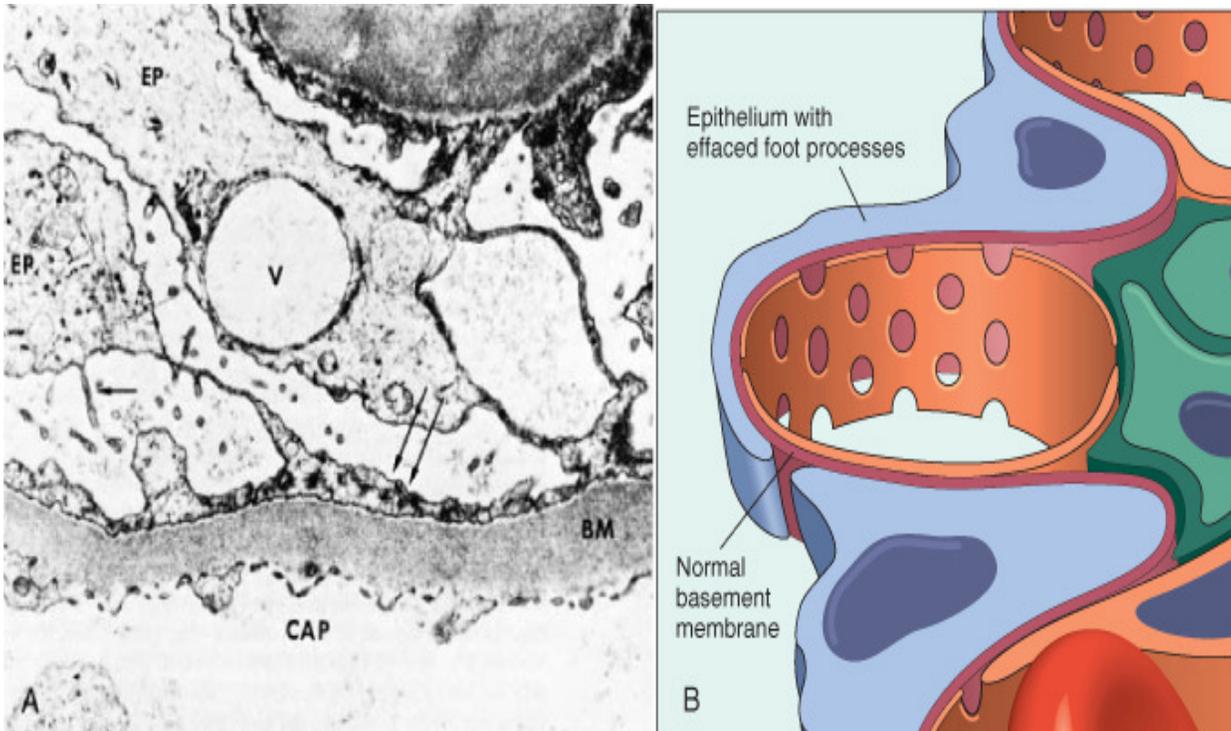
- **Clinical picture:**

- most common cause of NS in children
- 2 -- 6 years
- may follow URTI or immunization
- selective proteinuria
- responds to steroids
- renal function normal

- **Prognosis:**

- excellent in both children & adult

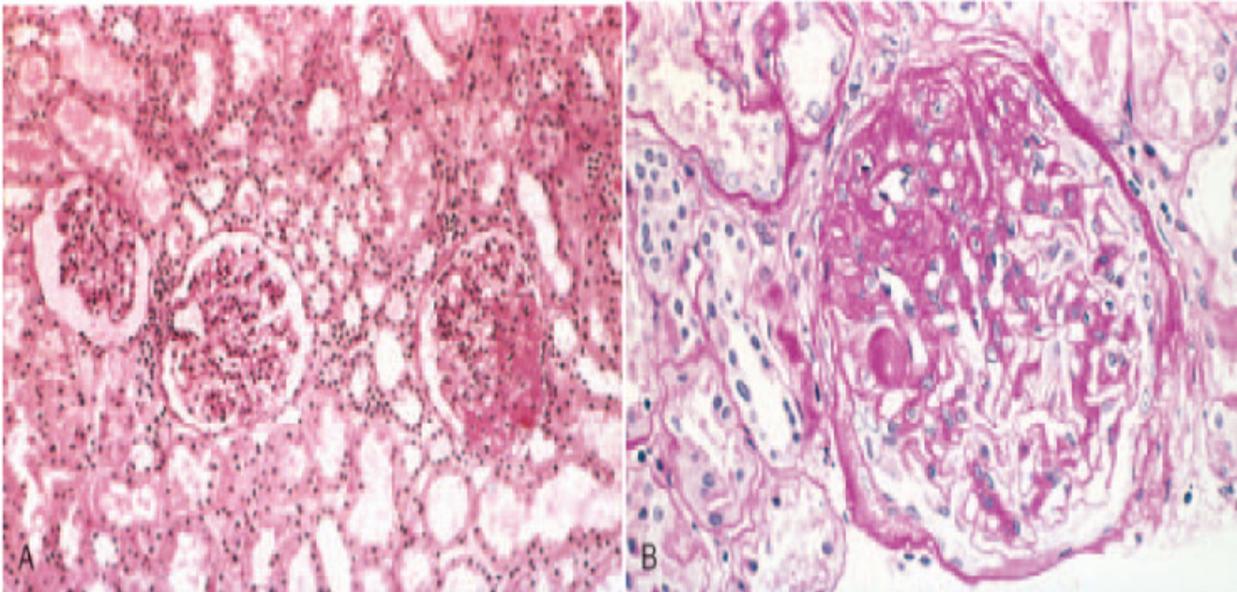
Minimal change glomerulopathy-ELECTRON MICROSCOPE



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IV. Focal segmental glomerulosclerosis:

- Focal, therefore some of glomeruli affected
 - Hyalinization of parts of the glomeruli hence the designation segmental
 - The disease is either primary (idiopathic) or secondary to other diseases as AIDS
 - Unresponsive to therapy
 - Sclerosis of some, but not all, glomeruli and only part of the glomerulus is involved.
 - Classification and types of FSGS
 - Association with HIV, Heroin addiction, sickle cell disease and Obesity.
 - Glomerular scarring in other forms of FGN, e.g. IgA nephropathy
 - Idiopathic.
- Light microscopy:**
- SCLEROTIC SEGMENTS SHOW COLLAPSE OF B.M. INCREASED MESANGIAL MATRIX, DEPOSITION OF HYALINE MASSES (HYALINOSIS)
- EM:**
- NON-SCLEROTIC SEGMENTS SHOW LOSS OF PODOCYTES & FOCAL DENUDATION OF EPITHELIAL CELLS
- IF:**
- IgM & C3 IN SCLEROTIC SEGMENTS



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FSGP

- CLINICAL PRESENTATION
 - NEPHROTIC SYNDROME
 - 10% CHILDREN
 - 15% ADULTS
 - PROTEINURIA
 - A higher incidence of hematuria, reduced GFR, and HT.
 - Nonselective proteinuria
 - poor or no response to steroids
- DIFFERENTIAL DIAGNOSIS
 - MCD&DMGN

V. **Glomerulopathies of non-immune origin:** This is seen in two clinical settings;

1. D.M.
 2. Amyloidosis
- Diabetic nephropathy: Occurs in two forms, diffuse or nodular (Kimmelsteil-Wilson disease). It presents as nephrotic syndrome
 - Amyloidosis: Could be a feature of multiple myeloma (primary amyloidosis) or a complication of chronic suppurative disease

Infections of the kidney:

Two routes:

1. Ascending infection as with lower UTI (obstruction and/or vesico-ureteric reflux)
2. Blood borne (hematogenous) by pyogenic organisms (septicemia) or tuberculosis.

Acute pyelonephritis:

- Commonest cause; E. coli, but others may be found as pseudomonas aeruginosa, streptococcus fecalis
- Mainly in women, WHY?
 - a. Colonic pathogens may cause fecal contamination of urethral orifice
 - b. Shorter urethra
 - c. Hormones facilitate bacterial adherence to mucosa
 - d. Urethral trauma during sexual intercourse (honey-moon cystitis)
- Increased susceptibility is seen in patients with;
 - a. Diabetes mellitus
 - b. Pregnancy
 - c. Urinary tract obstruction
 - d. Instrumentation
- Blood borne infection- Less common

Gross appearance:

1. Enlarged and swollen kidneys
2. C/S; small, yellow white abscesses with hemorrhagic rim, mainly in the cortex.

Histology:

1. Inflammation involving the interstitium (neutrophils) bursting into tubules with formation of focal abscesses.

Complications: More encountered in patients with diabetes mellitus and urinary tract obstruction.

Three important complications:

1. Papillary necrosis (necrotizing papillitis)- areas may resemble infarction-necrotic papillae are yellow-white (sharply defined) with congested borders.
2. Pyonephrosis- Renal carbuncle. Multilocular sac filled with pus.
3. Perinephric abscess

Chronic pyelonephritis:

Etiology:

1. Reflux nephropathy
2. Obstructive pyelonephritis

1. Reflux nephropathy: Vesico-ureteric reflux is common in children, especially girls due to congenital absence or shortening of the intra-vesical portion of the ureter so that the ureter is not compressed during micturition. Reflux-----Increased pressure in pelvis----urine forced into renal tubules----damage to kidney---scar formation.
2. Obstructive pyelonephritis (same concept)

Gross:

1. Small and contracted kidneys (unequal contraction)
2. Irregular scars of the kidneys, difficult to strip off the capsule (characteristic U-shaped depressed scars)
3. Dilatation of the pelvis, blunting of calyces

Histology:

1. Chronic inflammatory cells and fibrosis on interstitium
2. Atrophy and dilatation of tubules (eosinophilic material within tubules- thyroidization). Few tubules may contain neutrophils
3. Dilated pelvis; walls of pelvis and calyces show marked chronic inflammation + fibrosis.
4. Blood vessels show endarteritis obliterans
5. Periglomerular fibrosis, scarring and hyalinization
6. A variant called xanthogranulomatous pyelonephritis (foamy macros + chronic inflammatory cells + giant cells)

Tumors of the kidney

Benign – Usually small and incidental finding

Types:

1. Cortical adenoma:
 - a. Most common
 - b. Frequently multiple
 - c. Associated with chronic pyelonephritis and benign nephrosclerosis

Gross:

- Small, 3 cm. in diameter, encapsulated white-yellow

Histology:

- Cystic space
 - Tubular cords or papillary projections into this space. Cells show no atypia or mitosis
 - Very important note: Biologic behavior is determined by the size not histologically. If tumor size is more than 3 cm, it is considered potentially malignant and may metastasize
2. Other benign tumors are
 - a. Angiomyolipoma (hamartoma)
 - b. Medullary interstitial cell tumor
 - c. Juxtaglomerular tumor (reninoma). Excess rennin secretion...hypertension.

Malignant: Most common are;

a. Renal cell carcinoma (hypernephroma, Grawitz tumor):

- Hypernephroma is a misnomer (they previously thought that it arises from adrenal rests because the tumor cells resemble closely those of the adrenal cortex)
- Basically it arises from the tubular epithelium.
- 70-80% of all renal cancers
- Incidence: 50-70 years
- Sex incidence: Males affected more (2/1)
- Etiology:
 1. Cigarette smoking
 2. Certain viruses
 3. Long term dialysis
 4. Genetic factors (high incidence in Hippel-Lindau syndrome)

Morphology:

- Solitary, unilateral
- More often in the upper pole
- Large, golden yellow, well circumscribed
- C/S; hemorrhage and necrosis
- Tumor thrombus in renal vein extending in the inferior vena cava

Histology:

- Two types of cells seen; clear cells (abundant glycogen and lipids) with well defined borders, regular small pyknotic nucleus. Granular cells (pink eosinophilic cytoplasm). Most tumors have a mixture of both. If granular cells are more = Bad prognosis
- S & S: Classical triad of hematuria (60%), flank pain and a mass is found in 10% of patients. Others include polycythemia (erythropoietin secretion), hypercalcemia (PTH and prostaglandin secretion), Hypertension (rennin secretion), feminization or masculinization (gonadotrophins), Cushing's syndrome (ACTH secretion). N.B. Some of these are noted as part of the paraneoplastic syndrome (ectopic hormone production)
- Prognosis: 5 years- 45%

b. Wilm's tumor (nephroblastoma):

- Most common abdominal malignant tumor of young children
- Age incidence- 1-6 years (peak 1-3 years)
- Sex incidence: Equal (1/1)
- Arising from the primitive blastema cells

Morphology:

- Solitary, unilateral (5-10% bilateral)
- C/S; Soft, fish flesh, gray-white to creamy yellow)
- Invasion of renal veins- 50%

Histology:

- Primitive epithelial and mesenchymal elements- (carcino-sarcoma)
- Abortive tubules, poorly formed glomeruli

S & S: Palpable abdominal mass, fever, hematuria and hypertension

Prognosis: Following surgery and chemotherapy, 5-year survival rate is greater than 90%

Tumors of the urinary bladder

- More than 90%- transitional cell type
- It comprises 3% of all cancers of the body
- Most beyond the age of 40 years
- Males are affected more than females

Etiopathogenesis;

1. Industrial: Aniline dyes, rubber, plastic, textile industries (after long exposure of about 20 years). Carcinogenic agents responsible are benzene and beta-naphthylamine
2. Infective: Bilharziasis...local irritation----- squamous metaplasia----Squamous cell carcinoma
3. Dietary:
 - a. Carcinogenic metabolites excreted with urine
 - b. Artificial sweeteners (Saccharins)..used previously for diabetics
 - c. Coffee (caffeine)—controversial
4. Local lesions
 - a. Ectopia vesicae (extrophied bladder)=Congenital defect of the anterior wall of the bladder with splitting of anterior abdominal wall
 - b. Vesical diverticulum
 - c. Leukoplakia
 - d. In all of the above...squamous metaplasia-----squamous cell carcinoma
5. Smoking leads to increased risk by 2-3 fold (see 3-a)
6. Medications-Phenacetin, Immunosuppressives (cyclophosphamides)
 - Common location; trigone, region of the ureteric orifice, lateral walls
 - Gross appearance: 90% papillary, 10% flattened, indurated
 - Histology:
 - a. Transitional
 - b. Squamous
 - c. Glandular

Transitional cell papilloma:

- Single or multiple
- Less than 2 cm in diameter
- Papillary structures with branching patterns
- Each papilla consists of fibrovascular core covered by *NORMAL- LOOKING* cells with normal number of layers (not more than 6), no atypia, no mitosis, normal polarity
- For the above, designation is purely histologic and it does not imply an innocent behavior, because in fact it may behave in a malignant fashion

Transitional cell carcinoma:

- Commonest, divided into 3 grades(low ,intermediadte and high grades); depending on 2 features:
 - a. Anaplasia (cellularity, nuclear crowding, loss of polarity, pleomorphism, mitotic figures and giant cell formation

- b. Extent of invasion (invasion of the B.M; blood vessels ;lymphatic and neuronal) and underlying structures):

Squamous cell carcinoma:

- 5% of the histologic types
- Sessile, nodular, ulcerating, infiltrating

Adenocarcinoma:

- **Rare**
- Mainly seen in extrophy, cystic cystica, periurethral and periprostatic glands

Mixed carcinoma: Transitional and squamous cell carcinoma

Non-epithelial bladder tumors include:

- a. Benign (leiomyoma-most common)
- b. Malignant (rhabdomyosarcoma-most common)

**FIN
GOOD LUCK**