KIDNEY - 1

Dr.Swati Parikh

Associate professor

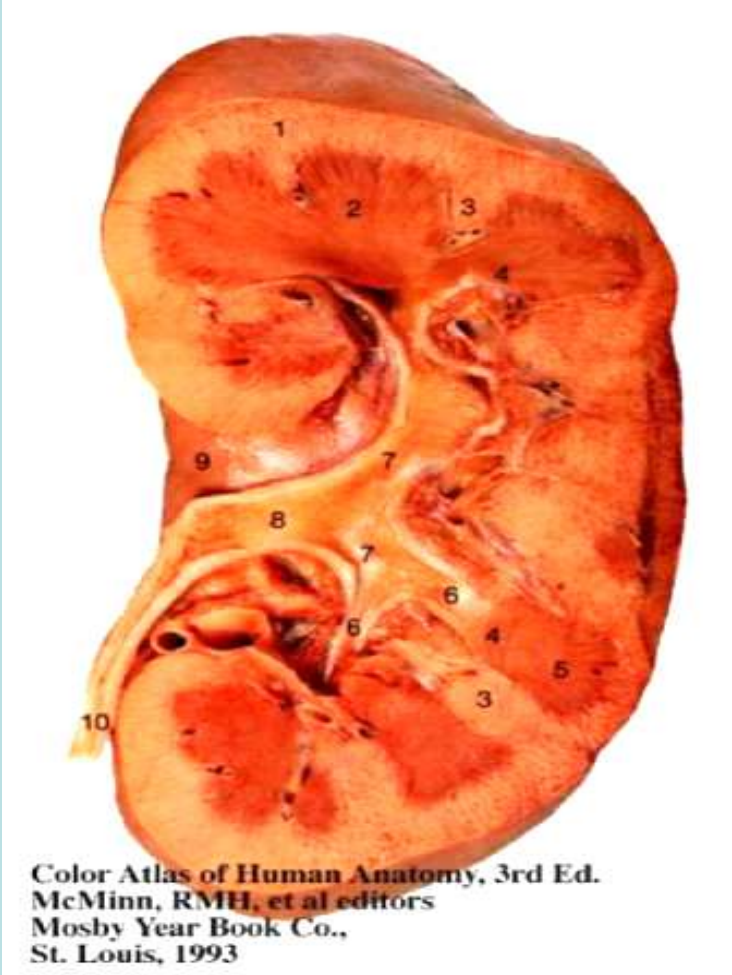
“What is man but an ingenious machine designed to turn with ‘infinite artfulness’, the red wine of shiraz into urine” …!

Isak Denison

FUNCTIONS OF KIDNEYS

- Excrete waste products of metabolism.
- Regulate body's concentration of salt and water.
- Maintain acid balance of plasma.
- Serve as an endocrine organ, secreting hormones like erythropoetin, renin and prostaglandins.

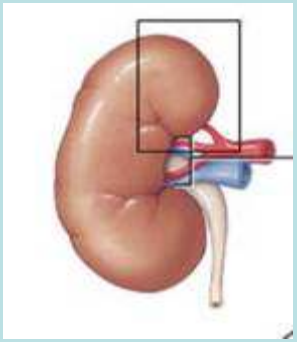
GROSS MORPHOLOGY

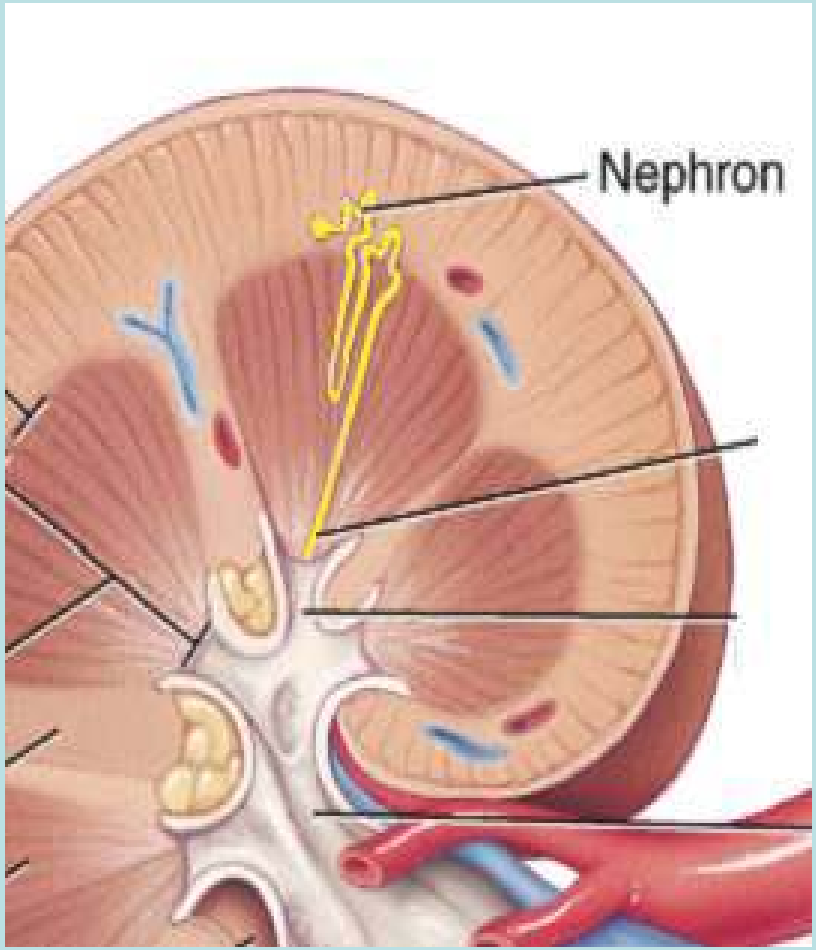


Color Atlas of Human Anatomy, 3rd Ed.
McMinn, RMH, et al editors
Mosby Year Book Co.,
St. Louis, 1993

- Each human kidney weighs about 150 grams.

Anatomy of Kidney





Note the positions of

Glomerulus

Loop of Henley

PCT, DCT, CT

Pelvis.

MICROSCOPY

- **Four components – blood vessels, glomeruli, tubules and interstitium.**

❖BLOOD VESSELS -Richly vascularised organ [25% of cardiac output].

- Cortex receives 90% of total renal circulation.

RENAL CIRCULATION

- Main renal artery ⟹ Anterior and Posterior sections ⟹ Inter lobar artery ⇨ Arcuate artery ⇨ Interlobular artery ⇨ Afferent arteriole ⇨ 20-40 capillary loops ⇨ Efferent arterioles ⇨ Peritubular vascular network and vasa recta.

IMPORTANT IMPLICATIONS

- Arteries are largely end arteries.
- Medulla is relatively avascular and prone for ischemia.
- Glomerular diseases have profound effect on tubules.

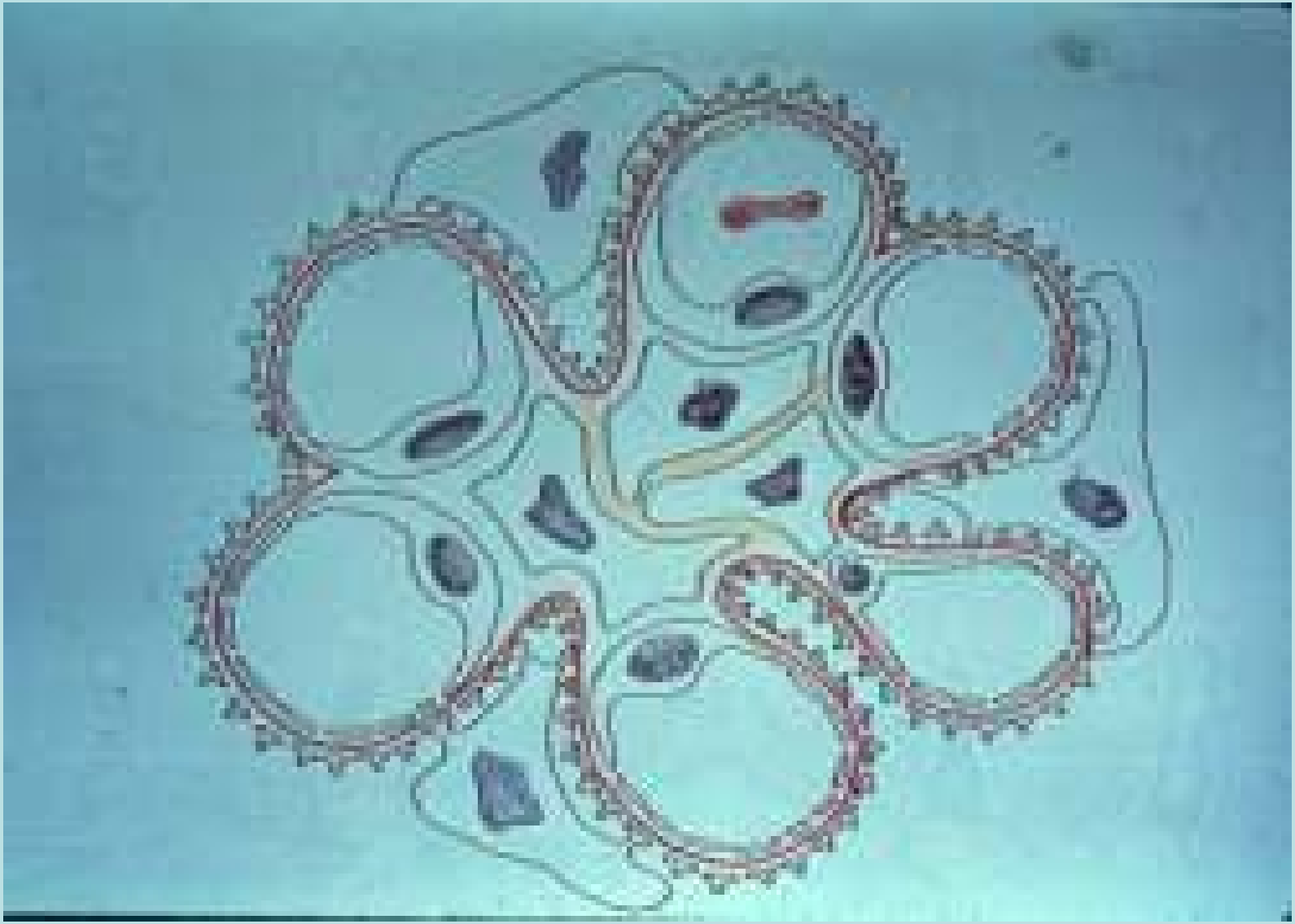
❖GLOMERULI

- Made up of anastomosing network of capillaries invested by two layers of epithelium-Visceral epithelium and Parietal epithelium.
- **ULTRASTRUCTURE OF GLOMERULI**
- GLOMERULAR CAPILLARY WALL:

  Filtering membrane.

  (1)Endothelial cells- Thin layer of fenestrated endothelial cells.(70-100 nm in diameter)

Normal Glomerulus



(2) GLOMERULAR BASEMENT MEMBRANE

- GBM is made up of thick electron dense central layer, Lamina densa & thinner electron lucent peripheral layers, Lamina rara interna and Lamina rara externa respectively.

STRUCTURE OF GBM

- **GBM consist of collagen mostly type 4, laminin, poly anionic proteoglycans (mostly heparan sulphate),fibronectin and several other glycoproteins.**
- **Type 4 collagen forms a network supra structure to which other glycoproteins attach. Collagen monomer is a triple helical molecule made up of 3 alpha chains. Each molecule consists of a 7s domain at amino terminus, a triple helical domain in the middle and a globular non collagenous domain at carboxyl terminus.**

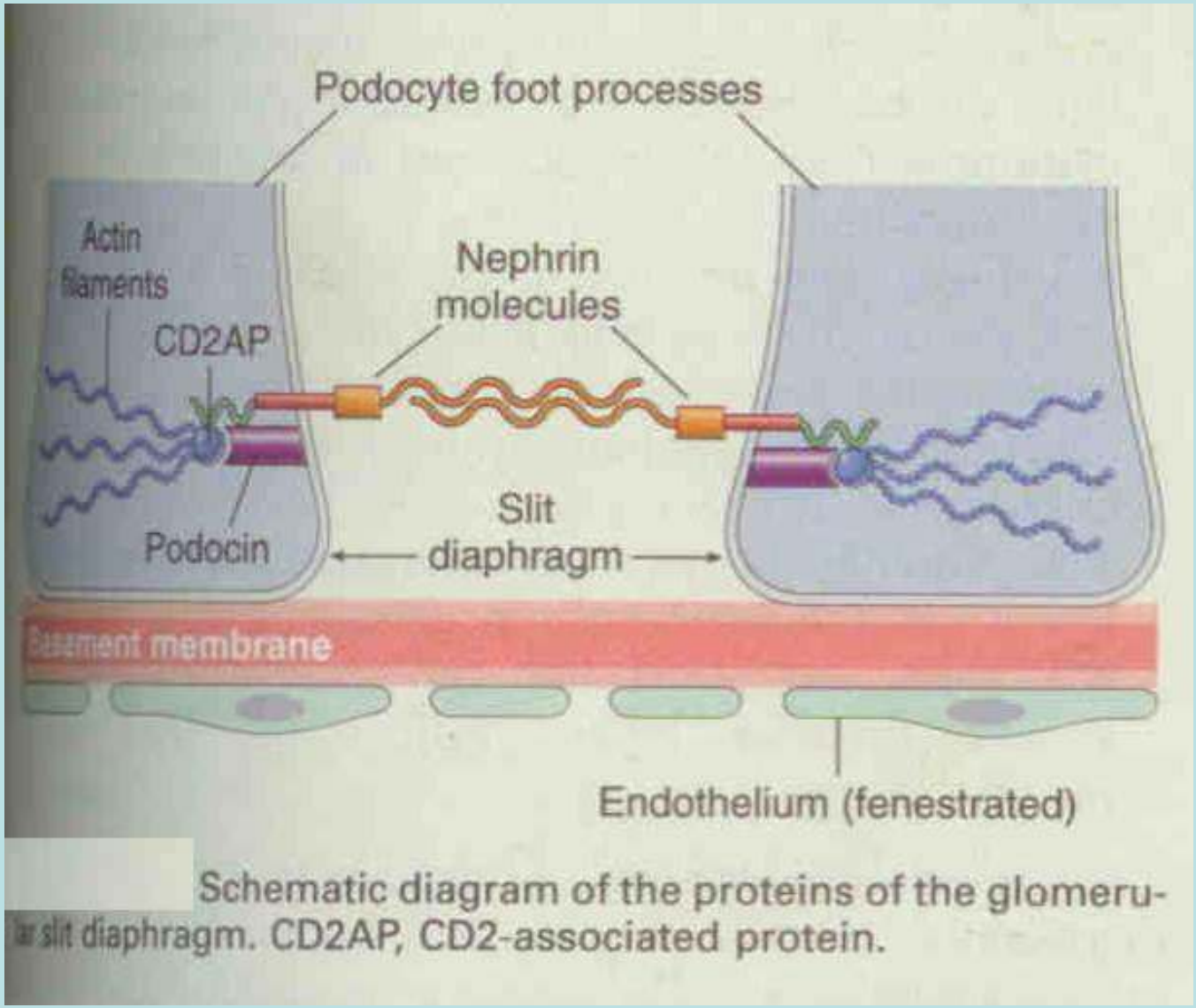
- NC domain is important for helical formation and also for assembly of collagen monomer in to dimer.7S domain is important for formation of tetramers and thus supra structure evolves.

(3)VISCERAL EPITHELIAL CELLS (Podocytes)
-Possess interdigitating processes, embedded in and adherent to lamina rara externa of basement membrane. Adjacent foot processes are separated by 20-30 nm wide filtration slits which are bridged by thin diaphragm.

- Size selective barrier

NEPHRIN

- Proteins located in slit diaphragm control the glomerular permeability.
- ***NEPHRIN***-trans membrane protein. Large extra cellular portion made up of immunoglobulin like domain. Nephrin molecules extend towards each other and dimerize across the slit diaphragm. Within the cytoplasm,nephrin forms molecular connections with podocin,CD2 associated protein and actin cytoskeleton.
- Mutation in genes encoding these proteins give rise to Nephrotic syndrome.



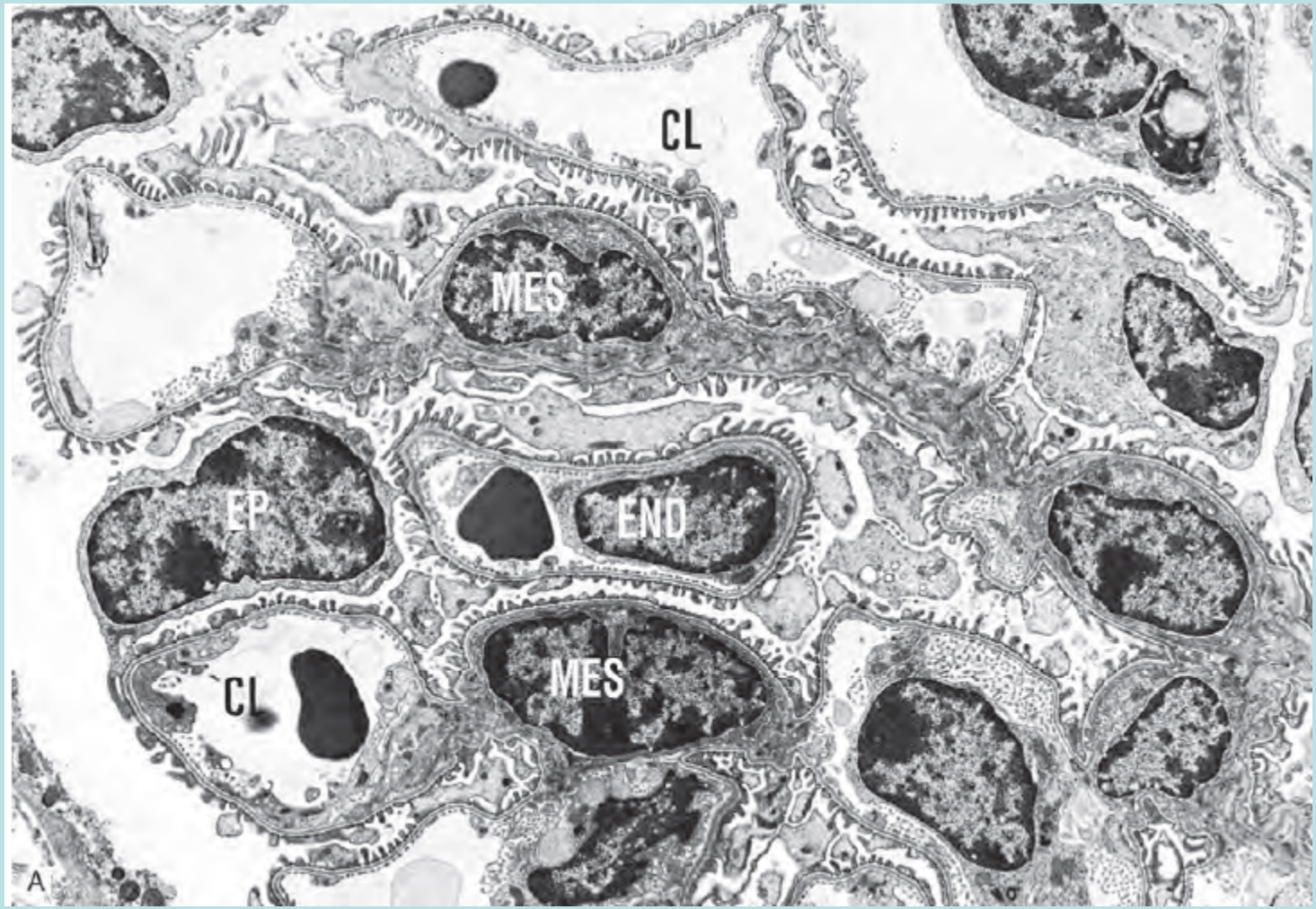
Schematic diagram of the proteins of the glomerular slit diaphragm. CD2AP, CD2-associated protein.

Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:902

MESANGIAL CELLS

- Entire glomerular tuft is supported by mesangial cells lying between capillaries.
- Mesenchymal origin.
- Cells are contractile, phagocytic, capable of proliferation, laying down both matrix and collagen and secreting number of biologically active mediators.

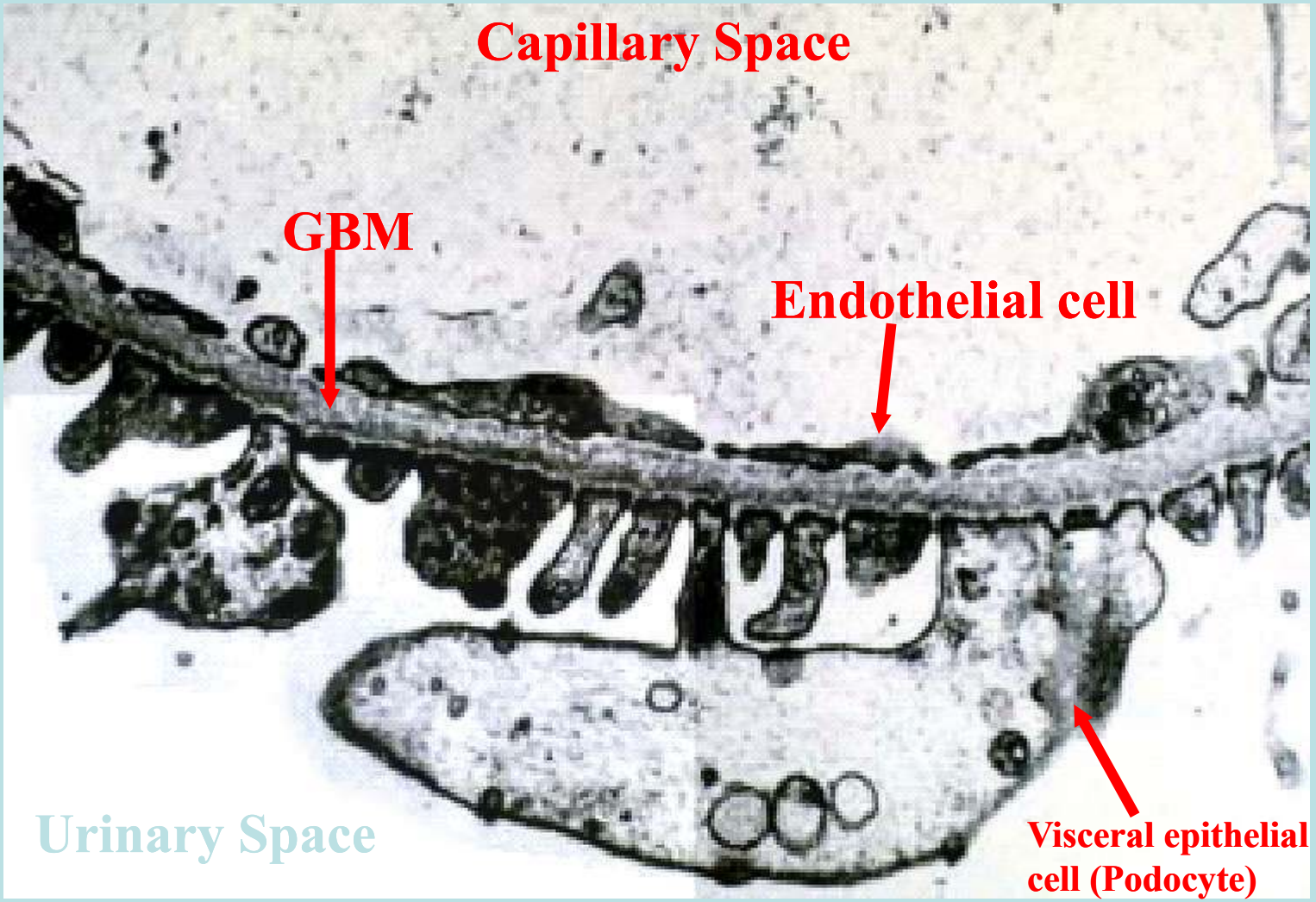
Normal EM of a glomerulus



Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:901

Filtration Membrane

Electron Micro.



Characteristics of glomerular filtration

- High permeability to water and small solutes.
- Impermeability to molecule of the size of ALBUMIN.

  Glomerular barrier function-discriminates various protein molecules depending on their size and charge.
- Complex structure of capillary wall, integrity of G.B.M., and many anionic moieties present within the wall.

❖ TUBULES

- Structure of renal tubular epithelial cells varies at different levels of nephron.
- Structure correlates with their major function.
- J.G.A. is a small endocrine organ, is a principal source of RENIN production.

❖ INTERSTITIUM

- Expansion is usually because of edema and infiltration by acute and chronic inflammatory cells.

Renal biopsy

- Two types: Open biopsy & Needle biopsy
- Adequacy: 5 to 10 glomeruli
- Sp. Stains: PAS, Methanamine silver, M.T.
- Routine fixative: Mercuric solutions
- Electron microscopy : (gluteraldehyde)
- Immuno fluroscent microscopy: (rapidly frozen tissue sections) Antisera IgG,IgA,IgM,C1q,C3,C4,Fibrinogen and fibrin

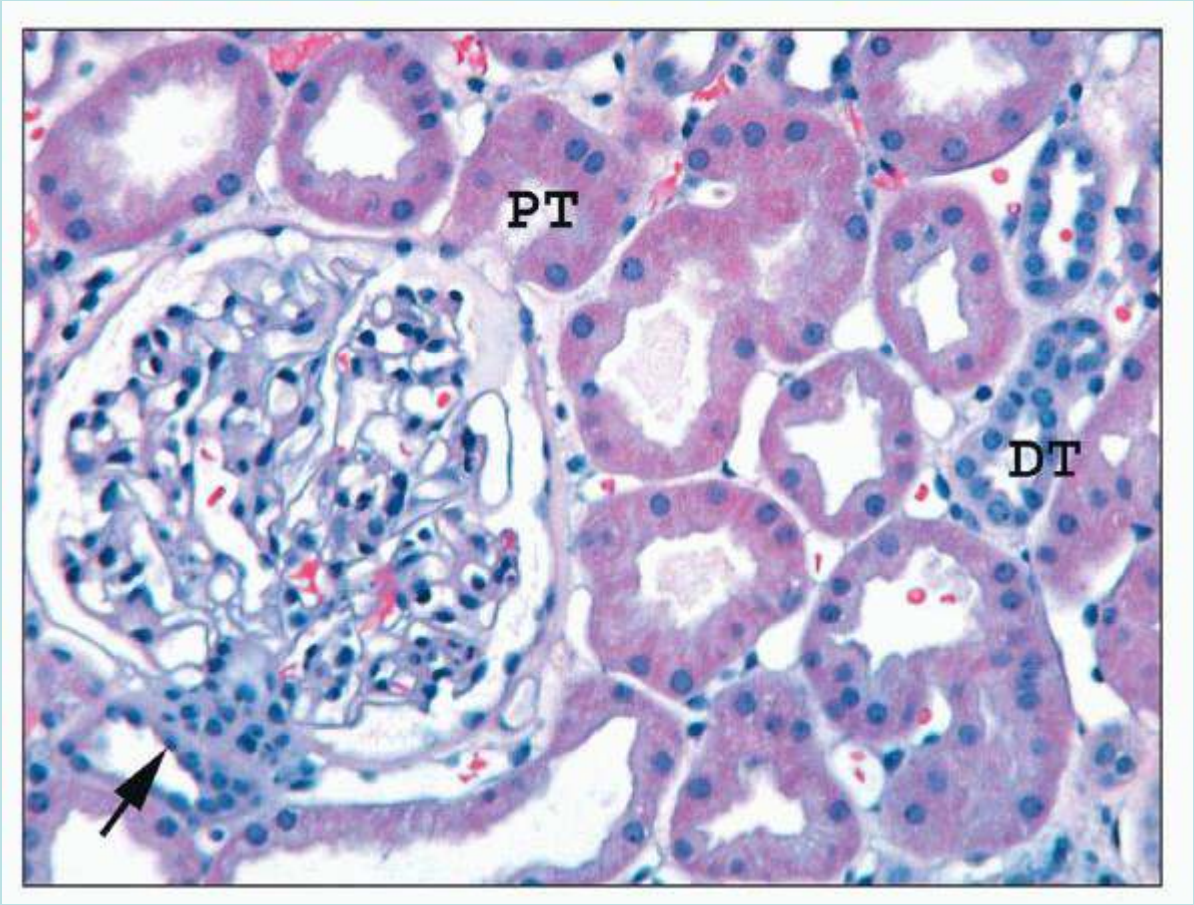
  -Granular/ Linear pattern

  - Glomerular region affected

  - Class of Ig or complement deposited

  - Intensity of immunofluroscence

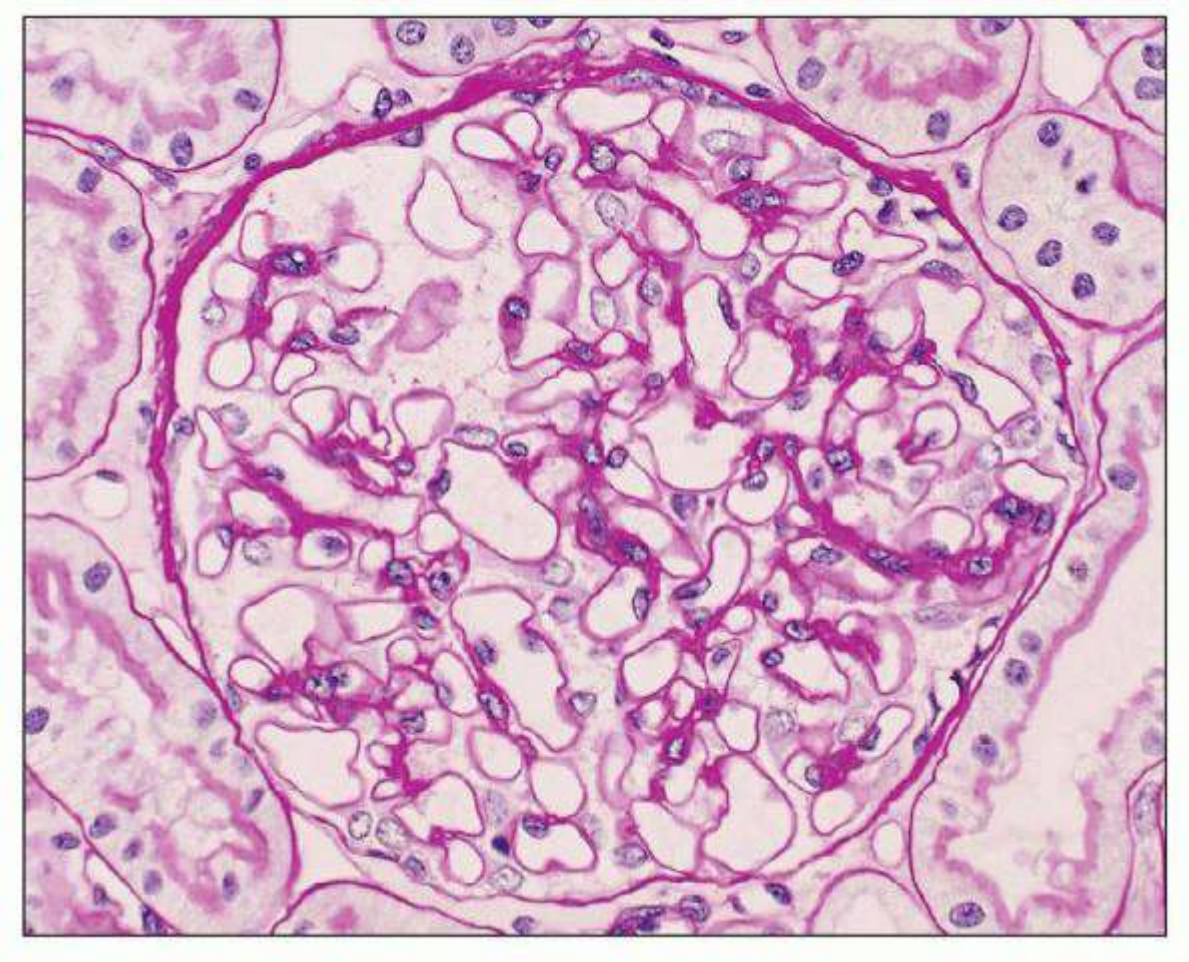
Normal Kidney:



(H&E stain)

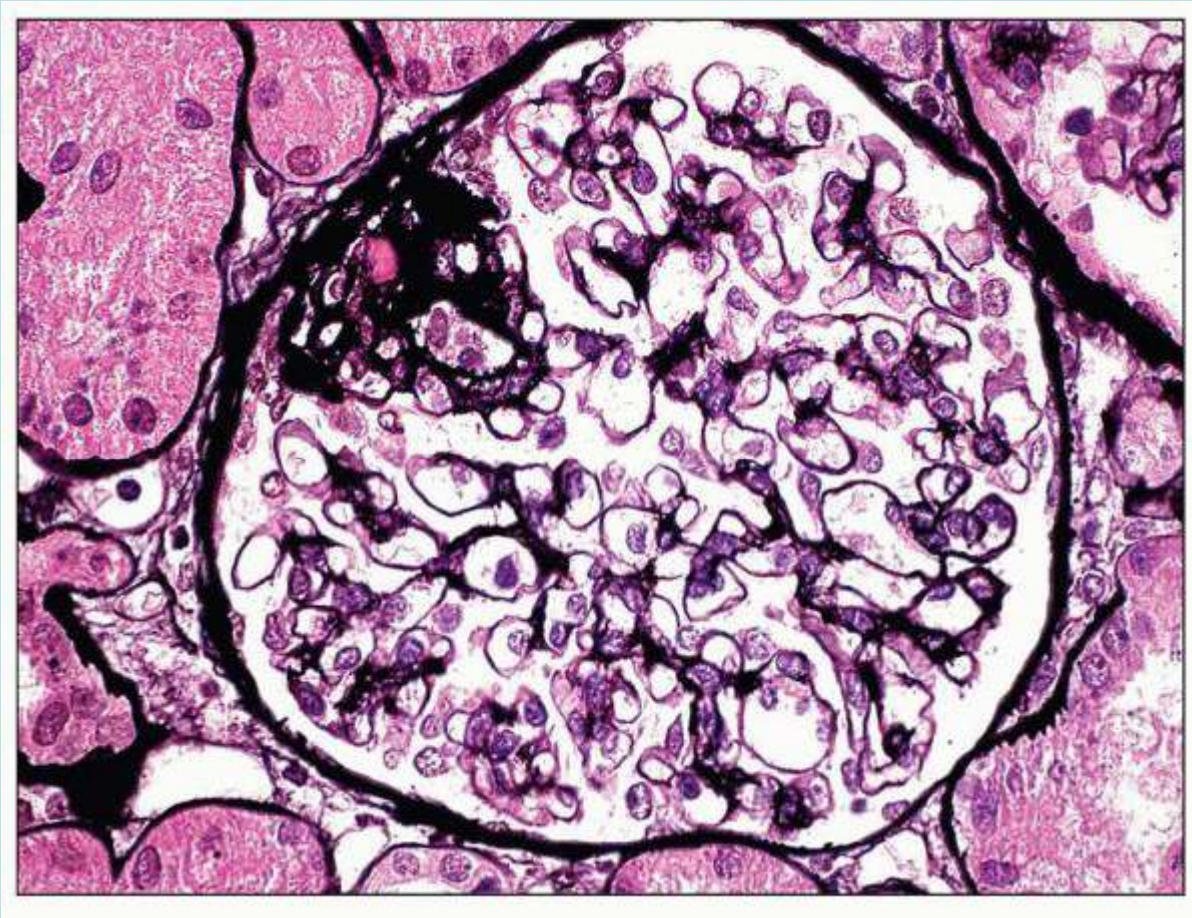
Ref: Heptinstall Pathology of the Kidney 7th Edition , Pg.64

Glomerulus (PAS stain)



Ref: Heptinstall Pathology of the Kidney 7th Edition ,Pg.496

Glomerulus
Silver Stain



Ref: Heptinstall Pathology of the Kidney ,7th Edition ,Pg.402

DISEASES OF KIDNEY

- ***AZOTEMIA***-Biochemical abnormality refers to an elevation of BUN, related to abnormal excretory function(GFR).

- When it is associated with clinical signs and symptoms it is termed as ***UREMIA***. Characterized not only by abnormal excretory function ,but also by metabolic and endocrine alterations,GIT,CVS and Neuromuscular involvements.

CAUSES OF AZOTEMIA AND UREMIA

- ***PRE RENAL*** -Hypo perfusion of kidney in conditions like hemorrhage ,shock, CCF and volume depletion.
- ***RENAL*** **-**All the renal diseases.
- ***POST RENAL*** -When urinary flow is obstructed below the level of kidney.

Overview of Renal Diseases

- Subdivided according to 4 basic components.
  - **Glomerular diseases**- most commonly immunologic disorders.
  - **Vascular diseases**- most commonly related to hypertension or diabetes.
  - **Tubular diseases**
  - **Interstitial diseases**- usually combined with tubular as **tubulointerstitial**-usually due to drug toxicity or infections

Glomerular diseases

- **Primary glomerulopathies**:

- Acute diffuse proliferative GN
  (post streptococcal, non post streptococcal)
- RPGN (Crescentic GN)
- Membranous GN
- Minimal change disease
- Focal segmental glomerulosclerosis
- MPGN
- IgA nephropathy
- Chronic GN

Ref- Robbins and Cotran: Pathologic basis of disease: 7th Edition, Pg:967

Glomerular diseases

- **Secondary GN:**

- SLE
- Diabetes mellitus
- Amyloidosis
- Good pasture syndrome.
- Glomerulopathy secondary to Multiple Myeloma
- Microscopic polyangitis / Polyarteritis Nodosa
- Granulomatosis with Polyangitis
- Henoch- Schonlein purpura, BE

- **Hereditary nephritis**

- Alport's syndrome.
- Fabry's disease

Ref- Robbins and Cotran: Pathologic basis of disease: 7th Edition, Pg:967

Various terms used to sub classify primary GN

- Diffuse-Involving all the glomeruli.
- Focal –Certain proportion of glomeruli.
- Global –Involving entire glomerulus.
- Segmental –Affecting part of each glomerulus.
- Mesangial –Mesangial region.

Glomerular Diseases

- **Primary Glomerular Diseases**
- Minimal-change disease
- Focal segmental glomerulosclerosis
- Membranous nephropathy
- Acute postinfectious glomerulonephritis
- Membranoproliferative glomerulonephritis
- IgA nephropathy
- Dense deposit disease
- C3 glomerulonephritis
- **Hereditary Disorders**
- Alport syndrome
- Fabry disease
- Podocyte/slit-diaphragm protein mutations

Ref: Robbins BASIC PATHOLOGY, Pg: 552

Clinical Syndromes:

- **Nephritic syndrome**.
  - Haematuria, Proteinuria, Hypertension, Oliguria
- **Nephrotic syndrome**.
  - Gross proteinuria, hypoalbuminemia, severe edema, hyperlipidemia, lipiduria
- **Acute renal failure**
  - Oliguria, loss of Kidney function - within weeks
- **Chronic renal failure**.
  - Over months and years - Uremia

Nephritic

- Hematuria
- Proteinuria
- Hypoalbuminemia
- Oliguria (GFR↓, Cr↑, BUN↑)
- Edema (salt and water retention)
- Hypertension

Nephrotic

- Proteinuria ("nephrotic range" >3.5g/24h)
- Hypoalbumimenia (<3 gm/dl)
- Edema
- Hyperlipidemia
- Lipiduria

CLINICAL MANIFESTATIONS

- Acute nephritis
- Rapidly progressive Glomerulo nephritis
- Nephrotic Syndrome
- Chronic Renal Failure
- Asymptomatic

BASIC TISSUE REACTIONS

- **Glomerular hypercellularity** – cellular proliferation, leukocytic infiltration and by formation of crescent.
- **Basement membrane thickening** –By L.M, appears as thickening of capillary walls. On E.M, thickening of B.M. proper in diabetic glomerulosclerosis and deposition of amorphous electron dense material on epithelial or endothelial side of B.M. or within the G.B.M. itself.

- **HYALINIZATION-** Accumulation of homogenous and eosinophilic material by L.M. When it obliterates the structural detail of glomerular tuft ,it is termed as ***SCLEROSIS.***

- **ADDITIONAL ALTERATIONS**
  -Deposition of fibrin, amyloid, lipid etc.
  -Intraglomerular thrombosis

Thank You