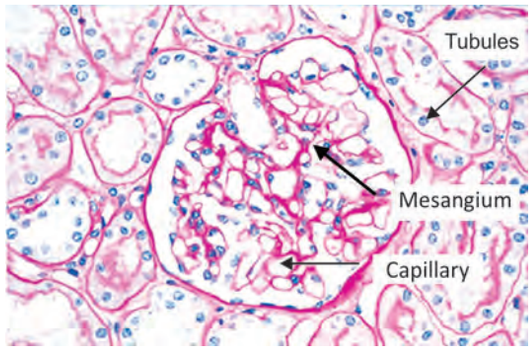
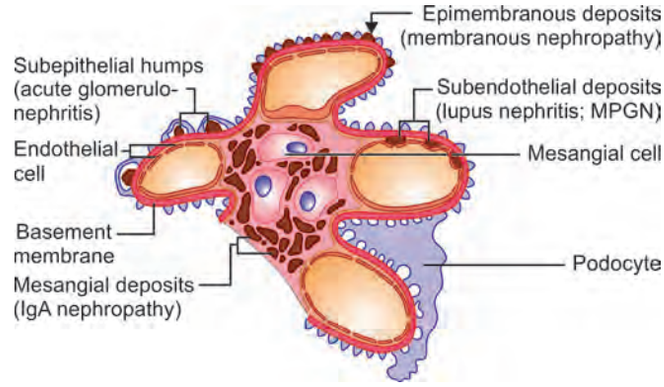
KIDNEY

GLOMERULUS



Structure of glomerulus



Types of glomerular deposits

PATHOLOGIC RESPONSES OF THE GLOMERULUS TO INJURY

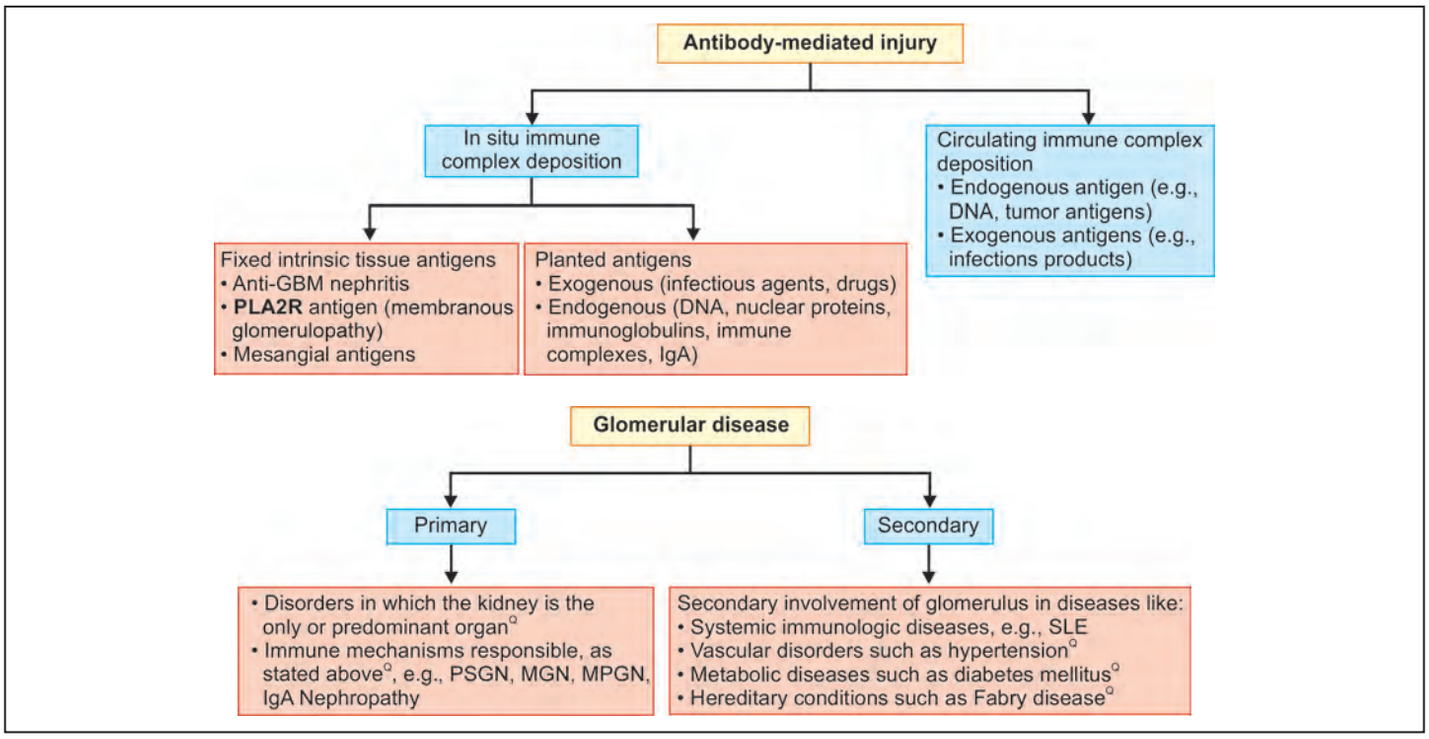
Site of glomerular deposits	Type of glomerulonephritis
Subepithelial deposits	• PSGN • Membranous GN • RPGN • Heymann Nephritis
Subendothelial deposits	• Lupus nephritis • MPGN-I
Membranous deposits	• MPGN II
Mesangial deposits	• IgA nephropathy • HSP

Terminologies used in kidney biopsy	
Terminology	**Description**
Diffuse	Involving **>50%** of the glomeruli in the kidney[Q]
Global	Involving the glomerulus **completely**[Q]
Focal	Involving **<50%** of the glomeruli in the kidney
Segmental	Affecting **a part of each glomerulus**[Q]
Capillary loop Mesangial	Affecting predominantly **capillary or mesangial regions**[Q]

Bowman's capsule- Lined by flattened cells (parietal epithelial cells)

Capillaries- Visceral epithelial cells having foot process (podocytes)
Every capillary has basement membrane lined by endothelial cells

All the capillaries are supported by mesangial matrix



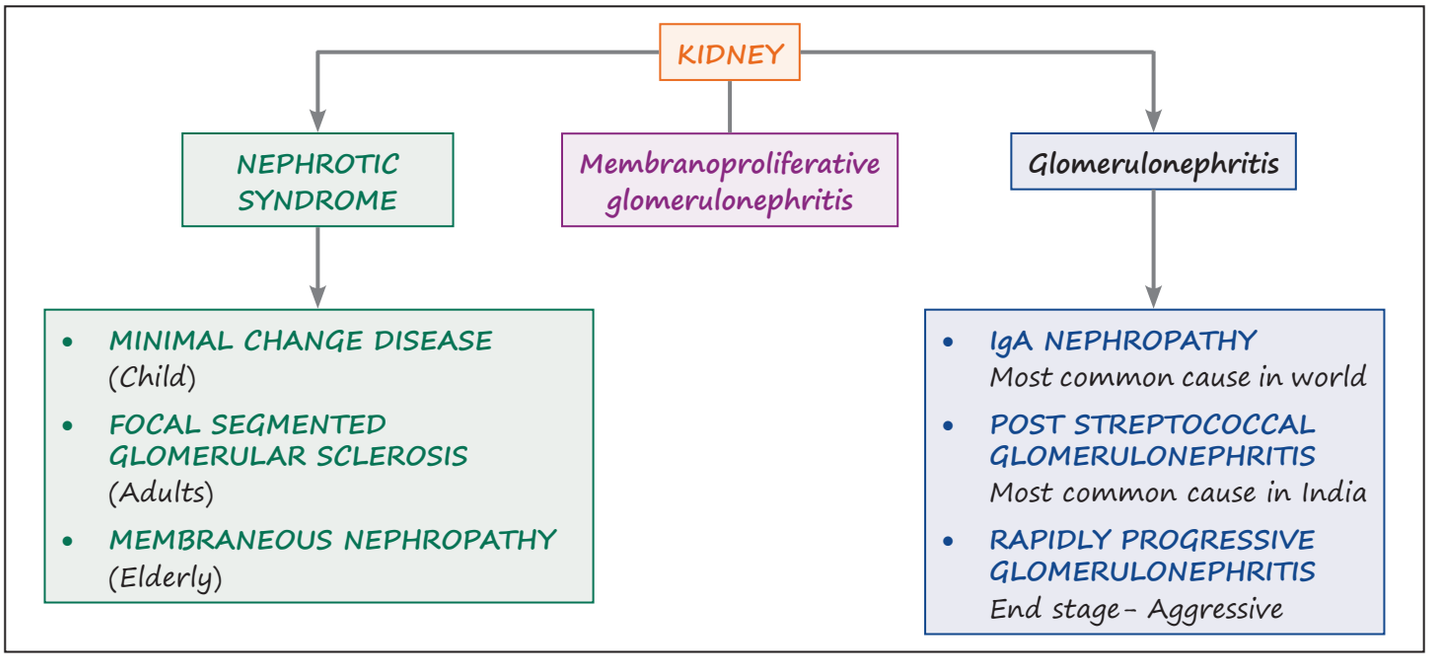
NEPHRON MUTATION

- Most common mutation
- Coded by NPHS-1
- Minimal change like presentation
- Respond to steroids

PODOCIN

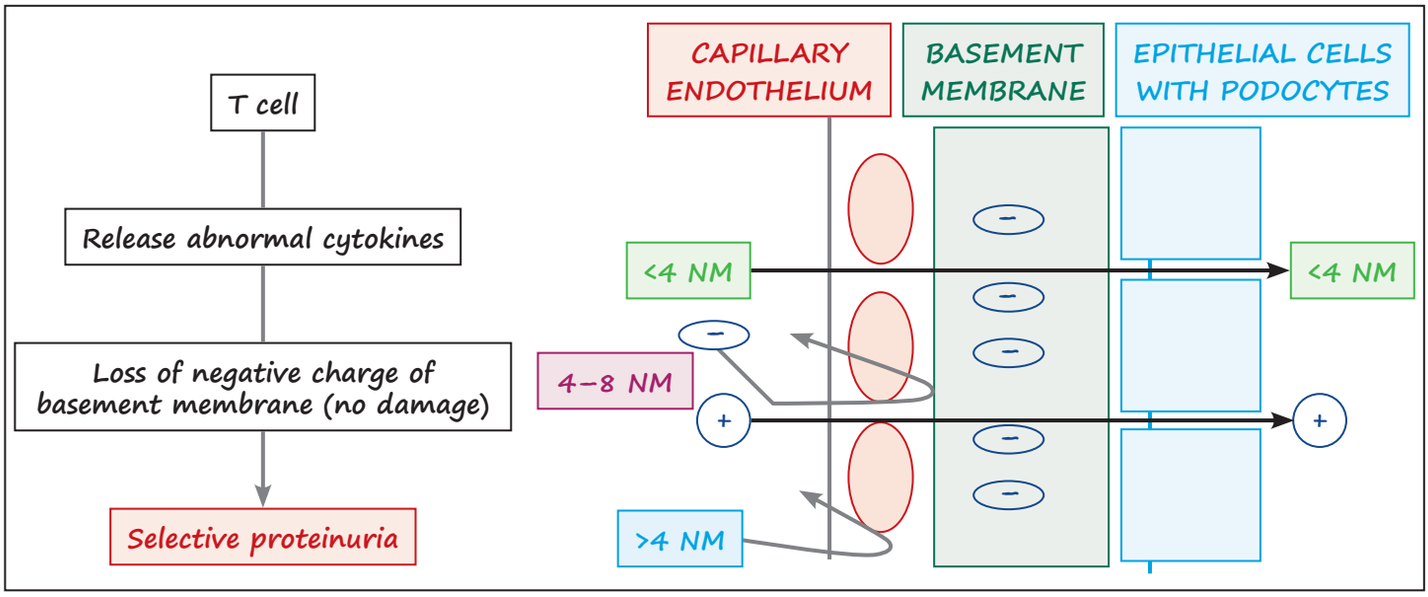
- Coded by NPHS-2
- FSGS like presentation
- Does not respond to steroids

Actin mutation also causes FSGS (α Actinin)



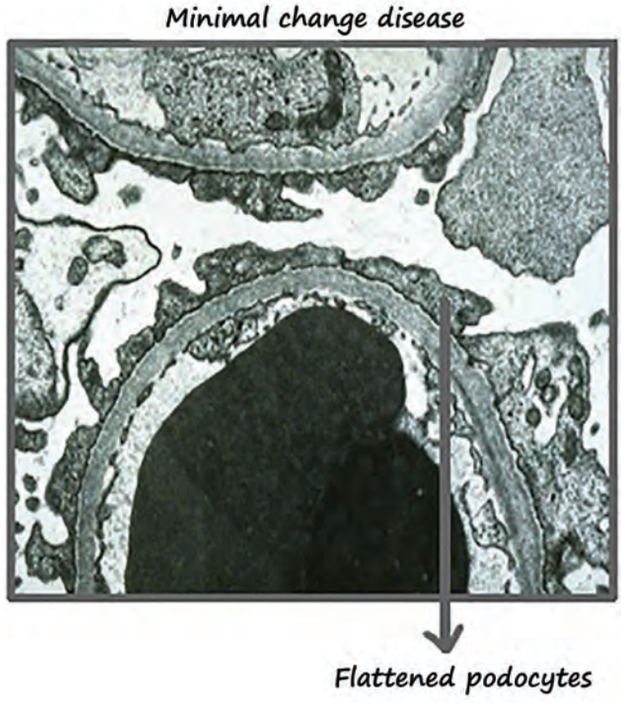
NEPHROTIC SYNDROME

MINIMAL CHANGE DISEASE



Albumin is released as it is negatively charged and smaller in size

- Cytokines also cause flattened podocytes– **Effacement seen in electron microscopy**
- No change in light microscopy and Immunofluorescence



- **Morphology:**
  - **Light microscopy: Glomeruli appear normal**[Q].
  - **Immunofluorescence microscopy: No Ig/ complement deposits.**
  - **Electron microscopy: Diffuse effacement of foot processes of podocytes ("podocytopathy")**[Q].
    - No electron-dense deposits[Q]
  - **Proximal tubules** cells get **laden with lipid** and protein due to tubular reabsorption of lipoproteins: **Lipoid nephrosis**[Q].

FOCAL SEGMENTED GLOMERULAR SCLEROSIS

Due to Podocytes injury

Caused by

- HIV
- Obesity
- Reflex
- Renal ablation
- Sickle cell anemia

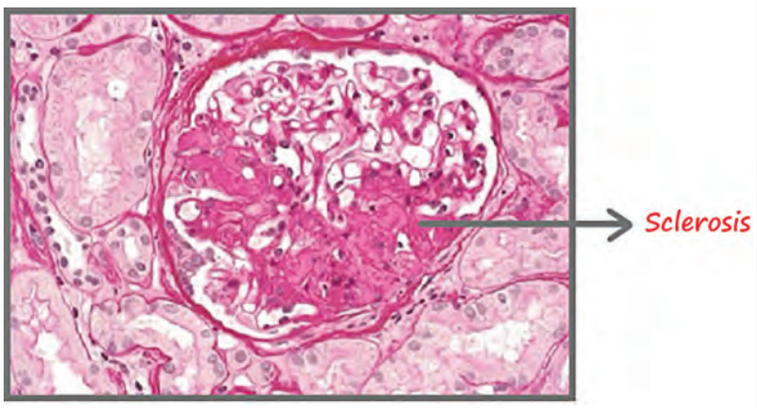
<50% of glomeruli- Focal segmented

Podocytopathies
- Minimal change disease
- FSGS

DAMAGED PODOCYTES → SCLEROSIS

HIVAN

- HIV associated nephropathy
- Collapsing nephropathy
- Proliferation of podocytes causes damage to other structures



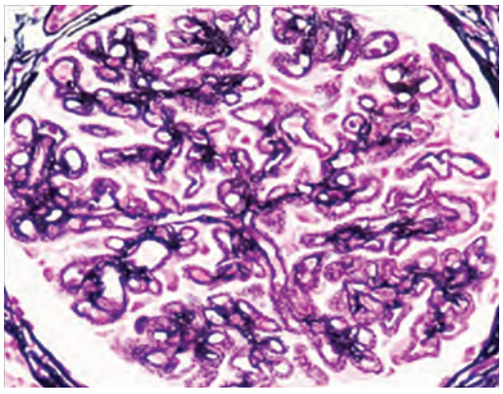
- **Morphology:**
  - **Light microscopy**
    - Collapse of capillary loops in sclerotic areas
    - Deposition of plasma proteins along capillary wall **(hyalinosis)**
  - **Immunofluorescence microscopy**
    - IgM + C3 deposition in sclerotic areas and/or in mesangium.
  - **Electron microscopy**
    - **Diffuse effacement** of foot processes of podocytes.
    - **Focal detachment** of the epithelial cells.
    - **Denudation** of the underlying GBM.

MEMBRANOUS NEPHROPATHY

- Immune complex mediated
- **Antigen - Phospholipid A2**

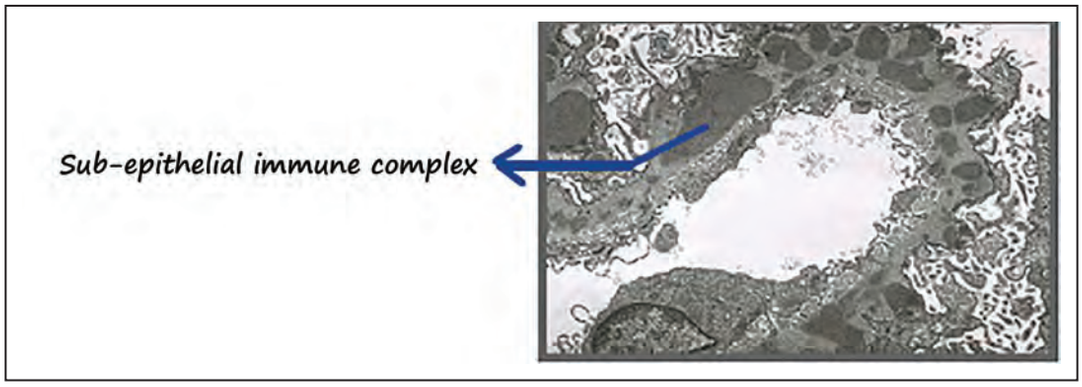
ON LIGHT MICROSCOPY

- Thickened BM
  PAS/Silver stain
- **SPIKES AND DOME PATTERN**



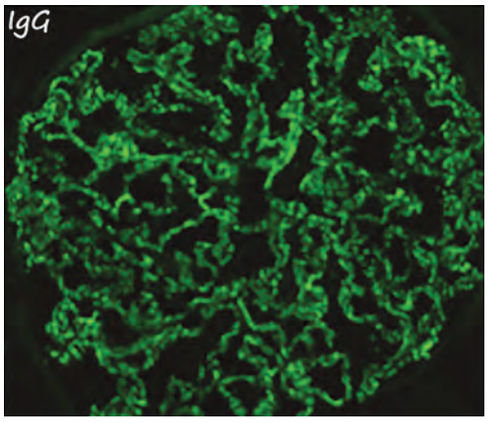
- **Morphology:**
  - **Light microscopy:** Uniform, diffuse thickening of the glomerular capillary wall.Q
  - **Immunofluorescence microscopy: Granular/Lumpy bumpy**Q electron dense immune complexes deposits
  - **Electron microscopy: Granular deposits (Ig + complement)**
    - **Effacement of podocyte** foot processesQ
  - **On Silver methenamine stain:** Prominent **"spikes" and "domes"**Q of silver-staining matrix.

ON ELECTRON MICROSCOPY



IMMUNOFLUORESCENCE

- Fluoro isothicyanate (green color)
- Granular immunofluorescence

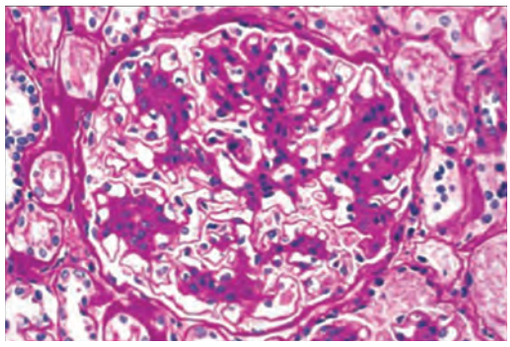


IgA NEPHROPATHY (BERGER'S DISEASE)

- Affects 25–40 years age group
- Due to excess of IgA or not able to metabolise IgA
- Occurs after upper respiratory or lower respiratory infection

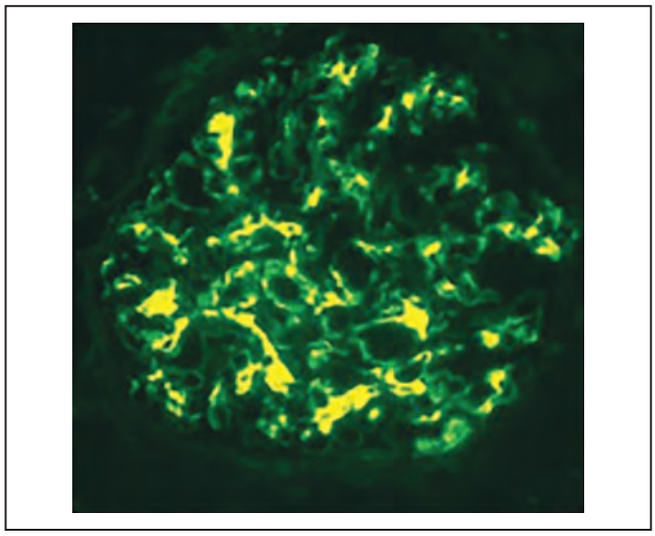
ON LIGHT MICROSCOPY

- Mesangial proliferation is seen



IN IMMUNOFLUORESCENCE

- Granular immunofluorescence (IgA, IgG, C3)
- IgA activates alternative complement pathway (C3)



ON ELECTRON MICROSCOPY

- Deposits increased mesangium

- **Presents with isolated hematuria**
- **Coeliac/liver disease patients have excess of IgA causing predeposition**
- **More prone to get IgA nephropathy**

TREATMENT

- Transplantation
- Reoccurs after transplantation

POST STREPTOCOCCAL GLOMERULONEPHRITIS

- Immune complex mediated
- Caused by B hemolytic streptococci

- **ANTIGEN- STREPTOCOCCAL PROGENITOR EXOTOXIN B - SPE B**

Antigen combines with Antibody

↓

ANTIGEN - ANTIBODY COMPLEX

↓

Deposited in the sub endothelium

↓

Neutrophil flooding in capillary

↓

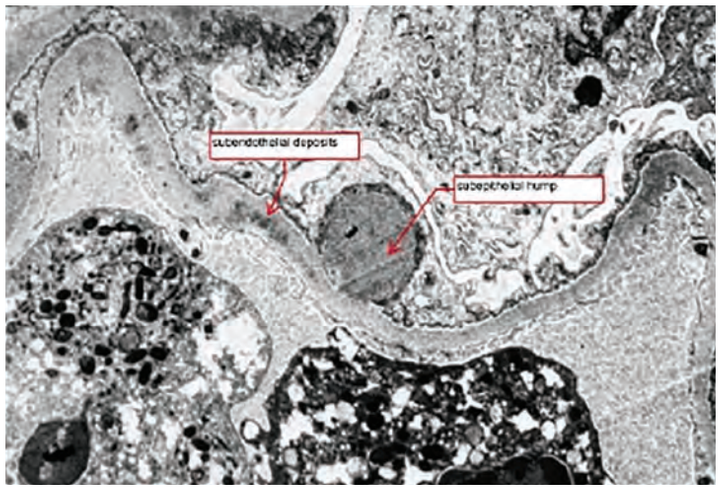
ENDOCAPILLARY PROLIFERATION

↓

Ag- Ab jumps from sub endothelium to subepithelium

↓

LARGE SUBEPITHELIAL HUMP



- Within 6 weeks heals by itself
- Complement deposition (C1, C3, C4)

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

Hallmark: BASEMENT MEMBRANE DAMAGE

Basement membrane damage

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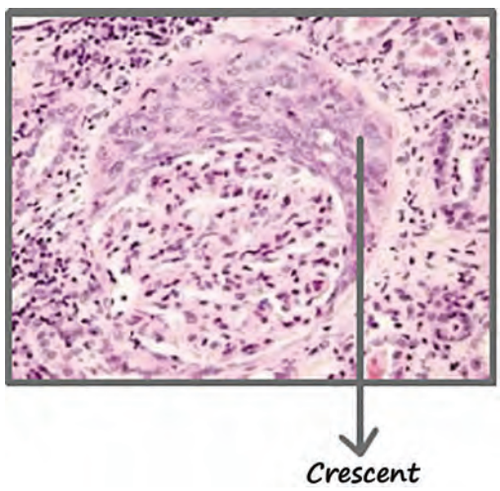
Coagulation protein leaks into bowman's capsule
Fibrinogen mainly

↓

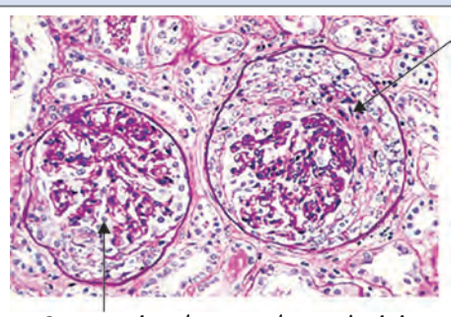
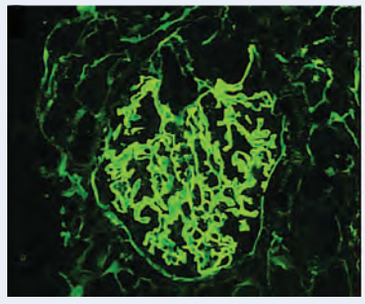
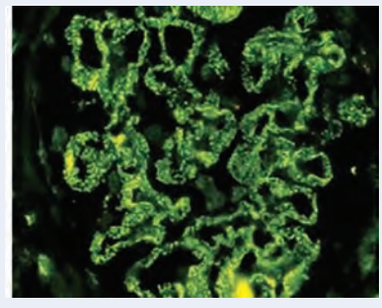
Parietal cells starts proliferating to eat up fibrogen

↓

CRESCENT



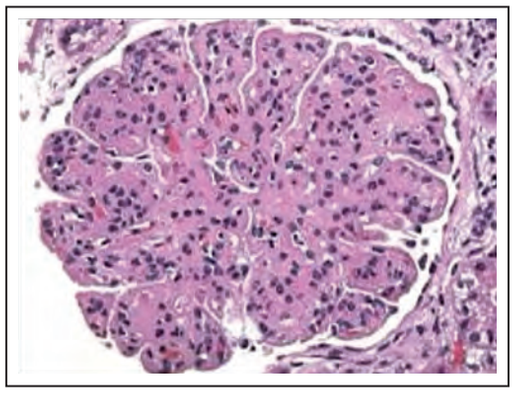
CRESCENT - Fibrinogen, inflammatory cells, parietal cells
Very big crescent can interact visceral epithelial cells

Entity	Type I (20%)	Type II (25%)	Type III (55%)
Mechanism	Anti-GBM antibody	Immune complex	Pauci-immune, c-ANCA/p-ANCA mediated
Etiology	Renal limited **Goodpasture syndrome**Q (Serum antibodies against **alpha 3 NC1 domain of collagen – IV**)	• **Postinfectious** ▪ Poststreptococcal glomerulonephritisQ ▪ Bacterial endocarditisQ • **Noninfectious** ▪ SLEQ, HSPQ ▪ Mixed cryoglobulinemiaQ • **Primary renal disease** ▪ MPGNQ ▪ IgA nephropathyQ	**ANCA-associated** • Idiopathic • **Granulomatosis with polyangiitis (Wegener granulomatosis)**Q • Microscopic polyangiitisQ • Hypersensitivity vasculitisQ
Grossly	Kidneys are enlarged and pale, often with **petechial hemorrhages** on the cortical surfaces. **(FLEA-BITTEN KIDNEY)**Q		
Light m/e	• **Glomeruli: Crescents** are HallmarkQ. • Focal and segmental necrosisQ, endothelial and mesangial proliferationQ. • **Pauci-immune: Segmental glomerular necrosis** is a feature characteristicQ.  Cresentic glomerulonephritis Crescents—formed by • Proliferation of **parietal cells**Q • Infiltration by **WBCs**Q • **Fibrin strands.**Q **Crescents** obliterate the urinary space and compress the glomerular tuft, hence **More the number of crescents → poorer the prognosis**Q		
Immunofluorescence m/e	**Linear GBM fluorescence**Q  **Type I RPGN (linear)**	**Granular immune deposits**Q  **Type II RPGN (granular)**	**No** deposition of immune reactantsQ **No deposits seen** **(Pauci-immune)**
Electron m/e	**Ruptures in the GBM**Q may be present, Type II shows immune complex deposits.		

DIFFERENTIATE BETWEEN TYPES OF RPGN

LIGHT MICROSCOPY	All crescents		
ELECTRON MICROSCOPY	All will show basement membrane damage		
IMMUNOFLUORESCENCE	I Linear	II Granular	III No IM

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS



SUBENDOTHELIAL DEPOSITION

↓

Mesangial cells proliferation

↓

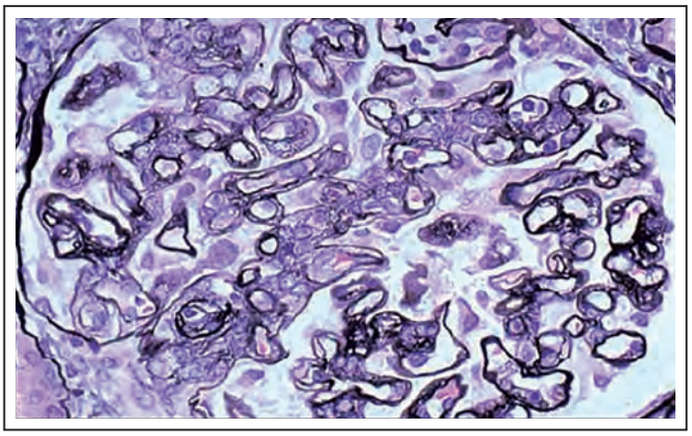
Lobular accentuation

↓

Splitting of BM

ON SILVER STAIN

- Basement membrane is broken
  Tram – Track appearance



MPGN TYPE 2

- **Known as** C3 GLOMERULONEPHRITIS
  DENSE DEPOSIT DISEASE
  COMPLEMENTOPATHIES
- C3 convertase- breakdown C3 to C3a and C3b

C3 → **C3a + C3b**

↑

C3 convertase

- C3 convertase is then broken down by Factor H and Factor I ⊖ **C3 NeF**

C3Ne F blocks the action of Factor H and I
Which causes more breakdown of C3 to C3a and C 3b
C3 will be decreased

- Deposition of dense material in laminate densa of BM (ribbon like)

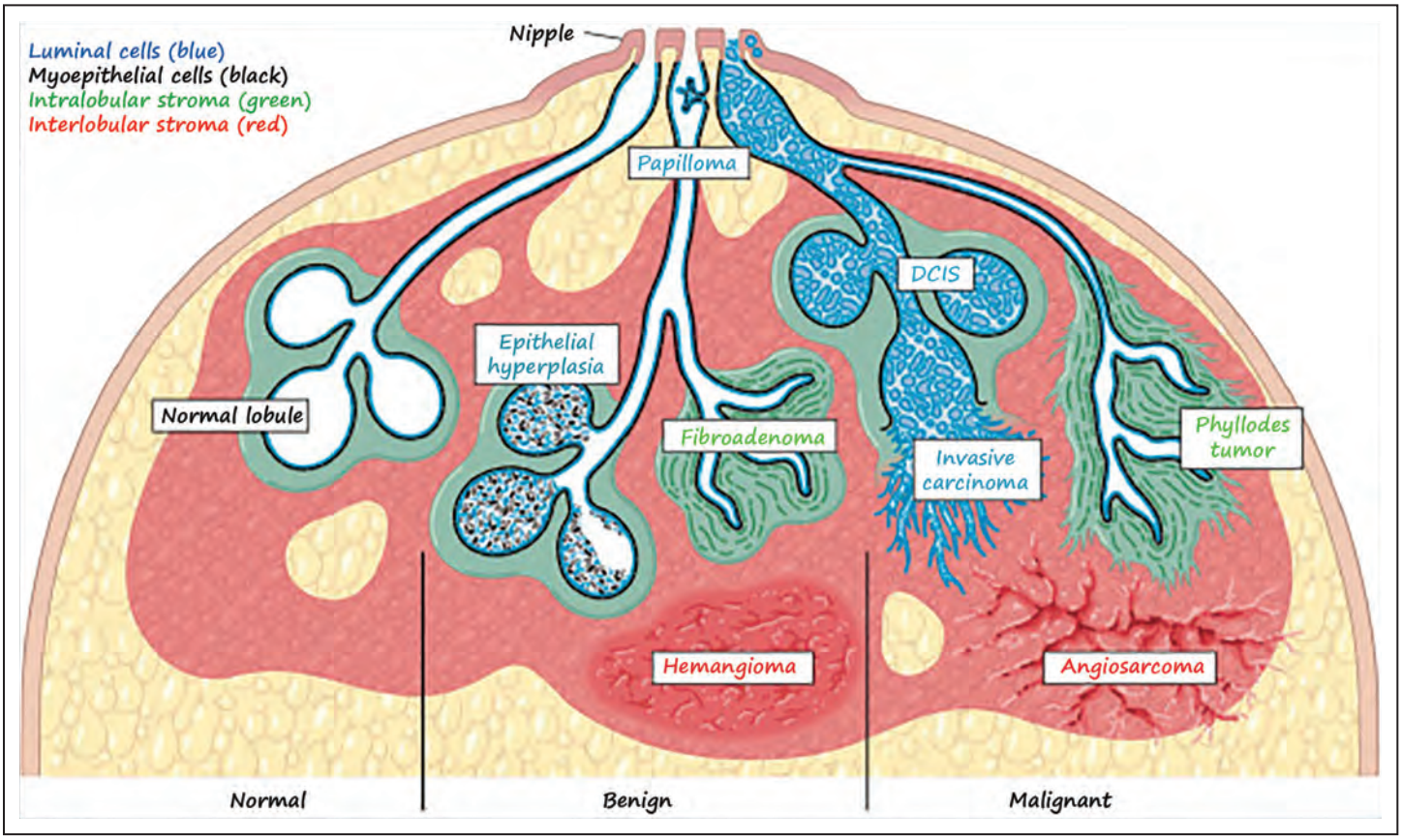
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

ISN/RPS (2003) classification of lupus nephritis	
Class I	Minimal mesangial LN
Class II	Mesangial proliferative LN
Class III	Focal LN (<50% of glomeruli) III (A): active lesions III (A/C): active and chronic lesions III (C): chronic lesions
Class IV	Diffuse LN (50% of glomeruli) Diffuse segmental (IV-S) or global (IV-G) LN IV (A): active lesions IV (A/C): active and chronic lesions IV (C): chronic lesions
Class V	Membranous LN
Class VI	Advanced sclerosing LN (90% globally sclerosed glomeruli without residual activity)
Adapted from weening jj, D'Agati VD, Schwartz MM	

BREAST

STRUCTURE OF BREAST

- **Breast include:**
  - Two major structures (ducts and lobules),
  - Two types of epithelial cells (luminal and myoepithelial),
  - Two types of stroma (interlobular and intralobular).
- Ducts and lobule are lined by inner luminal cells and outer myoepithelial cells.
- Each lobule is made up of acini and surrounded by intralobular stroma and interlobular stroma.



Proliferation of luminal and myoepithelial cells → Hyperplasia —Seen in→ Pregnancy and puberty

Hypertrophy → Lactating

Loss of Myoepithelial cells → **Malignancy**

Only luminal cells proliferate → Ductal carcinoma insitu
Myoepithelial cells are intact

If at any point, MEC disappear → Invasive carcinoma

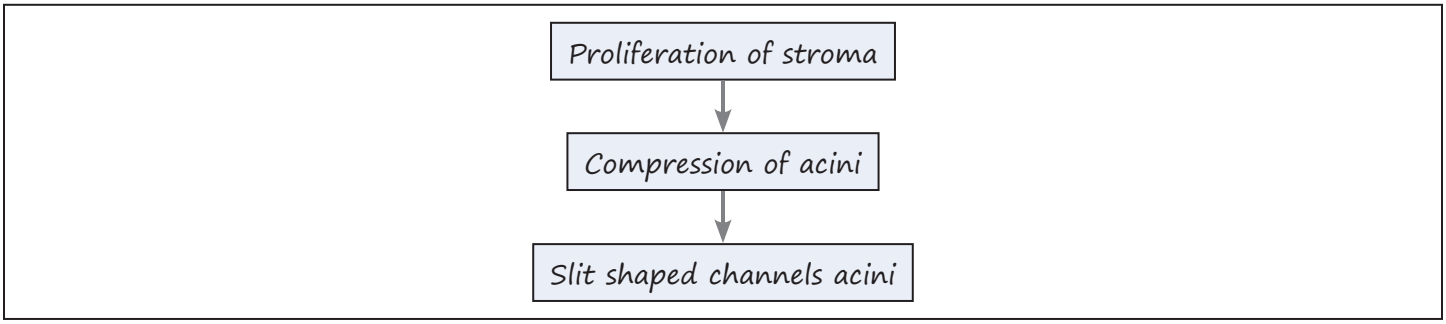
STAINS OF MEC

- P63
- Calponin
- S100
- Smooth muscle actin

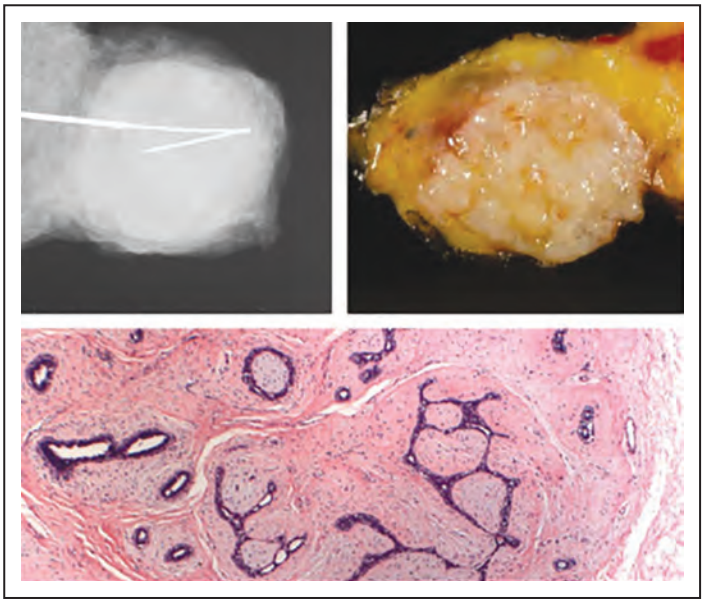
TUMORS OF THE BREAST

FIBROADENOMA

- Most common benign tumor of the female breast.
- Two-thirds of fibroadenomas harbor driver mutations in MED12.
- Arises from intralobular stroma
- Always benign, limited to intralobular stroma



- Tumors are well-circumscribed, rubbery, grayish white nodules that bulge above the surrounding tissue and often contain slit-like spaces lined by epithelium
- FNAC:
  - Intact duct
  - Proliferation of stroma
  - Spindle shaped ducts
  - Antler horn pattern



Proliferation of stroma and spindle shaped ducts

Antler horn pattern seen in FNAC