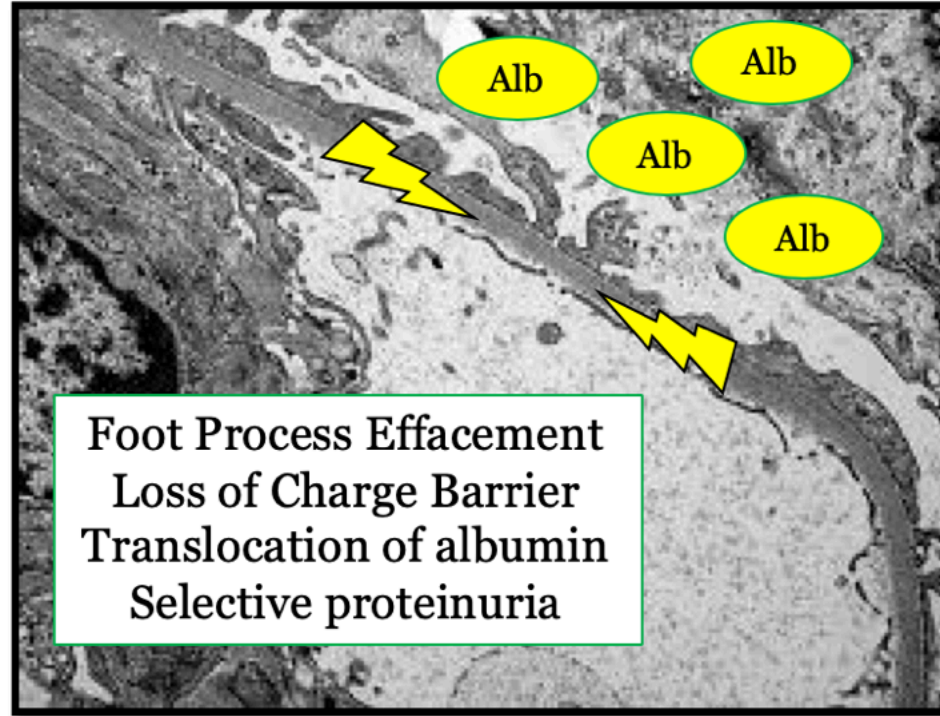


Part II. Nephrotic Disorders for USMLE Step One



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the **Language** of the Nephrotic Syndromes
(*Minimal Change, FSGS, Membranous*)
Proteinuria >3.5 gms/day

Edema

↓ Oncotic mm Hg

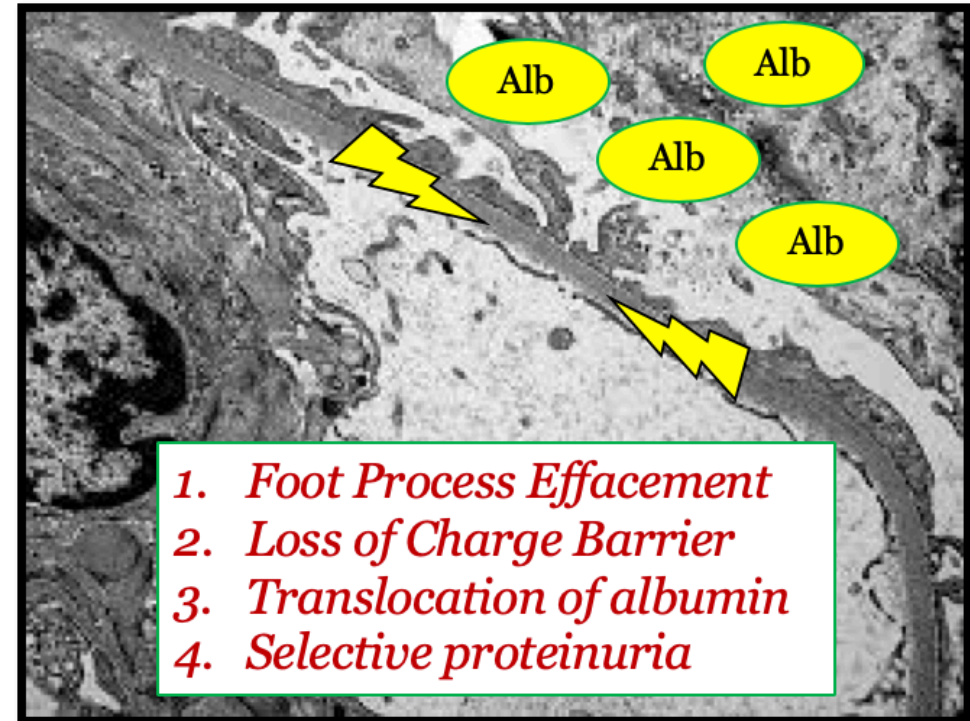
Thrombosis

Loss: *ATIII, plasminogen, C, S*
Gain: *fibrinogen*

Liver

↑ (Lipo-)protein synthesis

- Hyperlipidemia
- Frothy urine
- Lipiduria: *Fatty cast, Oval Fat Body, Maltese Cross*



Pathology derivatives

Disease Features

Nephritic

1. Oliguria/Azotemia
2. Hematuria
 - Color: Cola or Rust
 - RBC casts/Dysmorphic RBCs
3. HTN ('mild')
4. Edema/Proteinuria (mild/trace)

These patients *might* have:

- Edema
- Proteinuria (<3 gm)
- Hyperlipidemia

Nephrotic

- Proteinuria (>3.5 gm/day)
1. Frothy urine (lipoproteins)
 2. Hypoalbuminemia
 3. Edema
 4. Hypercoagulability
 5. Hyperlipidemia/-uria

These patients *might* have:

- Microscopic hematuria
- HTN
- Azotemia

Minimal Change
FSGS
Membranous

Disease Features

Nephritic

1. Oliguria/Azotemia
2. Hematuria
 - Color: Cola or Rust
 - RBC casts/Dysmorphic RBCs
3. HTN ('mild')
4. Edema/Proteinuria (mild/trace)

Nephrotic

Proteinuria (>3.5 gm/day)

1. Frothy urine (lipoproteins)
2. Hypoalbuminemia
3. Edema
4. Hypercoagulability
5. Hyperlipidemia/-uria

Context

- Clinical identifiers

Pathologic features

- Light/Electron Microscopy
- Immunofluorescence

Summary

- Unique Features

Minimal Change (MCD)
FSGS
Membranous (MN)

Disease Features

Nephritic

1. Oliguria/Azotemia
2. Hematuria
 - Color: Cola or Rust
 - RBC casts/Dysmorphic RBCs
3. HTN ('mild')
4. Edema/Proteinuria (mild/trace)

Nephrotic

Proteinuria (>3.5 gm/day)

1. Frothy urine (lipoproteins)
2. Hypoalbuminemia
3. Edema
4. Hypercoagulability
5. Hyperlipidemia/-uria

Context

- Clinical identifiers

Pathologic features

- Light/Electron Microscopy
- Immunofluorescence

Summary

- Unique Features

Overlap Syndromes:

MPGN
SLE

Minimal Change (MCD)

FSGS
Membranous (MN)

Systemic Disorders:

DM
Amyloid

Nephrotic: Demographic Features

Minimal Change

FSGS

Membranous

Kids >>> Adults

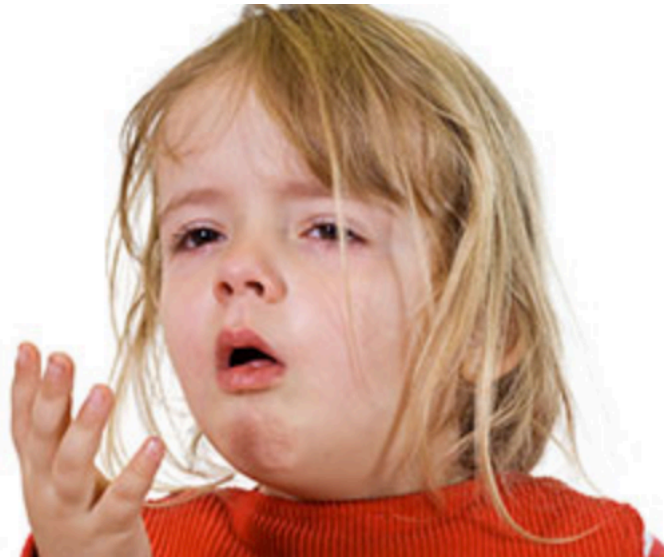


Nephrotic: Demographic Features

Minimal Change

Kids >>> Adults

Infection



Hodgkin Lymphoma

Reed-Sternberg

Triggers → Cytokine Release



Atopy

Nephrotic: Demographic Features

Minimal Change

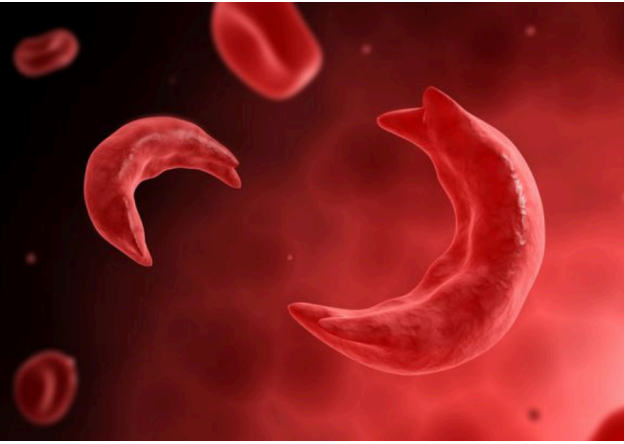
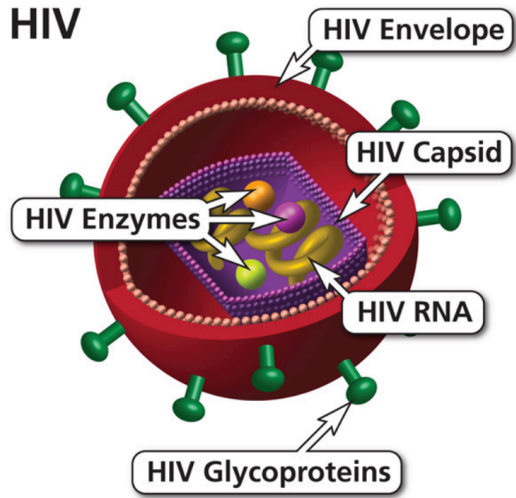
FSGS*

Membranous

Heroin

HIV infection

Sickle Cell Disease



***** Most common in Hispanics/African-Americans
FSGS will be identified by one of these risk factors *****

* FoKal SeGmental GlomeruloSclerosis (FSGS)

Nephrotic: Demographic Features

Minimal Change

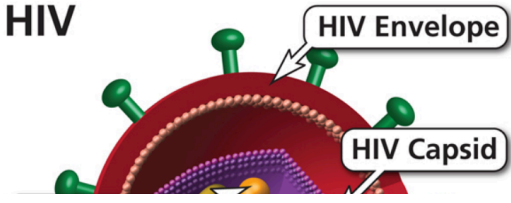
FSGS*

Membranous

Heroin

HIV infection

Sickle Cell Disease



*** FoKal SeGmental GlomeruloSclerosis (FSGS)**

FoKal: a portion of the kidney
SeGmental: a portion of the glomerulus

* FoKal SeGmental GlomeruloSclerosis (FSGS)

Nephrotic: Demographic Features

Minimal Change

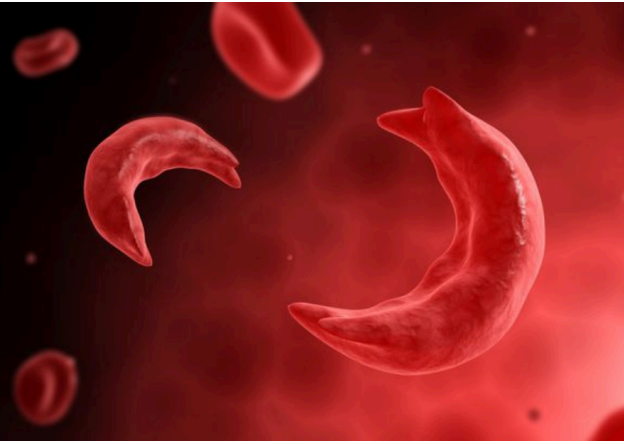
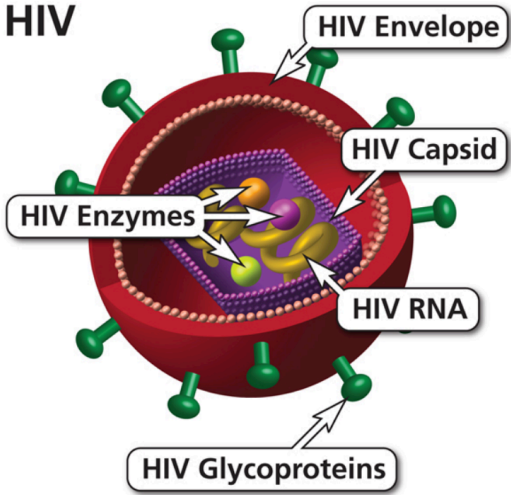
FSGS*

Membranous

Heroin

HIV infection

Sickle Cell Disease



***** Most common in Hispanics/African-Americans
FSGS will be identified by one of these risk factors *****

* FoKal SeGmental GlomeruloSclerosis (FSGS)

Nephrotic: Demographic Features

FSGS



Obesity

Anabolic Steroids

Nephrotic: Demographic Features

Minimal Change

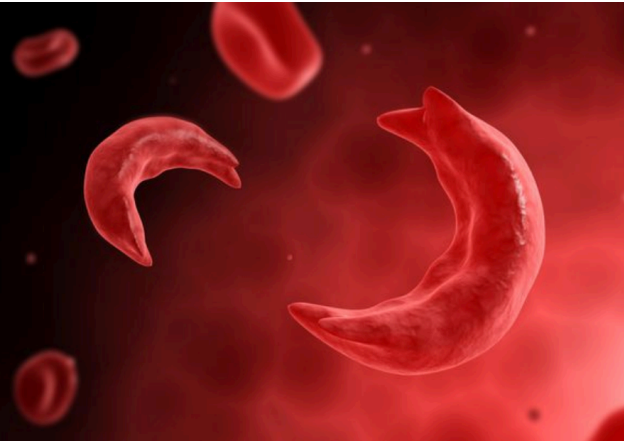
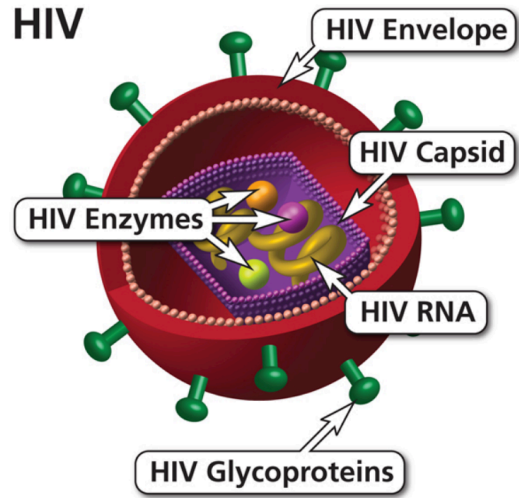
FSGS*

Membranous

Heroin

HIV infection

Sickle Cell Disease



***** Most common in Hispanics/African-Americans
FSGS will be identified by one of these risk factors *****

* FoKal SeGmental GlomeruloSclerosis (FSGS)

Nephrotic: Demographic Features

FSGS*

Heroin

Sickle Cell Disease

HIV infection

Patient with h/o IVDU presents with edema.
WBC 2.4; CD4 count 150 cells/ μ L
4+ protein on urine dipstick
What is the most likely cause for his presentation?



Most common in Hispanics/African-Americans
FSGS *will be identified by one of these risk factors*



* FoKal SeGmental GlomeruloSclerosis (FSGS)

Dipstick grading	Semi-quantitative urine protein (mg/dl)
Negative/nil	0
Trace	15-30
1+	30-100
2+	100-300
3+	300-1000
4+	>1000

Patient with h/o IVDU presents with edema.

WBC 2.4; CD4 count 150

4+ protein on urine dipstick

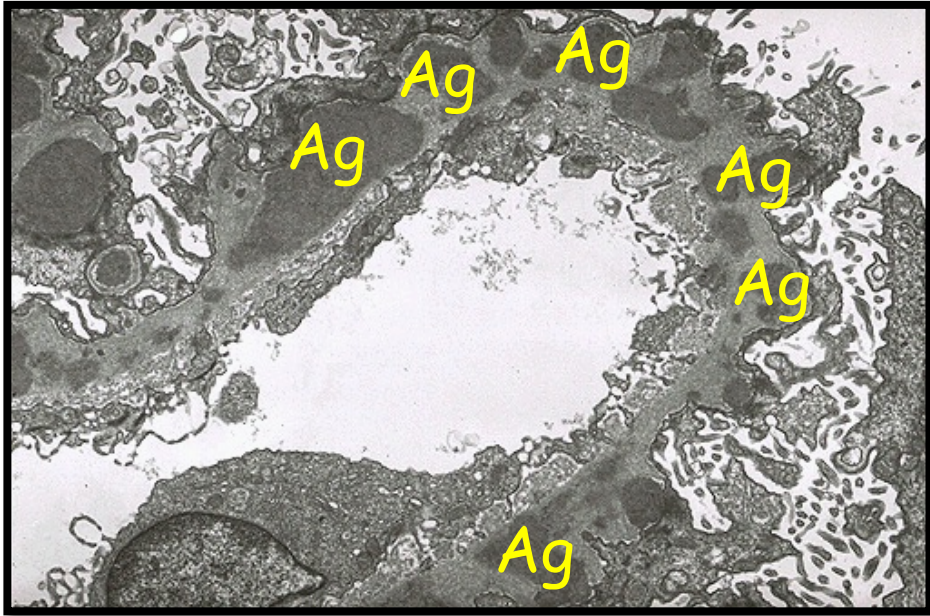
What is most likely cause for his presentation?

Nephrotic: Demographic Features

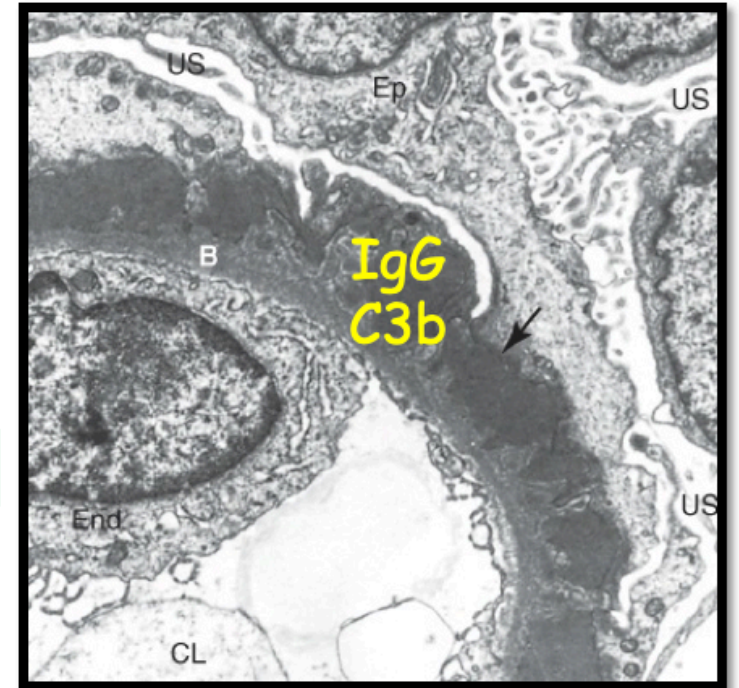
Minimal Change

FSGS

Membranous



Slow, *meandering* process



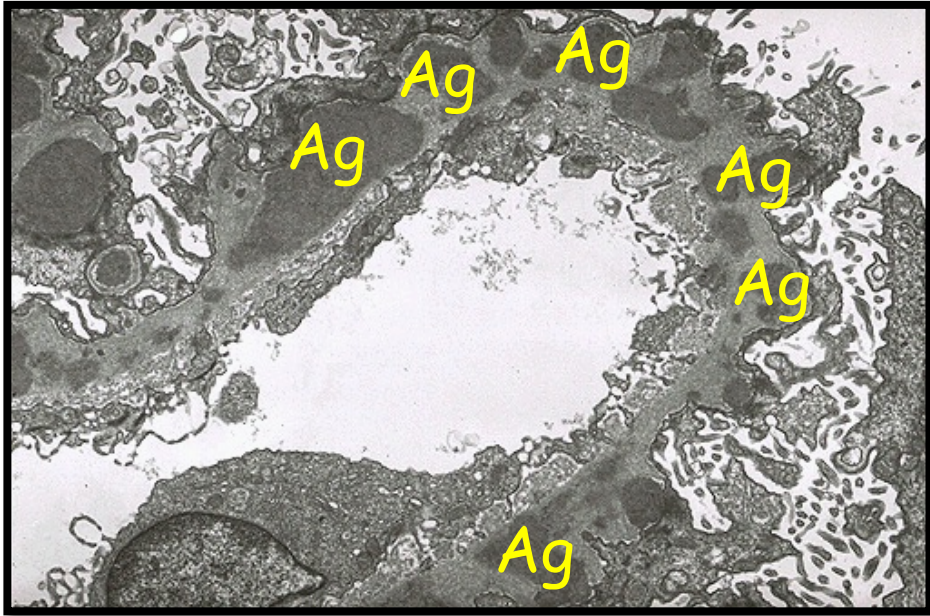
Antigens/IC deposit in the *Sub-Epithelial* portion of the GBM

Nephrotic: Demographic Features

Minimal Change

FSGS

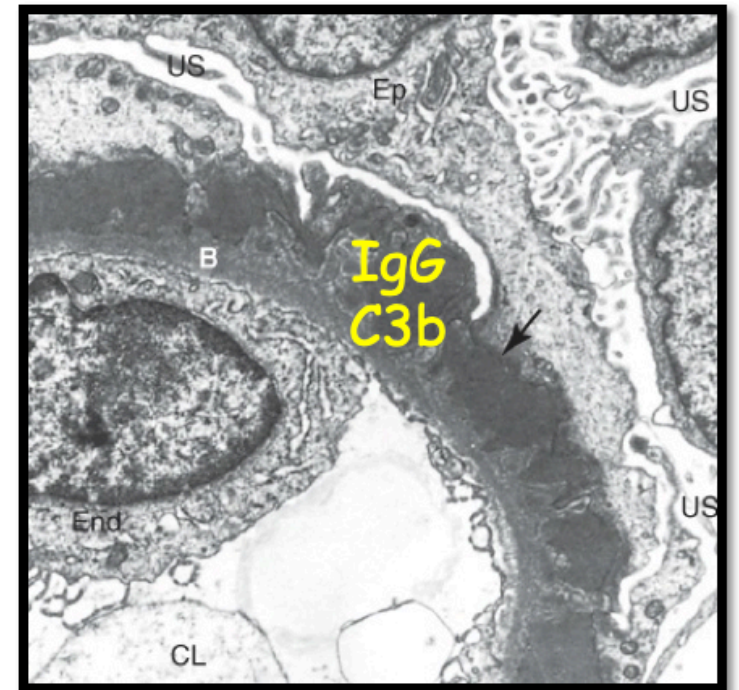
Membranous



Secondary
HBSAg, Tumor, SLE



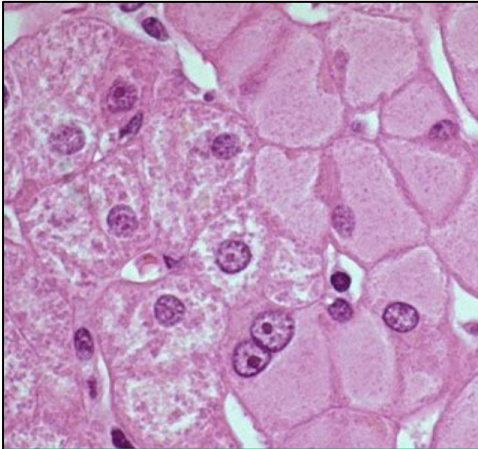
Indolent Onset



Primary
Autoimmune (PLA₂ Receptor)

Nephrotic: Demographic Features

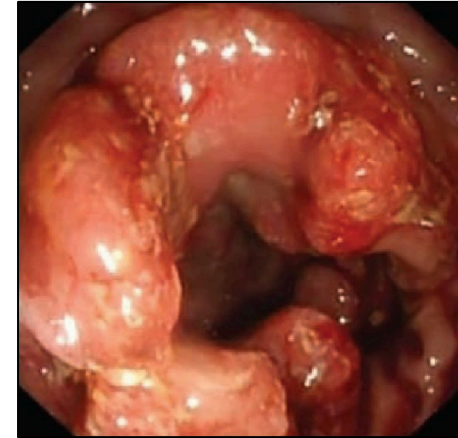
Membranous



Ground glass
hepatocytes (HBV)



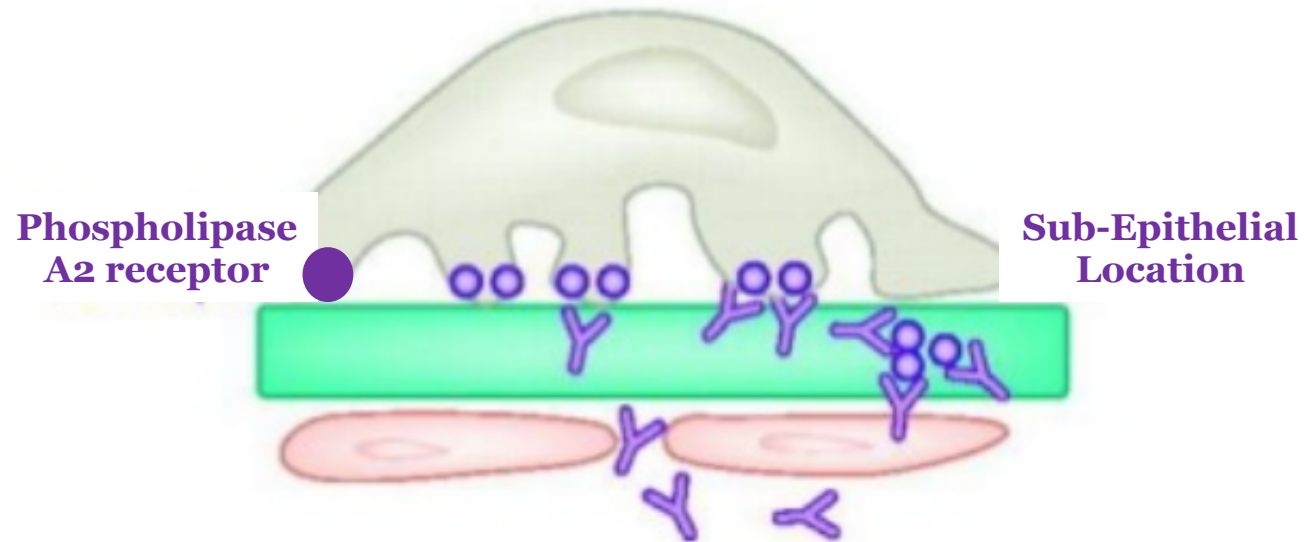
Malar Rash, SLE
(*Lupus nephritis, many*)



Neoplasm

Nephrotic: Demographic Features

Primary Membranous Nephropathy (75%)



Primary: PLA₂-r

Nephrotic Syndrome

Minimal Change

FSGS

Membranous

Demographic

Kids
Cytokine trigger

Heroin, HIV, SCD
Sclerosis = CKD

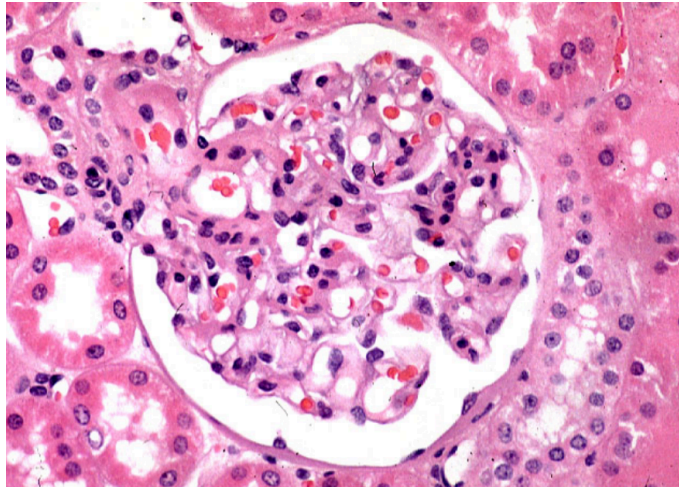
Planted Ag/IC
Tumor, HBSAg, SLE

Nephrotic: Pathology

Minimal Change

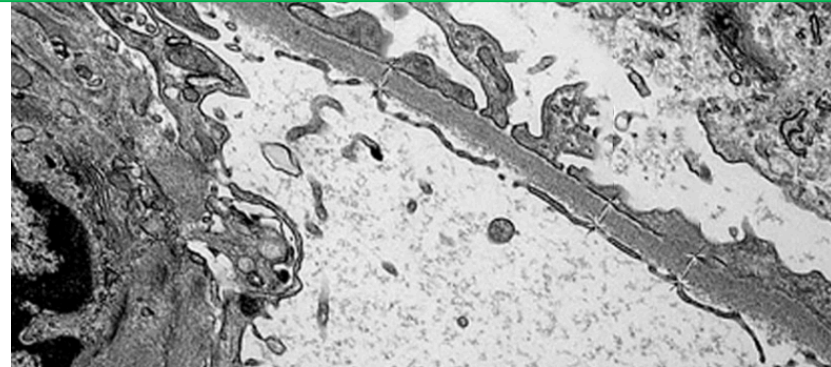
FSGS

Membranous



Normal Histology

1. Loss of **charge barrier**
2. Albumin translocation → **selective proteinuria**

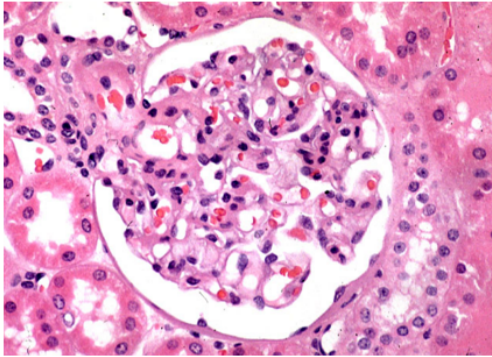


EM: Foot Process Effacement

Be familiar with these two derivatives

Nephrotic: Pathology

Minimal Change



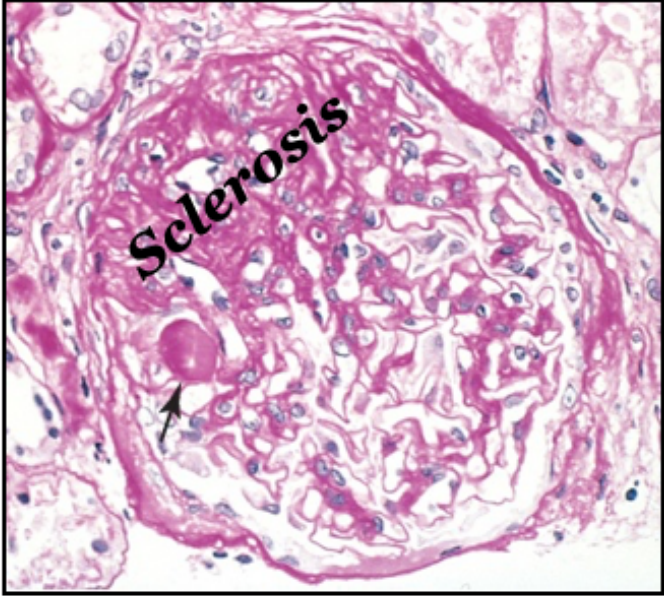
Normal Histology

FSGS

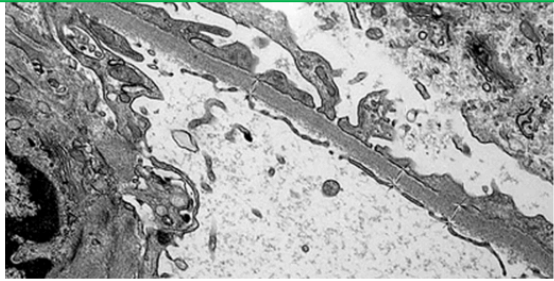
Pathoma: 'picture what would happen to Minimal Change if it progressed...'



Sclerosis



Loss of **charge barrier**
Albumin translocation → **selective proteinuria**



Foot Process Effacement

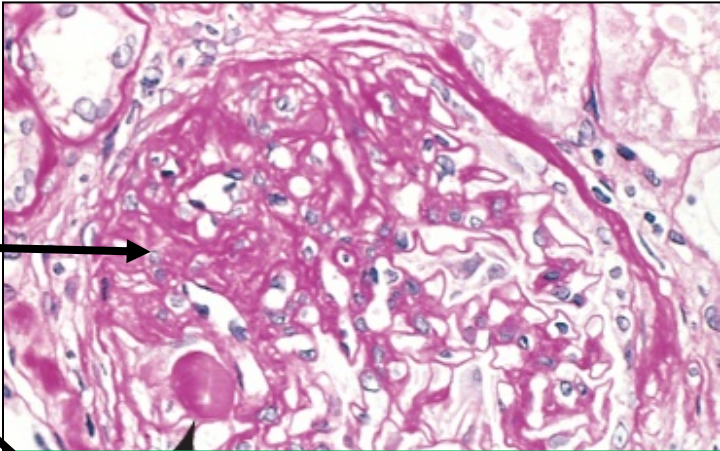
Nephrotic: Pathology

Minimal Change

FSGS

Membranous

Sclerosis



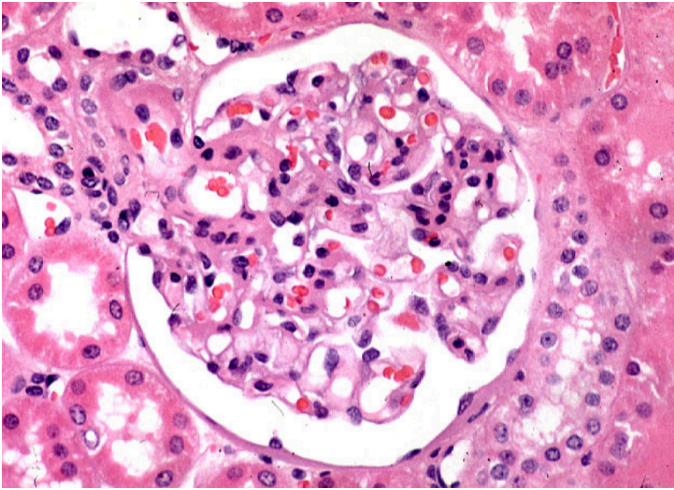
Creatinine elevation
HTN
Hematuria

FoKal **SeG**mental **G**lomerulo**S**clerosis

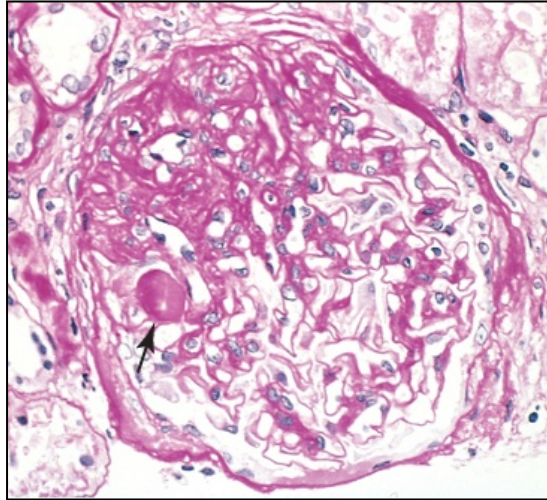
Fo**K**al: part of the kidney
Se**G**mental: part of the glomerulus

Nephrotic: Pathology

Minimal Change



FSGS

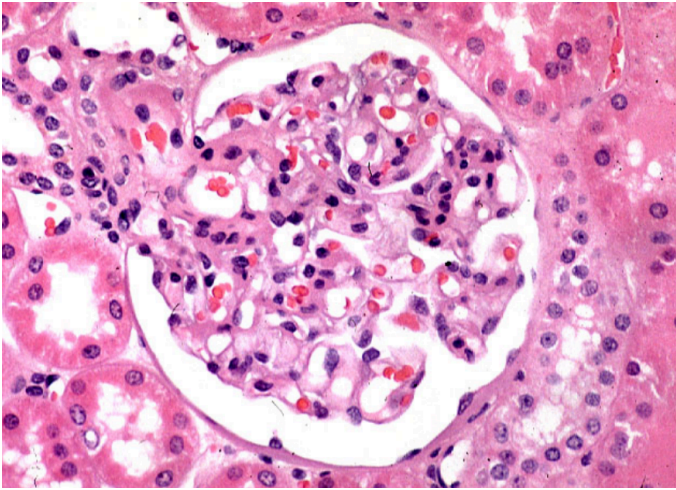


Membranous

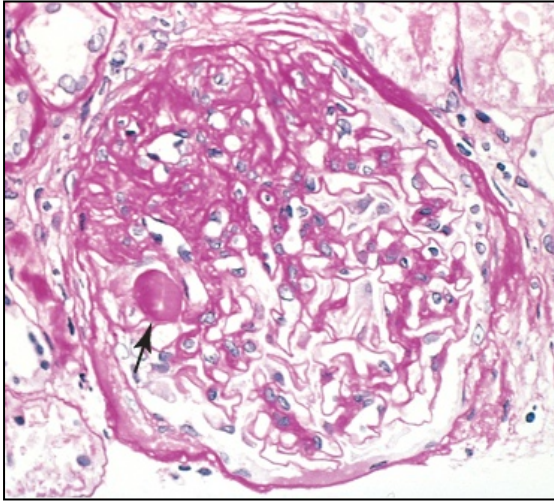
Nephrotic Syndrome and ***No Immunofluorescence***

Nephrotic: Pathology

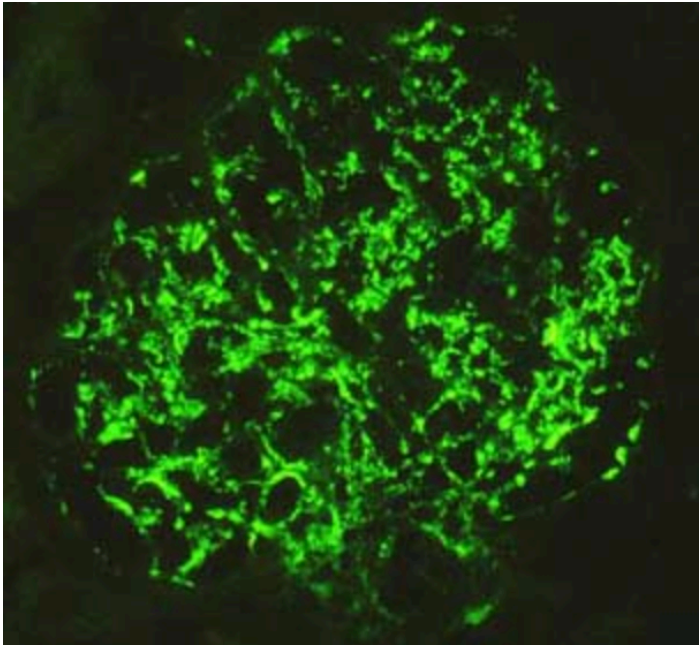
Minimal Change



FSGS



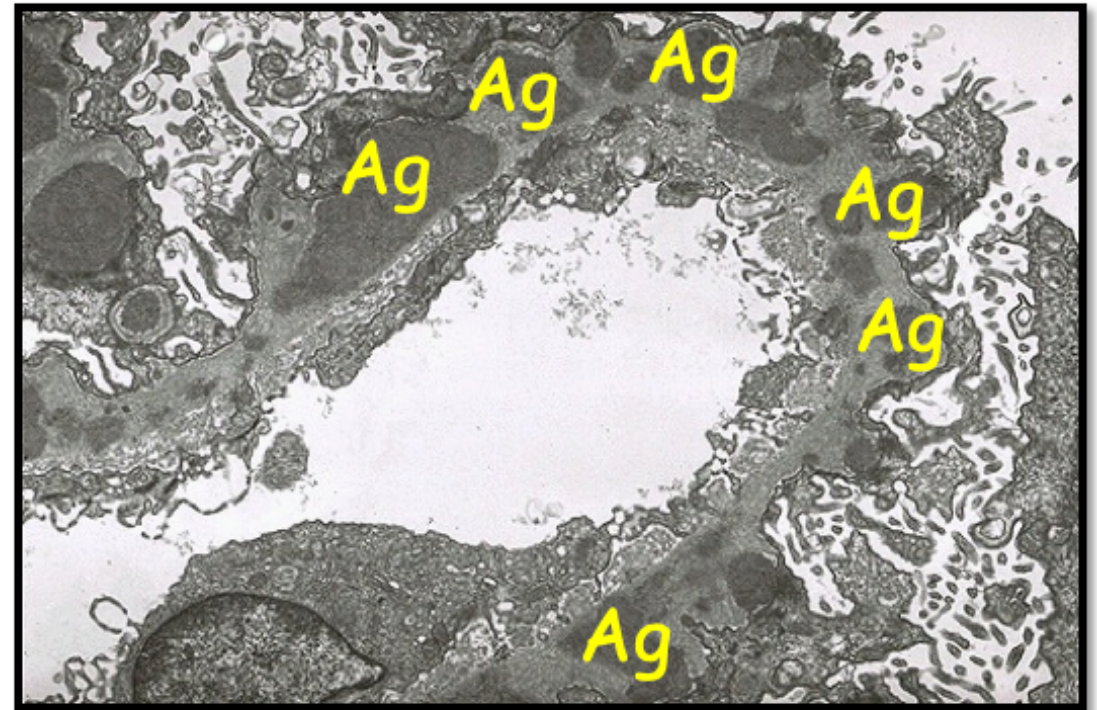
Membranous



Nephrotic Syndrome and *No Immunofluorescence*

Nephrotic: Pathology

Membranous Nephropathy

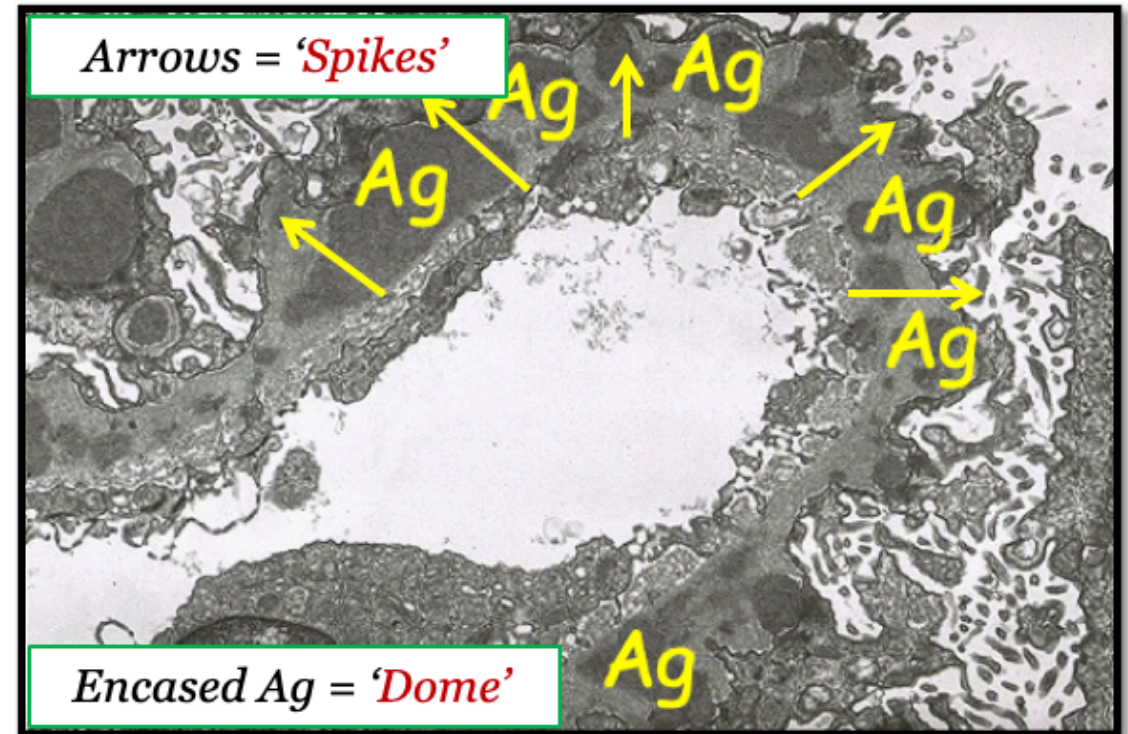
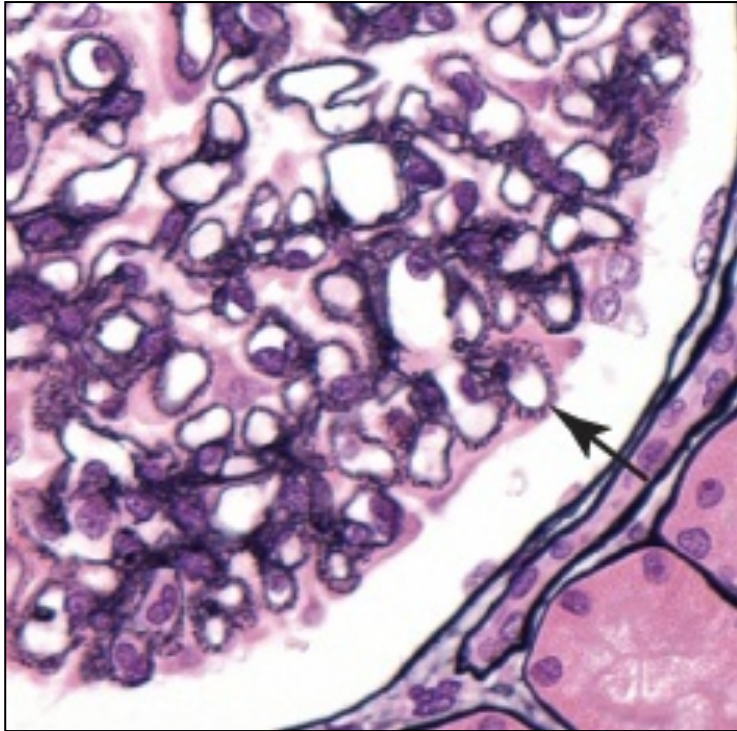


Electron Microscopy:

- Not pictured but the foot process is damaged → effacement/loss of charge barrier
- GBM is thickened (IC/'Planted Ag')
- Sub-epithelial location = repair of GBM by Podocyte AND non-proliferative

Nephrotic: Pathology

Membranous Nephropathy

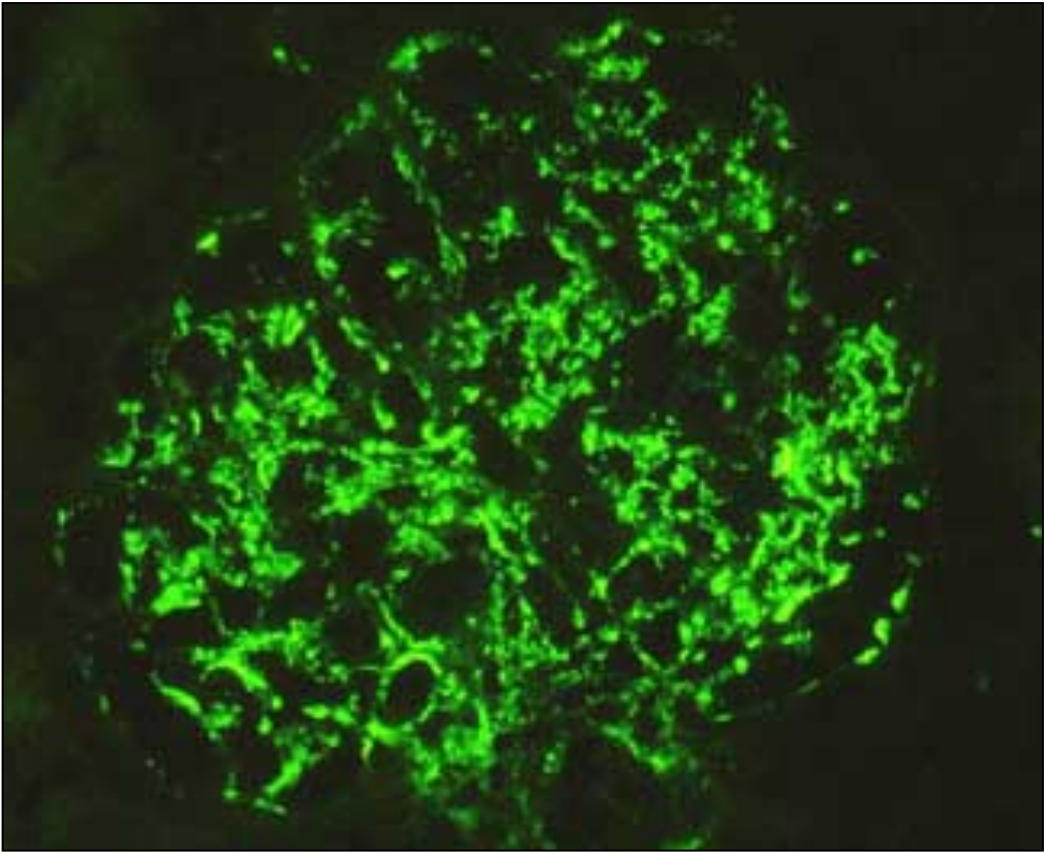


Electron Microscopy:

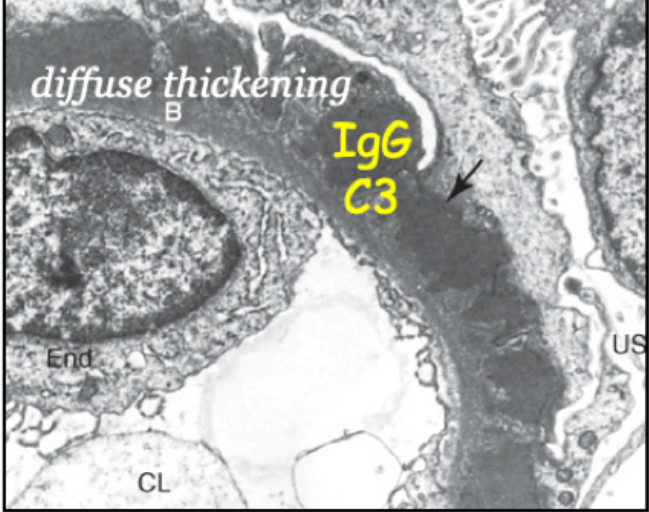
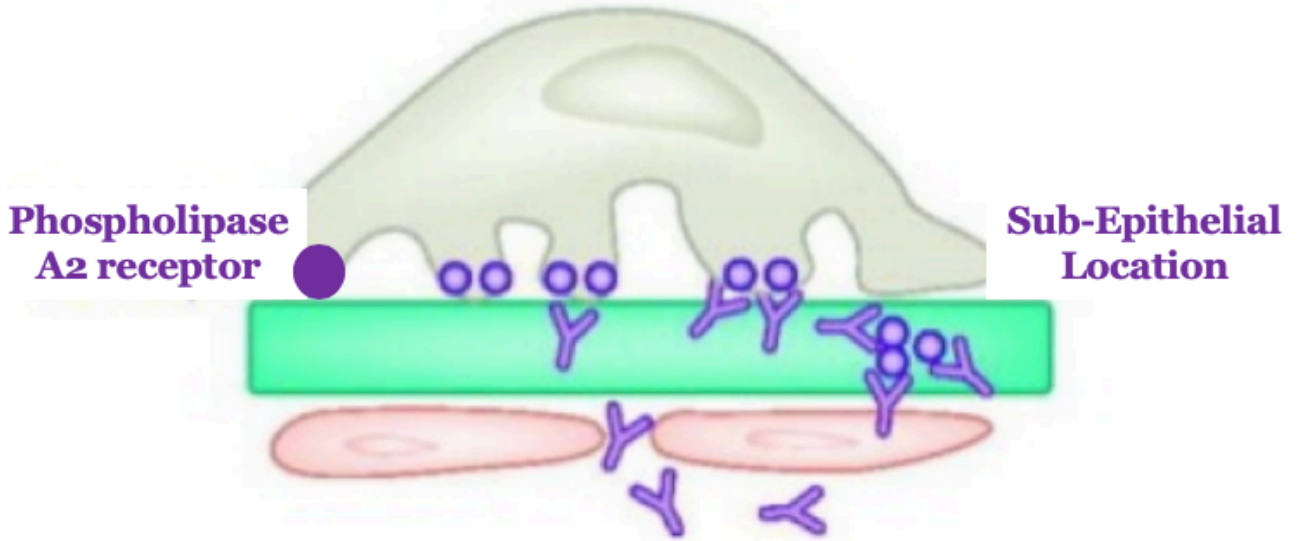
- Sub-epithelial location = repair of GBM by Podocyte
- 'Repair' = ECM and collagen; appears as 'spikes' between Ag/IC ('dome')

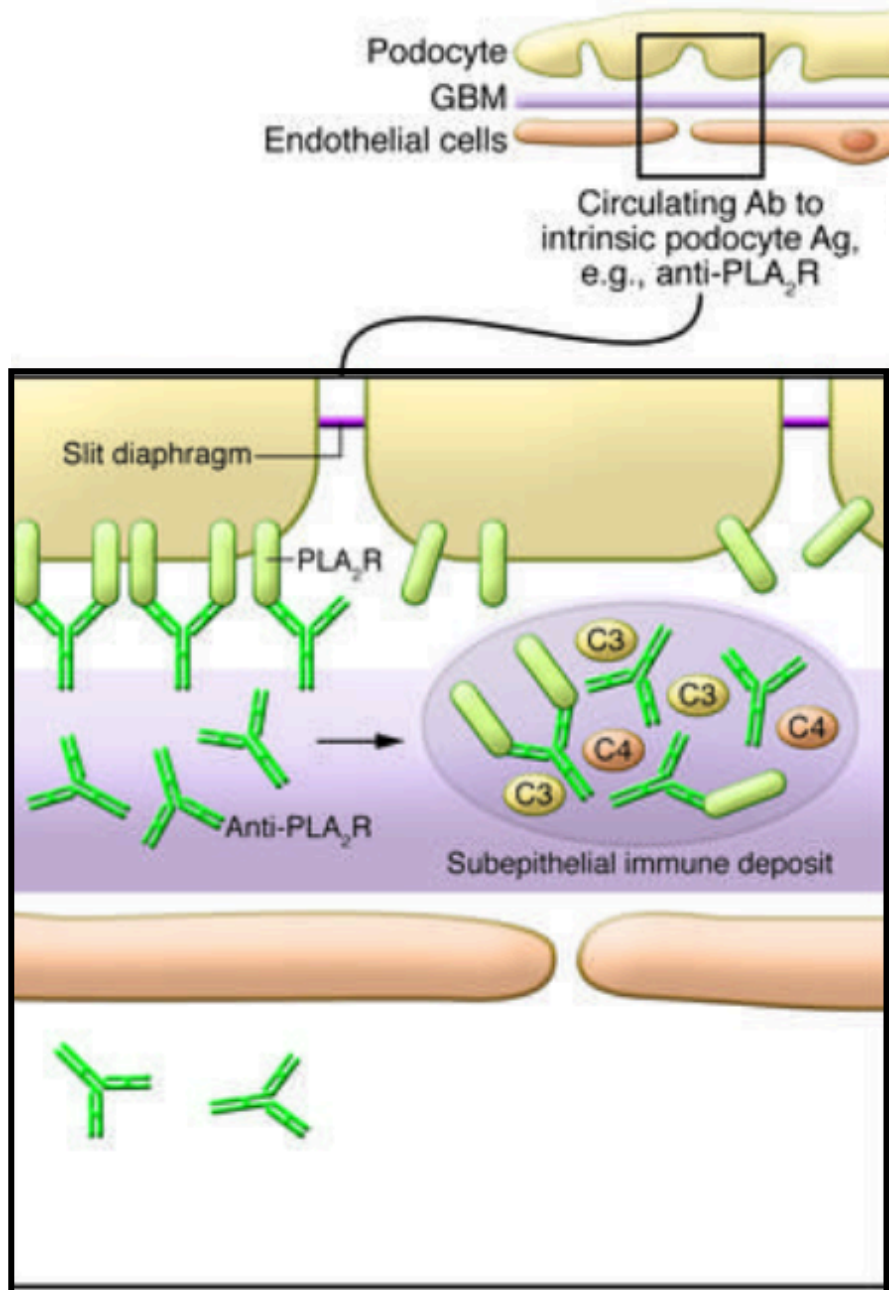
Nephrotic: Pathology

Membranous Nephropathy

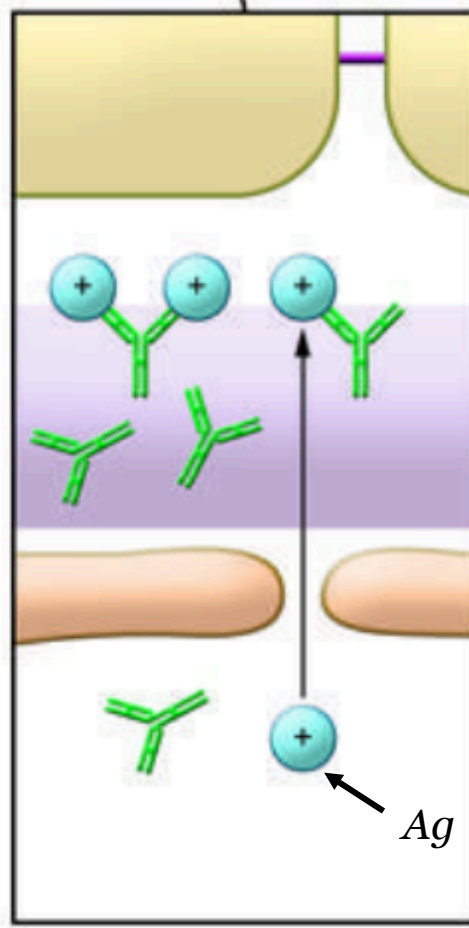
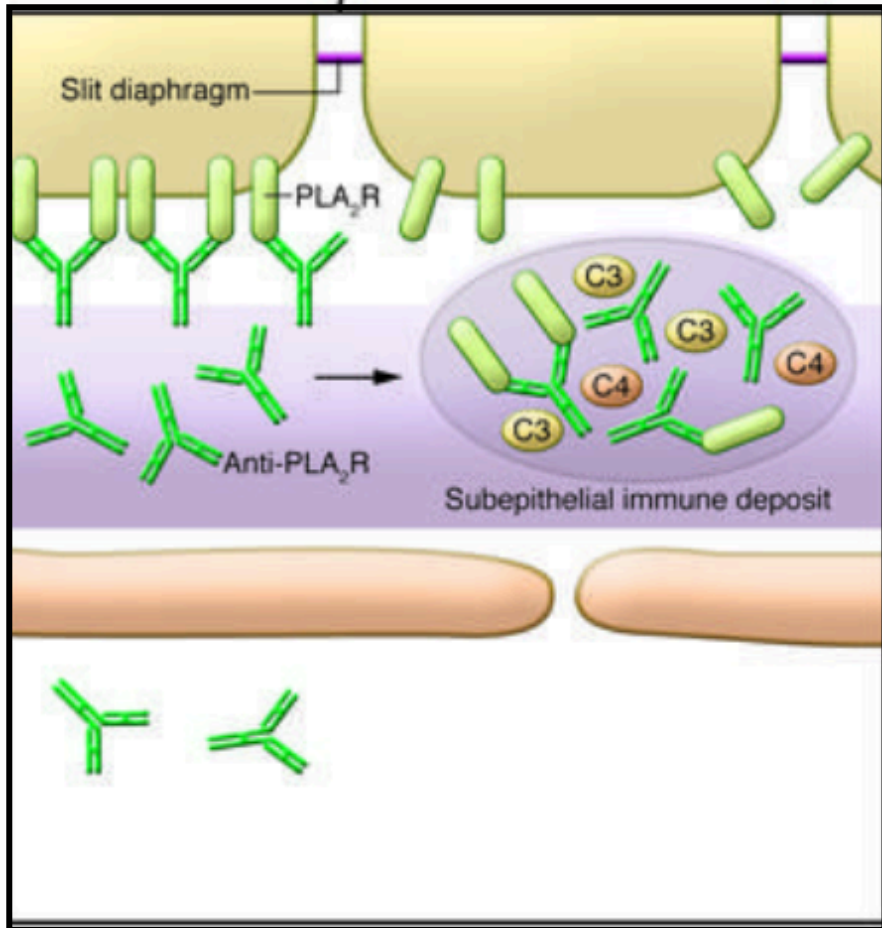
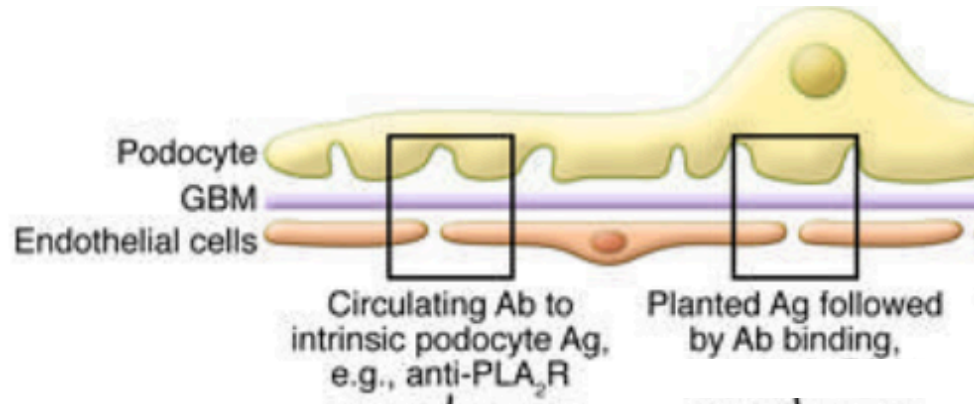


Immunofluorescence
Granular appearance with IgG and C3

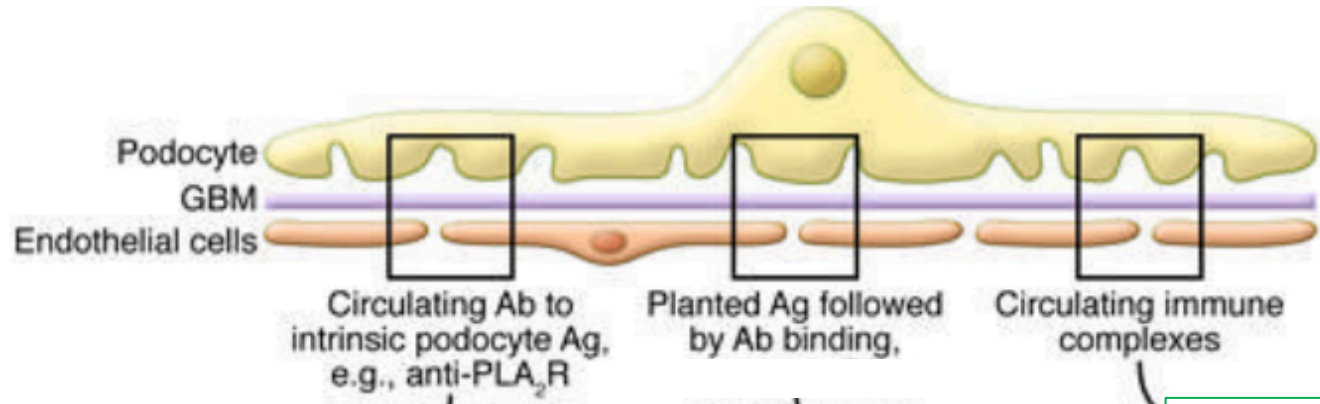




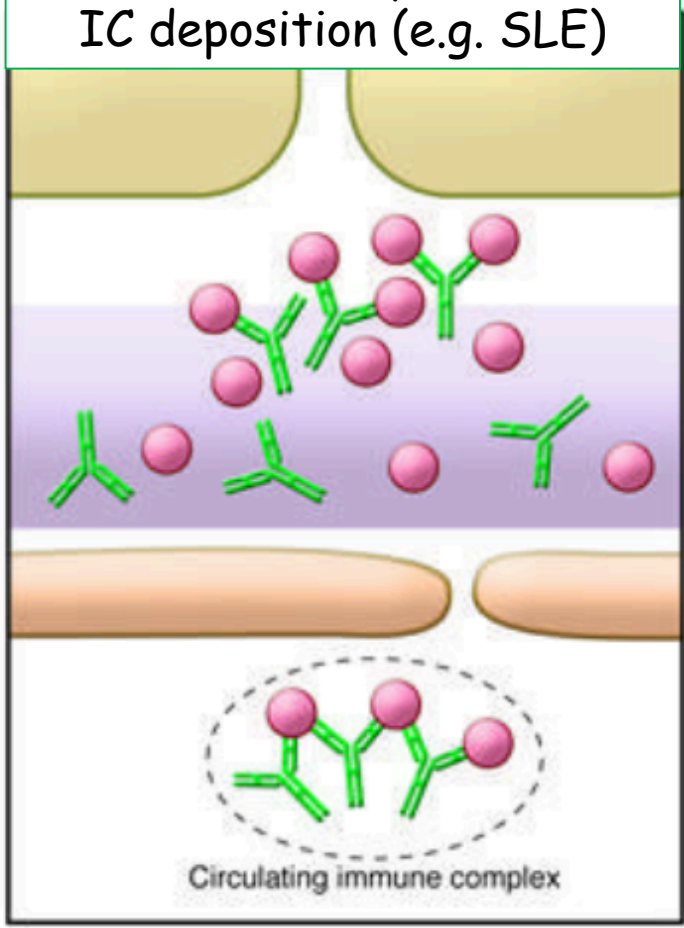
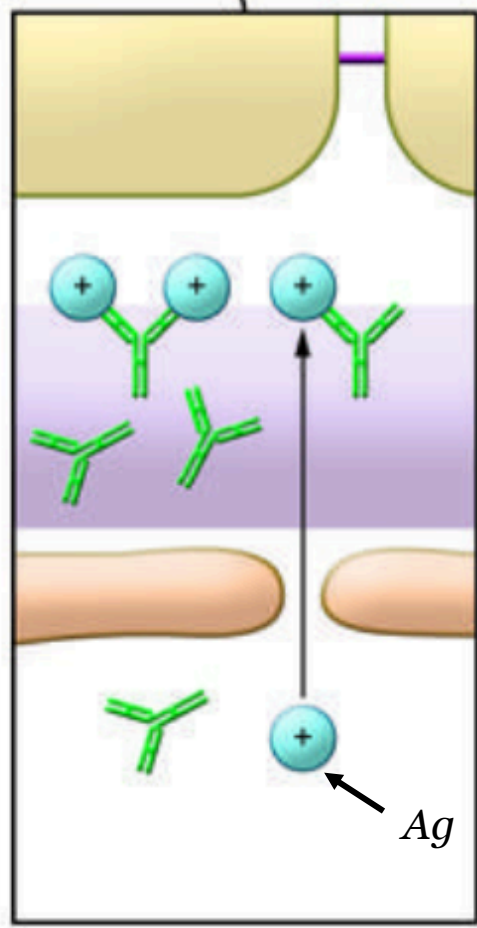
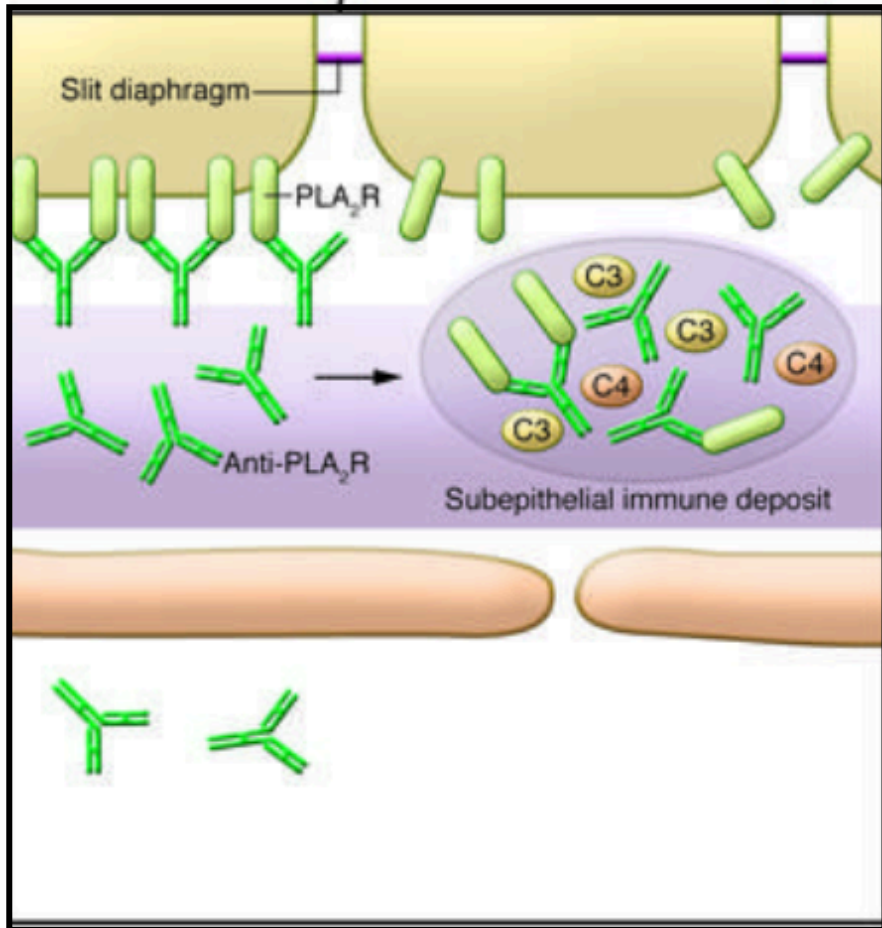
Primary MN:
 Subepithelial portion of GBM
 Foot processes are injured (*effaced*) with
 resultant damage to the slit diaphragm



Secondary MN
Antigen deposits ('planted')
in GBM with IgG response



Secondary MN
IC deposition (e.g. SLE)



Nephrotic Syndrome (>3.5 gms/d)

Minimal Change

FSGS

Membranous

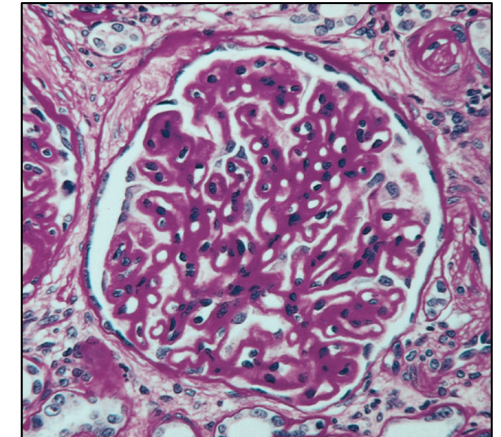
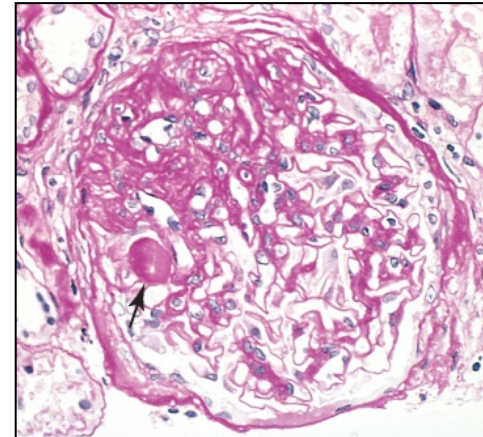
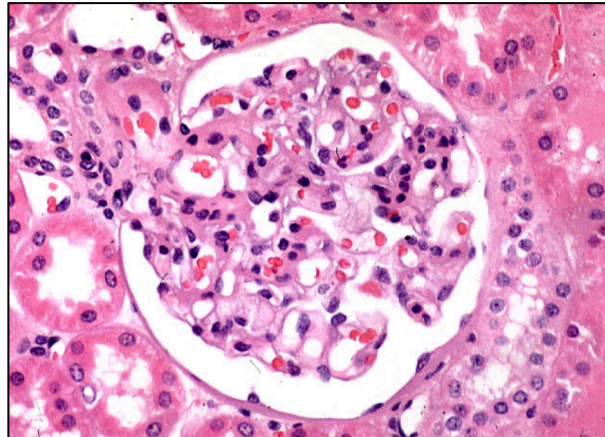
Demographic

Kids
Cytokine trigger

Heroin, HIV, SCD
Sclerosis = CKD

Planted Ag/IC
Tumor, HBSAg, SLE

Pathology: LM



Normal

Segmental Sclerosis

Thickened GBM

Nephrotic Syndrome (>3.5 gms/d)

Minimal Change

FSGS

Membranous

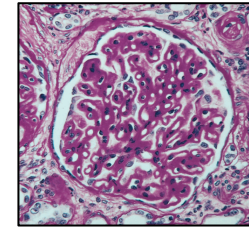
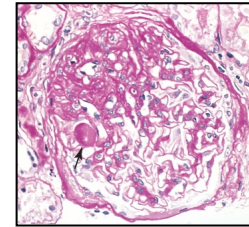
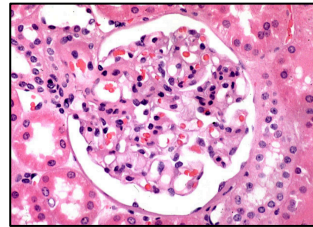
Demographic

Kids
Cytokine trigger

Heroin, HIV, SCD
Sclerosis = CKD

Planted Ag/IC
Tumor, HBSAg, SLE

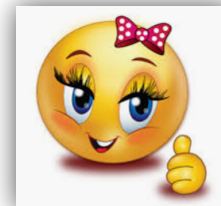
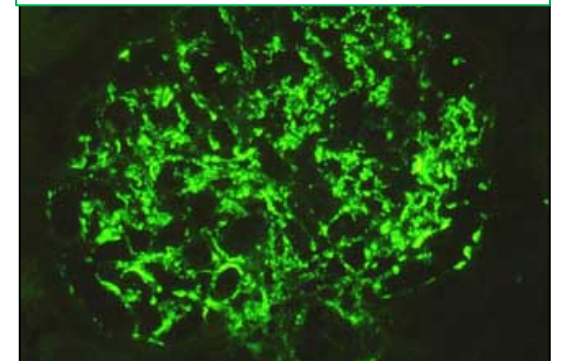
Pathology: LM



Pathology: IF

NA

Granular IF



Minimal Change

FSGS

Membranous

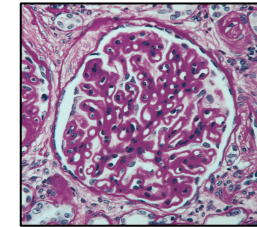
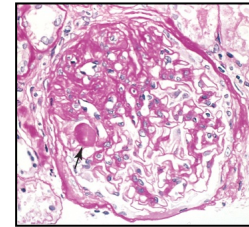
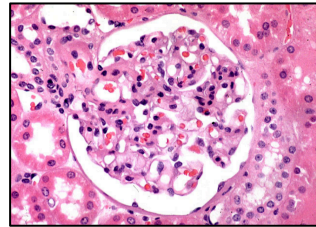
Demographic

Kids
Cytokine trigger

Heroin, HIV, SCD
Sclerosis = CKD

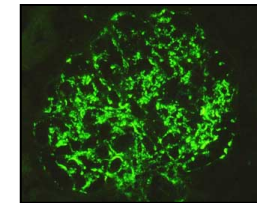
Planted Ag/IC
Tumor, HBSAg, SLE

Pathology: LM



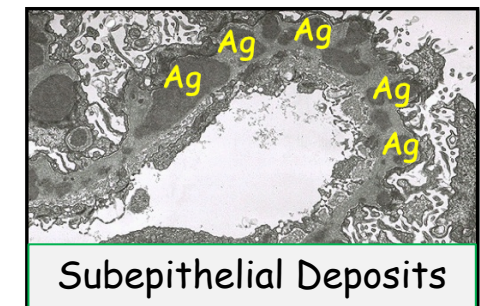
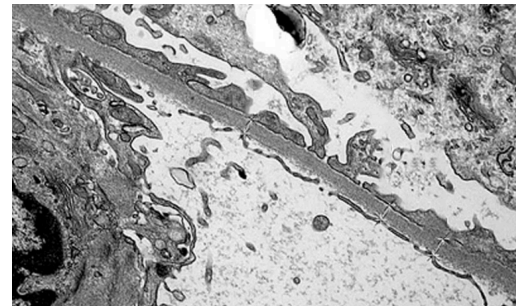
Pathology: IF

NA



Pathology: EM

← Effacement, Loss of Anionic Charge Barrier →



Subepithelial Deposits

Minimal Change

FSGS

Membranous

Demographic

Kids
Cytokine trigger

Heroin, HIV, SCD
Sclerosis = CKD

Planted Ag/IC
Tumor, HBSAg, SLE

Special Notes

Rx: Steroid Responsive

Best Rx for PSGN?

A. Observation and Supportive Care

Steroids do not help

Minimal Change

FSGS

Membranous

Demographic

Kids
Cytokine trigger

Heroin, HIV, SCD
Sclerosis = CKD

Planted Ag/IC
Tumor, HBSAg, SLE

Special Notes

Rx: Steroid Responsive

HTN
Hematuria (no casts)
Elevation of Creatinine

Proteinuria > 3.5 gms/day

Minimal Change

FSGS

Membranous

Demographic

Kids
Cytokine trigger

Heroin, HIV, SCD
Sclerosis = CKD

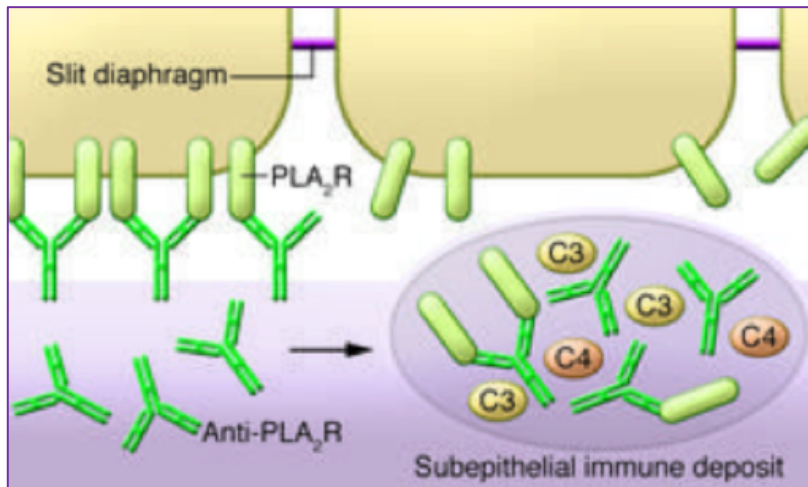
Planted Ag/IC
Tumor, HBSAg, SLE

Special Notes

Rx: Steroid Responsive

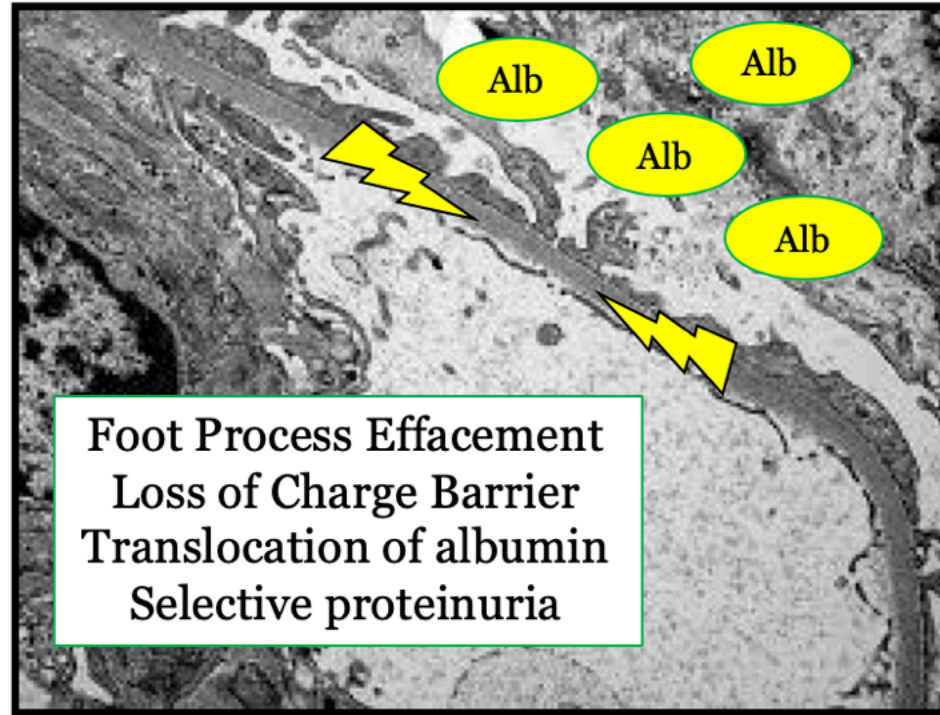
HTN
Hematuria (no casts)
Elevation of Creatinine

Proteinuria > 3.5 gms/day



Insidious onset
Dx: Anti-PLA₂ Aby

Part II. Nephrotic Disorders for USMLE Step One



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