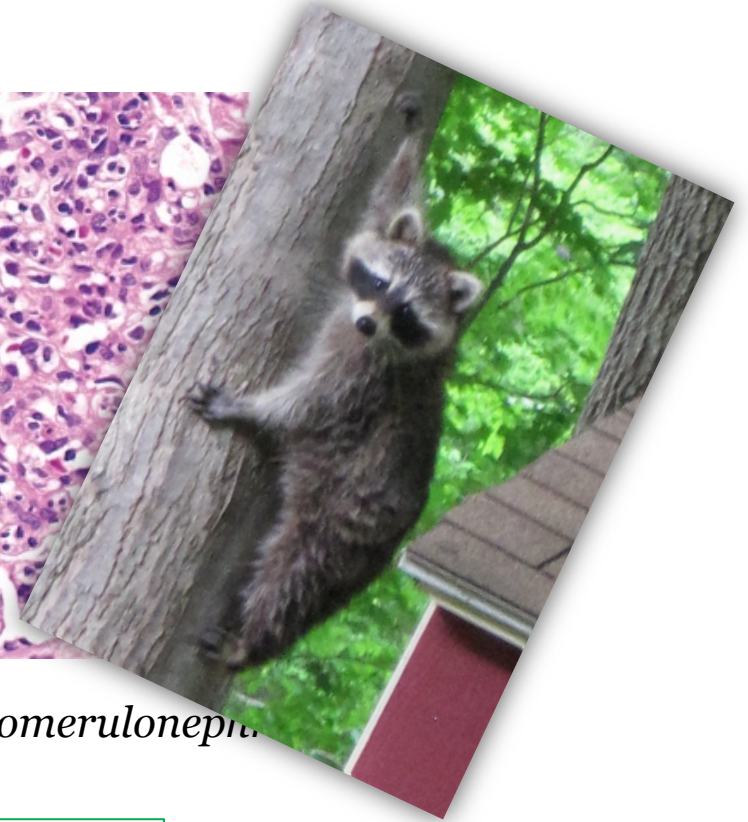
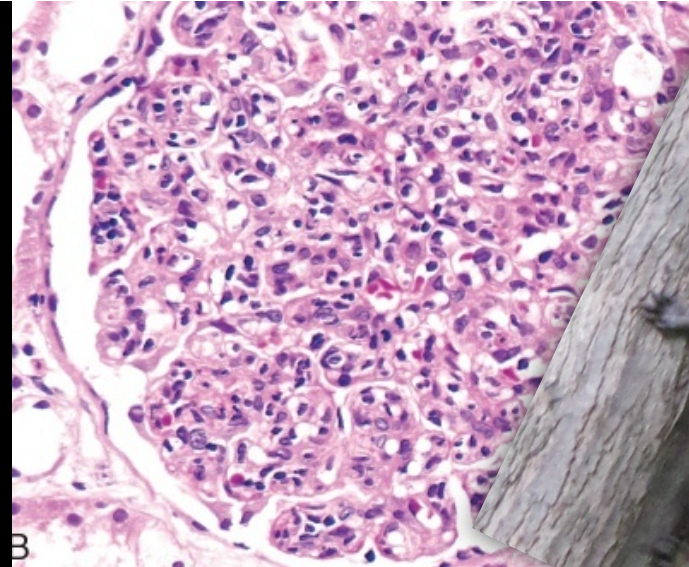
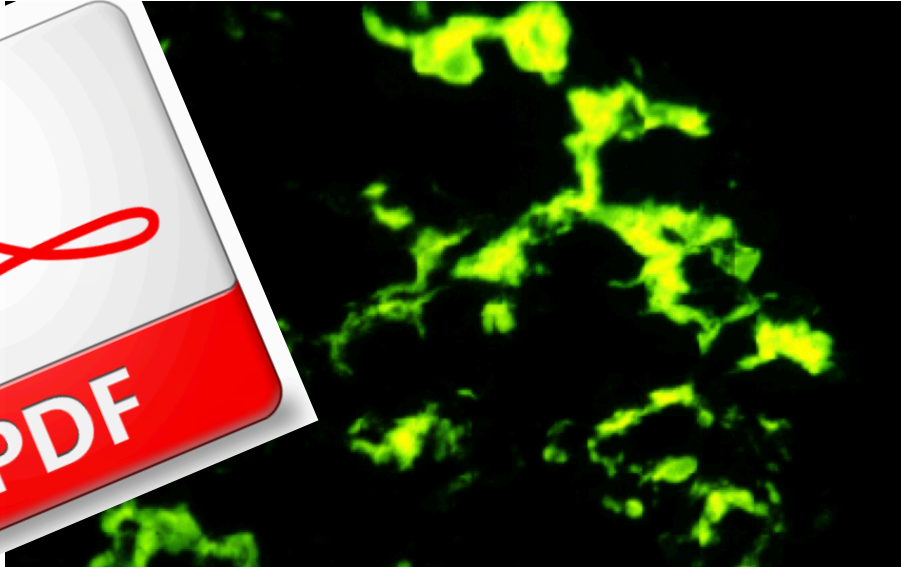


Part 3a. Nephritic Syndromes (**IgA Nephropathy** and **PSGN**) for USMLE Step One



**Post-Streptococcal Glomerulonephritis*

Howard J. Sachs, MD

Associate Professor of Medicine

UMass Medical School

www.12daysinmarch.com

E-mail: Howard@12daysinmarch.com

the Language of the Nephritic Syndromes

AKI/Elevated Cr

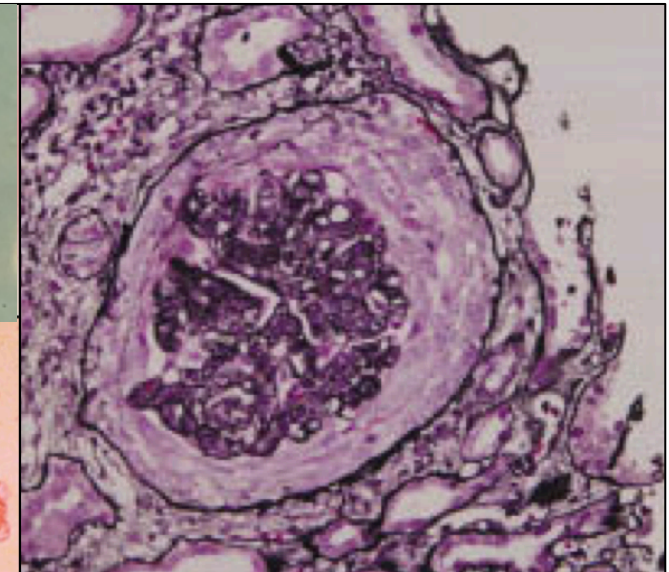
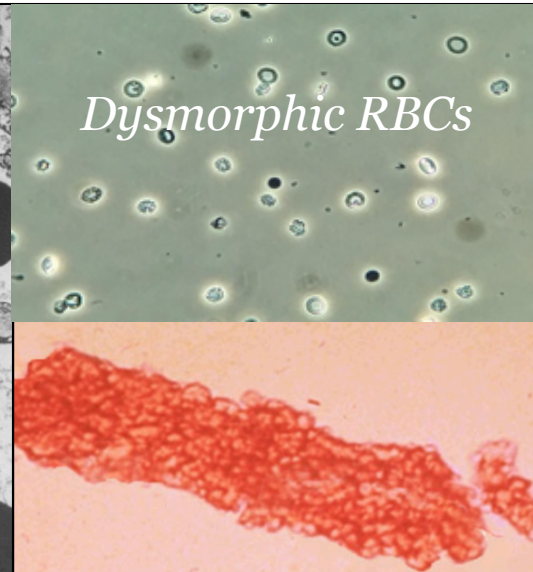
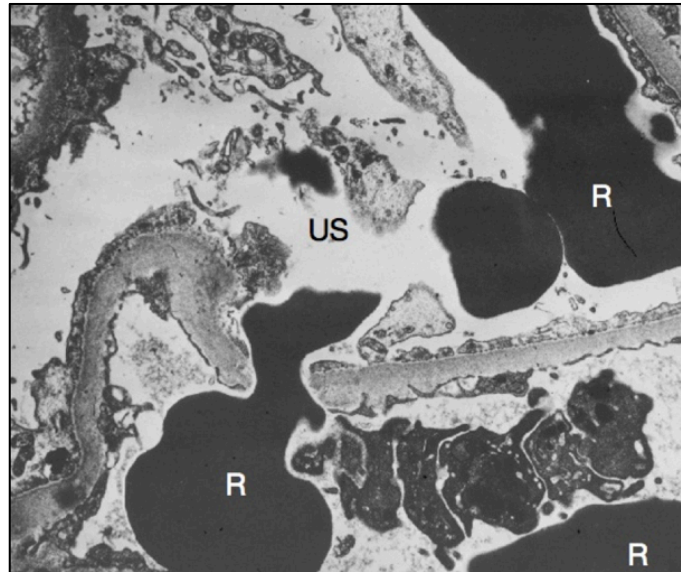
RBC Casts

RPGN/Crescents

Proteinuria, mild

Renal Injury:
Elevated Creatinine
HTN
Edema, mild (\downarrow GFR)

Clinico-Pathology
RPGN*
Crescents



The Players:

IgA Nephropathy
PSGN

Wegener's (GPA)
Anti-GBM (Goodpasture's)

Nephritic: What They Share in Common

IgA Nephropathy

PSGN

Kids
Infectious Triggers
Proliferative/RPGN
Hematuria



Nephritic: How They Differ

IgA Nephropathy

PSGN

Infectious

Viral trigger
2-3 days ago



'Flu-like illness'

Nephritic: How They Differ

IgA Nephropathy

PSGN

Infectious

Viral trigger
2-3 days ago

Strep Infection,
10-21 days ago



'Flu-like illness'



Honey, crusted lesions



Nephritic: How They Differ

IgA Nephropathy

PSGN

Infectious

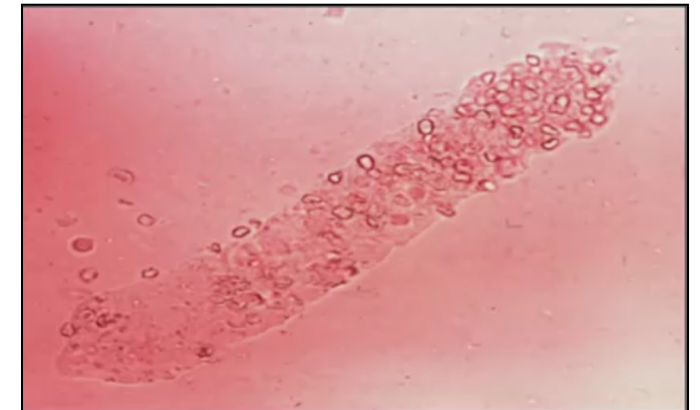
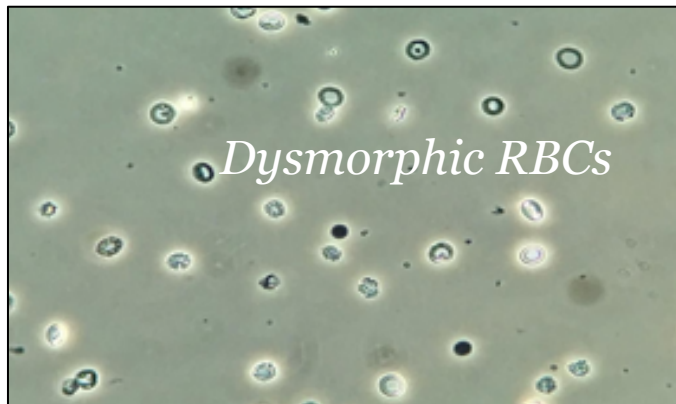
Viral trigger
2-3 days ago

Strep Infection,
10-21 days ago

Hematuria

Gross
Recurrent

Cola/Rust Colored
Isolated



Nephritic: How They Differ

IgA Nephropathy

PSGN

Infectious

Viral trigger
2-3 days ago

Strep Infection,
10-21 days ago

Hematuria

Gross
Recurrent

Cola/Rust Colored
Isolated

*'Patient presents with dark urine. Mom reports
he had same problem last summer...'*

Nephritic: How They Differ

IgA Nephropathy

PSGN

Infectious

Viral trigger
2-3 days ago

Strep Infection,
10-21 days ago

Hematuria

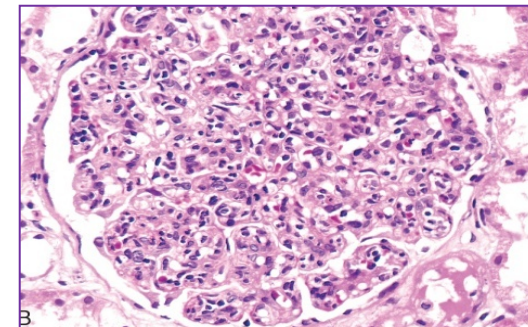
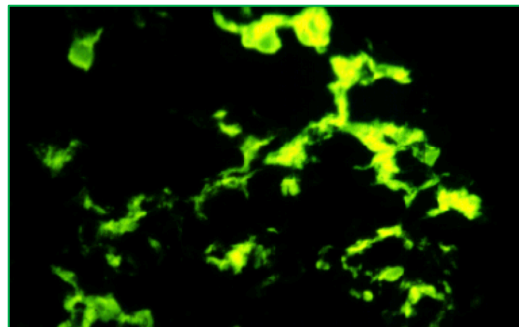
Gross
Recurrent

Cola/Rust Colored
Isolated

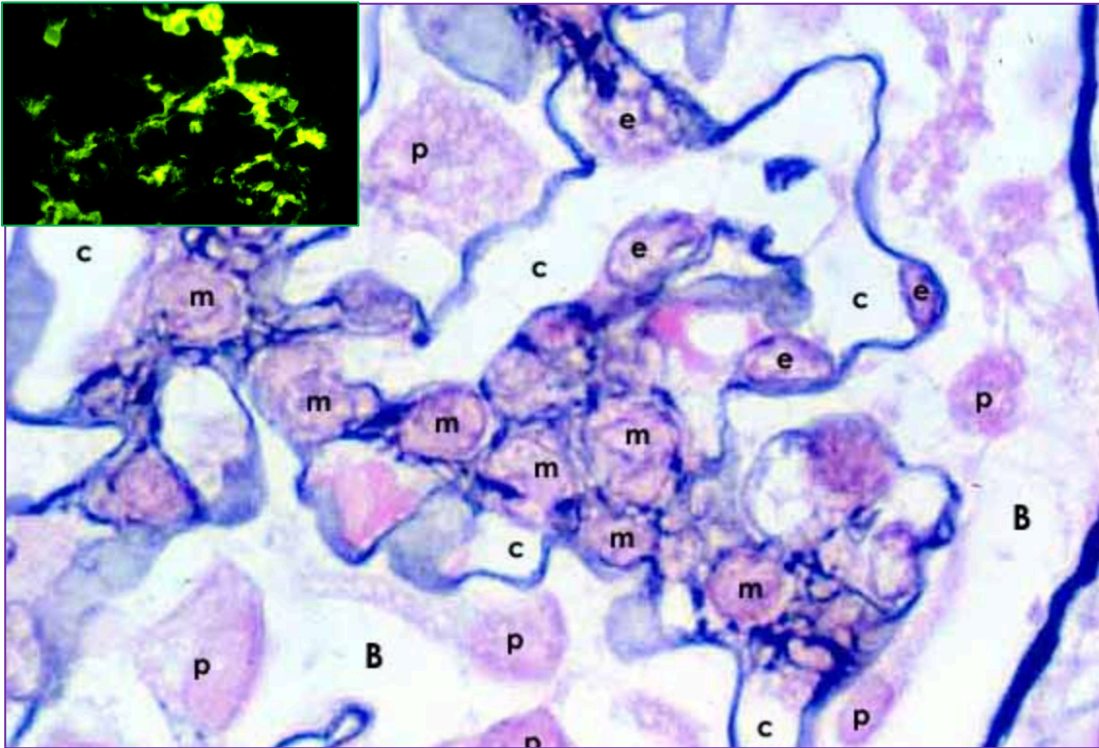
Key Pathology

Mesangial Cell
Smudgy IF

Subendothelial IC
Subepithelial 'humps'



Pathology: IgA Nephropathy



Silver stain: Interspersed appearance of intraglomerular mesangial cells

Mesangial

*Glomerular
Function/GBM*

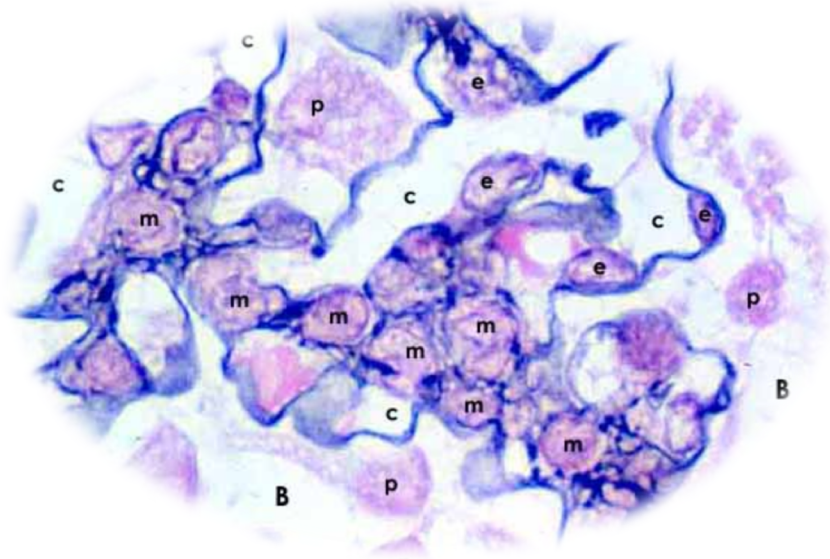
Podocyte

Endothelium



Cross talk

Pathology: IgA Nephropathy



Mesangial Cells*

*Generate extracellular matrix (e.g. nodular, lobular)
'Housekeeping' function (e.g. phagocytosis)*

Mesangial

*Glomerular
Function/GBM*

Podocyte

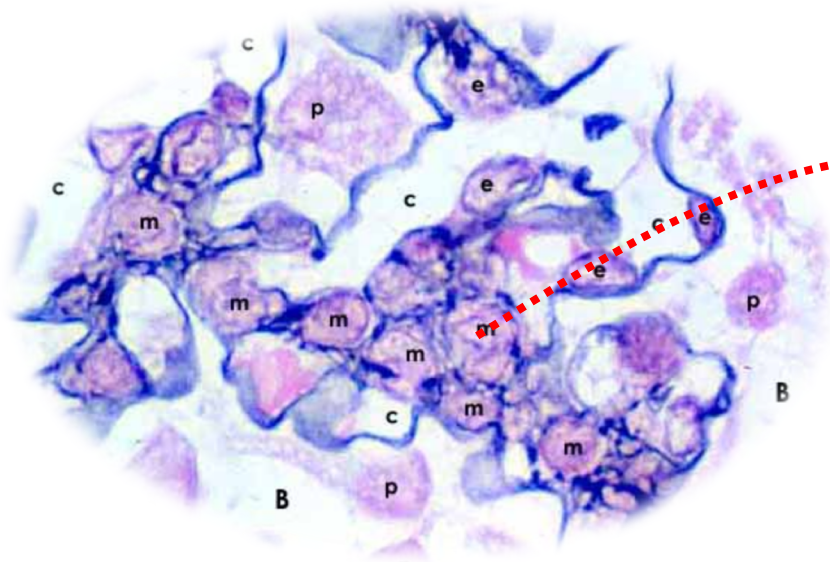
Endothelium



Cross talk

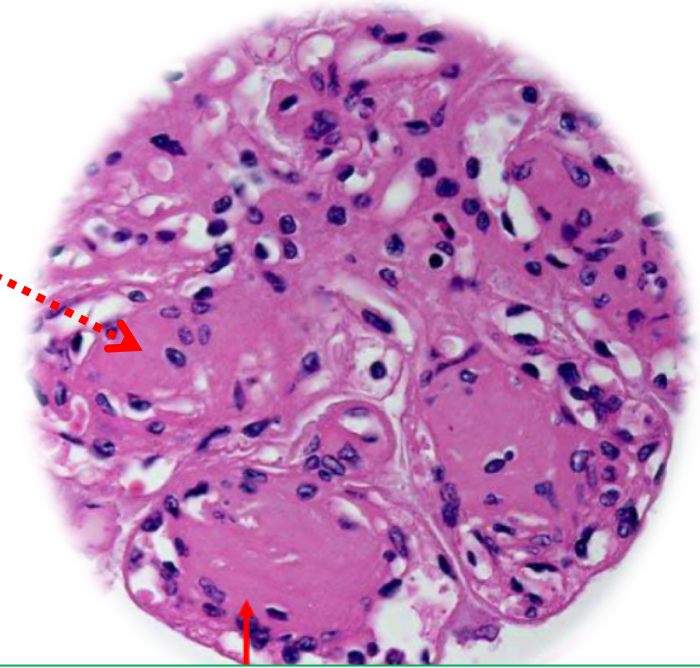
* J Am Soc Nephrol 20: 1179–1187, 2009

Pathology: IgA Nephropathy



Mesangial Cells*

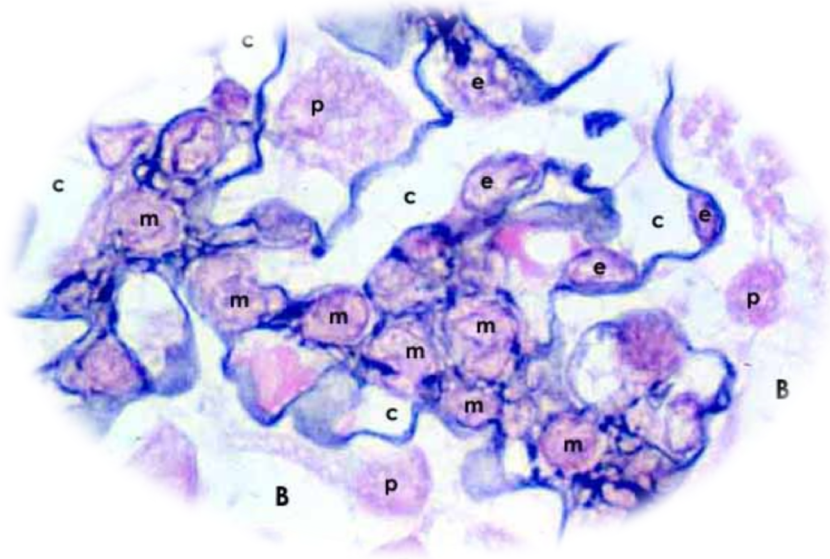
*Generate extracellular matrix (e.g. nodular, lobular)
'Housekeeping' function (e.g. phagocytosis)*



Nodular Glomerulosclerosis
(i.e. Kimmelstiel-Wilson Nodules)

* J Am Soc Nephrol 20: 1179–1187, 2009

Pathology: IgA Nephropathy



Mesangial Cells*

Generate extracellular matrix (e.g. nodular, lobular)
'Housekeeping' function (e.g. phagocytosis)

Mesangial

*Glomerular
Function/GBM*

Podocyte

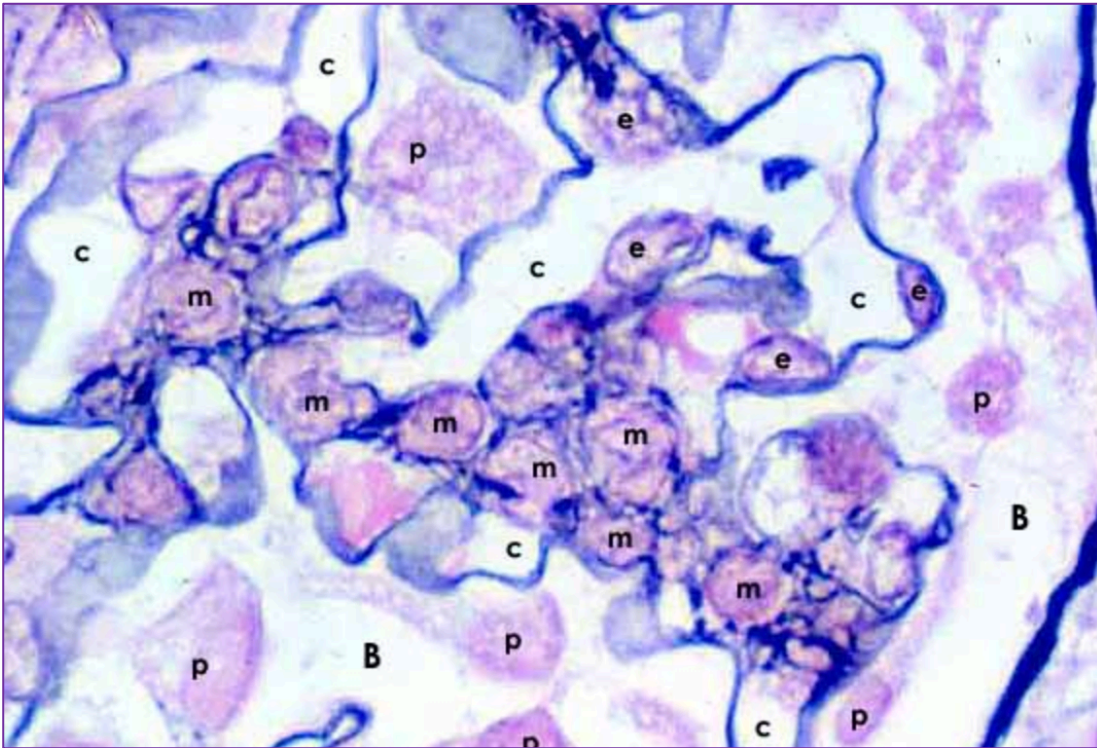
Endothelium



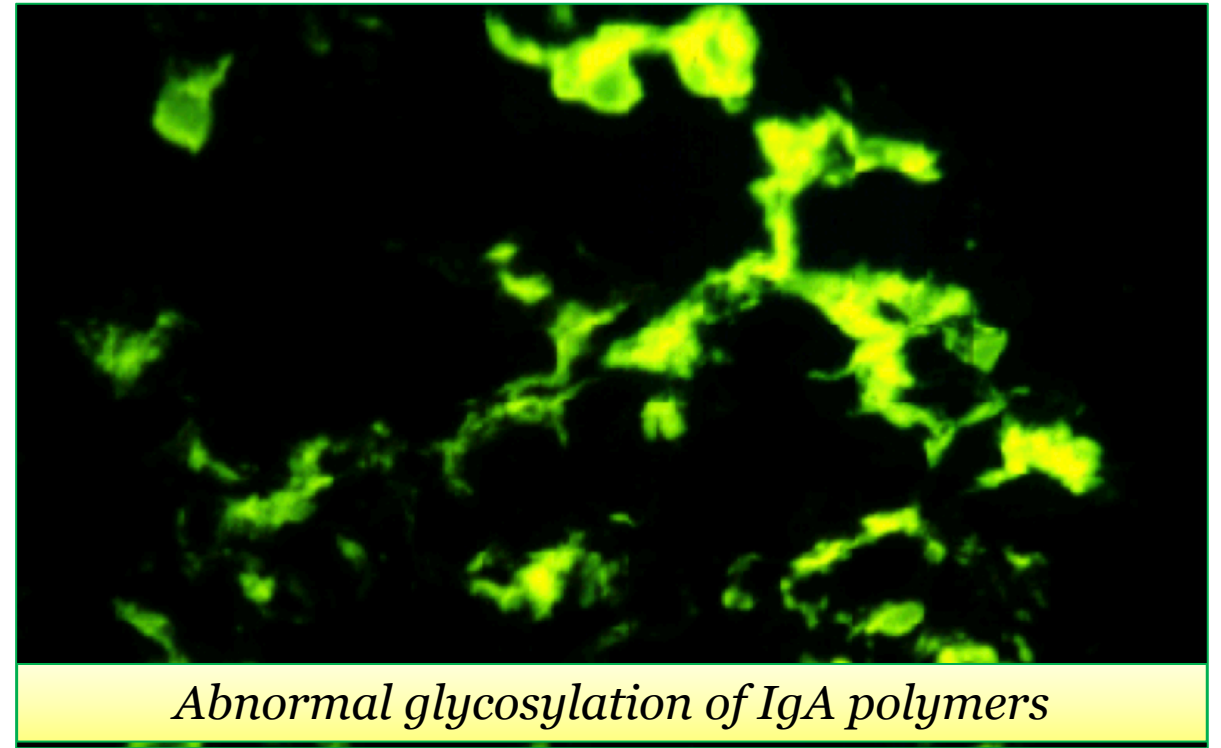
Cross talk

* J Am Soc Nephrol 20: 1179–1187, 2009

Pathology: IgA Nephropathy



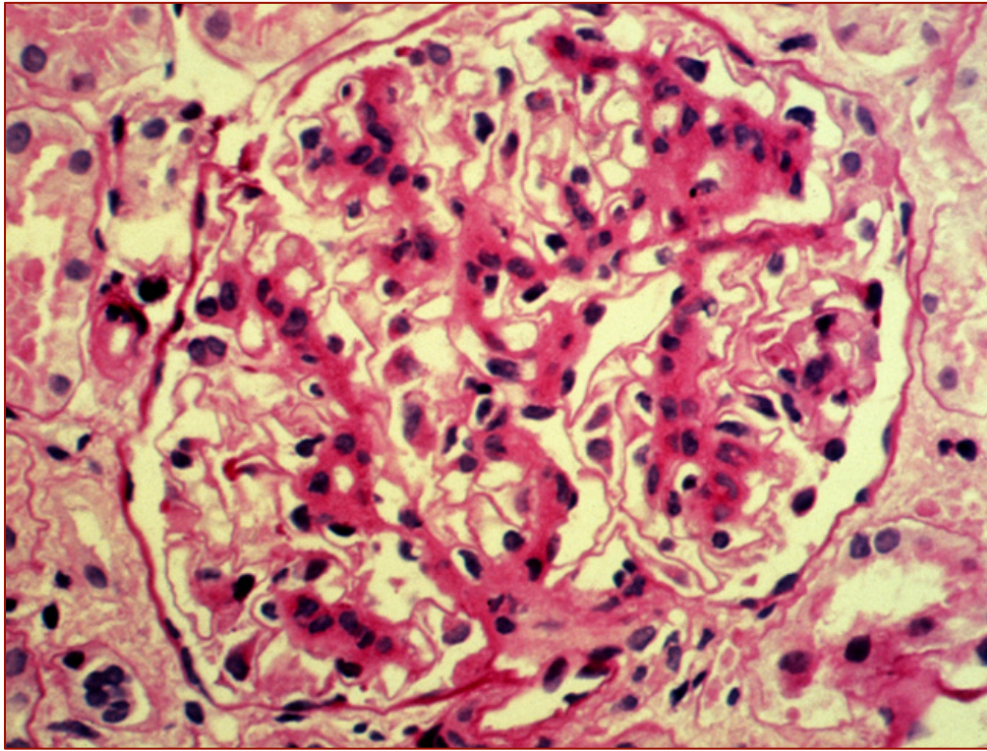
Silver stain: Interspersed appearance of intraglomerular mesangial cells



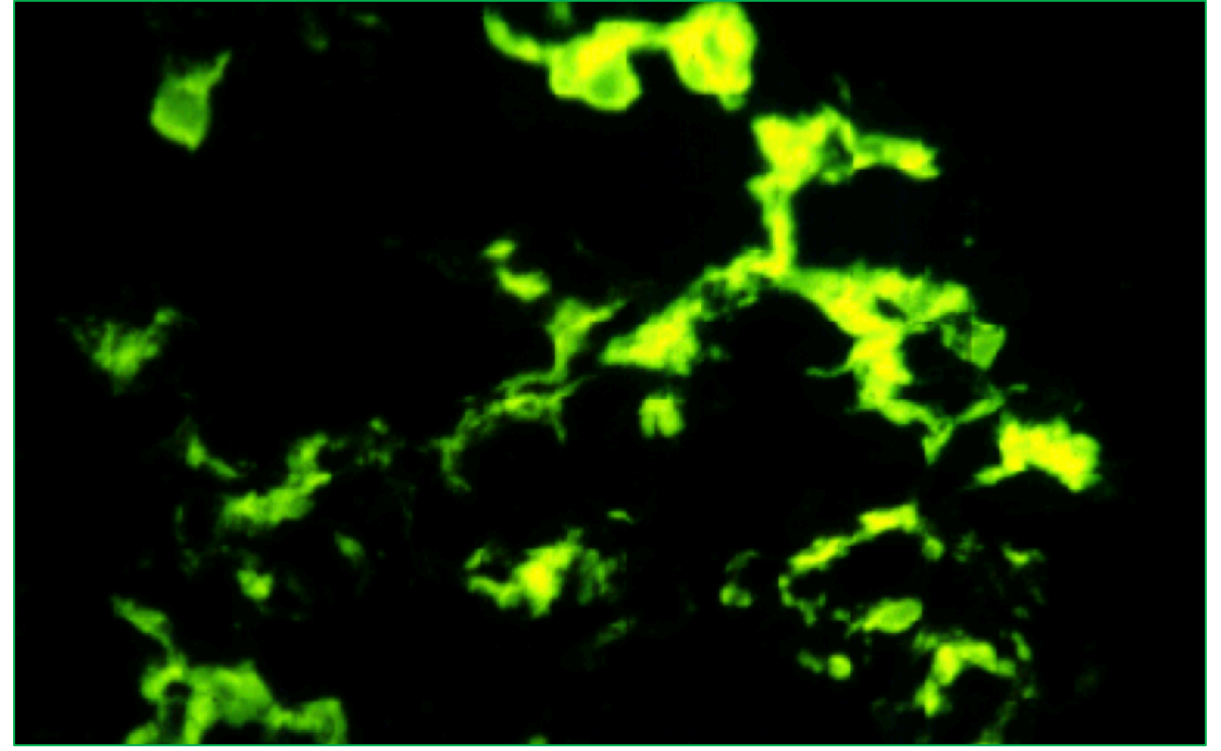
Abnormal glycosylation of IgA polymers

Classic Immunofluorescent Pattern:
Diffuse mesangial immunostaining for IgA

Pathology: IgA Nephropathy



Light microscopy: mesangial matrix expansion with mild cellular proliferation



Classic Immunofluorescent Pattern:
Diffuse mesangial immunostaining for IgA

Nephritic: How They Differ

IgA Nephropathy

PSGN

Infectious

Viral trigger
2-3 days ago

Strep Infection,
10-21 days ago

Hematuria

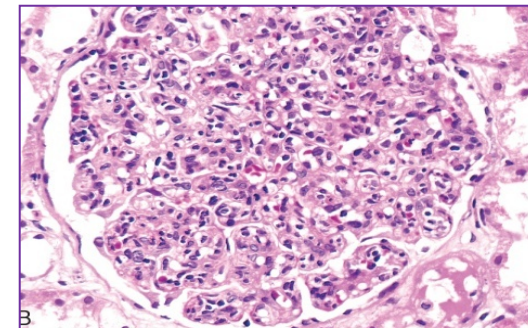
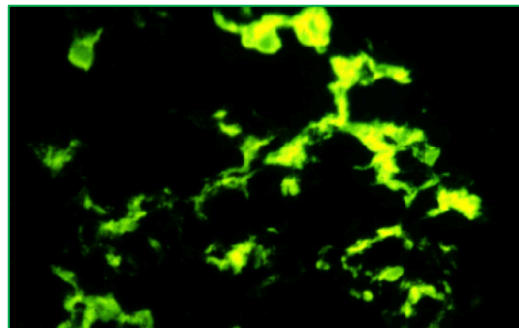
Gross
Recurrent

Cola/Rust Colored
Isolated

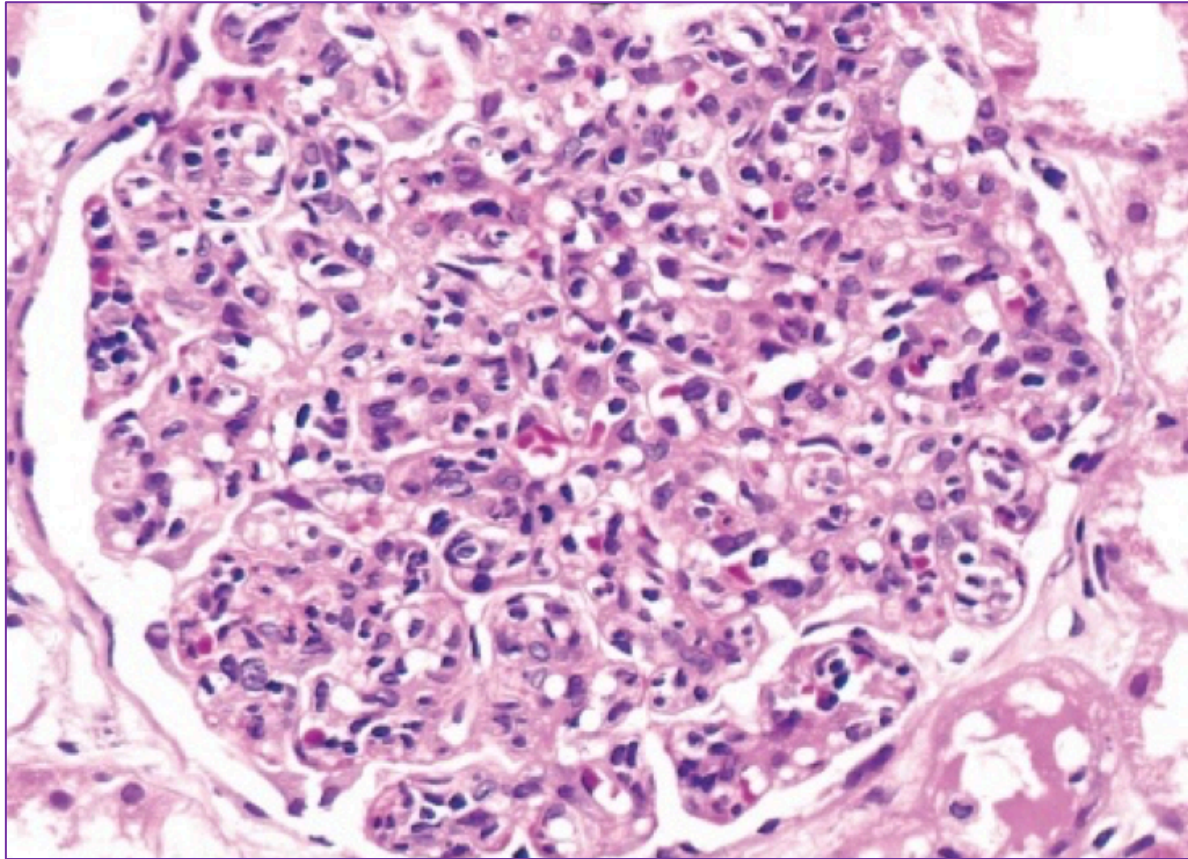
Key Pathology

Mesangial Cell
Smudgy IF

Subendothelial IC
Subepithelial humps



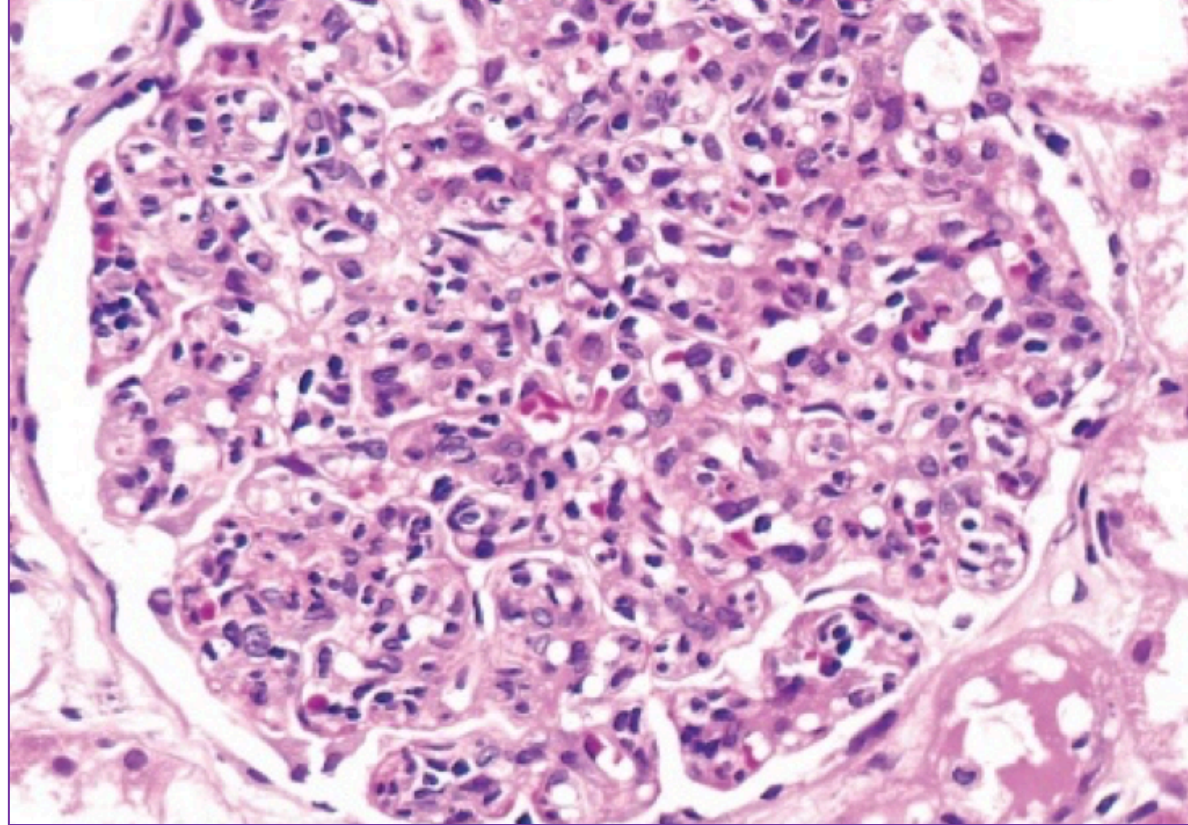
Pathology: PSGN



Acute Proliferative Glomerulonephritis

Proliferative (hypercellularity): infiltrate of inflammatory cells, endothelial and mesangial cell
Subendothelial deposition of **circulating immune complexes** with **complement activation**

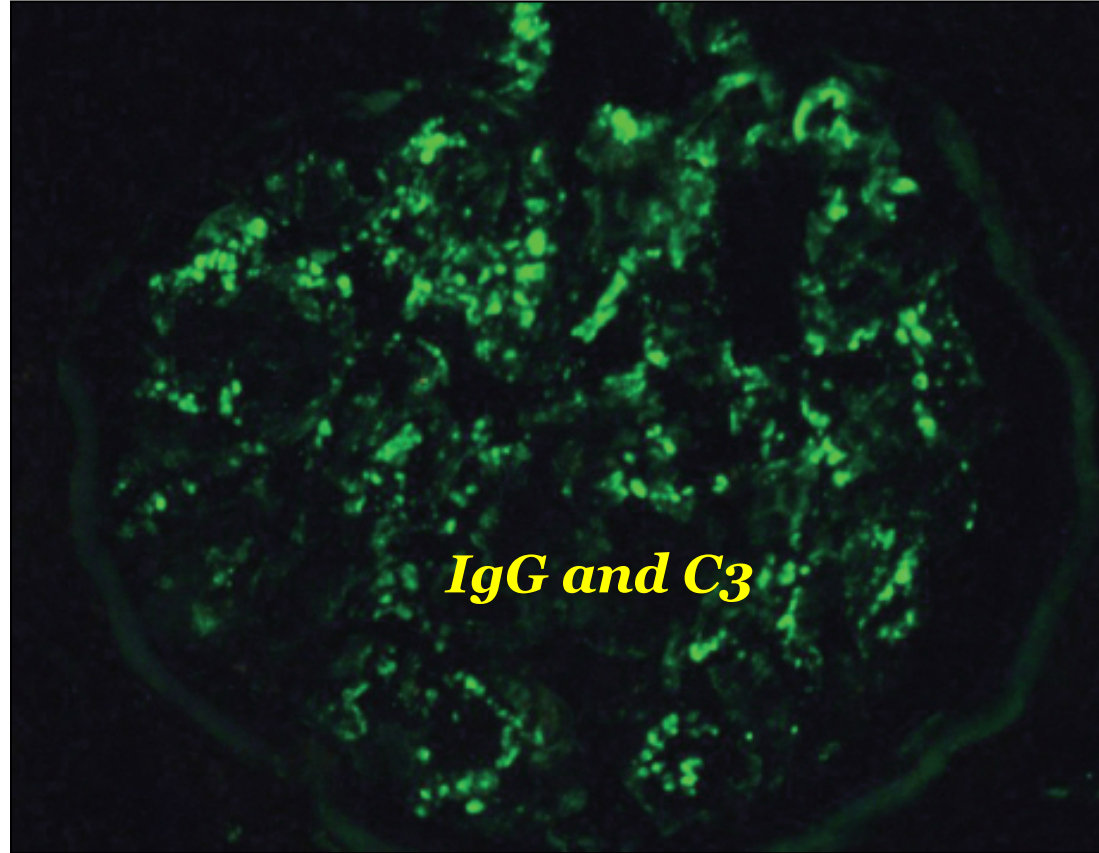
Same image for Diffuse Proliferative GN of SLE



Acute Proliferative Glomerulonephritis

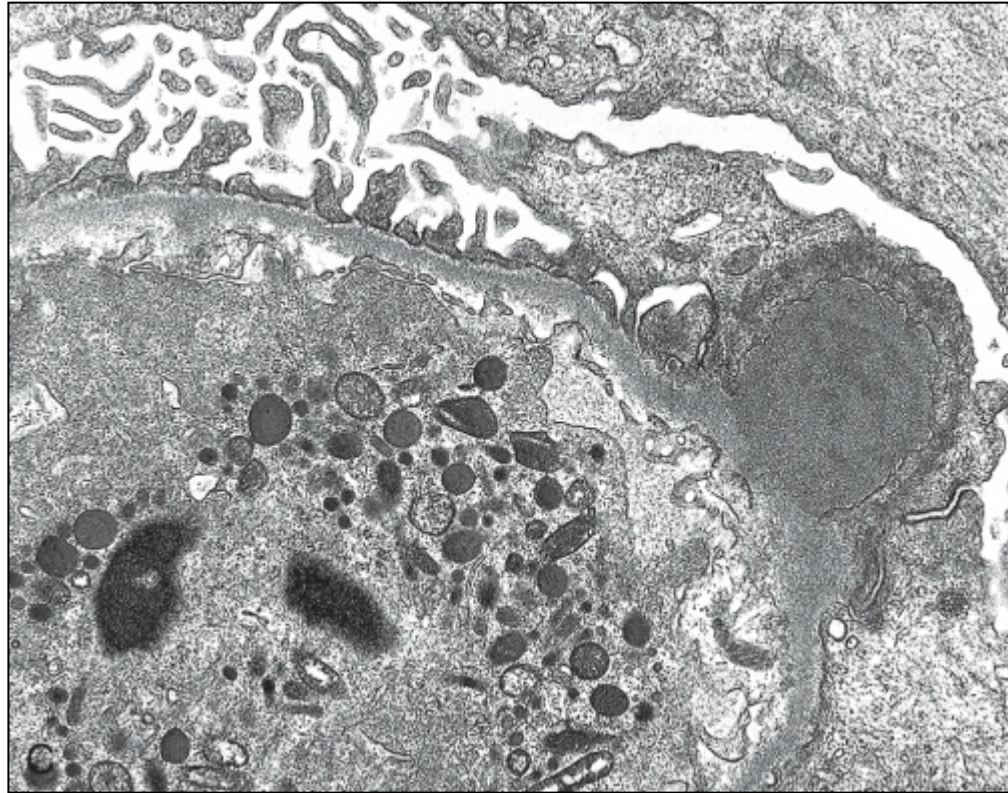
Proliferative (hypercellularity): infiltrate of inflammatory cells, endothelial and mesangial cell
Subendothelial deposition of **circulating immune complexes** with **complement activation**

Pathology: PSGN



Granular Immunofluorescence (immunostain IgG/C3)
'Lumpy-bumpy appearance' = **Focal** deposits in GBM

Pathology: PSGN

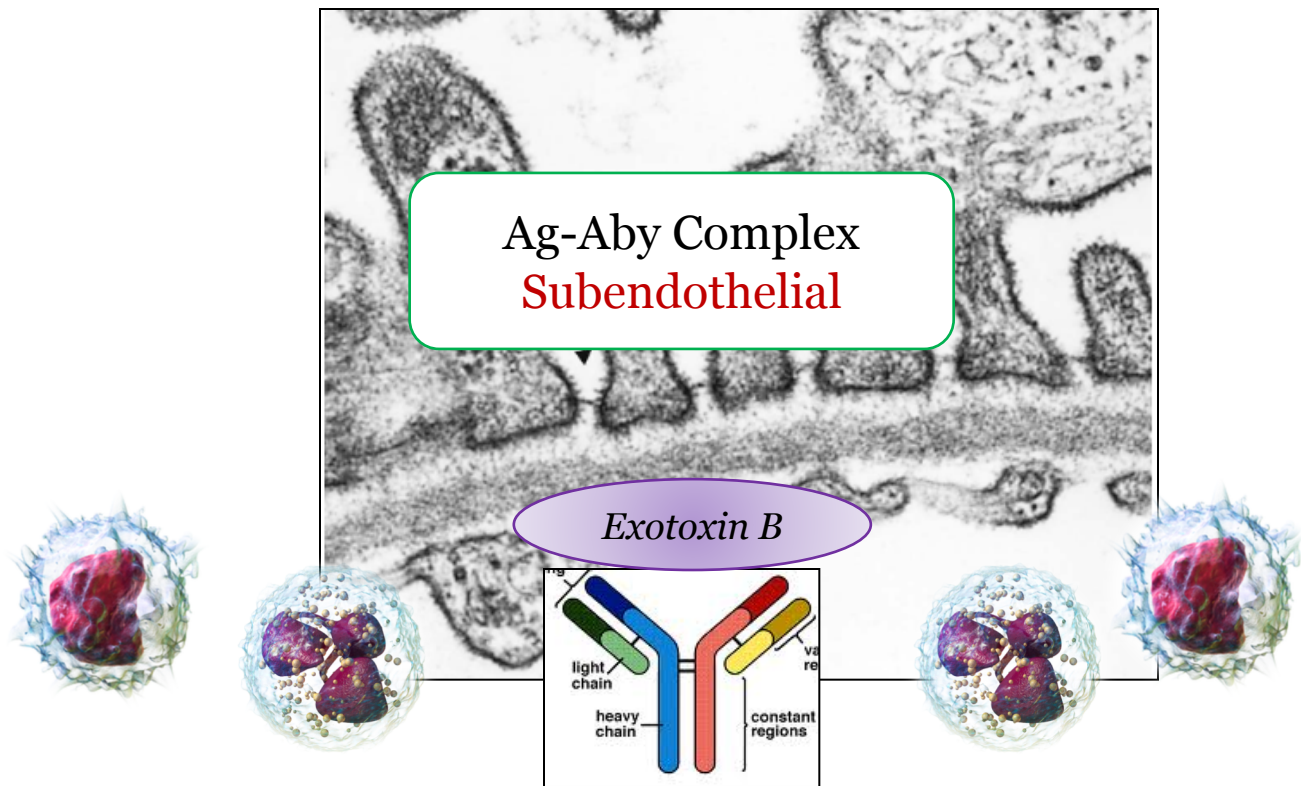


EM: sub-**ep**ithelial hump (*e.g. deposit*)

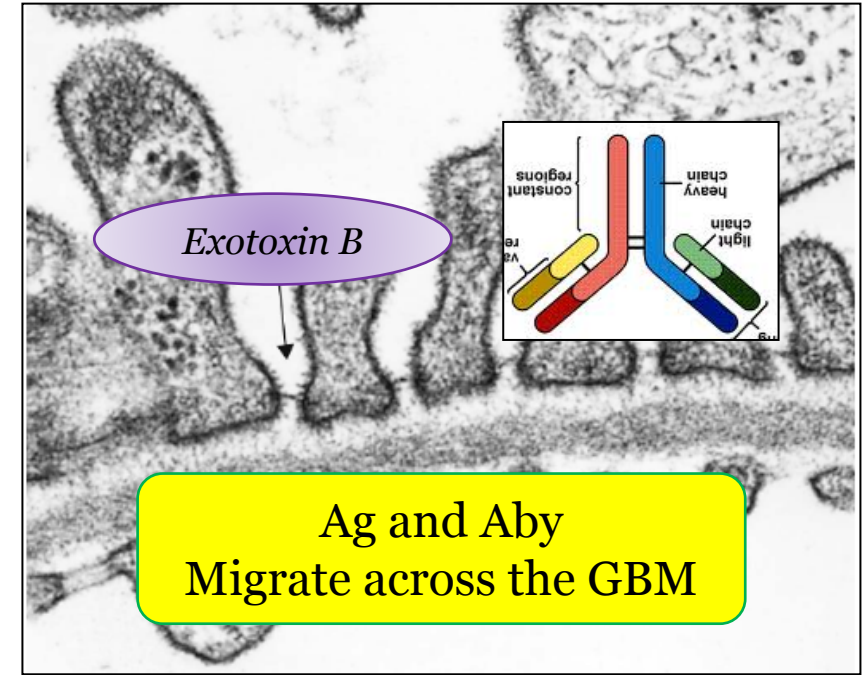
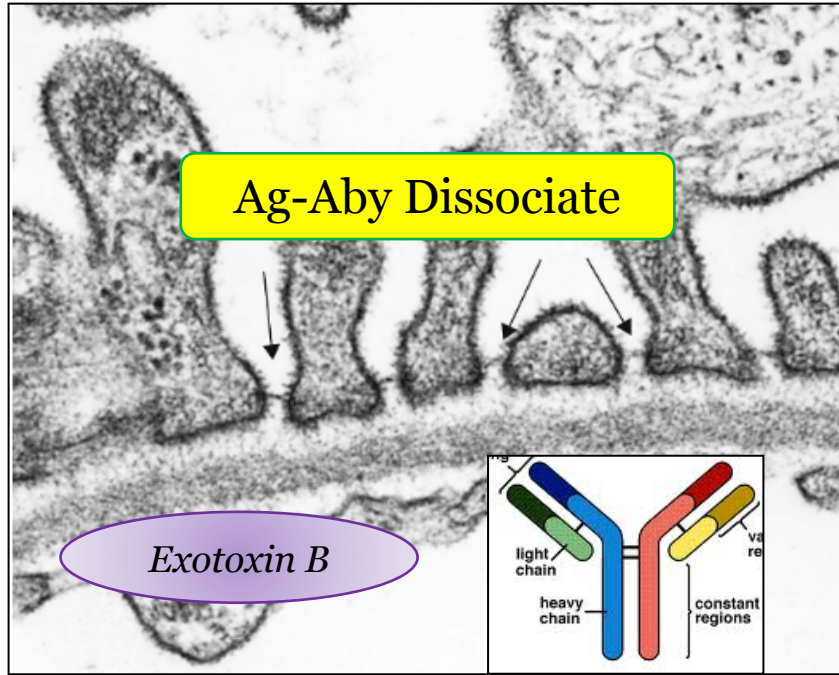
Poststreptococcal GN
Strep Pyogenes
Group A β -hemolytic (GAS)

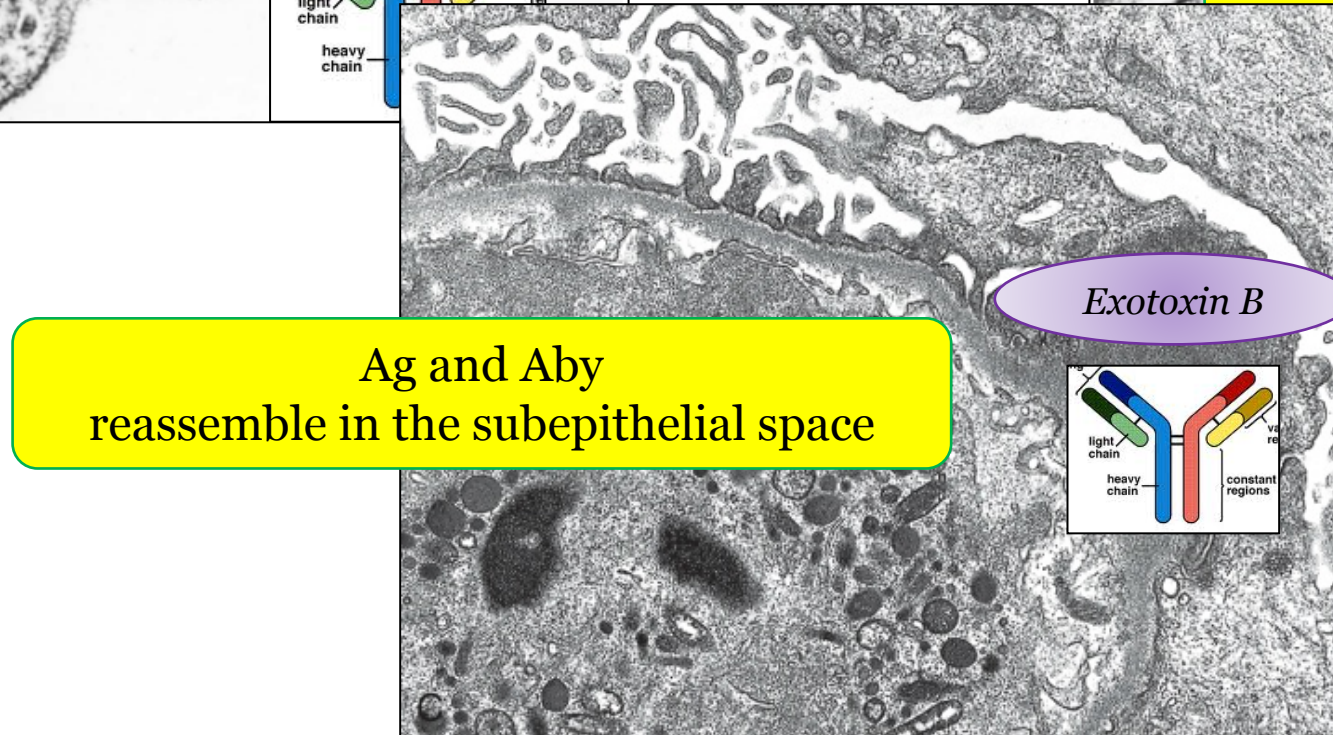
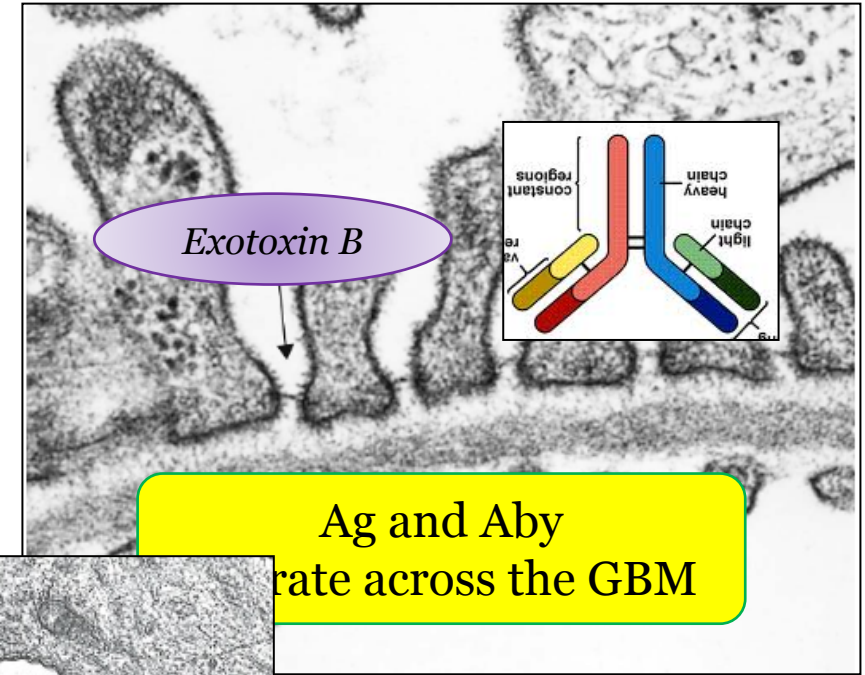
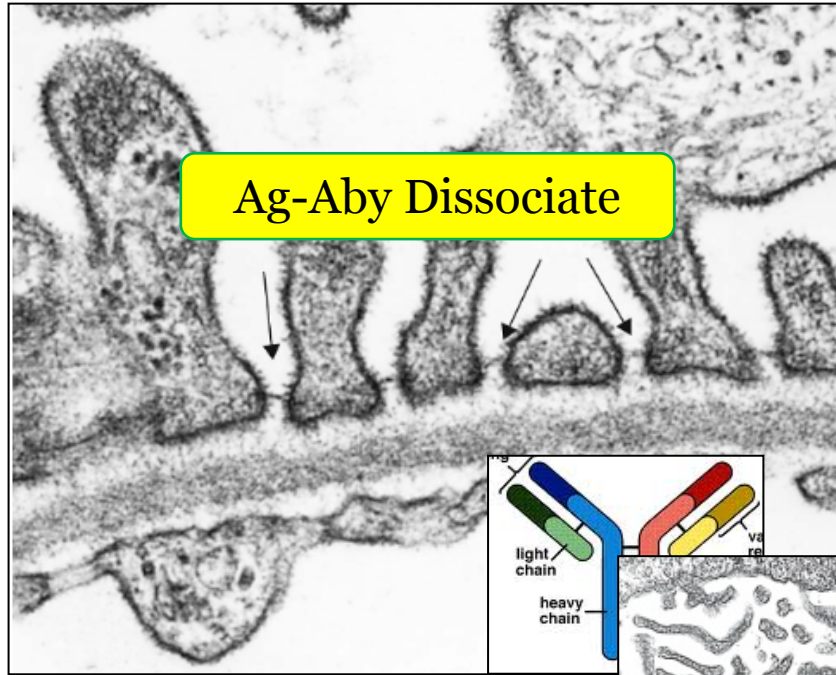


Nephritogenic Strains (Exotoxin B*)



* *Streptococcal pyogenic exotoxin B (SpeB)*





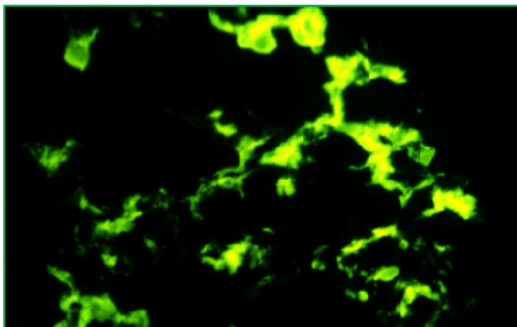
Nephritic: How They Differ

IgA Nephropathy

Viral trigger
2-3 days ago

Gross
Recurrent

Mesangial Cell
Smudgy IF

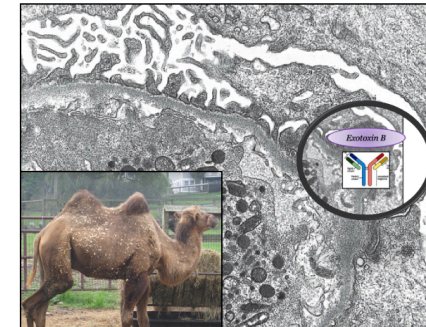
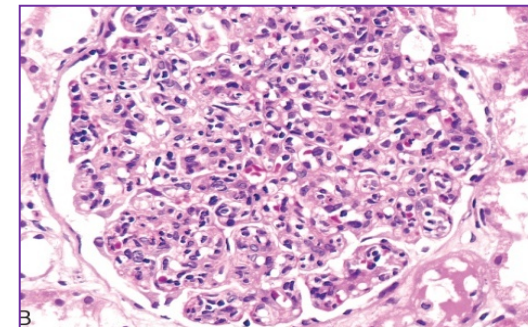


PSGN

Strep Infection,
10-21 days ago

Cola/Rust Colored
Isolated

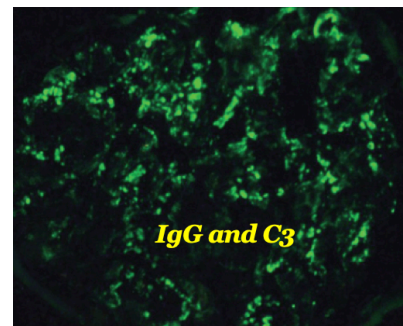
Subendothelial IC
Subepithelial humps



Infectious

Hematuria

Key Pathology



Nephritic: How They Differ

IgA Nephropathy

PSGN

Clinical Course and Associations

the Language of the Nephritic Syndromes

AKI/Elevated Cr

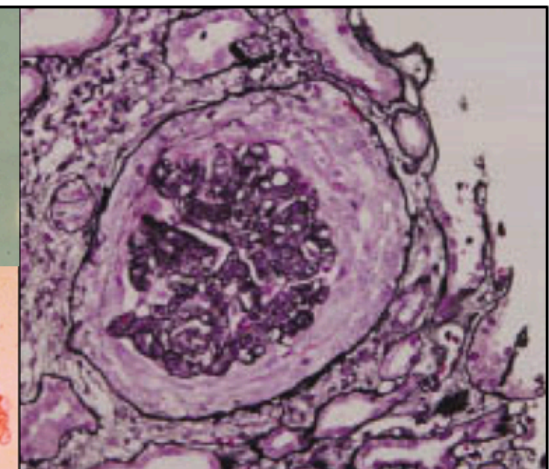
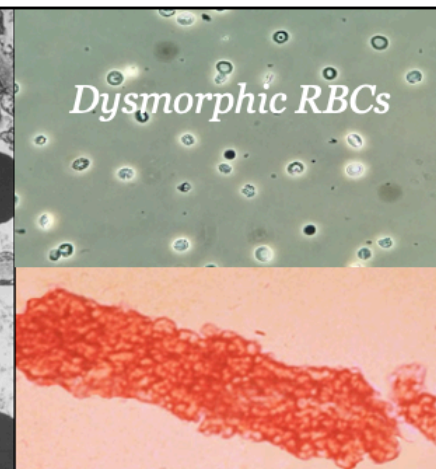
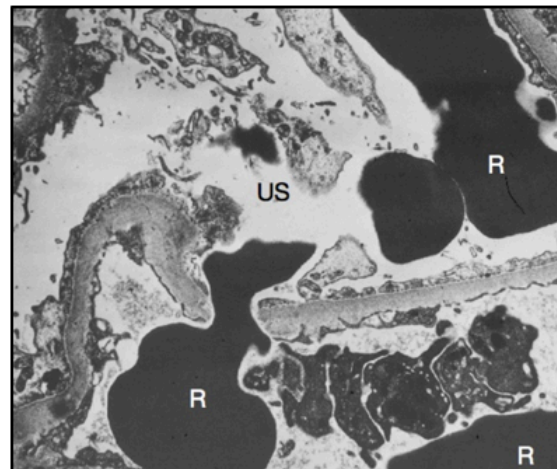
RBC Casts

RPGN/Crescents

Proteinuria, mild

Renal Injury:
Elevated Creatinine
HTN
Edema, mild (\downarrow GFR)

Clinico-Pathology
RPGN*
Crescents



Nephritic: How They Differ

IgA Nephropathy

Clinical Course and Associations

IgA Vasculitis
(*Henoch-Schonlein Purpura*)

the Tetrad

Skin: purpura
Hematochezia: GI sxs
Arthralgia: joint pain
Renal/Kidney: IgA



Nephritic: How They Differ

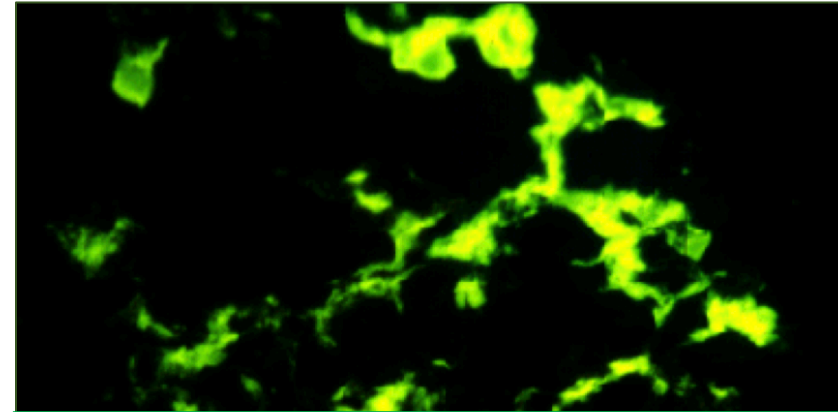
IgA Nephropathy

Clinical Course and Associations

IgA Vasculitis
(Henoch-Schonlein Purpura)

the Tetrad

Skin: purpura
Hematochezia: GI sx's
Arthralgia: joint pain
Renal/Kidney: IgA



IgA Vasculitis with identical renal manifestations to ***IgA Nephropathy***

Nephritic: How They Differ

Clinical Course and Associations

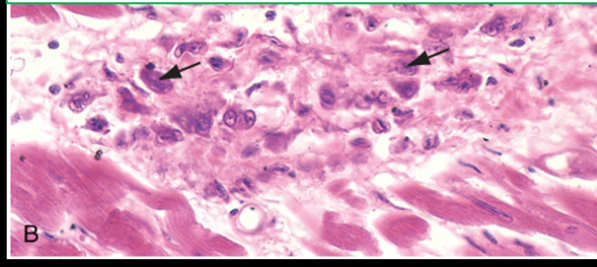
Strep Pyogenes, Group A β -hemolytic

Rheumatic Fever

Type II



Rheumatic Carditis
(Aschoff body)



Hypersensitivity

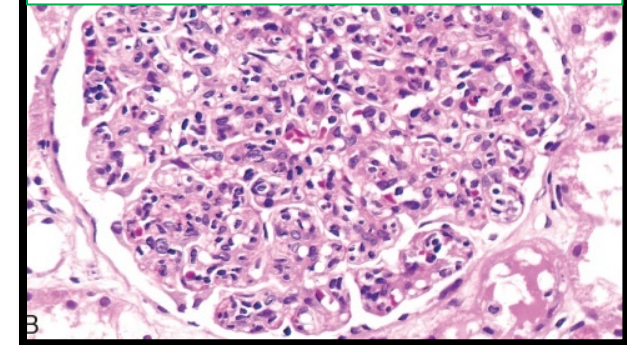


PSGN

Type III



APGN



Nephritic: How They Differ

Clinical Course and Associations

Strep Pyogenes, Group A β -hemolytic

Diagnostic Studies

Streptozyme test

(antibodies against extracellular streptococcal products):

- Streptolysin (ASO)
- Streptokinase (ASKase)
- Nicotinamide-adenine dinucleotidase (NAD)
- Hyaluronidase (AHase)
- DNAase B

skin

Decreased serum complement levels

Nephritic: How They Differ

PSGN

Clinical Course and Associations

Outcomes

Kids (6-10) > **Adults**

Favorable (95%) > **Less favorable (40% → CKD)**

Supportive therapy (no steroids)

Nephritic: How They Differ

PSGN

Clinical Course and Associations

Outcomes

Kids > Adults

Favorable (95%) > Less favorable (40% → CKD)

Supportive therapy (**no steroids**)

Minimal Change

Rx: Steroid Responsive

Best Rx for PSGN?

A. Observation and Supportive Care

Steroids do not help

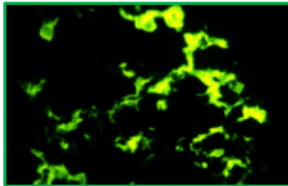
Nephritic: How They Differ

IgA Nephropathy

Viral trigger
2-3 days ago

Gross
Recurrent

Mesangial Cell
Smudgy IF



Skin: **purpura**
Hematochezia: **GI sxs**
Arthralgia: joint pain
Renal/**Kidney**: IgA



Infectious

Hematuria

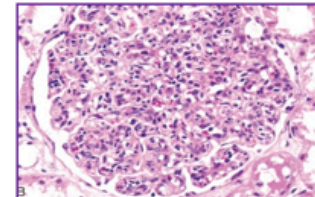
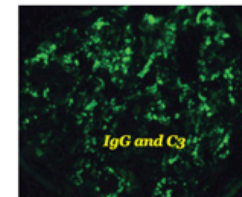
Key Pathology

PSGN

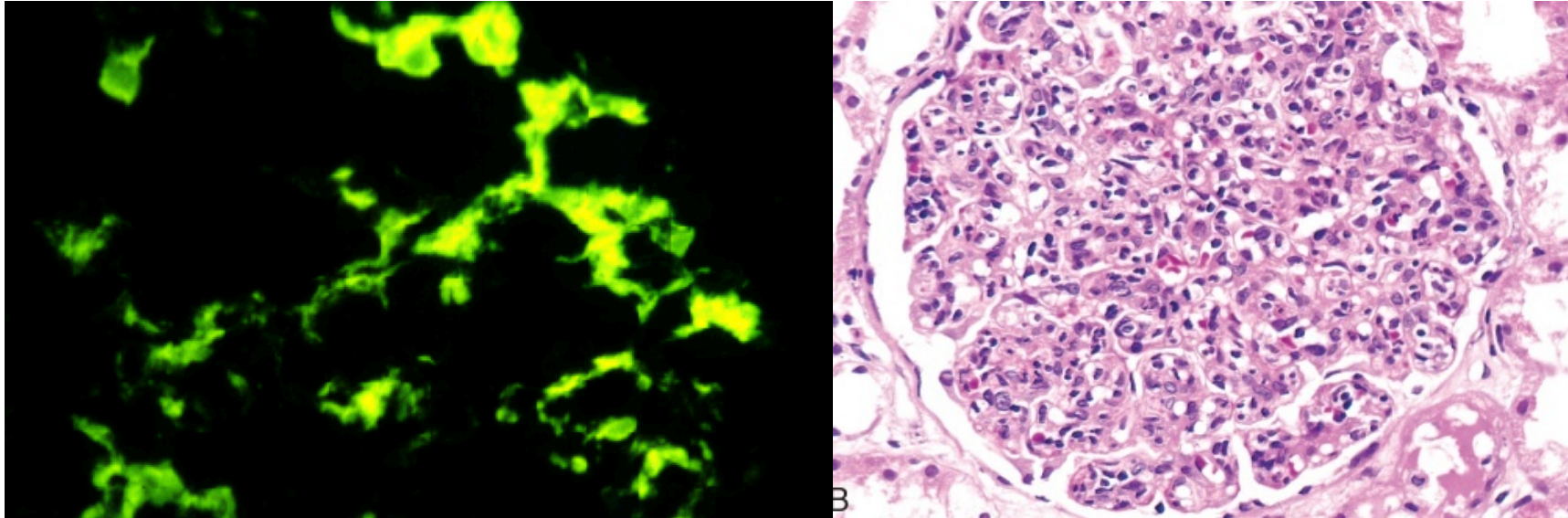
Strep Infection,
10-21 days ago

Cola/Rust Colored
Isolated

Subendothelial IC
Subepithelial humps



Part 3a. Nephritic Syndromes (**IgA Nephropathy** and **PSGN***) for USMLE Step One



**Post-Streptococcal Glomerulonephritis*

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