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Pathology GUS

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Pathology Lecture 3
Nephritic syndrome

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Nephritic Syndrome: Presentation

- **PHAROH**
- ***P**roteinuria*
  - *<3.5g/1.73m2/day*
- ***H**ematuria*
  - *Abrupt onset*
- ***A**zotemia*
  - *Increased creatinine and urea*
- ***R**BC Casts* Indicates glomerular origin of the hematuria.
- ***O**liguria* Decreased urine output and is a manifestation of the urinary impairment.
- ***H**TN* Related to the fluid retention and the azotemia.

non-nephrotic range of proteinuria, so it's less than 3.5

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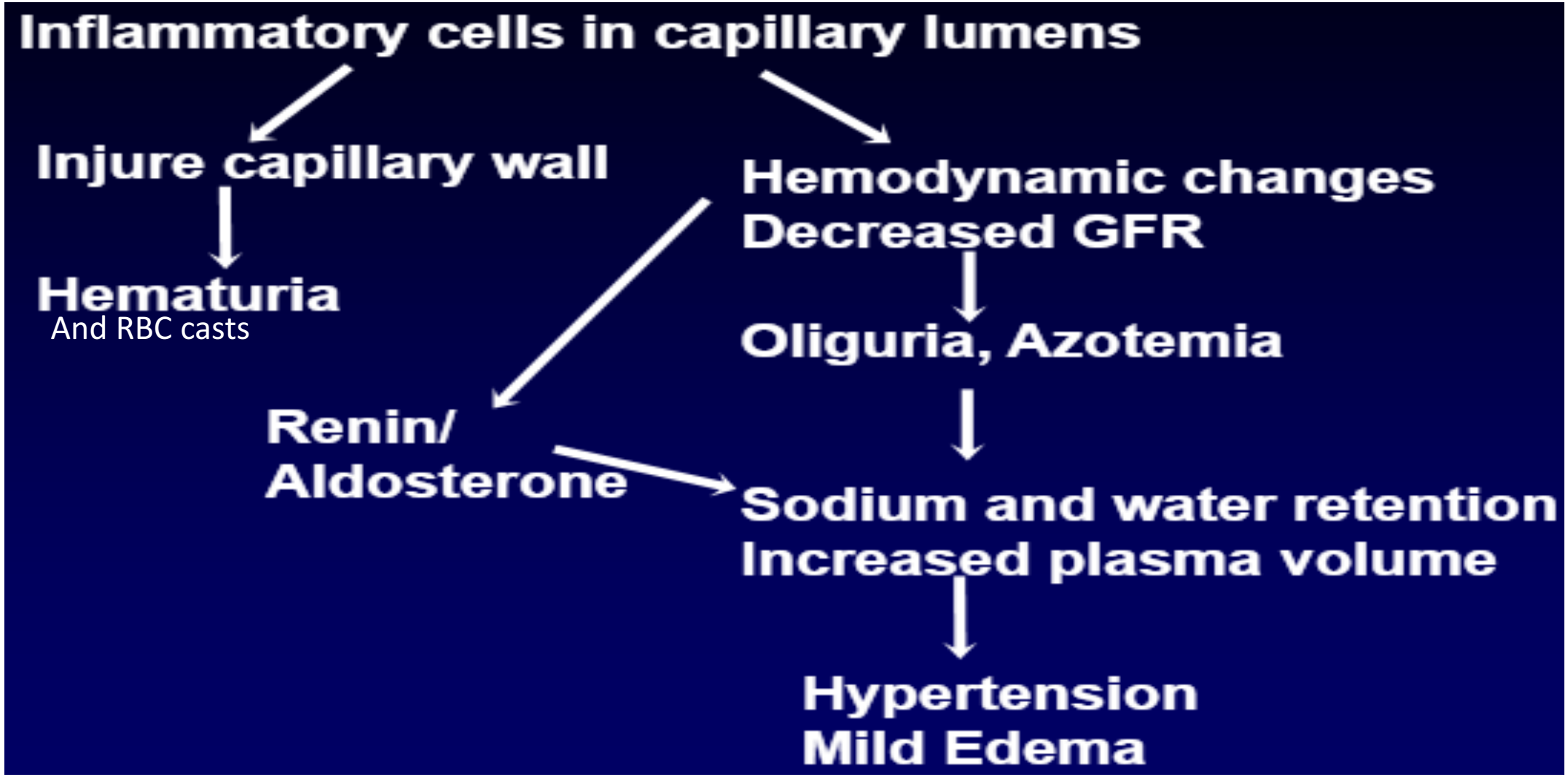
Peripheral Edema/Puffy Eyes

"Smoky Urine"

The Nephritic Syndrome

- Pathogenesis: glomerular inflammation
- **leukocytes & proliferation of cells in glomeruli**
- **Injury of capillary walls → escape of RBCs into urine (hematuria & RBC casts)**
- **↓ GFR → oliguria, fluid retention (edema), and azotemia.**
- **Hypertension (result of both fluid retention and ↑renin release from kidneys).**
- **May have some proteinuria (not heavy)**

Pathogenesis



Glomerular diseases mostly presenting with Nephritic syndrome

1-Membranoproliferative Glomerulonephritis (MPGN)

- **Abnormal proliferation of glomerular cells and inflammation**
- **Usually nephritic syndrome; some have a combined nephrotic-nephritic picture.**

- **<u>Types of MPGN:</u>**

1. **- type I (80% of cases)→ immune complex disease (The inciting antigen is not known)**
2. **- type II → excessive complement activation**

Type I MPGN

- **circulating immune complexes** (circulate , reach the kidney & get deposited inside the glomeruli >> elicit an inflammatory reaction >> begin the cascade of the different changes which will give us the pathogenesis of nephritic syndrome)
- **Many associations: hepatitis B and C; SLE** (systemic lupus erythematosus)**; infected A-V shunts.**

Type II MPGN (*dense-deposit disease) (DDD)*

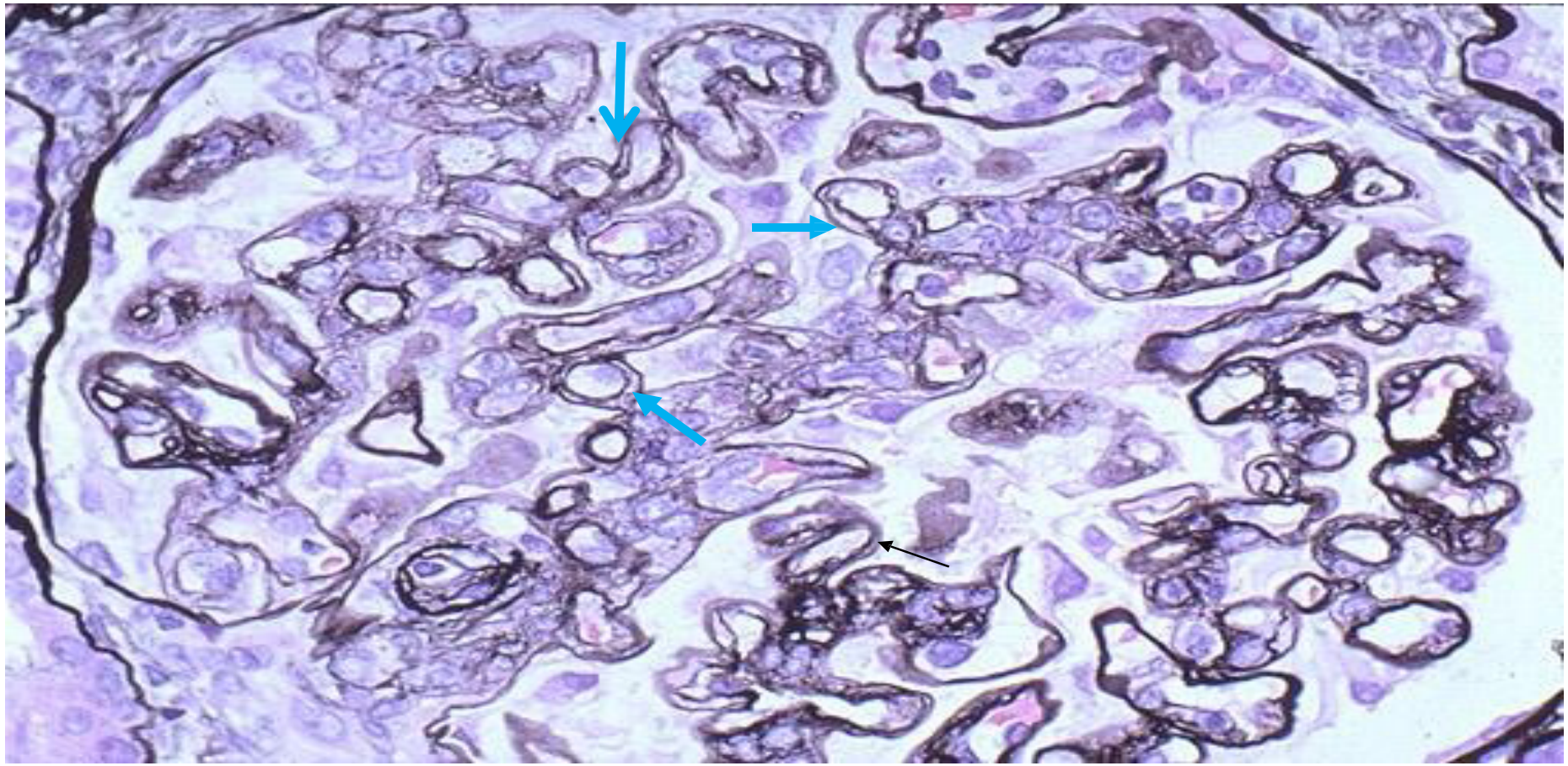
- ***Cause*: excessive complement activation**
- **autoantibody against C3 convertase called C3 nephritic factor (it stabilizes the enzyme and lead to uncontrolled cleavage of C3 and activation of the alternative complement pathway).**

- **<u>Result</u>: consumption of C3 complement and Hypocomplementemia**

The activated c3 particles will travel in the circulation and reach the glomeruli and get deposited there

- **Morphology**
- **LM**
- both types of MPGN are similar by LM.
- glomeruli are large with accentuated **lobular appearance** and show **proliferation of mesangial and endothelial cells** as well as infiltrating leukocytes
- **GBM** (because of the inflammation & the injury inside the basement membrane and the deposition of the immune complexes) **is thickened** (**double contour** or **"tram track"**)
- The **tram track** appearance is caused by **"splitting" of the GBM**

silver stain -double contour of the basement membranes("tram-track") that is characteristic of (MPGN)(arrows).

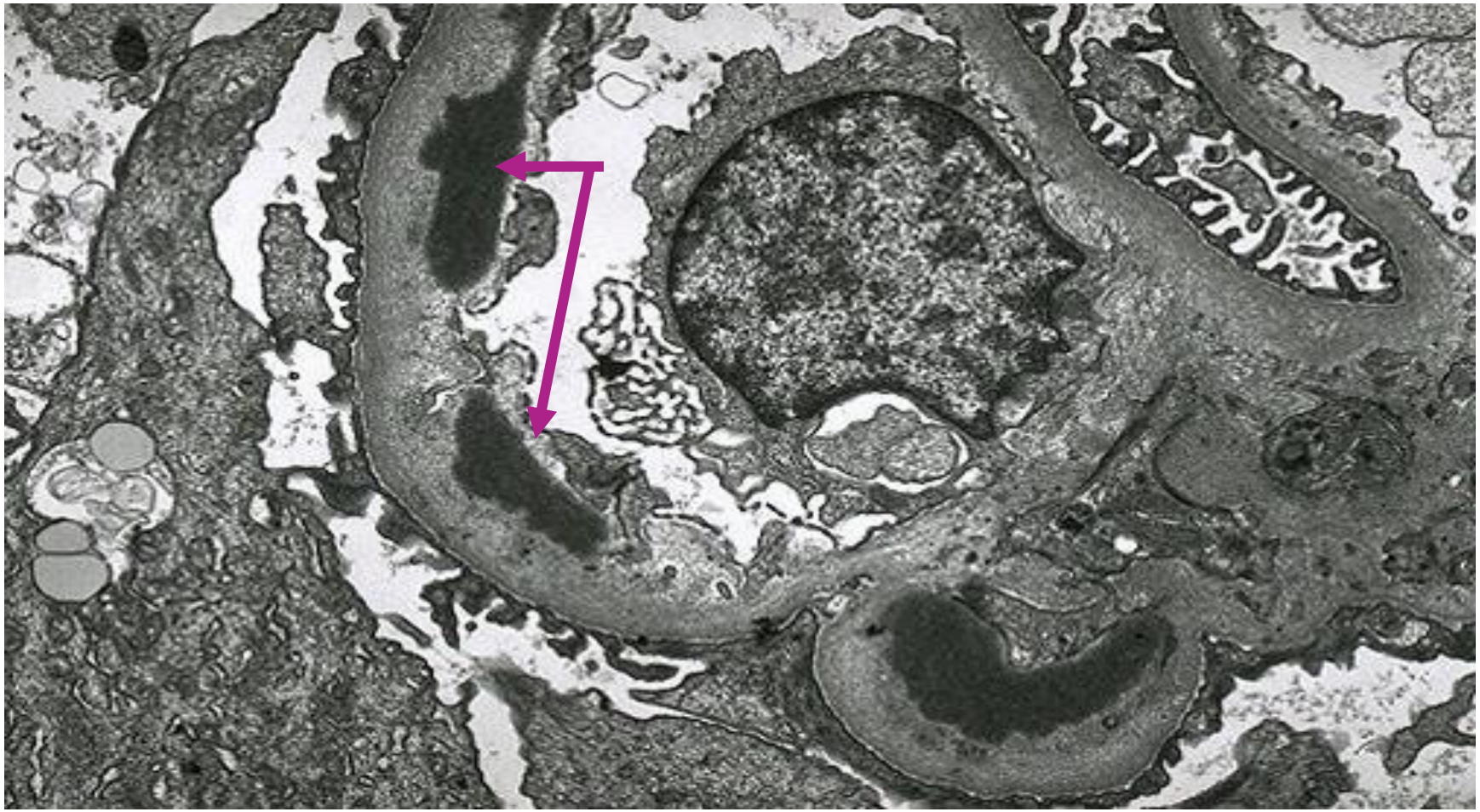


Silver stain>> for illustration of elastic fibers

- **IF (immunofluorescence)**

- **Type I MPGN →subendothelial electron- dense deposits** (**IgG** and **complement C1q and C4)**
- **Type II MPGN→ C3 alone in GBM**

EM- dense deposits in the basement membrane of MPGN type II in a ribbon-like mass (arrows)



- ***Clinical Course*** Regardless of the type
- **prognosis poor.**
- No remission.
- 40% progress to end-stage renal failure.
- 30% had variable degrees of renal insufficiency.
- **Dense-deposit disease (type II) has a worse prognosis.**
- **It tends to recur in renal transplant recipients**

Because the problem is in the immune system

2- Acute Postinfectious (Poststreptococcal) Glomerulonephritis (PSGN)

- deposition of **immune complexes** + proliferation of glomerular cells and leukocytes (neutrophils).
- Not direct infection of the kidney

- Cause: **an immune-mediated reaction to a previous infection of pharynx or skin**
- Post-streptococcal GN (most common).
- Infections by other organisms possible as pneumococci and staphylococci

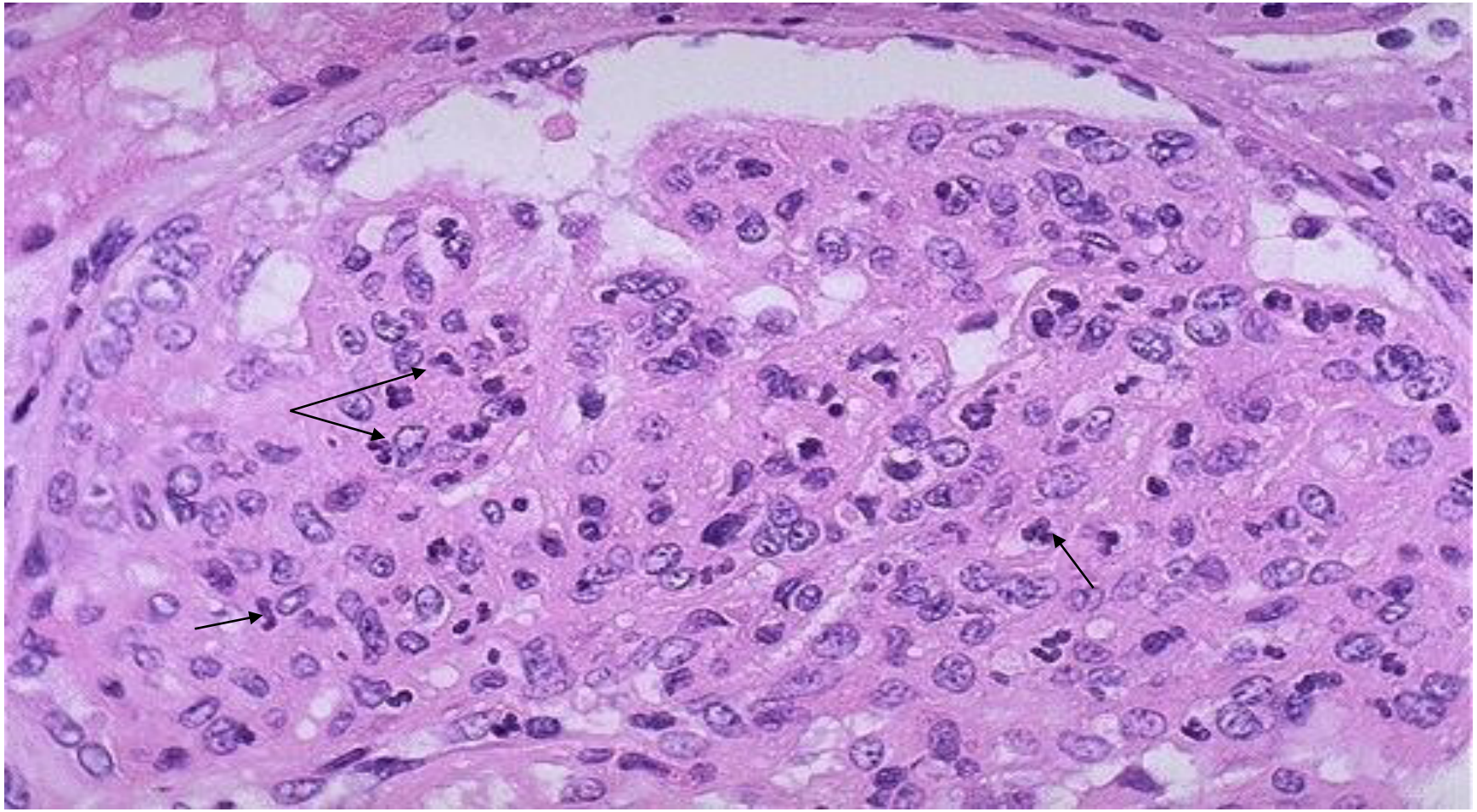
Poststreptococcal GN

- 1-4 wks after recovery from a group A streptococcal infection **(pharynx or skin).**
- A few strains (3%)of **β-hemolytic streptococci** are capable of this
- **Mechanism: binding of immune complexes to GBM proteins /**
- **or antibodies to bacterial antigens "planted" in the GBM**

This will lead to activation of the inflammatory cascade of the glomeruli--->nephritic syndrome

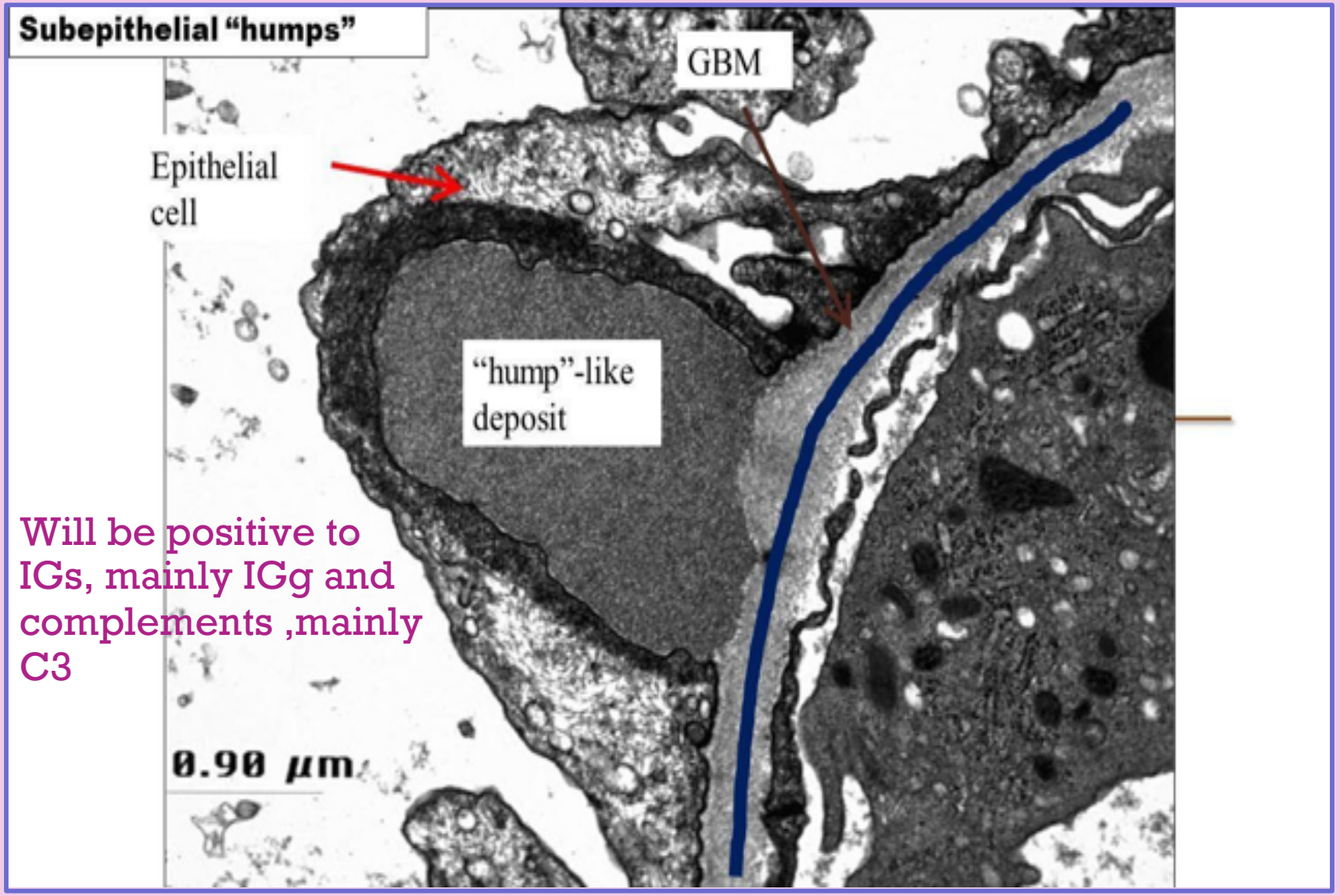
PSGN: increased epithelial, endothelial, and mesangial cells as well as neutrophils in and around the capillary loops (arrows)

Will lead to occlusion of the capillaries lumena



- **LM**
- proliferation of endothelial and mesangial cells and neutrophilic infiltrate.
- **IF**
- **deposits of IgG and complement** within the **capillary walls**
- **EM**
- immune complexes “**subepithelial "humps"** in GBM.

Looks like the humb of the camel



Will be positive to IGs, mainly IGg and complements ,mainly C3

PSGN- Clinical Course

- **acute onset .**
- **Many of patients are children**
- **fever, nausea, and nephritic syndrome.**
- **gross hematuria.**
- **Mild proteinuria.**
- **Serum complement levels are low during the active phase of the disease.** **Hypocomplementemia**
- **↑serum anti-streptolysin O antibody titers.** Evidence of a prior infection with streptococci
- **Recovery occurs in most children.** By clearance of antibodies after a period of time

3- IgA Nephropathy

- *one of the most common causes of recurrent microscopic or gross hematuria*
- children and young adults.
- hematuria (microscopic or gross) 1 or 2 days after **nonspecific** upper respiratory tract infection.
- Hematuria lasts several days and then subsides and then recur every few months. (Episodic)

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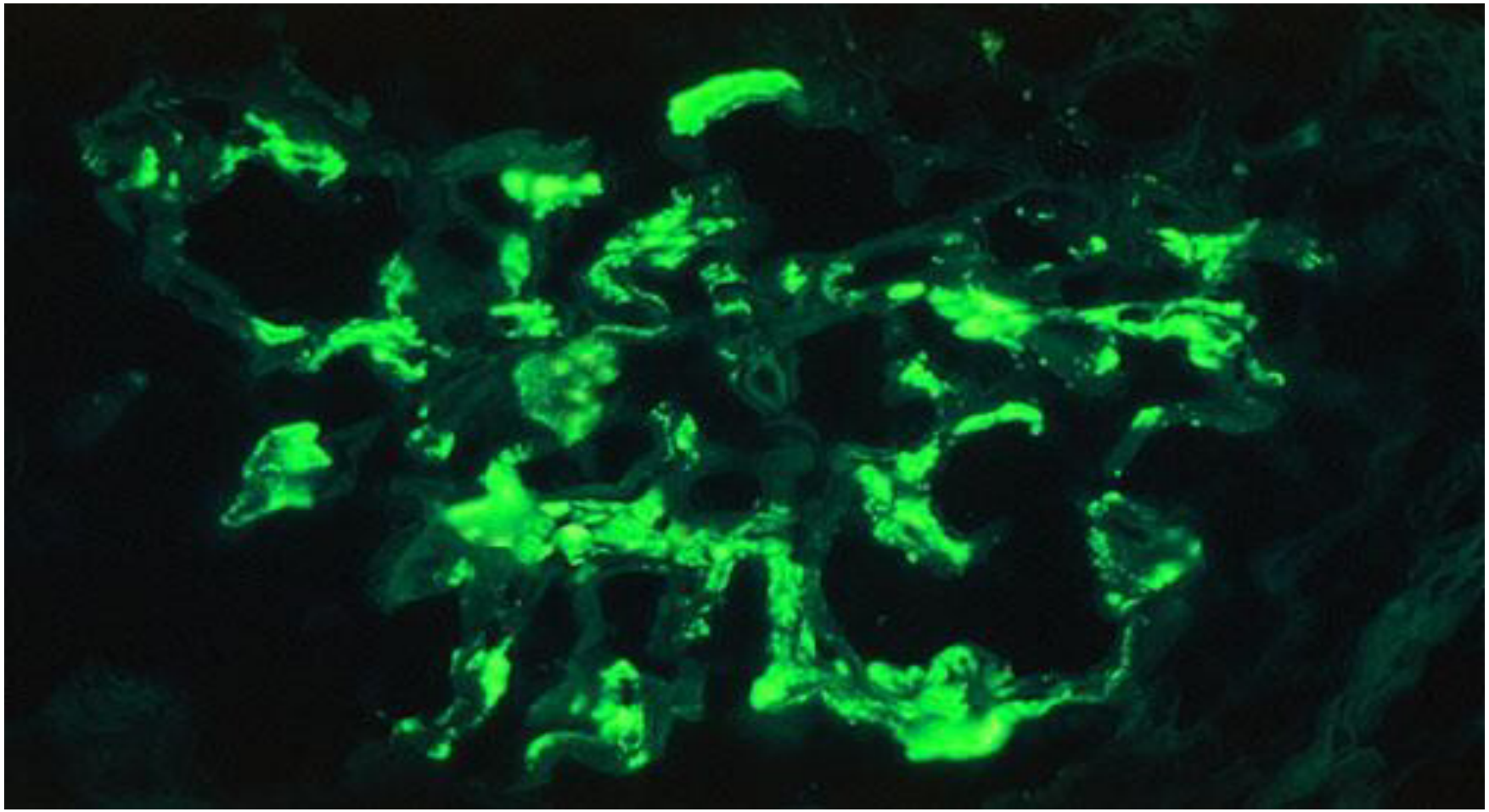
Pathogenesis

- abnormality in IgA production and clearance.

- LM: variable
- IF: mesangial deposition of IgA with C3
- EM: deposits in the mesangium

Very characteristic & diagnostic

IF : IgA mesangial staining.



This is the glomerulus, and you can appreciate the deposits in the mesangium (the fluorescent area)

Disease	Presentation	Age	LM	IF	EM	Prognosis
MCD	nephrotic	Children	none	negative	Effaced foot processes	good
FSGS	nephrotic	adults	Segmental sclerosis	negative	Effaced foot processes	Poor?
MNP	nephrotic	adults	Thickened GBM	IgG+ C3+	Sub-epithelial spikes and domes	Poor?
MPGN-type1	Nephritic/ nephrotic	adults	Tram track	Ig s	Subendothelial deposits	poor
MPGN-type2	Nephritic/ nephrotic	adults	Tram track	C3+	Dense deposits	poor
IgA nephropth	nephritic	Children, young adults	variable	IgA+	Mesangial deposits	variable
PSGN	nephritic	children	hypercellularity	IgG+ C3+	Subepithelial deposits (humps)	good
Alport syndrome	hematuria, hearing loss	children	variable	negative	Basket weave GBM	poor

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