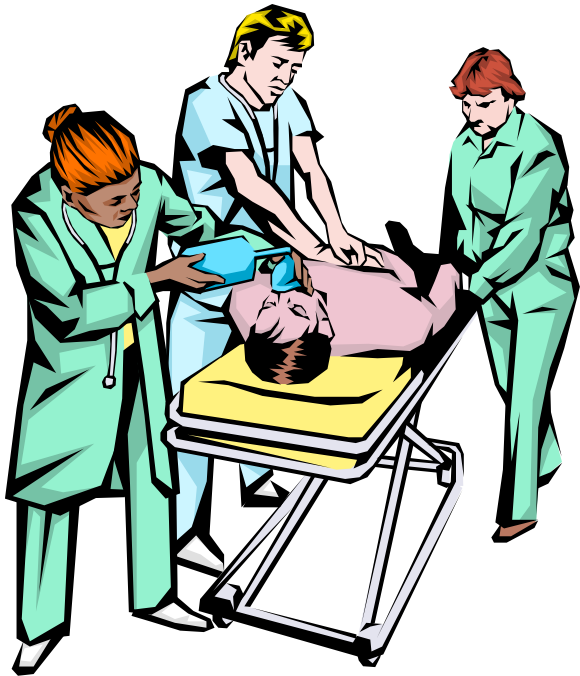
Acute Nephritic Syndrome

Acute Nephritic Syndrome

- A glomerular syndrome characterized by acute onset of:
  - Gross hematuria (with RBC casts in urine).
  - Mild - moderate proteinuria.
  - Azotemia, Oliguria , Edema, HTN.



Causes of acute nephritic syndrome

- Acute proliferative (Postinfectious) GN.
- IgA nephropathy (Berger disease).
- SLE.
- Crescentic glomerulonephritis:
  - RPGN: severe nephritic syndrome & ARF
  - Discussed separately.

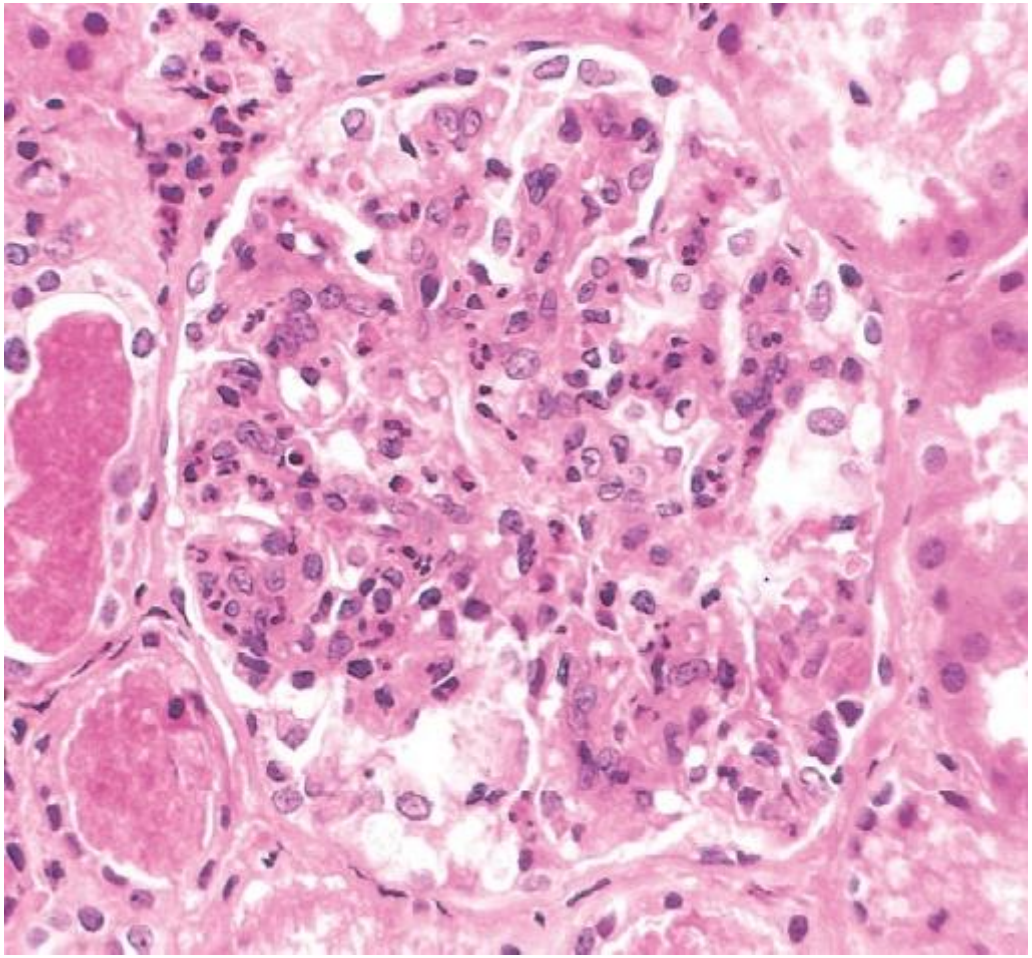
1. Acute diffuse proliferative (postinfectious) GN

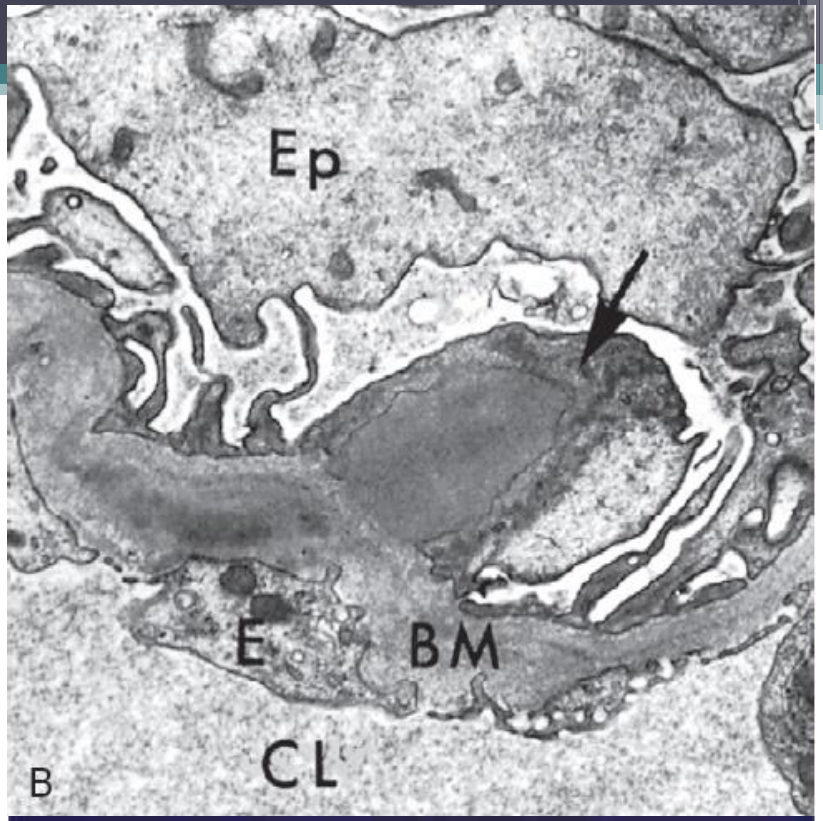
- Immune complex disease characterized by:
  - *Diffuse* proliferation of glomerular cells.
  - Influx of *leukocytes* especially <u>neutrophils.</u>

- Causes (infections):
  - *Strep. Pneumococcal (**common worldwide**), Staph., Measels, Mumps, HBV, HCV).*

Poststreptococcal GN

- Caused by certain "*nephritogenic*" strains of **group A β-hemolytic streptococci**.
- Acute nephritic syndrome affecting children usually (5-15 yrs).
- Presents **1–4 weeks** after a strep. infection of throat or skin (impetigo).
- **LM:**
  - *DIFFUSE* proliferation of glomerular cells & leukocytic infiltration. Crescents seen in few cases.
- **EM:**
  - ***Subepithelial humps*.***
- **IF:**
  - *Granular IgG & C3* in GBM & mesangium.

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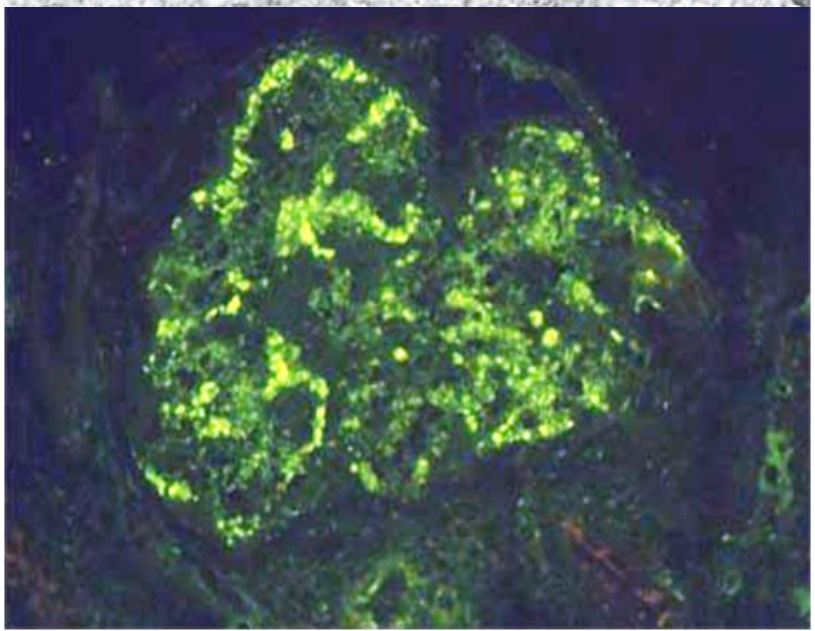


Clinical features

- Abrupt onset of malaise, fever & nausea.
- Acute nephritic syndrome.
- **Laboratory findings:**
  - Hypocomplementemia in the active phase.
  - ↑ anti-streptolysin O antibody titers.
- **Prognosis:**
  - Children >95% recover, 1% RPGN, 2% CRF.
  - Adults 15-50% develop ESRD.

2. IgA Nephropathy (IgA-N)

- The **most common GN** worldwide.
- Children & young adults.
- Usually 1 – 2 days after URTI.

- Primary IgA nephropathy.
- Secondary IgA nephropathy:
  - Henoch–Schönlein purpura
  - Celiac disease
  - Liver disease

Pathogenesis of IgA nephropathy

Genetic or acquired abnormality leading to:

- ↑ IgA synthesis in response to GI or respiratory exposure to Ags. **OR**
- Defective clearance

⇓

Deposition of IgA & IgA-immune complexes in mesangium

⇓

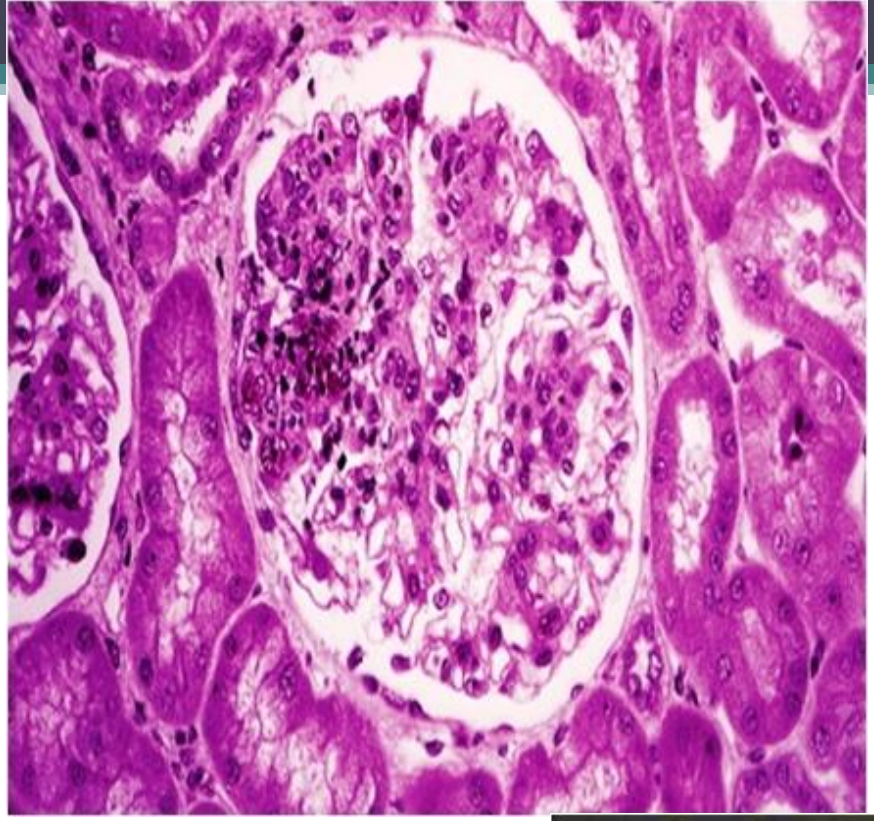
Activation of alternative complement pathway

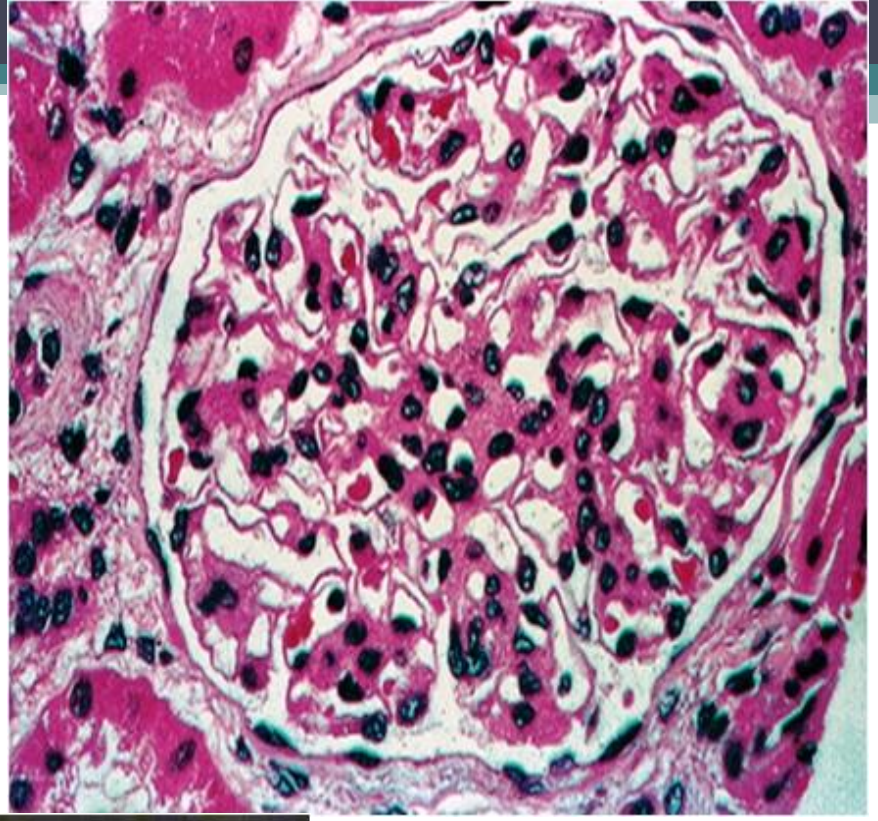
Morphology of IgA-N

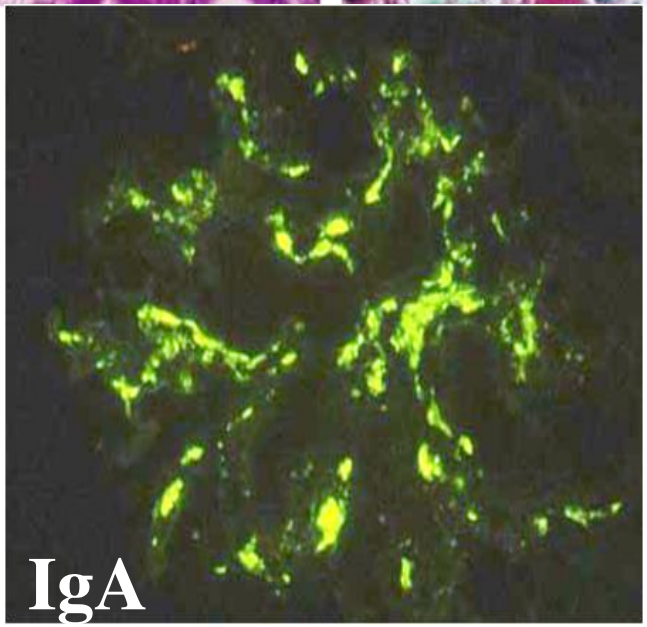
- **LM:** Variable*
  - *Normal* glomeruli.
  - Mesangial widening with focal & segmental inflammation (**Focal proliferative GN**).
  - Diffuse mesangial proliferation (**Mesangioproliferative**).

- **EM:**
  - Electron dense deposits in the mesangium.

- **IF:**
  - Deposition of **IgA in the mesangium** (hallmark).






IgA

Clinical features

- Typical presentation (in 50%):
  - An episode of **gross hematuria** occurs within 1 - 2 days of a nonspecific URT infection* → The hematuria lasts several days then subsides to recur every few months.
- Other manifestations:
  - Microscopic hematuria ± proteinuria.
  - Acute nephritic syndrome (least common).

- **Prognosis**:**
  - Initial benign course but slowly progress to CRF in 20 years (25 - 50%).

Rapidly Progressive Glomerulonephritis (RPGN)

Rapidly Progressive (Crescentic) glomerulonephritis –RPGN:

- RPGN is *not a single disease it is a syndrome* which could be caused by a number of diseases (both primary and systemic diseases).

- **Clinically** characterized by:
  - Rapid and progressive loss of renal function (ARF).
  - Features of the nephritic syndrome (more pronounced oliguria & azotemia).

- **Histologically** characterized by:
  - ***Crescent formation in > 50% of glomeruli.***

Types and causes

Type I (Anti-GBM Ab–Mediated) Crescentic GN –12%

-Idiopathic

-Goodpasture syndrome

Type II (Immune Complex –Mediated) Crescentic GN – 44%

-Idiopathic

-Postinfectious (PSGN)/infection related

- SLE

-Henoch-Schönlein Purpura/IgA nephropathy

Type III (Pauci-Immune/ANCA Associated) Crescentic GN– 44%

-Idiopathic

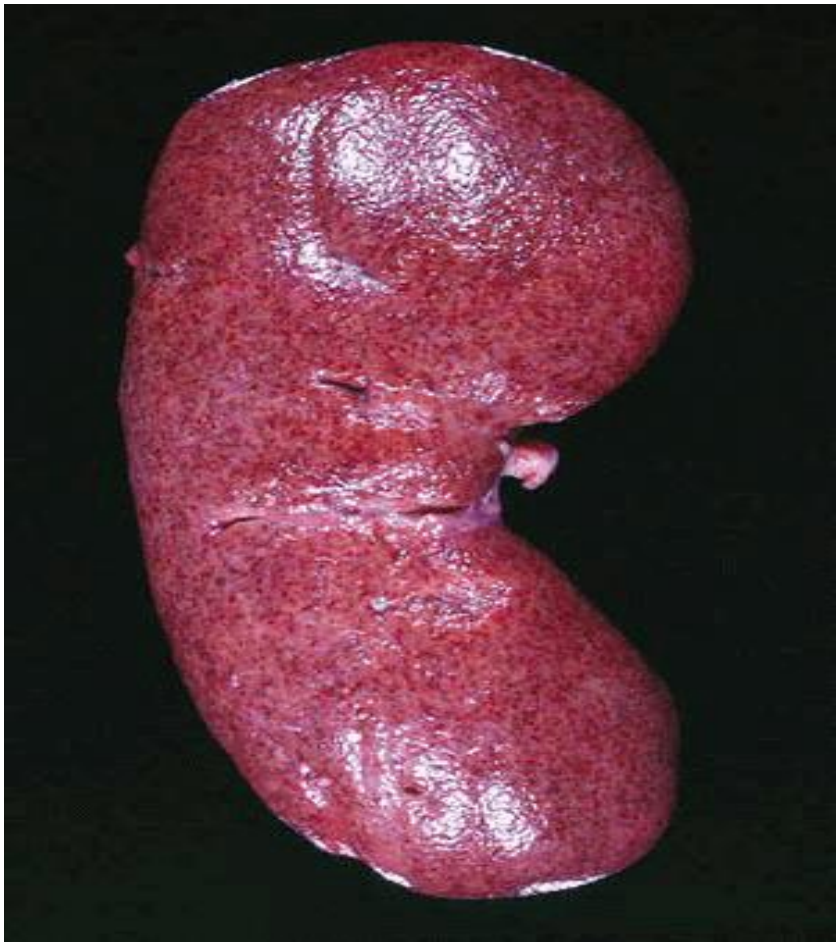
-Wegener granulomatosis

-Microscopic angiitis

**Idiopathic cases show pure renal involvement*

Common morphologic features for all types of crescentic GN

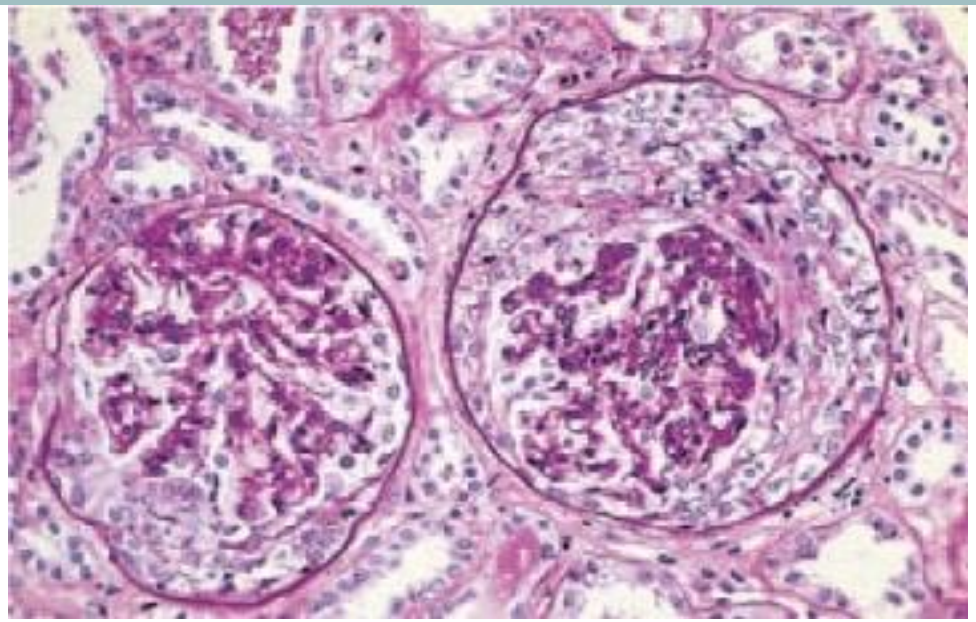
- **Gross:**
  - The kidneys are enlarged and pale with **petechial hemorrhages** on the cortical surfaces.

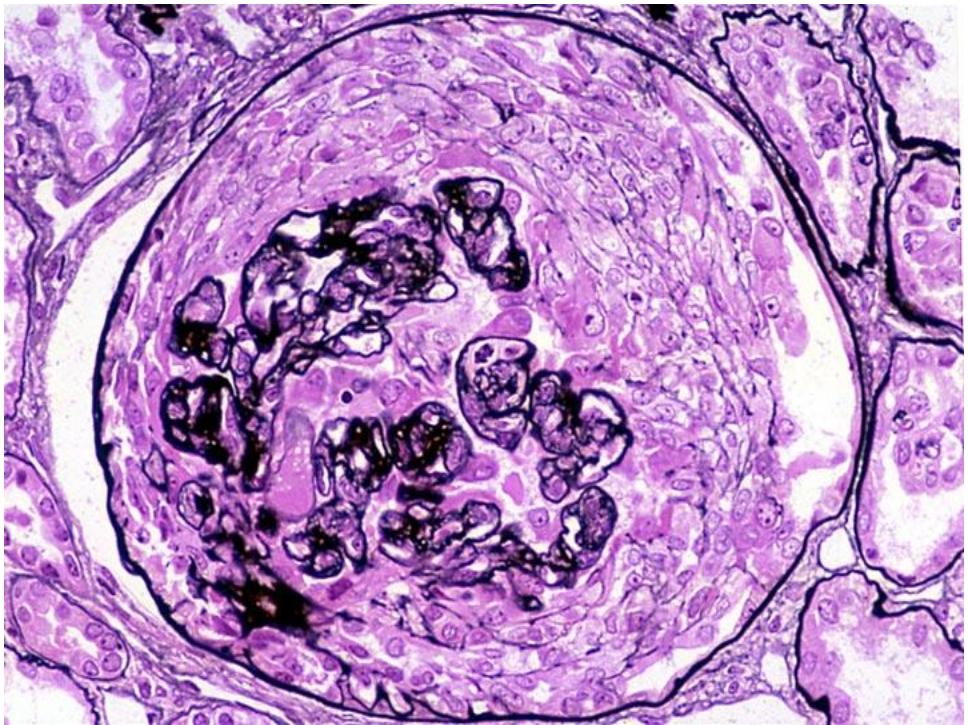


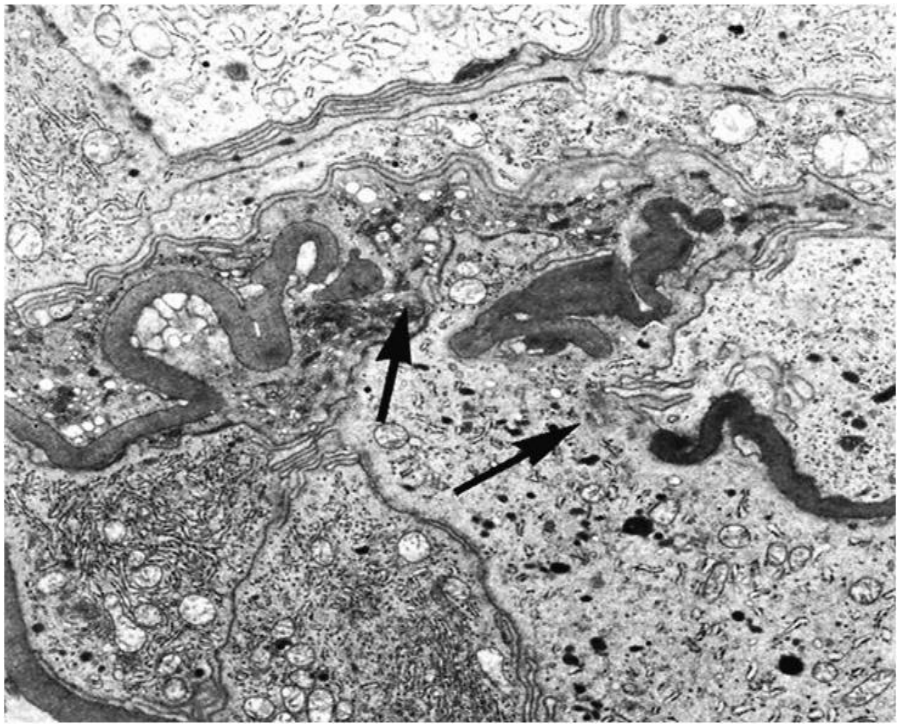
Common morphologic features for all types of crescentic GN

- **LM:**
  - Glomeruli show ***segmental necrosis***, ***GBM breaks and fibrin deposition.***
  - ***Crescent formation*** → compress the underlying glomeruli* & may undergo *scarring*.

- **EM:**
  - Wrinkling of GBM with focal disruption.



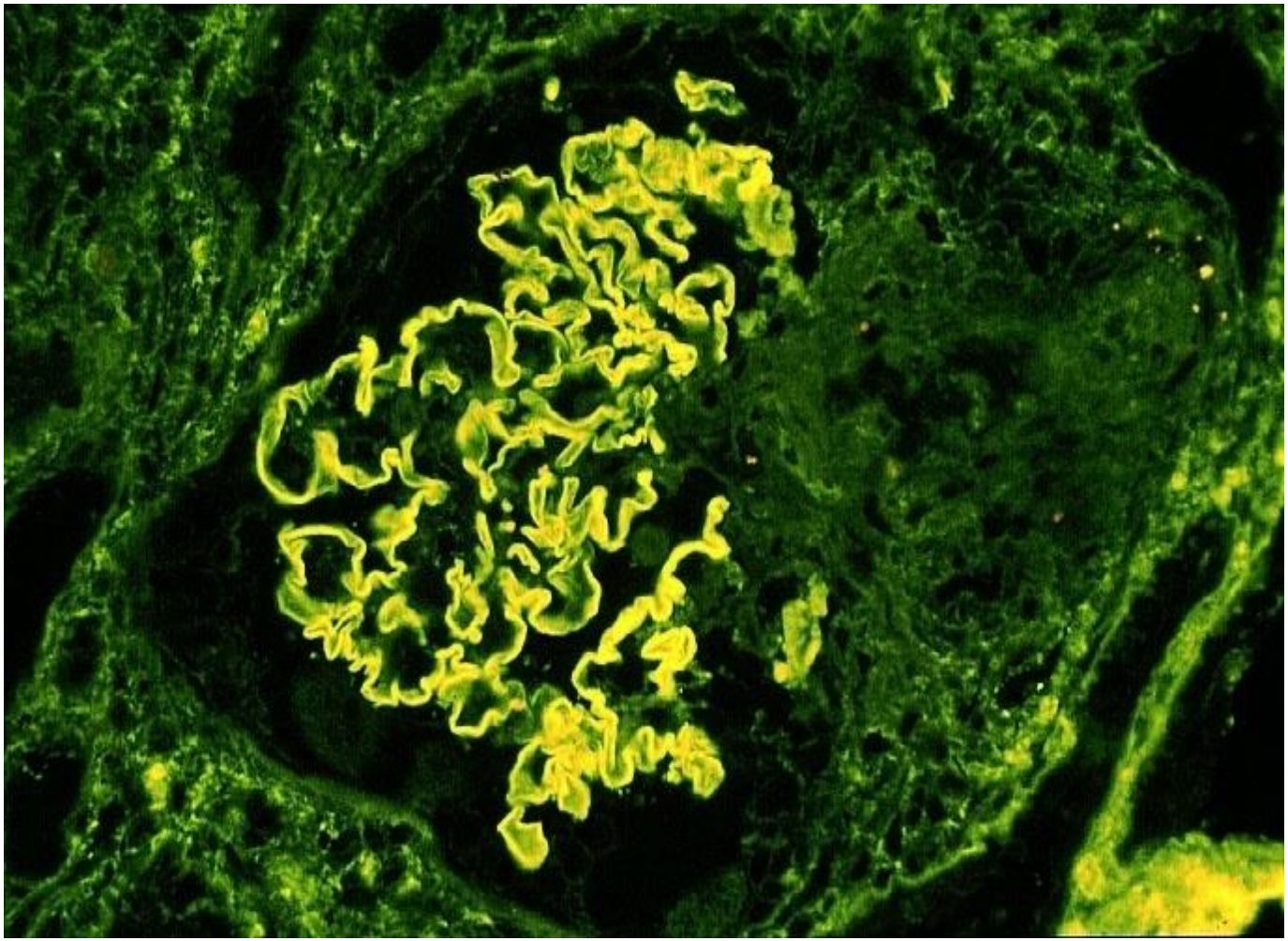




Type I (Anti-GBM Ab-Mediated) Crescentic GN

- Abs to GBM could cross react with *pulmonary alveolar BM* to produce the clinical syndrome of lung hemorrhage and renal failure (**Good Pasture`s syndrome**).
- **IF:**
  - **Linear** deposits of IgG & C3 along the GBM.
- **EM:**
  - **NO** deposits.
- Anti-GBM Abs are present in *serum* → may respond to plasmapharesis.

Anti-GBM GN – Linear IgG



Type II (Immune Complex - Mediated) Crescentic GN

- PSGN, SLE, IgA nephropathy & HSP or idiopathic
- **IF*:** Granular pattern of staining of Igs &/or complement in the GBM and/or mesangium.
- **E/M:** Subepithelial, subendothelial or mesangial deposits

Type III (Pauci-Immune/ANCA Associated) Crescentic GN- 44%

- Defined by the **lack of anti-GBM antibodies** or **immune complex deposition** by IF & EM.

- ANCA associated:
  - C-ANCA or P-ANCA detected in serum in **> 90%** of cases.
  - Associated with systemic vasculitis or idiopathic.

Prognosis of (RPGN)

- Depends roughly on the fraction of the involved glomeruli(> or < **80%**)*.
  - Renal involvement is **usually progressive leading to oliguria.**
  - Milder forms may subside.
- **Therapy:**
  - Plasmapheresis
  - Steroids
  - Cytotoxic drugs
- Some patients requires long term dialysis, and renal transplant.

Disease	Pathogenesis	L/M	IF	E/M
PSGN	Immune complexes	Diffuse proliferation Leucocyte infiltration	Granular IgG & C3 in GBM & mesangium	Subepithelial humps
IgA Nephropathy	IgA immune complexes & alternative complement	•Normal •Focal proliferative •Mesangio-proliferative	IgA & C3 in mesangium	Mesangial deposits
Crescentic GN				
Type I	Anti-GBM Ab	Segmental necrosis Fibrin Crescent formation	Linear IgG & C3	No deposits
Type II	Imune complexes		Granular IgG or IgA or IgM & complement	Deposits
Type III	ANCA		Negative	No deposits