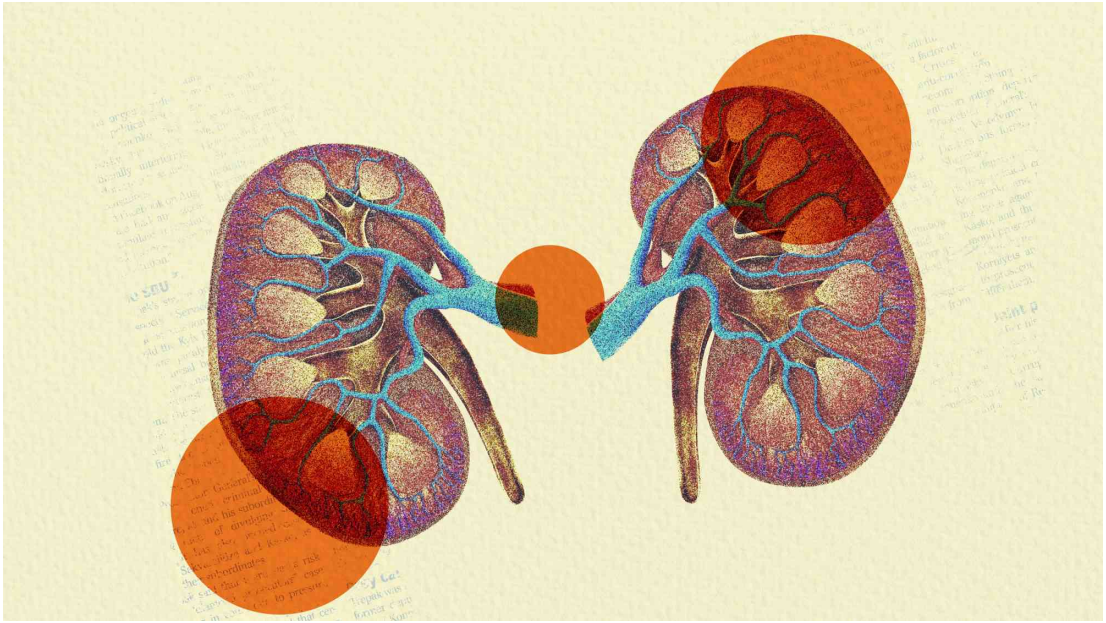
NEPHRITIC SYNDROME



An Overview of Pathophysiology , Diagnosis , and Management .

- PRESENTED BY :

  Reem Ghabayen

  Teeba Al tarawneh

CONTENTS

- **Glomerulonephritis** (definition, pathogenesis and histopathology).
- **Nephritic syndrome .**

1. Definition .
2. Classifications .
3. Pathophysiology .
4. Histology .
5. Investigation .
6. Treatment .

DEFINITION OF GLOMERULONEPHRITIS

- Inflammation of glomeruli in kidney .
- Immune mediated inflammation and subsequent damage of glomeruli .
- Could cause nephritic or nephrotic or mixed .

Quick HIT

Possible Presentations of Glomerular Disease

- Isolated proteinuria
- Isolated hematuria
- Nephritic syndrome—hematuria, HTN, azotemia
- Nephrotic syndrome—proteinuria, edema, hypoalbuminemia, hyperlipidemia

HISTOPATHOLOGY OF GLOMERULAR DISEASE

- GN is generally classified in terms of the histopathological appearance.

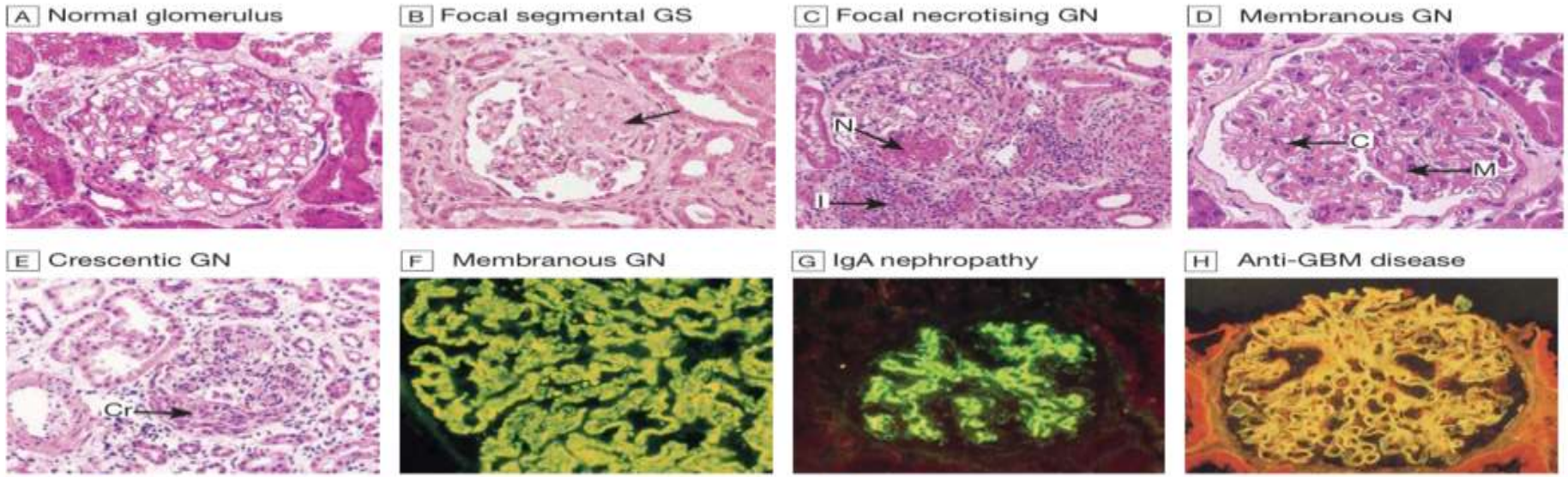


Fig. 15.12 Histopathology of glomerular disease. *(A–E Light microscopy)* A A normal glomerulus. Note the open capillary loops and thinness of their walls. B Focal segmental glomerulosclerosis (GS). The portion of the glomerulus arrowed shows loss of capillary loops and cells, which are replaced by matrix. C Focal necrotising glomerulonephritis (GN). A portion of the glomerulus (N = focal necrotising lesion) is replaced by bright pink material with some 'nuclear dust'. Neutrophils may be seen elsewhere in the glomerulus. There is surrounding interstitial inflammation (I). This is most commonly associated with small-vessel vasculitis and may progress to crescentic nephritis (see E). D Membranous glomerulonephritis. The capillary loops (C) are thickened (compare with the normal glomerulus) and there is expansion of the mesangial regions by matrix deposition (M). However, there is no gross cellular proliferation or excess of inflammatory cells. E Crescentic glomerulonephritis. The lower part of Bowman's space is occupied by a semicircular formation ('crescent', Cr) of large pale cells, compressing the glomerular tuft. This is seen in aggressive inflammatory glomerulonephritis. *Antibody deposition in the glomerulus. (F–H Direct immunofluorescence)* F Granular deposits of IgG along the basement membrane in a subepithelial pattern, typical of membranous GN. G Immunoglobulin A (IgA) deposits in the mesangium, as seen in IgA nephropathy. H Ribbon-like linear deposits of anti-GBM antibodies along the glomerular basement membrane in Goodpasture's disease. The glomerular structure is well preserved in all of these examples. *(A, C, D, E) Courtesy of Dr J.G. Simpson, Aberdeen Royal Infirmary. (F, G, H) Courtesy of Dr R. Herriot.*

TERMS

Nomenclature of glomerular disorders

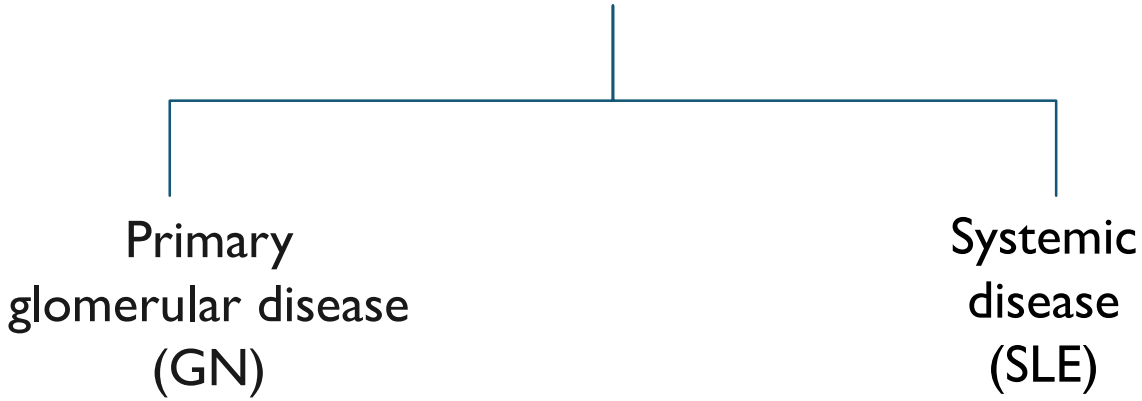
TYPE	CHARACTERISTICS	EXAMPLE
Focal	< 50% of glomeruli are involved	Focal segmental glomerulosclerosis
Diffuse	> 50% of glomeruli are involved	Diffuse proliferative glomerulonephritis
Proliferative	Hypercellular glomeruli	Membranoproliferative glomerulonephritis
Membranous	Thickening of glomerular basement membrane (GBM)	Membranous nephropathy
Primary glomerular disease	1° disease of the kidney specifically impacting the glomeruli	Minimal change disease
Secondary glomerular disease	Systemic disease or disease of another organ system that also impacts the glomeruli	SLE, diabetic nephropathy

DEFINITION OF NEPHRITIC SYNDROME

- Glomerulonephritis that causes decrease in GFR and filtration of both protein and RBCs .

❖ **Causes and pathogenesis :**

Proliferation of the cells within the glomeruli accompanied by leukocytes infiltration causing capillary injury that leads to escape of RBCs into the urine and decrease in GFR .



PATHOGENESIS OF NEPHRITIC SYNDROME

- Its immune complex mediated .
- Antigen attached to antibody and forms Ag-Ab complex .
- Hereditary nephritis (Alport syndrome)

- In some cases , antibodies are produced against antigens of basement membrane (this is called **anti-GBM antibody induced glomerulonephritis**) .

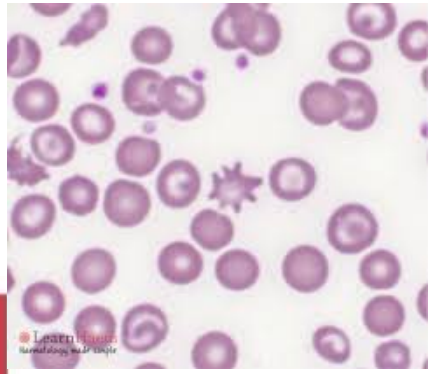
SYMPTOMS OF NEPHRITIC SYNDROME

- **<u>Nephritic syndrome classically present with the following :</u>**

I. Oliguria (less than 0.5 ml / kg / hour) .

II. Hypertension. due to activation of RAAS which increases AGII, Aldosterone and ADH

III. Hematuria is defining as >3 erythrocytes in urinalysis . (RBCs cast or dysmorphic RBCs 'Acanthocytes') .



❖ Microscopic hematuria is more commonly glomerular in origin .
❖ Gross hematuria is more commonly non glomerular or urologic in origin .

Quick HIT

If the patient has no other symptoms associated with hematuria, and thorough workup fails to reveal a cause, the prognosis is excellent. (There is usually mild glomerular/interstitial disease.)

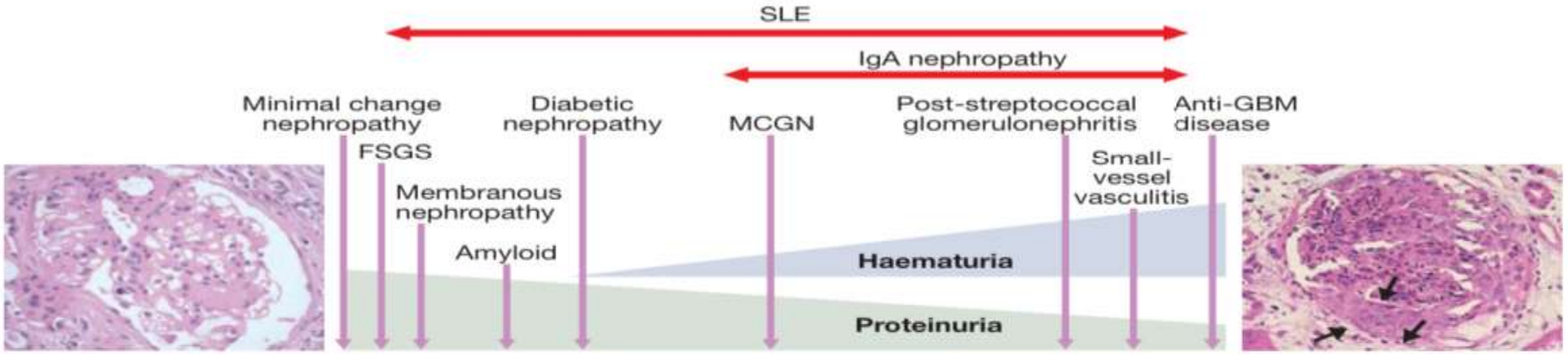
CONT…

IV. Subnephrotic proteinuria (1-2 g / 24 h) .

V. Edema (due to volume overload not hypoalbuminemia as in nephrotic) .

VI. Azotemia (high blood urea nitrogen (BUN) and creatinine // reflects a decreased GFR with no clinical manifestation) .

NEPHRITIC VS. NEPHROTIC



Nephrotic

Mechanism
- Injury to podocytes
- Changed architecture
  - Scarring
  - Deposition of matrix or other elements

Clinical features
- Overt proteinuria: usually > 3.5 g/24 hrs (urine may be frothy)
- Hypoalbuminaemia (> 30 g/L)
- Oedema and generalised fluid retention
- Possible intravascular volume depletion with hypotension, or intravascular expansion with hypertension

Nephritic

Mechanism
- Inflammation
- Reactive cell proliferation
- Breaks in GBM
- Crescent formation

Clinical features
- Haematuria (red or brown urine)
- Oedema and generalised fluid retention
- Hypertension
- Oliguria
- Reduced renal function

Fig. 15.9 Nephritic and nephrotic syndrome. At one extreme, specific injury to podocytes causes proteinuria and nephrotic syndrome. The histology to the left shows diabetic nephropathy. At the other end of the spectrum, inflammation leads to cell damage and proliferation, breaks form in the glomerular basement membrane (GBM) and blood leaks into urine. In its extreme form, with acute sodium retention and hypertension, such disease is labelled nephritic syndrome. The histology to the right shows a glomerulus with many extra nuclei from proliferating intrinsic cells, and influx of inflammatory cells leading to crescent formation (arrows) in response to severe post-infectious glomerulonephritis. (FSGS = focal and segmental glomerulosclerosis; IgA = immunoglobulin A; MCGN = mesangiocapillary glomerulonephritis; SLE = systemic lupus erythematosus)

NEPHRITIC VS. NEPHROTIC

TABLE 7-5 Nephritic Versus Nephrotic Syndrome

	Nephritic Syndrome	Nephrotic Syndrome
Pathogenesis	Inflammation of glomeruli due to any of the causes of glomerulonephritis	Abnormal glomerular permeability due to a number of conditions
Causes	Poststreptococcal glomerulonephritis is the most common cause, but may be due to any of the causes of glomerulonephritis	Many conditions. Membranous glomerulonephritis is the most common cause in adults. Other causes include diabetes, SLE, drugs, infection, glomerulonephritis (focal segmental and others) Minimal change disease is the most common cause in children
Laboratory Findings	Hematuria AKI—azotemia, oliguria Proteinuria, if present, is mild and not in nephrotic range	Urine protein excretion rate >3.5 g/24 hr Hypoalbuminemia Hyperlipidemia, fatty casts in urine
Clinical Findings	HTN Edema	Edema Hypercoagulable state Increased risk of infection

POST STREPTOCOCCAL GLOMERULONEPHRITIS

(Most common cause of nephritic syndrome)

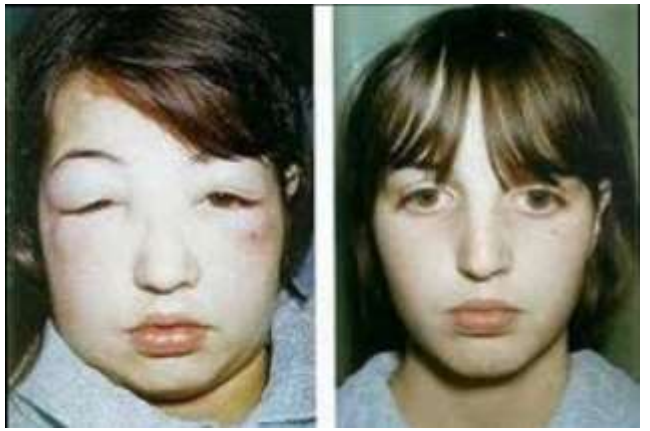
- Most frequently seen in children between (2-6y.o) after two to four weeks of group A beta hemolytic streptococcal infection of pharynx and skin .

❖ **Pathophysiology:**

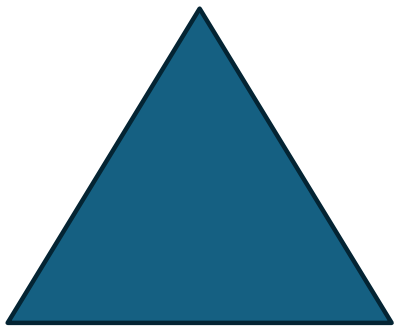
Ag-Ab complex deposition (type 3 hypersensitivity)

❖ **Clinical manifestations:**

Hematuria (Smoky Cola colored urine) .



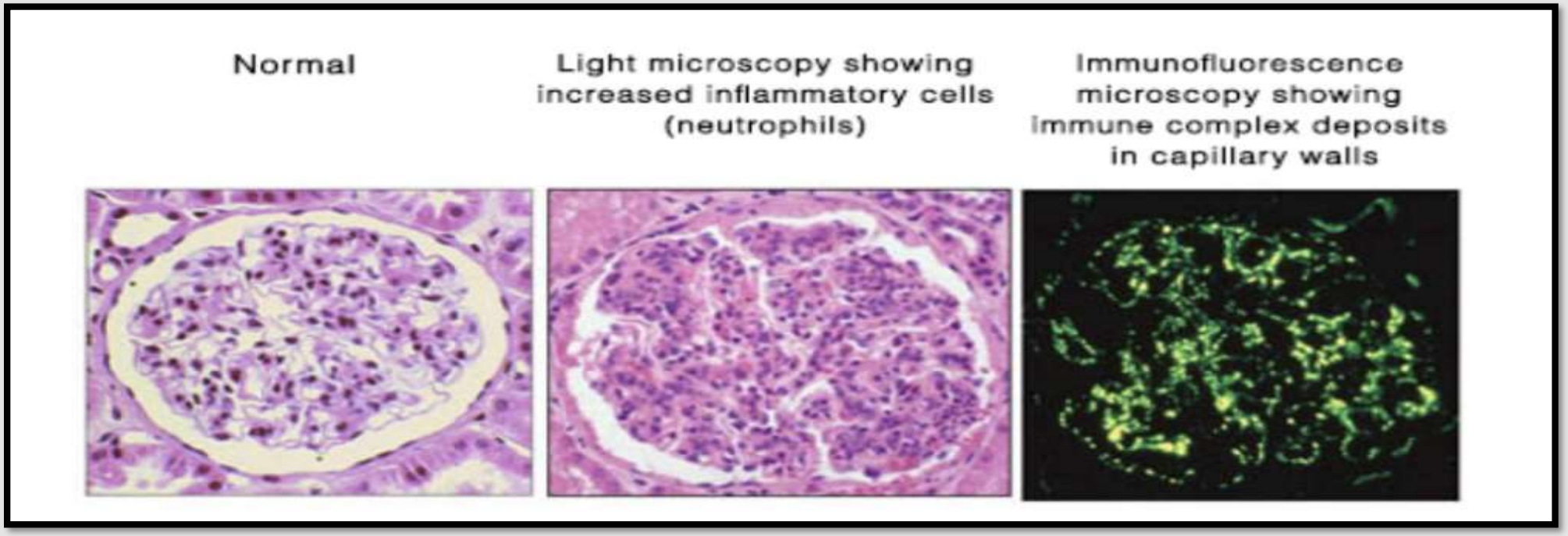
Periorbital and peripheral edema .



Hypertension

❖ **Histology :**

- LM : enlarged & hyper cellular glomeruli .
- IF : granular (starry sky appearance) (lumpy bumpy) , due to IgM – IgG – C3 "C3 consumption" deposition along GMB & mesangium .
- EM : subepithelial immune complex humps .



❖ **Diagnosis :**

1. Decrease serum complement level .
2. Increase antistreptolysin O (ASO) titer (it is produced against streptococcal antigens)
3. Urinalysis (hematuria & RBCs cast) .
4. RFT (high BUN & creatinine) .

❖ **Treatment :**

*Self-limited (from weeks to months) with excellent prognosis.

*supportive treatment

1. Anti-hypertensive drugs .
2. Loop diuretics (for edema) .
3. Steroid maybe helpful in sever cases .

IGA NEPHROPATHY (BERGER DISEASE)

(One of the most common causes of hematuria)

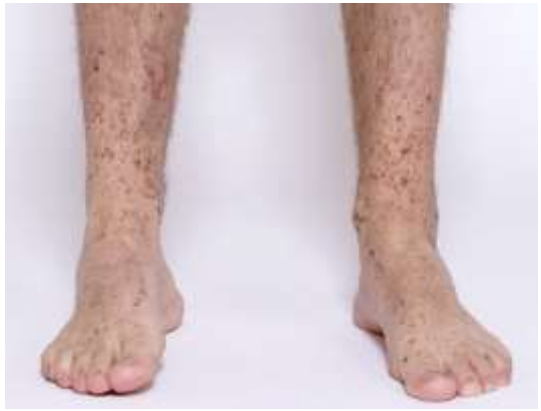
- An immune mediated disease of young ages groups , associated with over production of IgA antibody that deposits in the mesangium .
- Usually idiopathic , flares triggered by URTI (ex : sore throat) , liver disease , coeliac disease .

❖ Pathophysiology:

- The deposits of IgA triggers inflammation and progressive damage of the filtration system .

❖ Clinical manifestation :

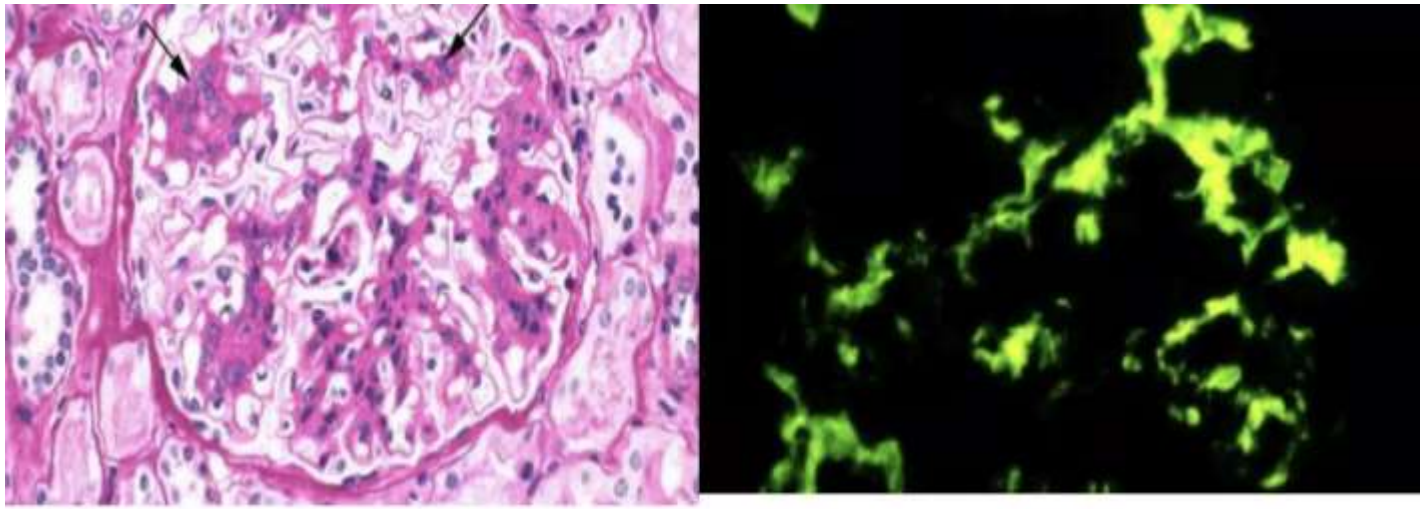
1. Hematuria & hypertension .
2. Henoch-Schönlein Purpura (HSP) .



Petechial rash affecting buttocks & lower legs .

❖ Histology :

- LM : mesangial proliferation .
- EM : mesangial immune complex deposition .
- IF : IgA based immune complex deposits In the mesangium .



❖ Treatment :

*Supportive .

*Steroids for unstable diseases .

*but no therapy has been proven to be effective .

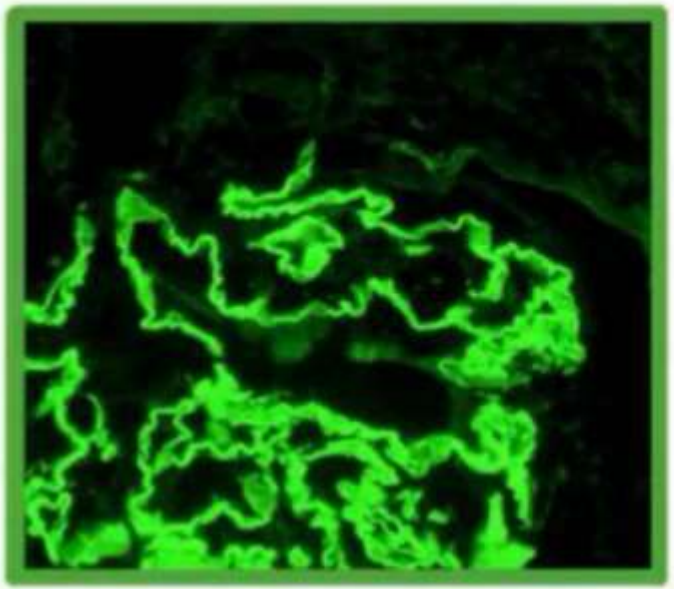
RAPIDLY PROGRESSIVE GN (CRESCENTIC)

- Severe form of nephritic syndrome characterized by rapid loss of kidney function .

	Type 1 **(Anti GBM disease)** **(Good pasture syndrome)**	**Type 2** **(Diffuse proliferative GN)** **(Immune complex mediated GN)**	**Type 3** **(focal necrotizing GN)** **(Pauci immune)**
Pathophysiology	Antibody against GMB and alveolar BM .	Immune complexes trigger glomerular inflammation. Causes: *post infectious GN *SLE	Small vessels vasculitis often ANCA mediated
Clinical Manifestations	➢ Haemoptysis and haematuria .	➢ HTN ➢ Haematuria ➢ Oliguria	➢ Primary or secondary small vessel vasculitis
IF	Linear IgG deposition	Granular IgG-IgA C3 deposition	Negative or minimal staining (pauci immune)
Treatment	❖ Plasmapheresis ❖ Corticosteroids ❖ Cyclophosphamide	TREAT THE UNDERLYING CAUSE ❖ Immune suppression for	❖ Glucocorticoid ❖ Immunosuppressant

IMMUNOFLUORESCENCE

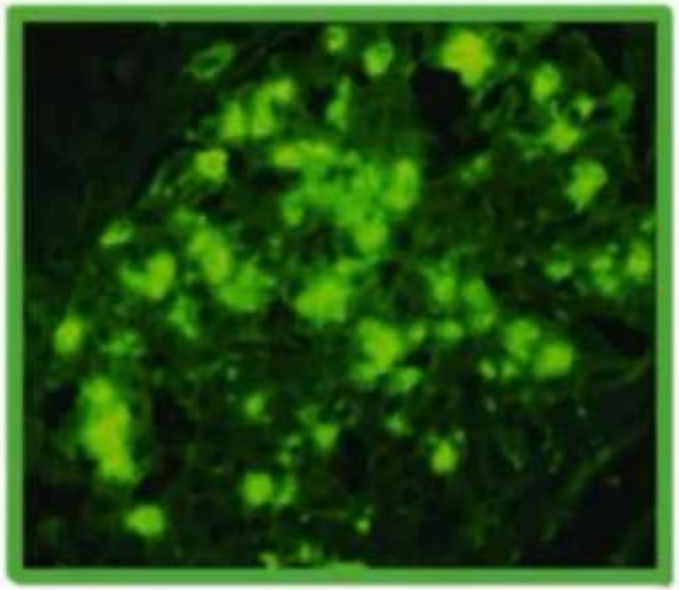
TYPE I



"LINEAR"

* ANTI-GBM binds to COLLAGEN of GBM

TYPE II



"GRANULAR"

* Immune complex deposition in subendothelium

TYPE III

* NEGATIVE *

MEMBRANOPROLIFERATIVE GN

- Nephritic syndrome that often co-present with nephrotic syndrome .

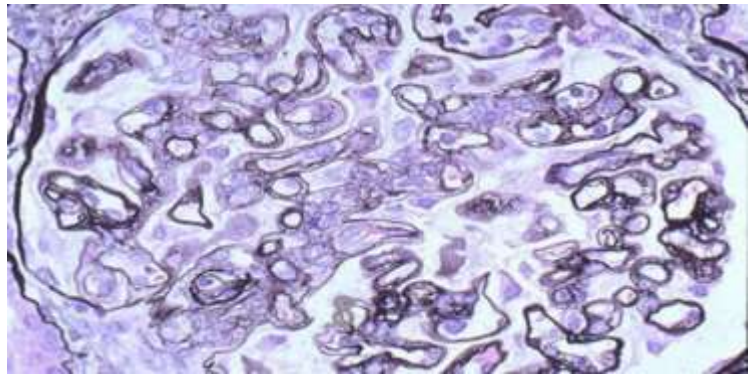
Type I

- ✓ Idiopathic or secondary to hepatitis B or C .
- ✓ Subendothelial IC deposits with granular in IF .

Type II

- ✓ Associated with C3 nephritic factor .
- ✓ Intra membranous deposits also called dense deposit disease .

➢ In both types ; mesangial ingrowth > GBM splitting (tram track) on H&E and PAS stains .



ALPORT SYNDROME

- Hereditary nephritis X-linked or autosomal dominant inheritance with variable presentations .

❖ **Pathophysiology:**

- Accumulation of abnormal collagen IV results in progressive degeneration of GBM .

❖ **Clinical manifestations** include haematuria , pyuria , proteinuria , high frequency hearing loss without deafness (because type IV collagen is found in the cochlear membrane) and progressive renal failure .

❖ **There is no effective treatment.**

“REFERENCES”

- Davidson’s Principles & Practice of Medicine .
- Step-Up to Medicine .
- FIRST AID FOR THE USMLE STEP 1 .

THANK YOU ☺