بسم الله الرحمن الرحيم

# GLUMERULONEPHRITIS

- Lecture by Dr. Zaidan Jayed

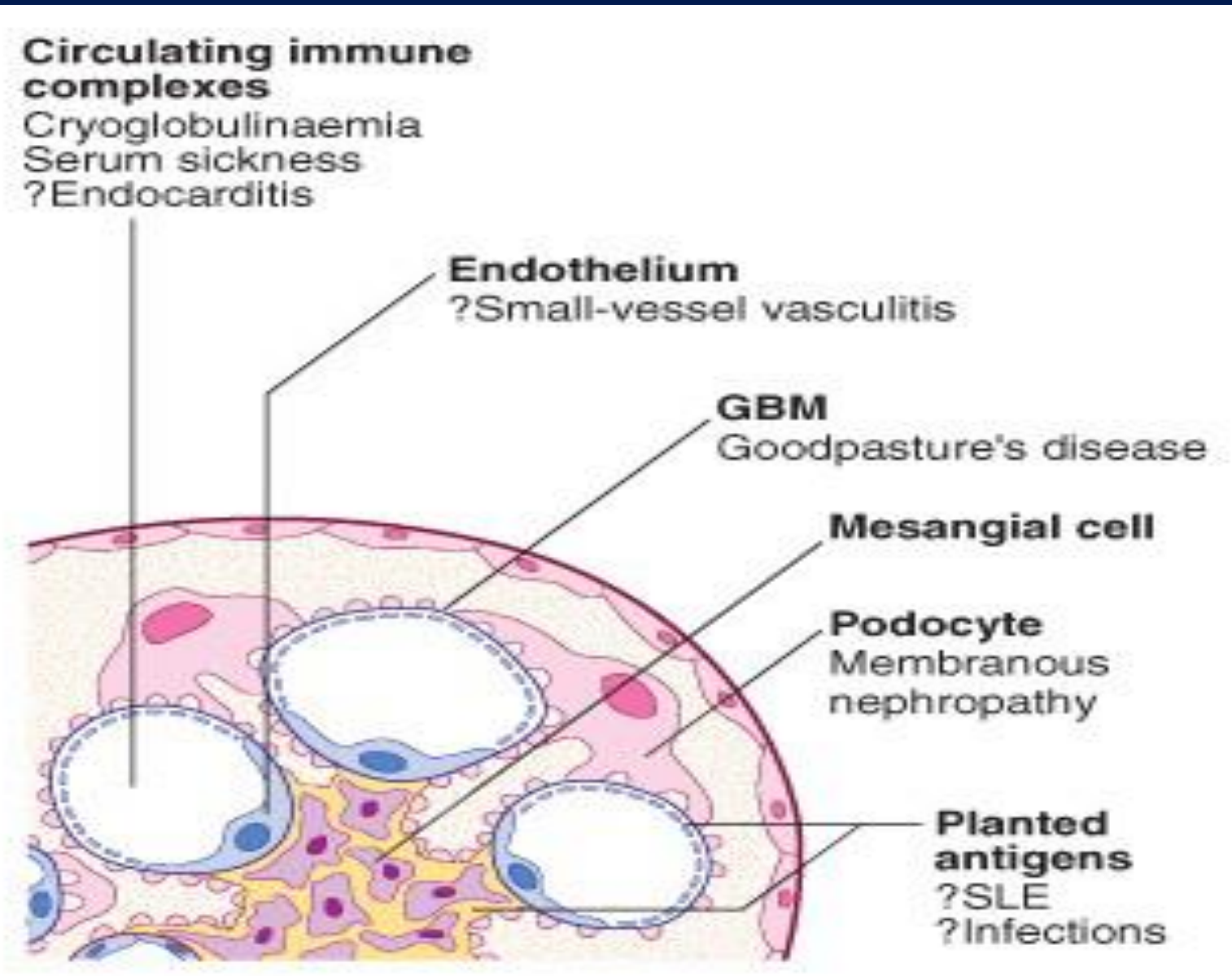
# Learning objectives

At the end of this lecture, students should be able to :

- 1- Define glomerulonephritis (GN).
- 2- List the presentation of GN.
- 3- Recognize nephritic and nephrotic syndrome.
- 4- Identify causes, clinical features, diagnosis and management of common causes of nephritic syndrome.

# Definition

Glomerulonephritis literally means 'inflammation of glomeruli' and, although inflammation is not apparent in all varieties ('glomerulopathy' is sometimes used to denote this), the name sticks.


Circulating immune complexes
Cryoglobulinaemia
Serum sickness
?Endocarditis
Endothelium
?Small-vessel vasculitis
GBM
Goodpasture's disease
Mesangial cell
Podocyte
Membranous nephropathy
Planted antigens
?SLE
?Infections

# Presentation of glomerulonephritis

1-Nephritic syndrome and rapidly progressive glomerulonephritis.

2-Nephrotic syndrome.

3-Asymptomatic abnormalities of urinary sediment.

# NEPHRITIC AND NEPHROTIC SYNDROMES

**Nephritic syndrome**

1-Haematuria (brown urine)

2-Oedema and generalised fluid retention

3-Hypertension

4-Oliguria

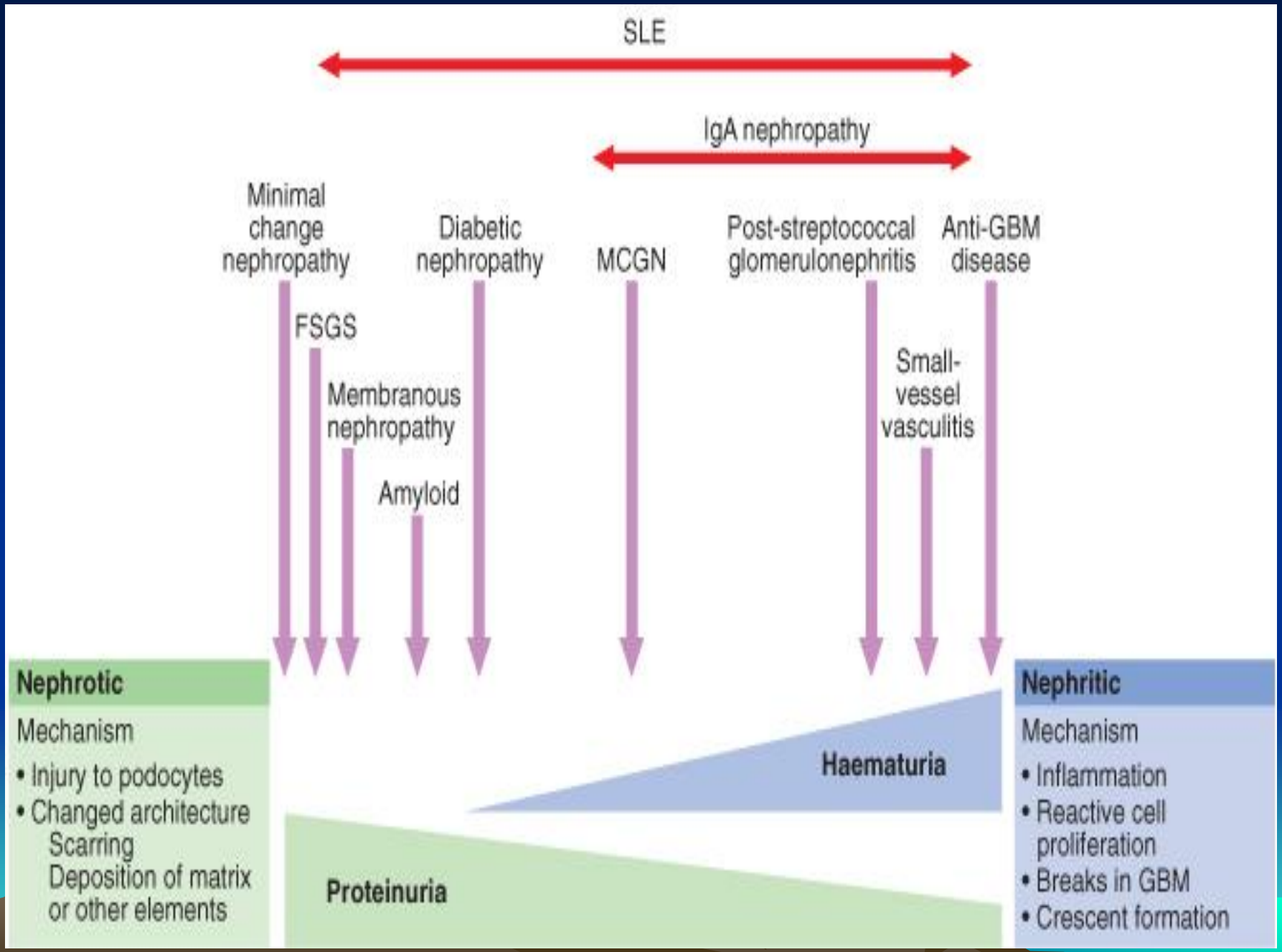
**Nephrotic syndrome**

1-Overt proteinuria-usually > 3.5 g/24 hrs (urine may be frothy)

2-Hypoalbuminaemia (< 30 g/l)

3-Oedema and generalised fluid retention

4-Intravascular volume depletion with hypotension, or expansion with hypertension, may occur


SLE
IgA nephropathy
Minimal change nephropathy
FSGS
Membranous nephropathy
Amyloid
Diabetic nephropathy
MCGN
Post-streptococcal glomerulonephritis
Small-vessel vasculitis
Anti-GBM disease
Nephrotic
Mechanism
• Injury to podocytes
• Changed architecture
Scarring
Deposition of matrix or other elements
Haematuria
Proteinuria
Nephritic
Mechanism
• Inflammation
• Reactive cell proliferation
• Breaks in GBM
• Crescent formation

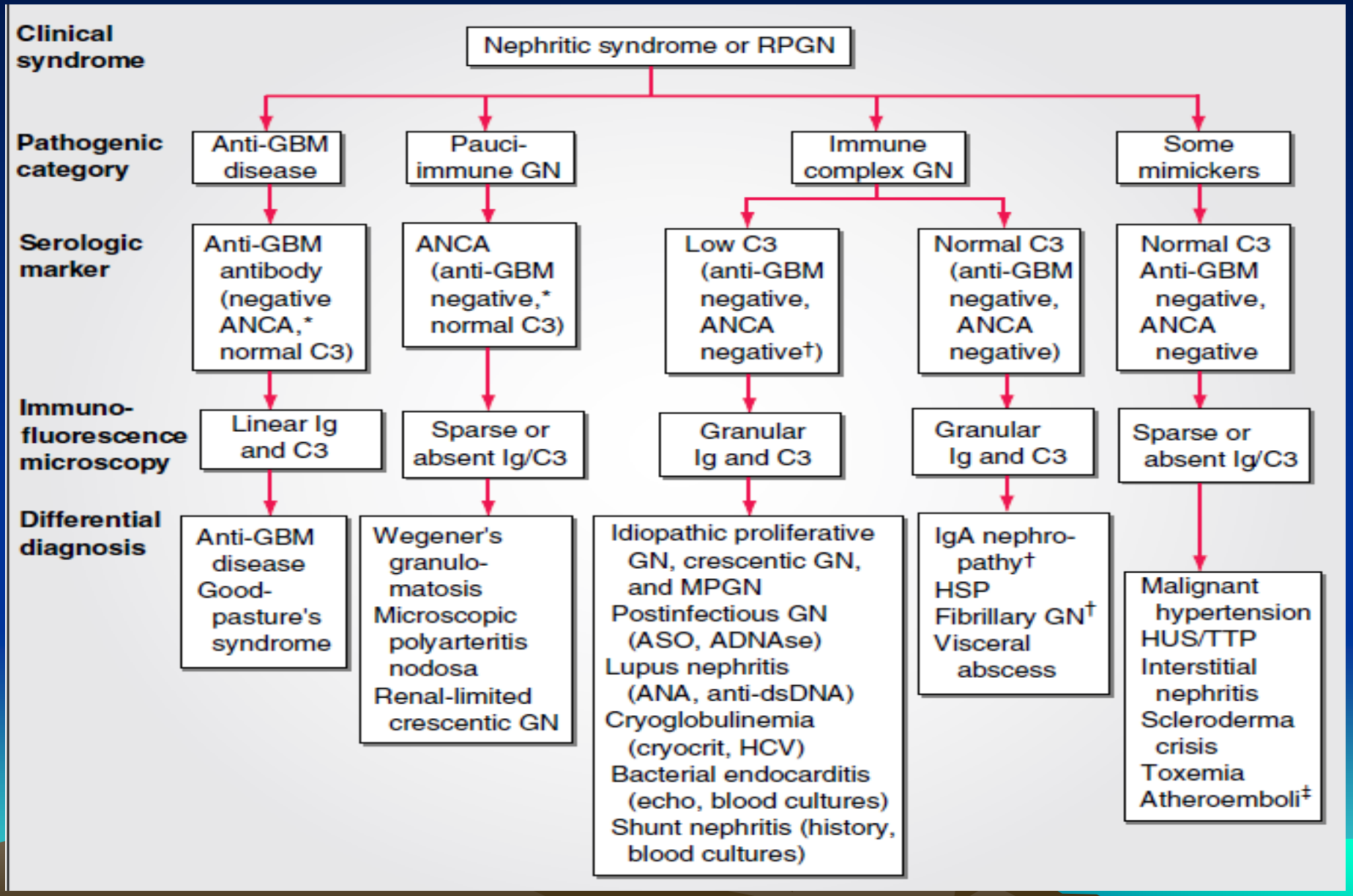
# ACUTE NEPHRITIC SYNDROME AND RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

- The *acute nephritic syndrome* is the clinical correlate of acute glomerular inflammation.In its most dramatic form, the acute nephritic syndrome is characterized by sudden onset (i.e., over days to weeks) of acute kidney injury and oliguria (less than 400 mL/day of urine). Extracellular fluid volume expansion, edema, and hypertension develop because of impaired GFR and enhanced tubular reabsorption of salt and water.

- As a result of injury to the glomerular capillary wall, urinalysis typically reveals red blood cell casts, dysmorphic red blood cells, leukocytes,and subnephrotic proteinuria of less than 3.0 g per 24 h (“nephritic urinary sediment”). Hematuria is often macroscopic. The classic pathologic correlate of the nephritic syndrome is *proliferative glomerulonephritis*

- *RPGN* is the clinical correlate of more subacute glomerular inflammation. Patients develop renal failure over weeks to months in association with a nephritic urinary sediment, subnephrotic proteinuria and variable oliguria, hypervolemia, edema, and hypertension.The classic pathologic correlate of RPGN is crescent formation involving most glomeruli (*crescentic glomerulonephritis*). In practice, the clinical term *rapidly progressive glomerulonephritis* and the pathologic term *crescentic glomerulonephritis* are often used interchangeably.

# ETIOLOGY AND DIFFERENTIAL DIAGNOSIS



# Acute post-infectious glomerulonephritis

- This is most common following infection with certain strains of streptococcus and therefore is often called post-streptococcal nephritis, but it can occur following other infections. It is much more common in children than adults but is now rare in the developed world. The latency is usually about 10 days after a throat infection or longer after skin infection, suggesting an immune mechanism rather than direct infection.

- An acute nephritis of varying severity occurs. Sodium retention, hypertension and oedema, are particularly pronounced. There is also reduction of GFR, proteinuria, haematuria and reduced urine volume. Characteristically, this gives the urine a red or smoky appearance. There are low serum concentrations of C3 and C4 and evidence of streptococcal infection (perform antistrepto-lysin O (ASO) titre, culture of throat swab, and other swab tests if skin infection is suspected).

- Renal function begins to improve spontaneously within 10-14 days, and management by fluid and sodium restriction and use of diuretic and hypotensive agents is usually adequate. Remarkably, the renal lesion in almost all children and most adults seems to resolve completely despite the severity of the glomerular inflammation and proliferation seen histologically.

## CAUSES OF GLOMERULONEPHRITIS ASSOCIATED WITH LOW SERUM COMPLEMENT

- 1-Post-infection glomerulonephritis
- 2-Subacute bacterial infection-especially endocarditis
- 3-SLE
- 4-Cryoglobulinaemia
- 5-Mesangiocapillary glomerulonephritis-usually type II.

# SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) (LUPUS NEPHRITIS)

- Renal involvement is clinically evident in 40 to 85% of patients with SLE; it varies from isolated abnormalities of the urinary sediment to full-blown nephritic or nephrotic syndrome or chronic kidney disease. Renal biopsy has proven very useful for identifying the different patterns of immune-complex glomerulonephritis in SLE, which are diverse, portend different prognoses, and do not necessarily correlate with the clinical findings.

- Patients with active lupus nephritis have a range of serologic abnormalities. Hypocomplementemia is present in 75 to 90% of patients and is most striking with diffuse proliferative glomerulonephritis. Antinuclear antibodies (ANA) are usually detected (95 to 99%), although not specific for SLE. ANA titers tend to fall with treatment, and ANA may not be detected during remissions. Anti-double-stranded DNA (dsDNA) antibodies are highly specific for SLE, and changes in their titers correlate with the activity of lupus nephritis.

## TREATMENT

- The treatment of lupus nephritis is controversial and based largely on the class of injury and disease activity. Because there is relatively poor correlation between clinical features (urinalysis findings, serum creatinine) and histologic class, the renal biopsy findings are an important guide to therapy. Treatment is not indicated for those with a normal biopsy or only mesangial deposits of immunoglobulins, as these histologic patterns portend an excellent prognosis (100% and 90% 5-year survival rates, respectively).

Glucocorticoids and cyclophosphamide are the mainstays of therapy for patients with proliferative nephritis. High-dose steroids given as intravenous boluses (pulse therapy) are usually effective at rapidly controlling acute glomerular inflammation. Cyclophosphamide and azathioprine are important adjuncts to steroid therapy and appear to afford better long-term preservation of renal function than steroids alone. Intravenous pulse cyclophosphamide is as efficacious as oral therapy and appears to be less toxic.

- 

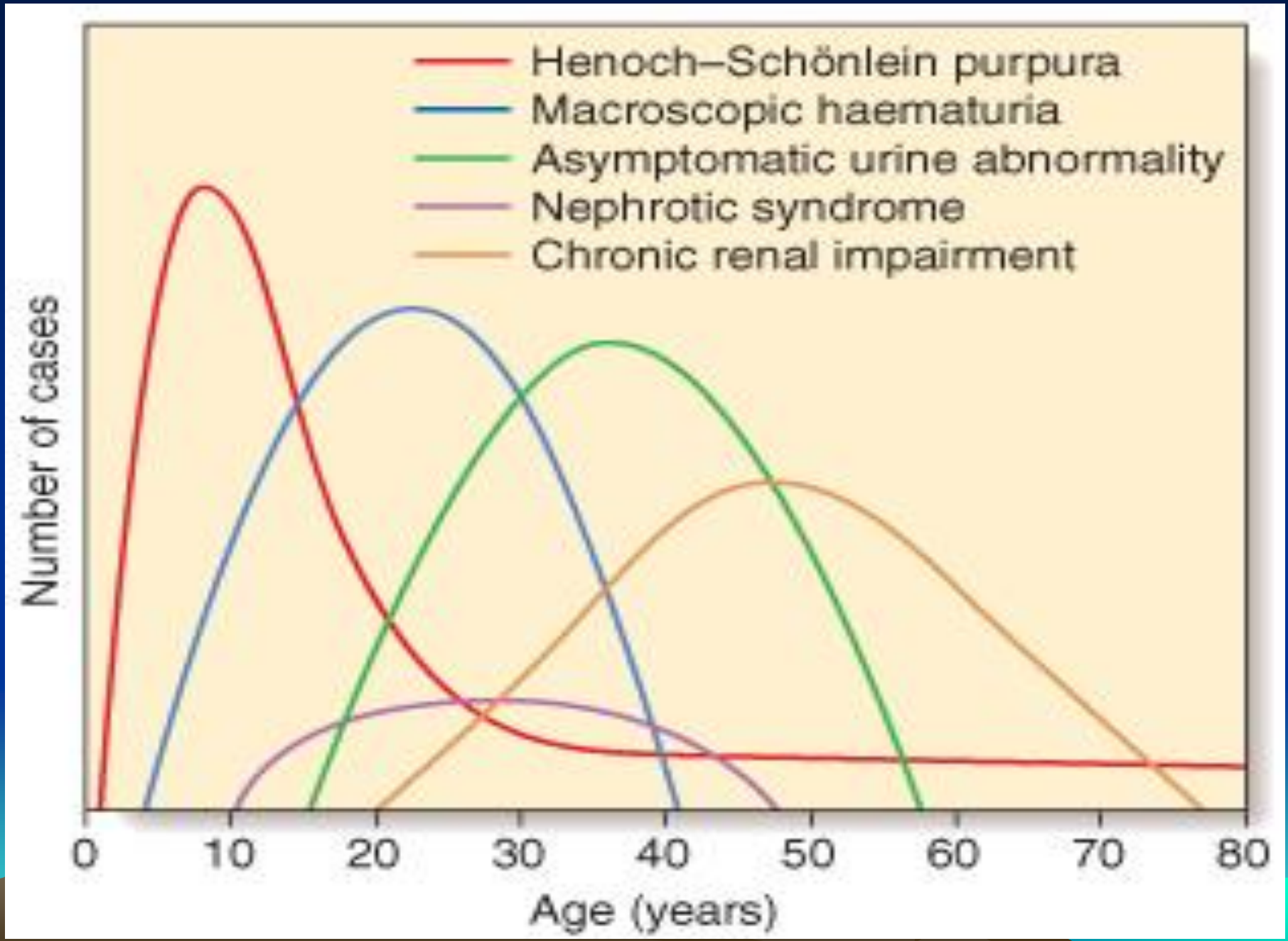
عش مع ربك بين الخوف والرجاء

ومع نفسك بين المنع والعطاء

# IGA NEPHROPATHY AND HENOCH-SCHO¨ NLEIN PURPURA

IgA nephropathy is the most commonly recognised type of glomerulonephritis and can present in many ways.

- 


Henoch–Schönlein purpura
Macroscopic haematuria
Asymptomatic urine abnormality
Nephrotic syndrome
Chronic renal impairment
Number of cases
0
10
20
30
40
50
60
70
80
Age (years)

- Haematuria is almost universal, proteinuria usual, and hypertension very common. There may be severe proteinuria and nephrotic syndrome, or in some cases progressive loss of renal function. The disease is a common cause of ESRF. A particular hallmark in some individuals is acute exacerbations, often with gross haematuria, in association with minor respiratory infections. This may be so acute as to resemble acute post-infectious glomerulonephritis, with fluid retention, hypertension and oliguria with dark or red urine. Characteristically, the latency from clinical infection to nephritis is short: a few days or less. These episodes usually subside spontaneously.

- In children, and occasionally in adults, a systemic vasculitis occurring in response to similar infections is called Henoch-Schönlein purpura. A characteristic petechial rash (cutaneous vasculitis, typically affecting buttocks and lower legs) and abdominal pain (gastrointestinal vasculitis) usually dominate the clinical picture, with mild glomerulonephritis being indicated by haematuria. When the disease occurs in older children or adults, the glomerulonephritis is usually more prominent. Renal biopsy shows mesangial IgA deposition and appearances indistinguishable from acute IgA nephropathy .Occasionally, IgA nephropathy progresses rapidly and crescent formation may be seen. The response to immunosuppressive therapy is usually poor. The management of less acute disease is largely directed towards the control of blood pressure in an attempt to prevent or retard progressive renal disease.

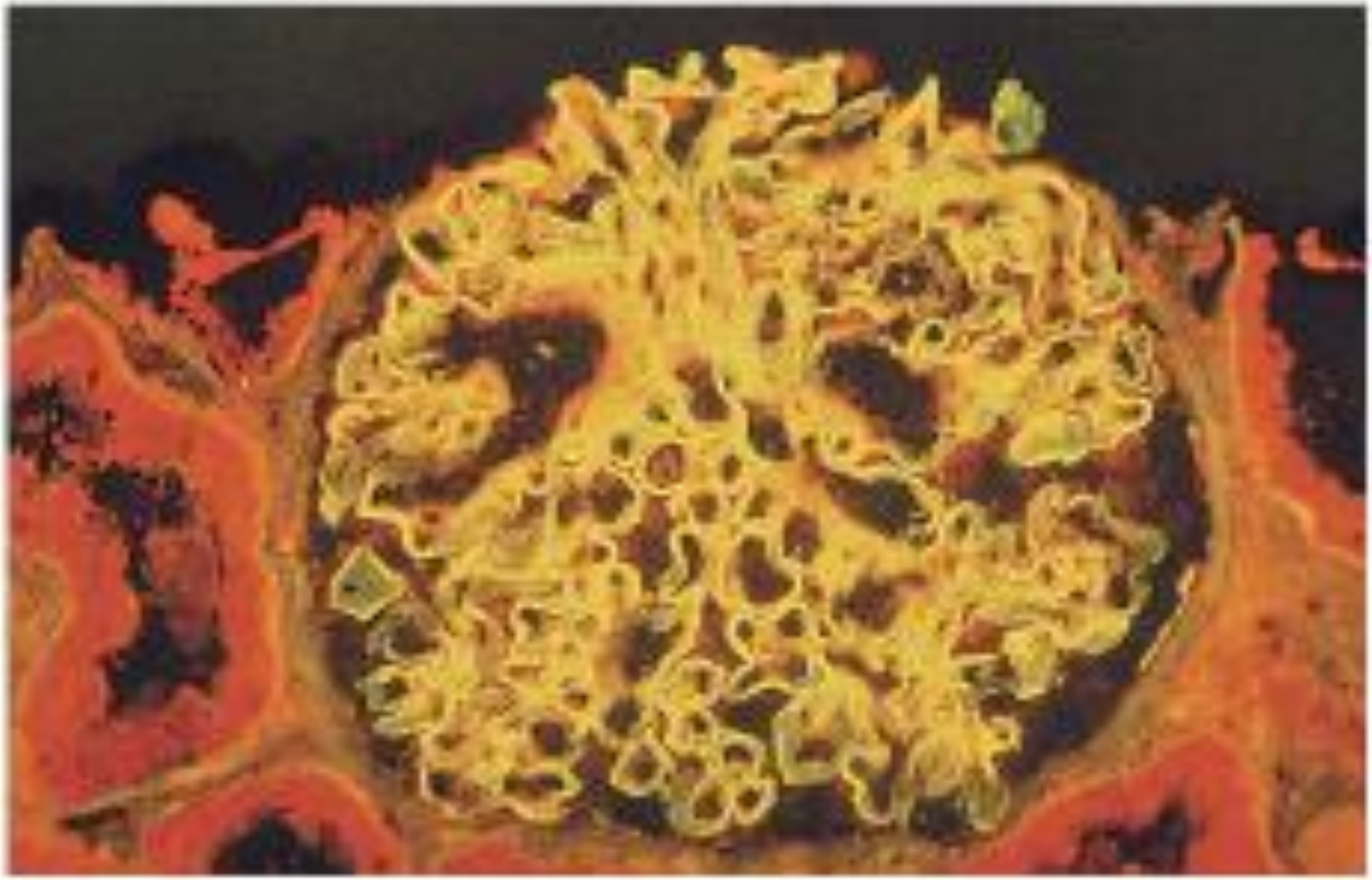
# NEPHRITIC SYNDROME AND RPGN DUE TO ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE (GOODPASTURE'S SYNDROME)

- Anti-GBM disease is an autoimmune
- disease in which autoantibodies directed against type IV collagen induce RPGN and crescentic glomerulonephritis. Acute nephritic syndrome is rare. Between 50 and 70% of patients have lung hemorrhage; the clinical complex of anti-GBM nephritis and lung hemorrhage is referred to as *Goodpasture's syndrome*.
- Patients with this syndrome are typically young males (5 to 40 years; male-female ratio of 6:1). In contrast, patients presenting during the second peak in the sixth decade rarely suffer lung hemorrhage and have an almost equal sex distribution.

- Anti-GBM disease commonly presents with hematuria, nephritic urinary sediment, subnephrotic proteinuria, and rapidly progressive renal failure over weeks, with or without pulmonary hemorrhage.When pulmonary hemorrhage occurs, it usually predates nephritis by weeks or months. Hemoptysis can vary from fluffy pulmonary infiltrates on chest x-ray and mild dyspnea on exertion to life-threatening pulmonary hemorrhage; hypertension is unusual.

- The diagnostic serologic marker is circulating anti-GBM antibodies with a specificity for the type IV collagen. Anti-GBM antibodies are detected in the serum of 90% of patients with anti-GBM nephritis by specific immunoassay. Renal biopsy is the gold standard for diagnosis of anti-GBM nephritis. The typical morphologic pattern on light microscopy is diffuse proliferative glomerulonephritis, with focal necrotizing lesions and crescents in 50% of glomeruli (crescentic glomerulonephritis). Immunofluorescence
- microscopy reveals linear ribbon-like deposition of IgG along the GBM.

H Linear IgG–anti-GBM disease



## TREATMENT

- Prior to the introduction of immunosuppressive therapy, 80% of patients with anti-GBM nephritis developed ESRD within 1 year, and many patients died from pulmonary hemorrhage or complications of uremia. With early and aggressive use of plasmapheresis, glucocorticoids, cyclophosphamide, and azathioprine, renal and patient survival have improved dramatically. In general, emergency plasmapheresis is performed daily or on alternate days until anti-GBM antibodies are not detected in the circulation (usually 1 to 2 weeks). Prednisone (1mg/kg per day) is started simultaneously, in combination with either cyclophosphamide (2 to 3 mg/kg per day) or azathioprine (1 to 2 mg/kg per day) to suppress new synthesis of anti-GBM antibodies. The speed of initiation of therapy is a critical determinant of outcome. One year renal survival approaches 90% if treatment is started before serum creatinine exceeds 442 mol/L (5 mg/dL) and falls to about 10% if renal failure is more advanced.

# References


1- Harrison’s Principles of Internal Medicine.

2- Davidson’s Principle and Practice of Medicine.

# THANK YOU • FOR LISTENING