CLINICAL PRESENTATION OF GN

Clinical Presentations of Glomerular Disease

Asymptomatic

Proteinuria 150 mg to 3 g per day

Hematuria >2 red blood cells per high-power field in spun urine or $>10 \times 10^6$ cells/liter (red blood cells usually dysmorphic)

Macroscopic hematuria

Brown/red painless hematuria (no clots); typically coincides with intercurrent infection

Asymptomatic hematuria ± proteinuria between attacks

Nephrotic syndrome

Proteinuria: adult >3.5 g/day; child >40 mg/h per m^2

Hypoalbuminemia <3.5 g/dl

Edema

Hypercholesterolemia

Lipiduria

Nephritic syndrome

Oliguria

Hematuria: red cell casts

Proteinuria: usually <3 g/day

Edema

Hypertension

Abrupt onset, usually self-limiting

Rapidly progressive glomerulonephritis

Renal failure over days/weeks

Proteinuria: usually < 3 g/day

Hematuria: red cell casts

Blood pressure often normal

May have other features of vasculitis

Chronic glomerulonephritis

Hypertension

Renal impairment

Proteinuria often > 3 g/day

Shrunken smooth kidneys

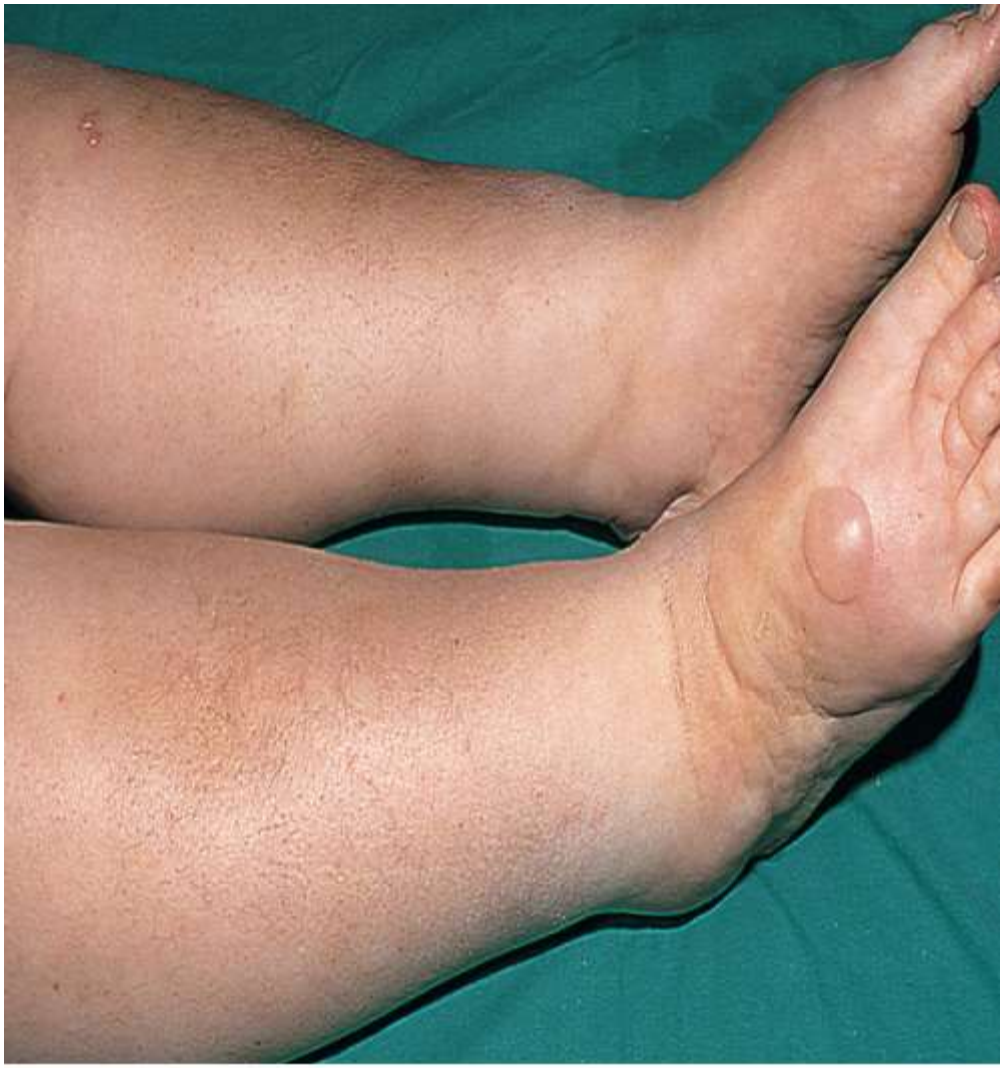
DIAGNOSIS

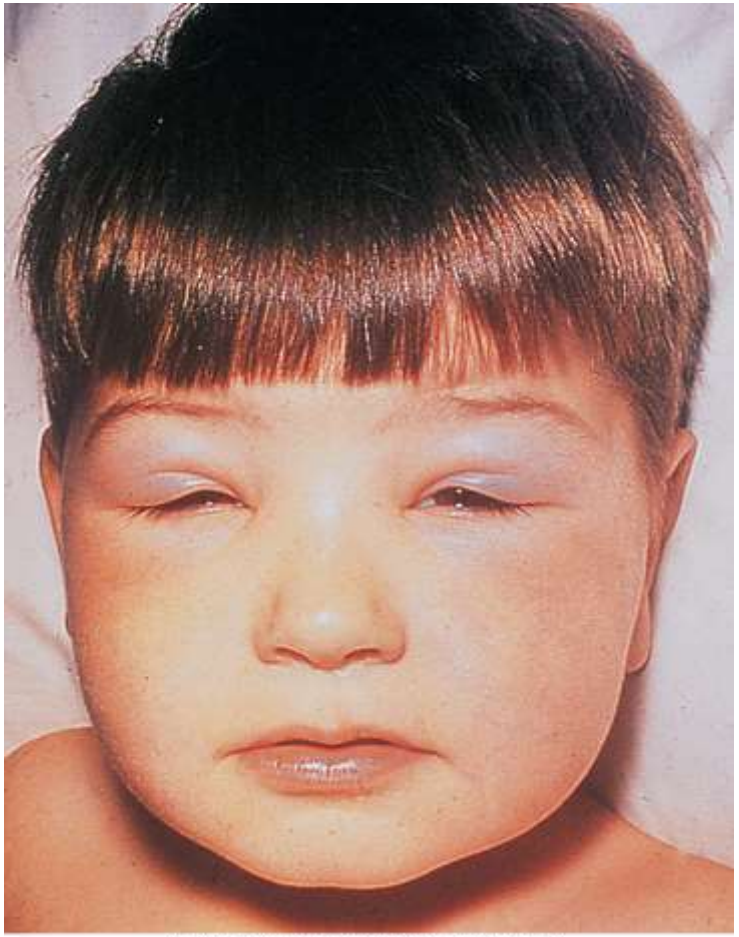
- History .
- Physical exam.
- Investigations:
  - Labs.
  - Imaging.
  - Renal biopsy.

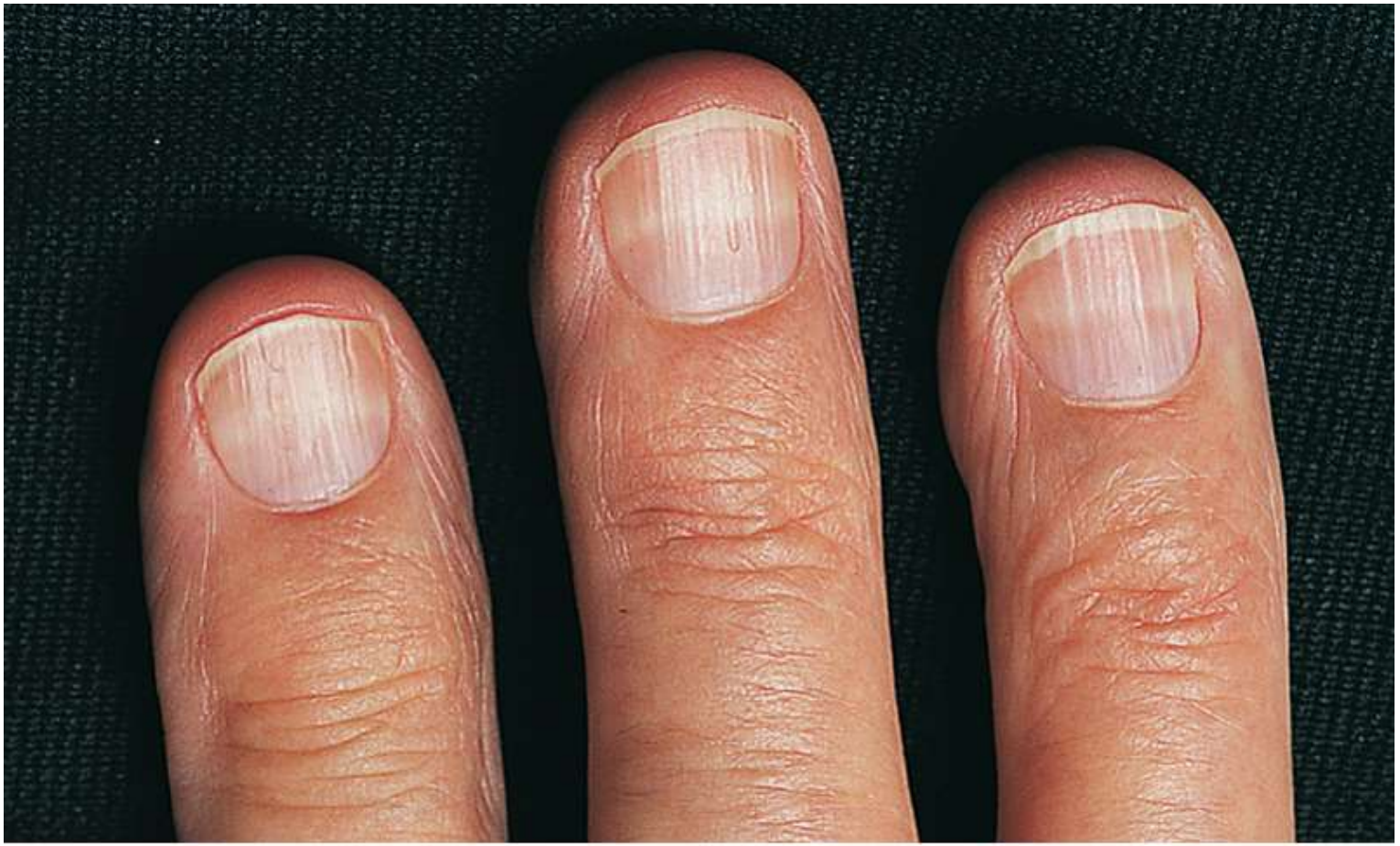
History

- Onset (sudden or gradual).
- Symptoms: edema,hematuria,proteinuria,etc.
- Family history.
- Drug history.
- Past history of infections or malignancy.

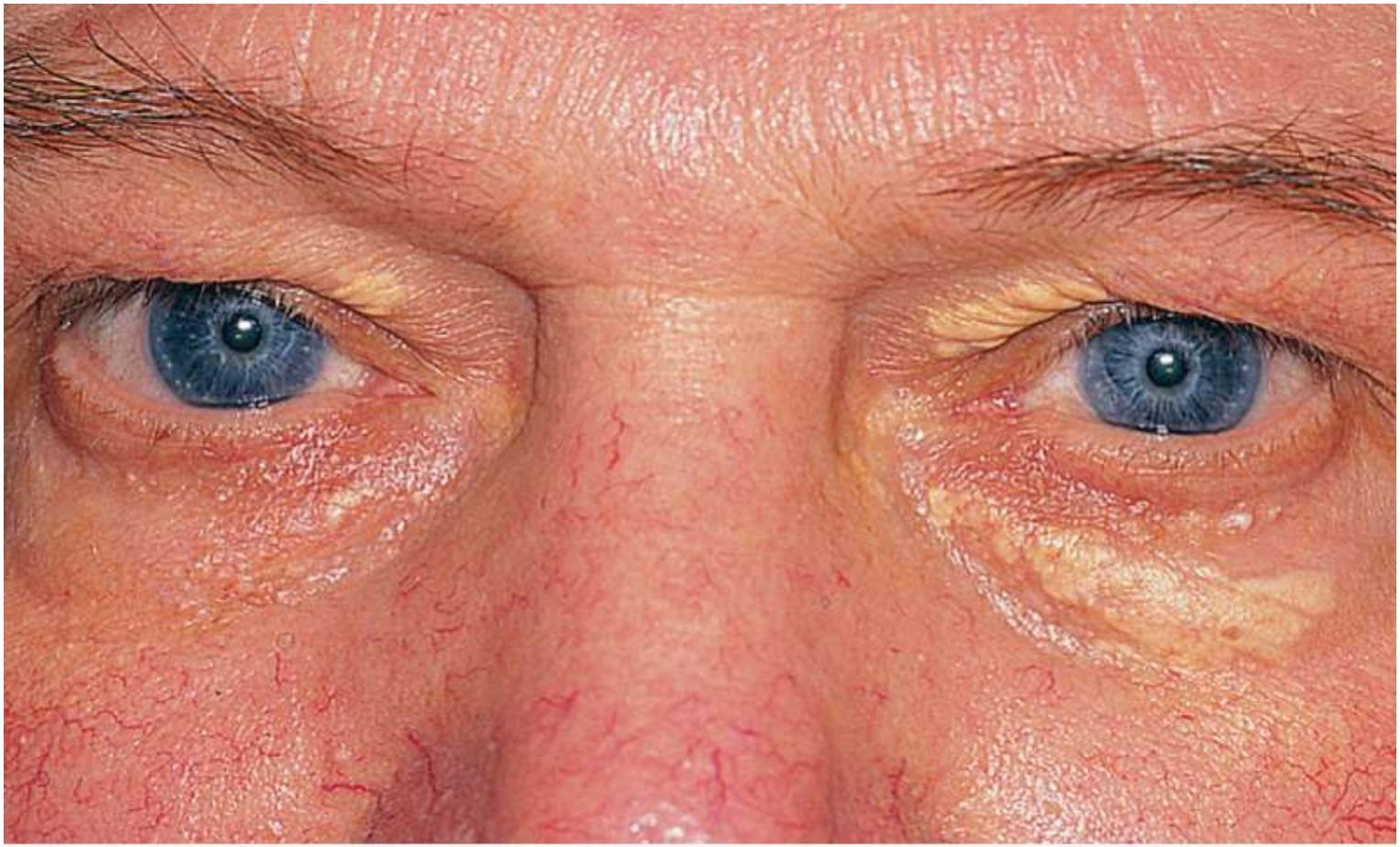
PE







Muehrcke lines (bands) in nephrotic syndrome. The white line grew during a transient period of hypoalbuminemia caused by the nephrotic syndrome.



Xanthelasmas in nephrotic syndrome.

LAB work up

- antinuclear and anti-DNA antibodies for lupus,
- cryoglobulins and rheumatoid factor suggesting cryoglobulinemia.
- anti–glomerular basement membrane (anti-GBM) antibodies for Goodpasture disease, antineutrophil cytoplasmic autoantibody (ANCA) for vasculitis,
- antistreptolysin O titer or streptozyme test for poststreptococcal glomerulonephritis

- Hepatitis profile.
- ASO titer.
- Serum and urine electrophoresis(MM,LCD,HCD)
- Measurement of systemic complement pathway activation by testing for serum C3, C4, and CH50 (50% hemolyzing dose of complement) is often helpful in limiting the differential diagnosis.

Imaging

- You need to make sure you have both kidneys.
- Size :normally 10-13 cm in adults.
- No anatomical or structural abnormalities.
- Presence of hydronephrosis.

Hypocomplementemia in glomerular disease DDX

- *Classical pathway activation* (low C3,low C4,low CH50):Lupus nephritis (especially Class IV),Cryoglobulinemia,Membranoproliferative GN type 1.
- **Alternative pathwayactivation**(C3 ↓, C4 normal, CH50 L):Poststreptococcal GN
  GN associated with other infection* (e.g., endocarditis, shunt nephritis),HUS, Atheroembolic renal disease.

Renal biopsy

- Aid in diagnosis.
- Help to expect prognosis.

- WHEN TO DO IT??

this is debatable sometimes between nephrologist.

Indications

- For diagnosis of ?primary GN.
- Unexplained AKI.
- First presentation of CKD in young adult.
- When kidney disease is part of systemic illness and the kidney is the easiest to access for Dx.
- Evaluation of RPGN.

NOT indicated

- **Isolated glomerular hematuria.**
- **Isolated non-nephrotic proteinuria.**
- **Nephrotic syndrome:** when one of the following is present:

➢ DM

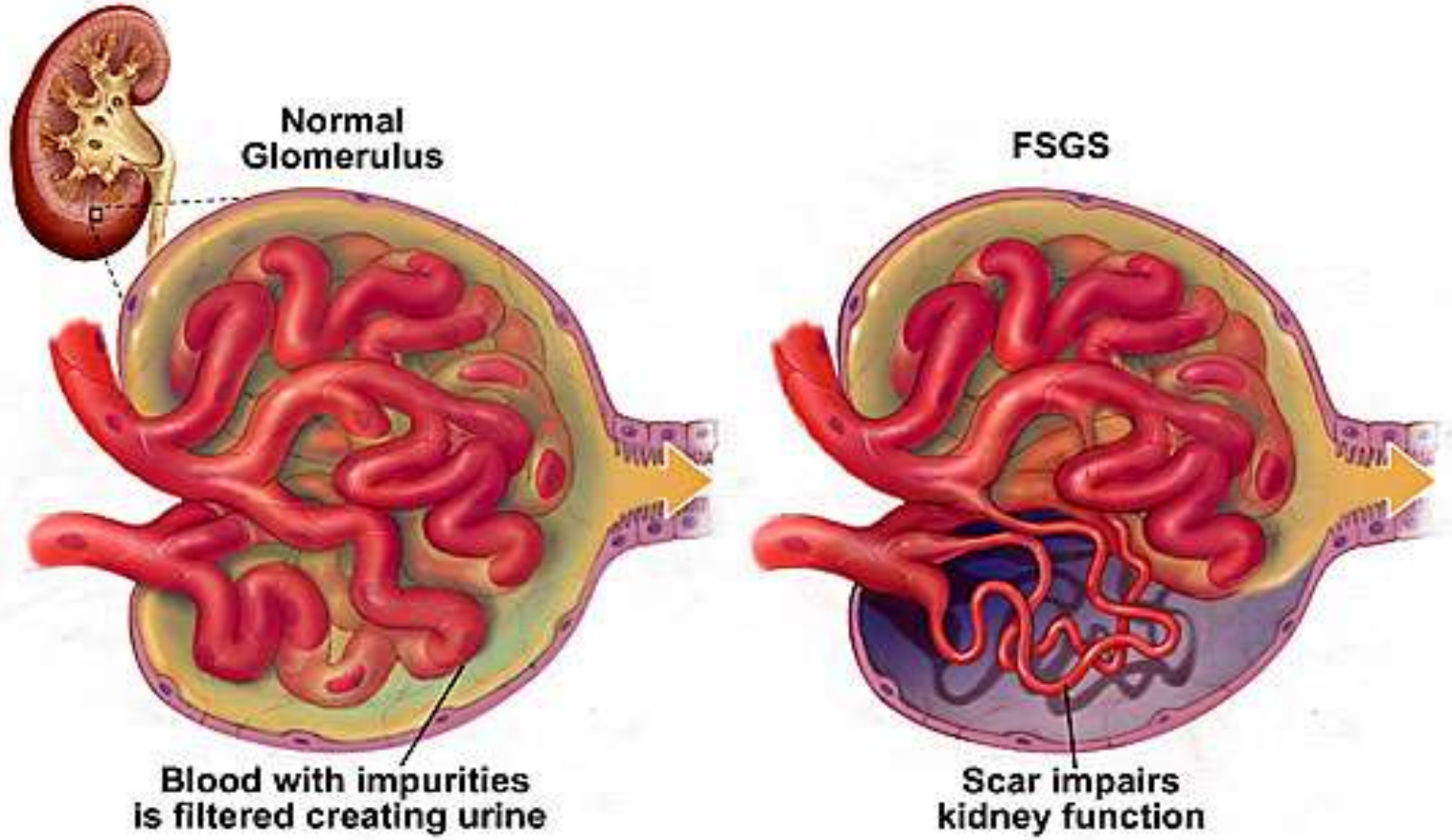
➢ history and presence of extrarenal involvement(eg: amyloidosis)

➢ Children under the age of six years with the acute onset of nephrotic syndrome.

➢ Malignancy, massive obesity.

Terminology

- Glomerulonephritis: inflammation of the kidney (glomerulos)
- Diffuse: process that involve all glomeruli,>50%
- Focal: involvement of some glomeruli **NOT** all,<50%
- Global: if the whole glomerular tuft is involved,
- Segmental: only part of the tuft involved


Normal
Glomerulus
FSGS
Blood with impurities
is filtered creating urine
Scar impairs
kidney function

Mechanisms of glomerular inflammation

- Both humoral and cell-mediated immune mechanisms play a part in the pathogenesis of glomerular inflammation

- Two basic mechanisms of antibody-mediated glomerular injury have been identified:

  - antibodies can bind either to a structural component of the glomerulus or to material that is not intrinsic to the glomerulus

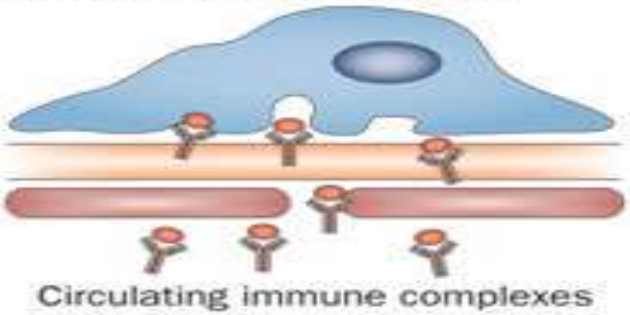
Mechanism..cont'd

- circulating antigen–antibody complexes form, escape clearance by the reticuloendothelial system, and are deposited in the glomerulus

- activation of cell-mediated immunity can also induce glomerular injury

a Deposition of immune complexes from the circulation

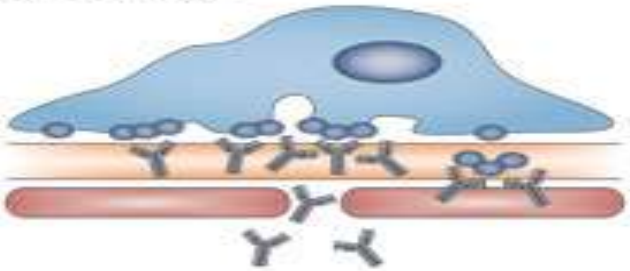
Animal model
Rabbit
Chronic serum sickness
- Low-avidity antibody and oligovalent antigen



Human MN
No evidence yet

b *In situ* formation of immune deposits

Animal model
Heymann nephritis
- Megalin

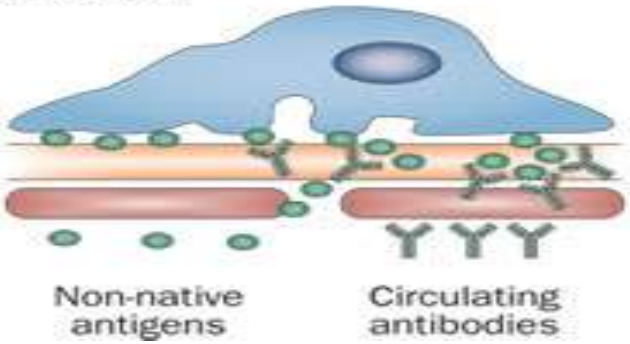


Human MN
Alloimmune MN
- Neutral endopeptidase

Autoimmune MN
- Phospholipase A_2 receptor

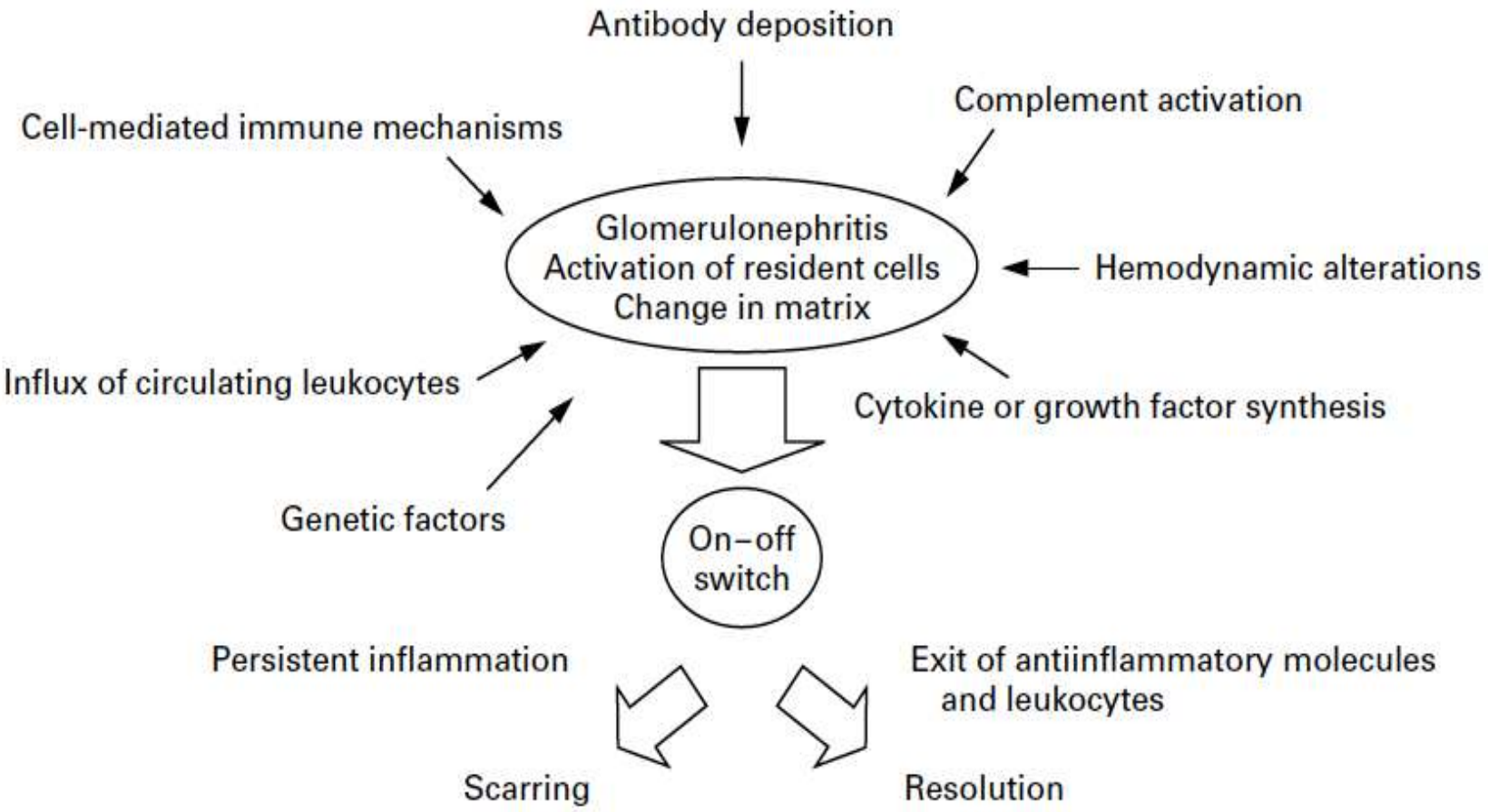
c Exogenous planted antigen targets

Animal model
Rabbit or mouse
- Cationic BSA



Human MN
Early-childhood MN
- Cationic BSA

Mechanism..cont'd



Classification Schemes

- Clinical
  - Primary and Secondary
  - Nephrotic and Nephritic
  - Acute and Chronic

Pathologic Classification

- Non Proliferative
- Proliferative

GN Pathologic Classification

- Non Proliferative
  - Minimal Change GN
  - Focal Segmental Glomerulosclerosis
  - Membranous GN
- Proliferative
  - Focal proliferative
  - Membranoproliferative
  - Diffuse Proliferative
  - Crescentic (RPGN)

TABLE 1. CLASSIFICATION OF GLOMERULAR DISEASES ACCORDING TO THE PRESENCE OR ABSENCE OF PROLIFERATIVE CHANGES.

TYPE OF DISORDER	PROLIFERATIVE CHANGES	NO PROLIFERATIVE CHANGES
Primary renal disorder	IgA nephropathy IgM nephropathy Other mesangioproliferative glomerulonephritides Crescentic glomerulonephritis With immune deposits Pauci-immune Membranoproliferative glomerulonephritis	Focal segmental glomerulosclerosis Membranous glomerulopathy Minimal-change disease Thin basement membrane disease
Secondary disorder	Lupus nephritis Postinfectious glomerulonephritis Glomerulonephritis related to hepatitis B or C Systemic vasculitides Wegener's granulomatosis Polyarteritis nodosa Henoch–Schönlein purpura Idiopathic	Diabetic nephropathy Amyloidosis Light-chain nephropathy Human immunodeficiency virus nephropathy Alport's syndrome Drug-induced glomerulopathies

Nephrotic Syndrome

- Proteinuria > 3.5 g/d
- Edema
- Hyperlipidemia/oval fat bodies
- Hypoalbuminemia

Complications of nephrotic syndrome

- Increased risk of atherosclerosis
- Elevated levels of
  - Total and low density lipoprotein cholesterol
  - Lipoprotein (a)
- Low or normal high density lipoprotein cholesterol
- It is related to the hypoproteinemia and low serum oncotic pressure of nephrotic syndrome, which then leads to reactive hepatic protein synthesis, including of lipoproteins

Complications of nephrotic syndrome…cont'd

- Increase risk of thrombosis- DVT,PE… due to urinary anti-thrombin III loss

- Increase risk of infections due to urinary Ig loss.