Renal Block

Editing File

color index:

Black: Main text

Red: important

Gray: Notes & explanation

Immune Complex Nephritis

Immunology

MED438

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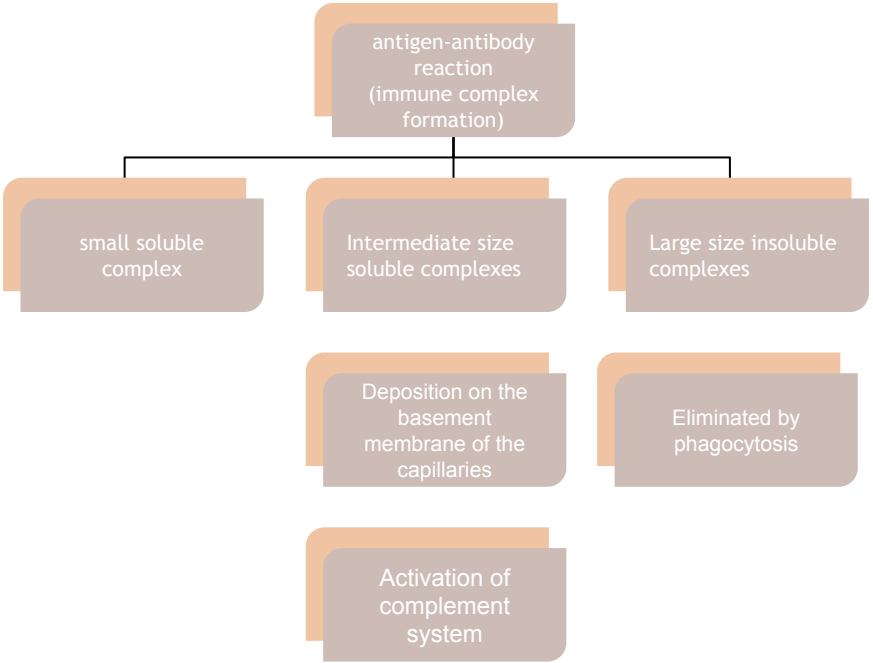
Objectives:

- Understand the importance of immune complexes in the pathogenesis of renal injury.
- Learn that immune complexes form in the circulation and may deposit in different tissues.
- Understand the dynamics of deposition of complexes which depend on the size and rate.
- Identify the different types of renal disease based on the site of deposition of the immune complexes.

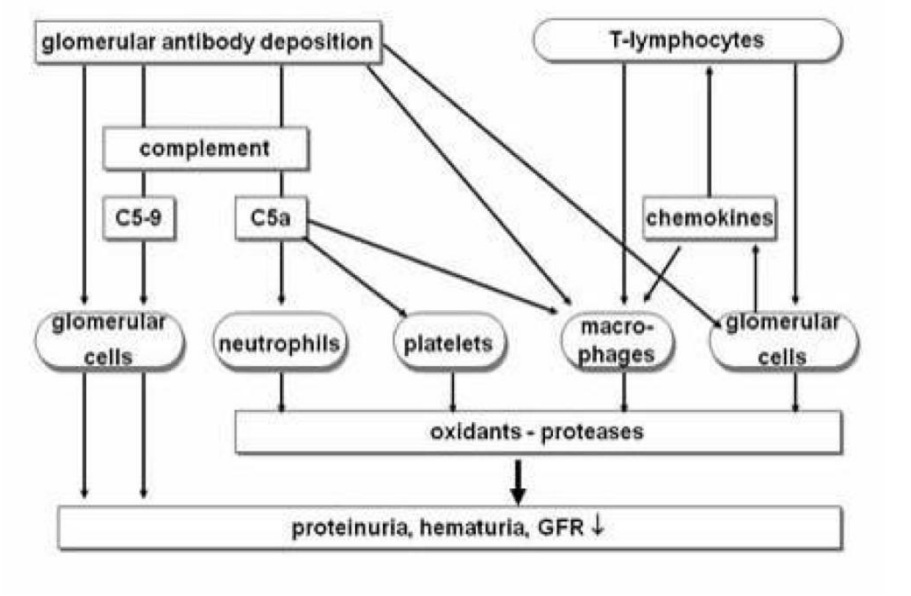
Pathogenesis of Immune-Complex Nephritis: (Type III hypersensitivity reactions)

quick review for type III hypersensitivity

Complexes of antibody with various microbial or self antigens induce type II or III hypersensitivity reactions in the kidney.

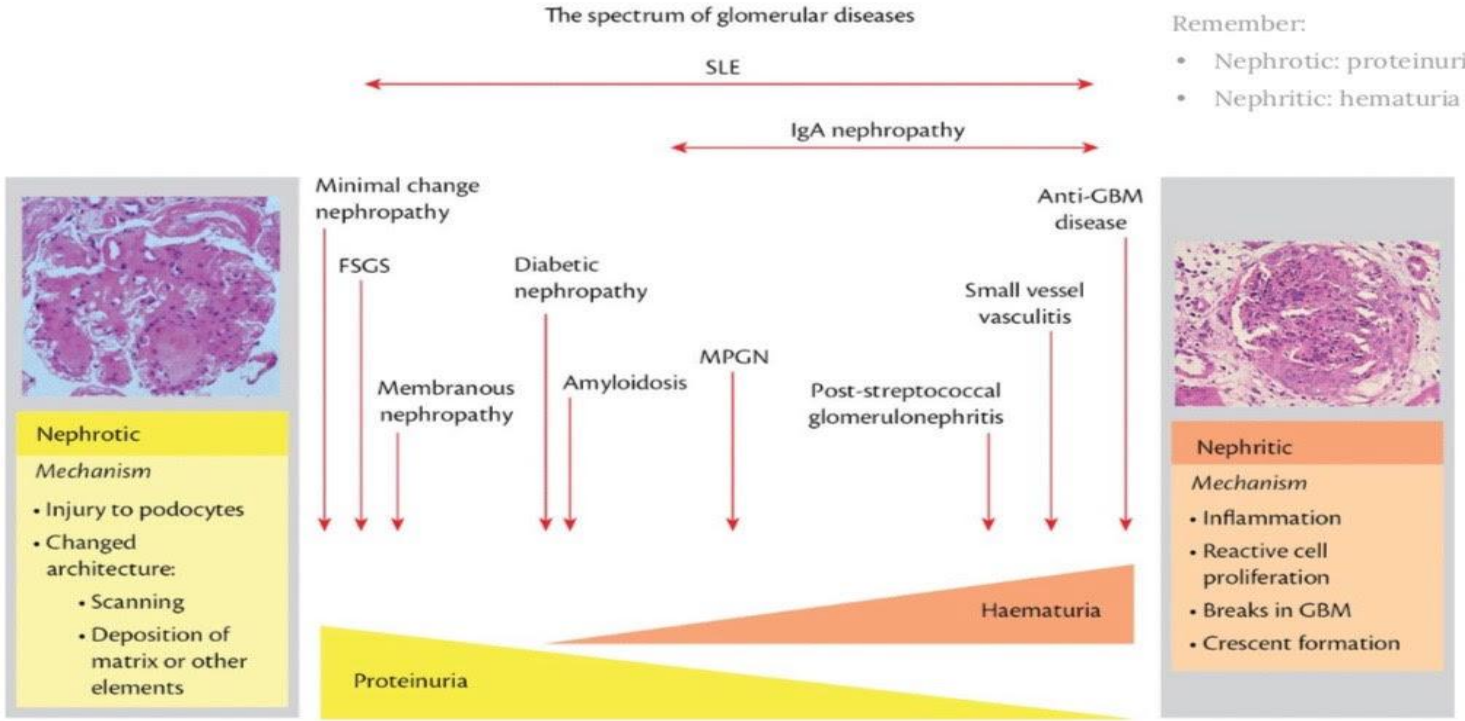


Immune-mediated glomerular injury



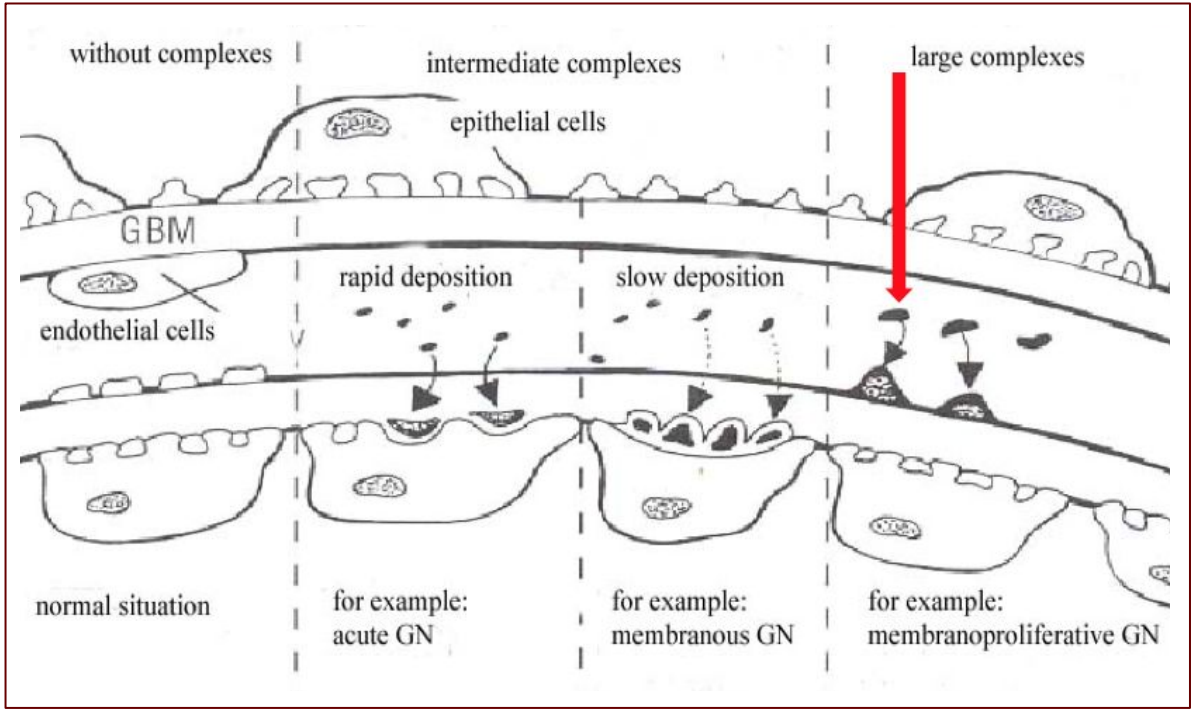
Site of deposition: Complexes accumulate in tissues where **filtration** of plasma occurs. This explains the high incidence of:

- Glomerulonephritis (deposition in the **kidney**)
- Vasculitis (deposition in the **arteries**)
- Arthritis (deposition in **synovial joints**)

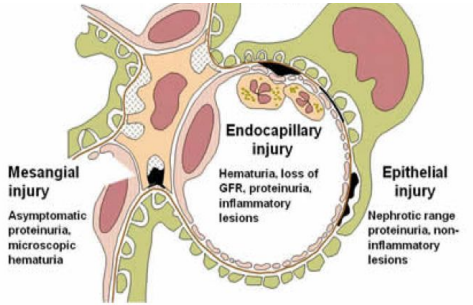


Immune Complex Nephritis

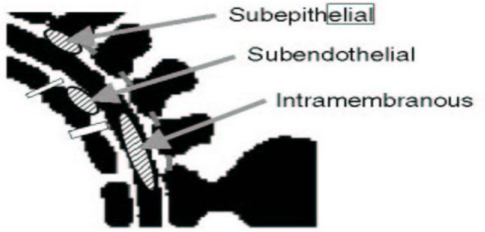
The magnitude of the reaction depends on the quantity of immune complexes as well as distribution within the wall of glomerular capillary



Glomerular Injury is determined by immune complex localization as are the clinical symptoms



Location of immune deposits in the glomerular Capillary wall



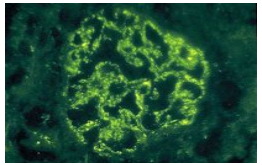
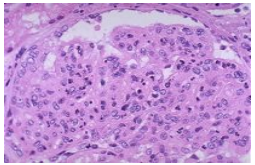
Types of immune-mediated renal injury:

1. Post Infectious Glomerulonephritis (GN) (Post-streptococcal)

Presentation:
• 7-14 days after pharyngitis or 14-21 days after (skin infection)
• Abrupt onset (Acute nephritic syndrome)
• Strep antigens trigger antibodies that cross-react to glomeruli
• Circulating immune complexes during filtration in the glomerulus deposit in the kidney activating the complement system.

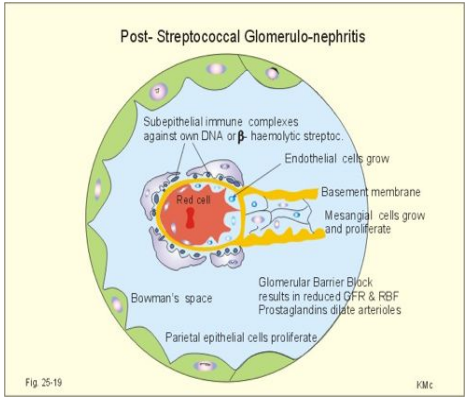
Features of Acute glomerulonephritis:
- Diffuse proliferative GN (PGN)
- Diffuse proliferation of glomerular cells and frequent infiltration of leukocytes (especially neutrophils)

Typical features of immune complex disease:
1- Hypocomplementemia
2- Granular deposits of IgG & complement on GBM

the immune deposits are distributed in the capillary loops in a granular, bumpy pattern because of the focal nature of the deposition process.

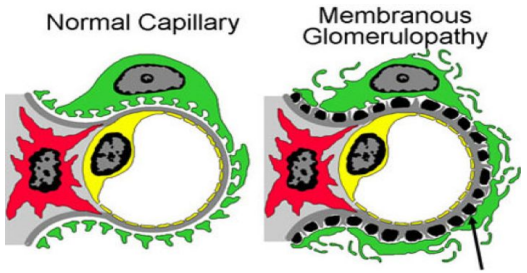
Post-streptococcal GN:
• Caused by known streptococcal types called: nephritic strains
- In most children bacterial culture will be negative & Anti-streptolysin-O antibody (ASO) will be the only evidence.
The anti-DNAse B titre is a better indicator of streptococcal skin sepsis than the ASO titre.
- Cholesterol and lipids in skin suppress the ASO antibody response but not the anti-DNAse B antibody titre.



2. Membranous Glomerulonephritis (Membranous nephropathy)

- A slowly progressive disease
- A form of chronic immune-complex nephritis
- Most common between 30 - 50 years but rare in children.
- Most common cause of primary nephrotic syndrome in Caucasian adults above 40 years.
- 60% of cases are primary whereas the remaining cases are secondary to conditions such as cancer, infection and drugs

- M-type phospholipase A2 receptor 1 (PLA2R) represents the major target antigen in primary membranous nephropathy.
- Anti-PLA2R antibodies are present in 70%-80% of patients with primary membranous nephropathy.



Types of immune-mediated renal injury:

3- Membranoproliferative Glomerulonephritis (MPGN) OR Mesangiocapillary GN

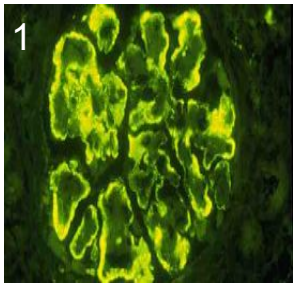
It is a chronic progressive glomerulonephritis that occurs in older children and adults:

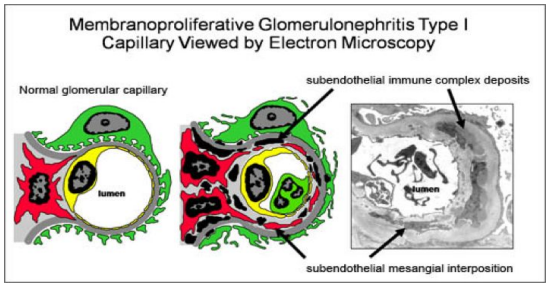
1 Type I MPGN (80% of cases)

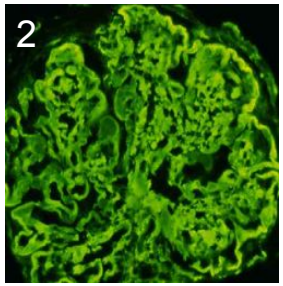
- Circulating immune complexes have been identified
- May occur in association with **hepatitis B & C antigenemia**, **extra-renal infections** or **SLE**
- Characterized by **subendothelial** and **mesangial deposits**

2 Type II MPGN Also known as : dense deposit disease

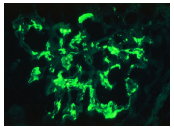
The fundamental abnormality is:
- **Excessive complement activation.**
- Some patients have autoantibody against **C3** convertase called: **C3 nephritic factor.**
- Characterized by **intramembranous** dense deposits







4. IgA Nephropathy (Berger disease)



- The most common form of primary glomerulonephritis in the world
- Affects children and young adults.

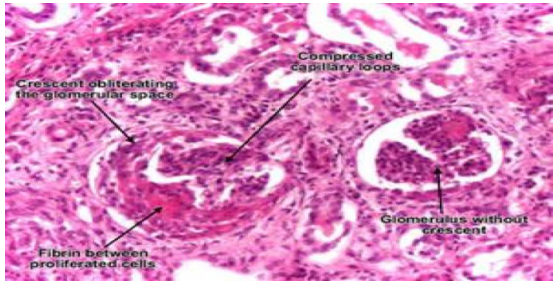
- Begins as an episode of gross **hematuria** that occurs within 1-2 days of a **nonspecific** upper respiratory tract infection
- The pathogenic hallmark is the production of aberrantly glycosylated **IgA** and development of autoantibodies against those **under-lycosylated IgA antibodies**.
- The immune complexes are deposited in the masangium.

- Histology findings: Deposition of **IgA** & complement **C3** in the mesangium
- There is evidence of : Activation of complement by the **alternative** pathway (**serum complement C2 and C4 will be normal** (classical pathway))

Types of immune-mediated renal injury:

5. Rapidly Progressive (Cresentic) Glomerulonephritis (RPGN)

- **RPGN** is a clinical syndrome and not a specific form of GN
- Crescents are defined as the presence of two or more layers of cells in the Bowman space.
- The presence of **crescents** in glomeruli is a marker of severe injury.
- In most cases the glomerular injury is immunologically mediated
-The initiating event is the development of a physical disruption in the **GBM**.
-The lesions are mediated by processes involving macrophages and cell-mediated immunity.
-Following disruption of the glomerular capillary, circulating cells, inflammatory mediators, and plasma proteins pass through the capillary wall into the Bowman space.
-**CrGN** is classified into three groups based on immunological findings

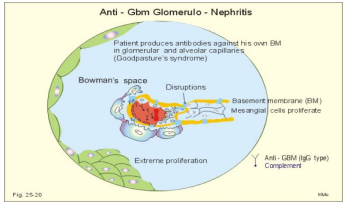


1 Type I (Anti-GBM antibody) (Cresentic GN)

Characterized by linear deposition of **IgG** and **C3** on the GBM

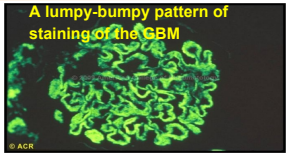
Goodpasture syndrome

Antibodies bind also in the pulmonary alveolar capillary basement membranes



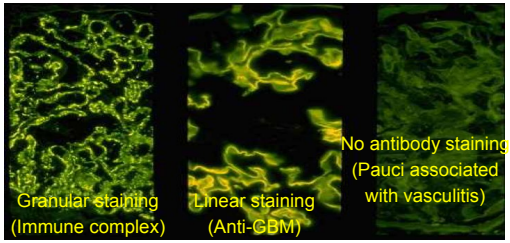
2 Type II (Immune complex - mediated Cresentic GN)

•May occur as a complication of any of the immune complex nephritides
- **Post infectious.**
-**SLE**
- **IgA nephropathy**
• Characteristic granular (lumpy-bumpy) pattern of staining of the GBM for immunoglobulin & complement.



3 Type III (Pauci-immune) Cresentic GN

- Defined by the lack of anti-GBM antibodies.
-Most cases are associated with: Anti-neutrophil cytoplasmic antibodies in serum (**ANCA**) and systemic vasculitis



Take Home Messages

1) Immune complexes underlie the pathogenesis of many of the glomerulonephritides.

2) Activation of the complement system is an integral part of the process, and measurement of the complement proteins help in diagnosis and follow- up of patients.

3) Immunofluorescence of renal biopsy demonstrate the presence of immune complexes and confirm the diagnosis.

Quiz:

1- the feature of post infectious Glomerulonephritis:
A- Hypocomplementemia
B- Anti-PLA2R antibodies
C- Granular deposits of IgG
D- both A & C

2- A disease characterized by intramembranous dense deposits:
A- membranous glomerulonephritis
B- Type I MPGN
C- Type II MPGN
D- Berger disease

3- Type III (pauci-immune) cresentic GN associated with
A- SLE
B- Deposition of IgG and C3 on the GBM
C- ANCA
D- Goodpasture syndrome

4- A disease characterized by decline C3 while the C2 and C4 will be normal ?
A- Berger disease
B- Post infection glomerulonephritis
C- Membranoproliferative (GN)
D- A and B

5- A disease characterized by production of aberrantly glycosylated IgA & autoantibodies against those under-lycosylated IgA antibodies
A- IgA nephropathy
B- Berger disease
C-Post infection glomerulonephritis (GN)
D- Membranoproliferative glomerulonephritis

6- Which of the following may occur with hepatitis B or C?
A- IgA nephropathy
B- Membrano-proliferative glomerulonephritis
C- Membranous glomerulonephritis
D- Crescentic glomerulonephritis

1.D 2.C 3.C 4.A 5.A 6.B

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إنّ الله يعطي أصعب المعارك لأقوى الجُنود فاستمر

Good Luck !

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