LECTURE 1

IMMUNOLOGY OF NEPHRITIS

Introduction

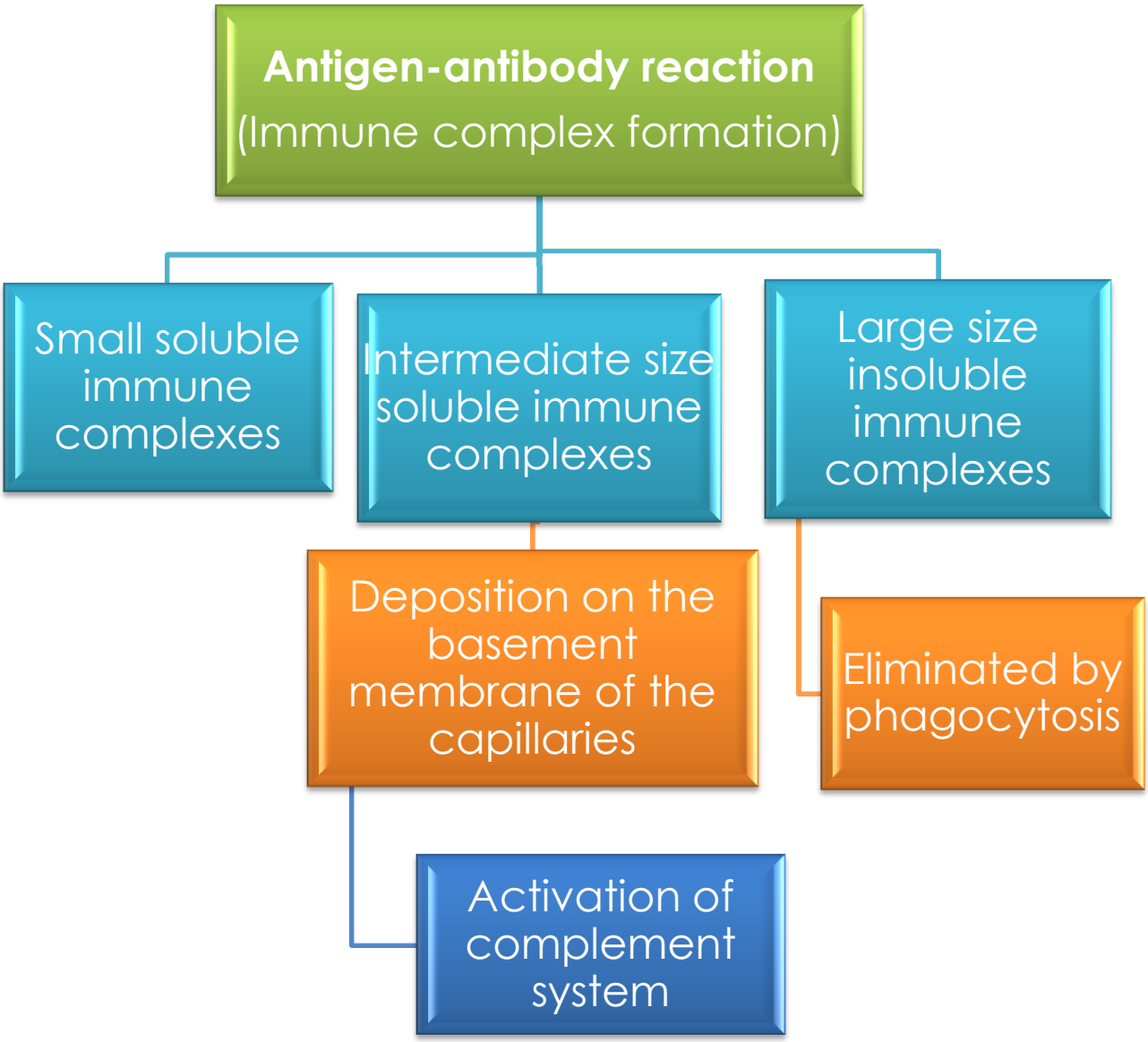
In this lecture the main Hypersensitivity reaction is II and III:

Hypersensitivity II:

Antigens are part of the cell membrane of any tissue >> antibodies bend to them forming immune complex >> induce inflammation.

Hypersensitivity III:

Antigens are circulating in the blood > antibodies bend to them forming immune complex.



The complex is based on it's size:

- **The *small* soluble immune complex is filtered in the glomerulus, it wont cause disease.**
- **The *large* insoluble is easily picked by kupffer cells, and eliminated.**
- **The *intermediate* causes disease.**

Site of Deposition:

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

- **Glomerulonephritis** (kidney)
- **Vasculitis** (arteries)
- **Arthritis** (synovial joints)

Types of immune-mediated renal injury:

- Antibody-mediated Injury:
  - **Membranous glomerulonephritis**
  - **IgA nephropathy**
  - **Membrano-proliferative glomerulonephritis**
  - **Post infectious glomerulonephritis**
  - **Anti-glomerular basement membrane disease**

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

- ✓ **7-14 days** after pharyngitis.
- ✓ **14-21 days** after (skin infection)
- ✓ **Abrupt onset** (Acute nephritic syndrome)

This disease is caused by special type of streptococcal called (nephritic strains)

Antibodies fight Streptococcal antigens then cross-reacted with glomeruli antigens.

circulating immune complex (type 3 hypersensitivity) during filtration in glomerulus deposit in the kidney.

Tests:

- Bacterial culture: in children it will be negative .
- ASO*: is the only evidence of the disease.
- Anti- DNAse B titter: in skin infection it's better than AOS.

Why ? Cholesterol and lipids in skin supress the ASO antibody responses.

Immune complex are deposited in the capillary loops in granular (glomeruli).

Microscopically: lumpy bumpy pattern

*anti- streptolysin-O antibody

Features of Acute glomerulunephritis

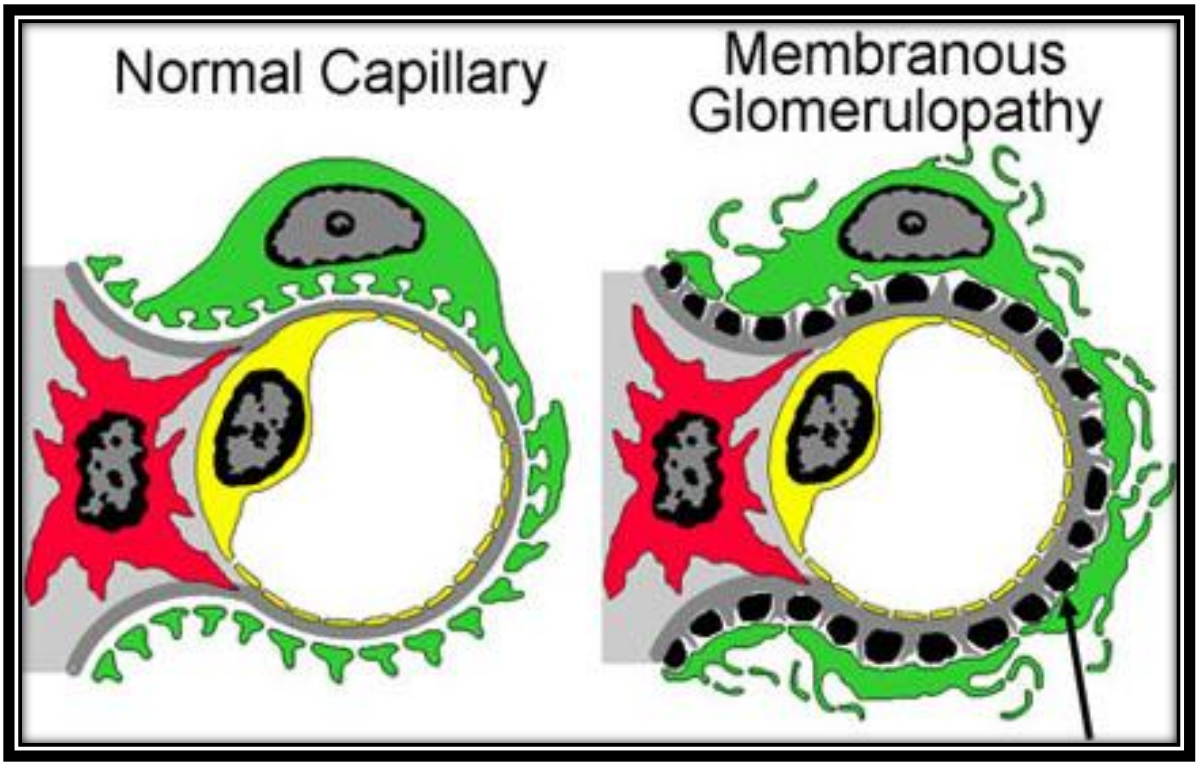
Diffuse proliferation of glomerular cells and frequent infiltration of leukocytes (especially neutrophils)

Typical features of immune complex disease:

- Hypo-complementemia
- Granular deposits of **IgG & complement** on GBM

2. Membranous Glomerulonephritis (Membranous nephropathy)

- ✓ A slowly progressive disease
- ✓ A form of **chronic immune-complex nephritis**
- ✓ Most common between 30 - 50 years

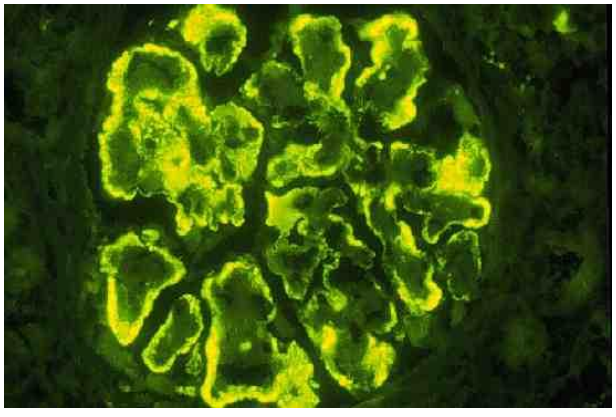


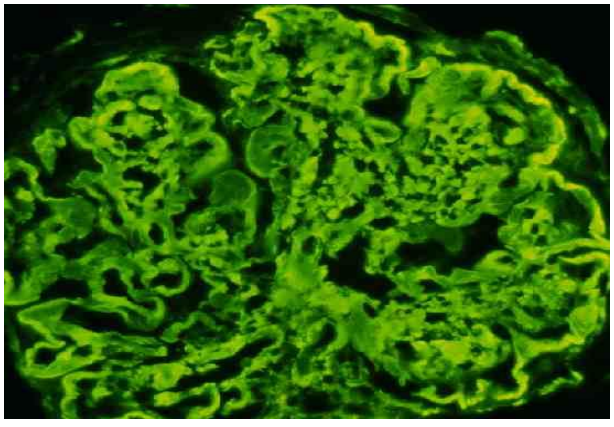
3.Membranoproliferative Glomerulonephritis (MPGN) OR Mesangio-capillary GN

- ✓ It is a chronic progressive glomerulonephritis that occurs in
- ✓ older children and adults.

❑ **2 main types:**

Type I MPGN (80% of cases)	Type II MPGN
➢ Circulating immune complexes have been identified. ➢ May occur in association with hepatitis B&C anti-genemia, Extra-renal infections or SLE. ➢ Characterized by sub-endothelial and mesangial deposits.	➢ 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.





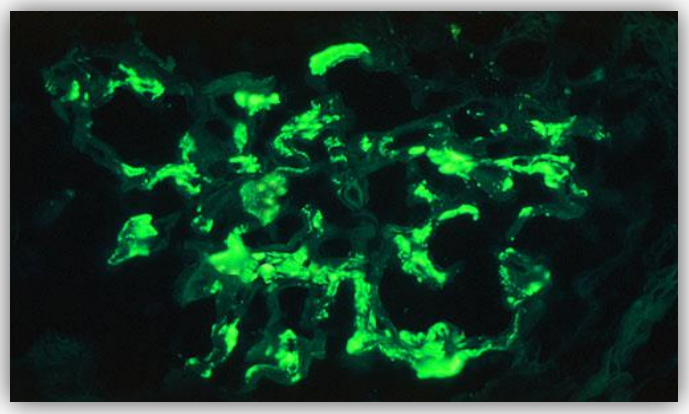
4. IgA Nephropathy (Berger disease)

- ✓ 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 non specific **upper respiratory tract infection**

❑ The pathogenic hallmark* is :

- Deposition of **IgA & complement C3** in the mesangium.
- Evidence of activation of complement by the alternative pathway (serum complement C2 and C4 will be normal)

- This **immunofluorescence** pattern demonstrates positivity with antibody to IgA.
- The pattern is that of mesangial deposition in the glomerulus. This is IgA nephropathy.

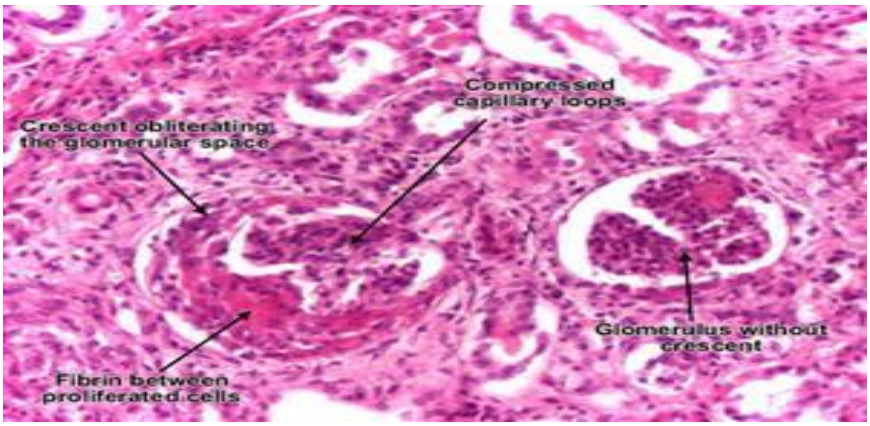


*Hallmark: a sure sign

5. Rapidly Progressive (Cresentic) Glomerulonephritis (RPGN)

- ✓ RPGN is a clinical syndrome and not a specific form of GN
- ✓ In most cases the glomerular injury is immunologically mediated
- ✓ The practical classification of **CrGN** based on the immunologic findings:

- **Type I (Anti-GBM antibody) (Cresentic GN).**
- **Type II (Immune complex - mediated Cresentic GN).**
- **Type III (Pauci-immune) Cresentic GN.**



Rapidly Progressive (Cresentic) Glomerulonephritis

Type I (AntiGBM antibody) Cresentic GN	Type II (Immune complex – mediated) Cresentic GN	Type III (Pauci-immune) Cresentic GN
Characterized by linear deposition of **IgG and C3** on the GBM. (glomerular basement membrane)	May occur as a complication of any of the immune complex nephritides Post infectious, **SLE, IgA nephropathy**	Defined by the **lack of anti-GBM antibodies.**
Goodpasture syndrome*	Characteristic **granular** (microscopically): - A lumpy-bumpy pattern of staining of the GBM	Most cases are associated with: -Anti-neutrophil cytoplasmic antibodies in serum (**ANCA**) and systemic Vasculitis
Antibodies bind also in the pulmonary alveolar capillary basement membranes		

*Extra: Goodpasture Syndrome is a rare disease that can involve quickly worsening kidney failure and lung disease some forms of the disease involve just the lung or the kidney but not both.

Take Home Message

- ✓ Immune complexes underlay the pathogenesis of many of the glomerulo-nephritides.
- ✓ 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.
- ✓ Immunofluorescence of renal biopsy demonstrate the presence of immune complexes and confirm the diagnosis.

MCQs

- **Post Infectious Glomerulonephritis occurs 7-14 days after which f the following?**

A-Nephritic Syndrome B-Pharyngitis C-Skin Infection

- **Which of the following may occur with hepatitis B or C?**

A- Membranous glomerulonephritis B- IgA nephropathy

C- Membrano-proliferative glomerulonephritis

- **What is the hallmark of Berger's Disease?**

A- Serum complement C2 & C4 B-IgG C-IgA & complement C3

- **What is type III Cresentic GN characterized by?**

A- ANCA B- SLE C- IgG & C3

- **Which of the following tests confirms the diagnosis of an immune complex GN?**

A- Bacterial Culture B- Immunofluorescence C- ASO

1:B, 2:C, 3:C,4:A, 5:B