Renal Block

Immunology

Lecture 1

Immune Complex Nephritis

In this document you will find some main points gathered from the 1st lecture..This document is NOT a replacement for the lecture..If you need additional information go back to the lecture or use a book as a reference so you understand everything correctly.

Hopefully all the information is correct and Hope you find them Useful.

Good Luck to everyone.

430 Immunology Team

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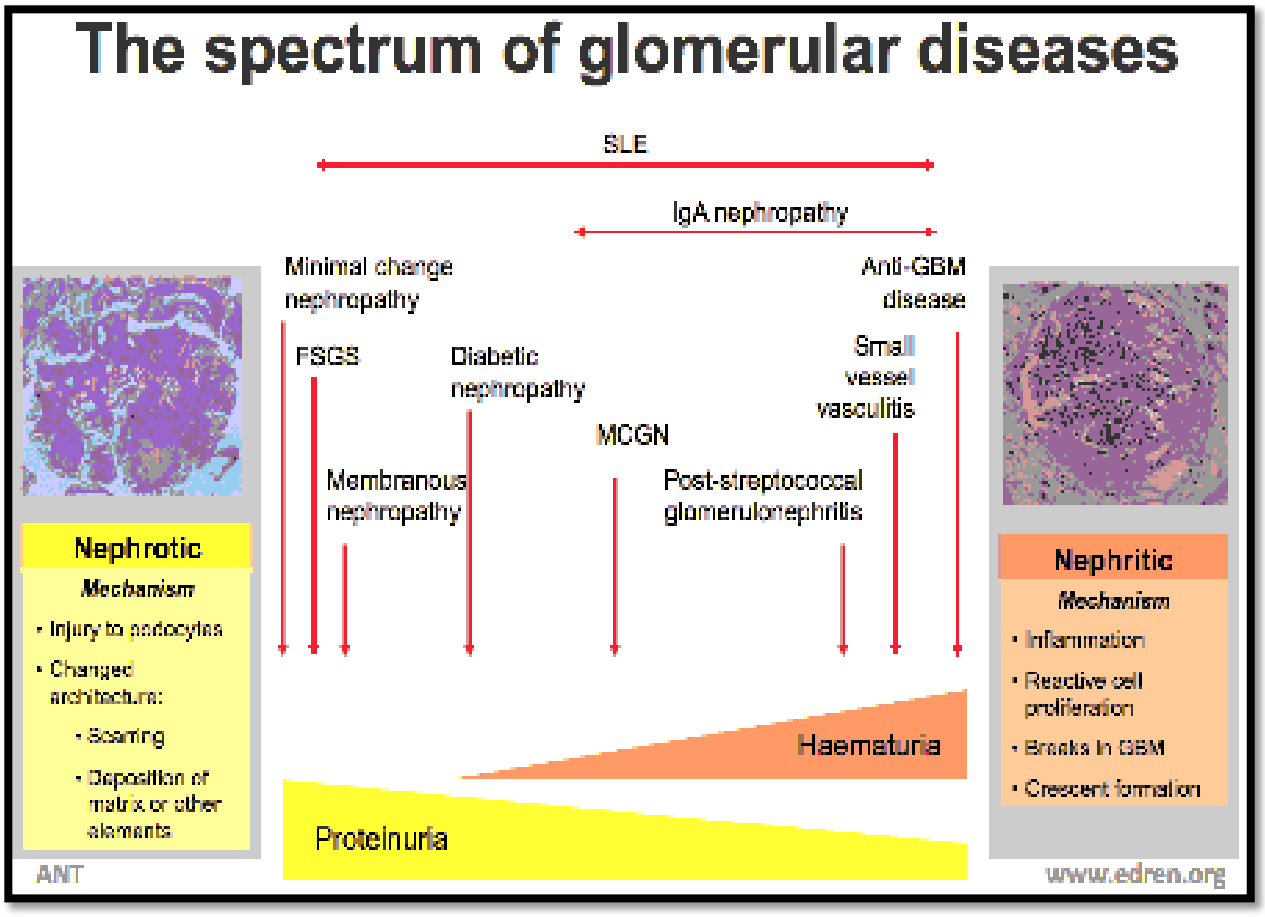
Immunology

Some main points you can go through and revise from:

Complexes of antibody with various bacterial, viral, parasitic OR self antigens have been shown to induce a variety of type II & III hypersensitive reactions in the kidney :



Pathogenesis of immune-complexes

Soluble antigen + Antibody = Immune complex

Fates of different complexes:

Small soluble Immune complex	**Excreted with urine**
Intermediate soluble Immune complex	**Deposit on the basement membrane c capillaries → activate complement sys**
Large insoluble Immune complex	**Eliminated by phagocytosis**

To help you understand

This basically means that "Intermediate soluble Immune complexes" are most likely to cause more damage than the other two

Site of deposition:

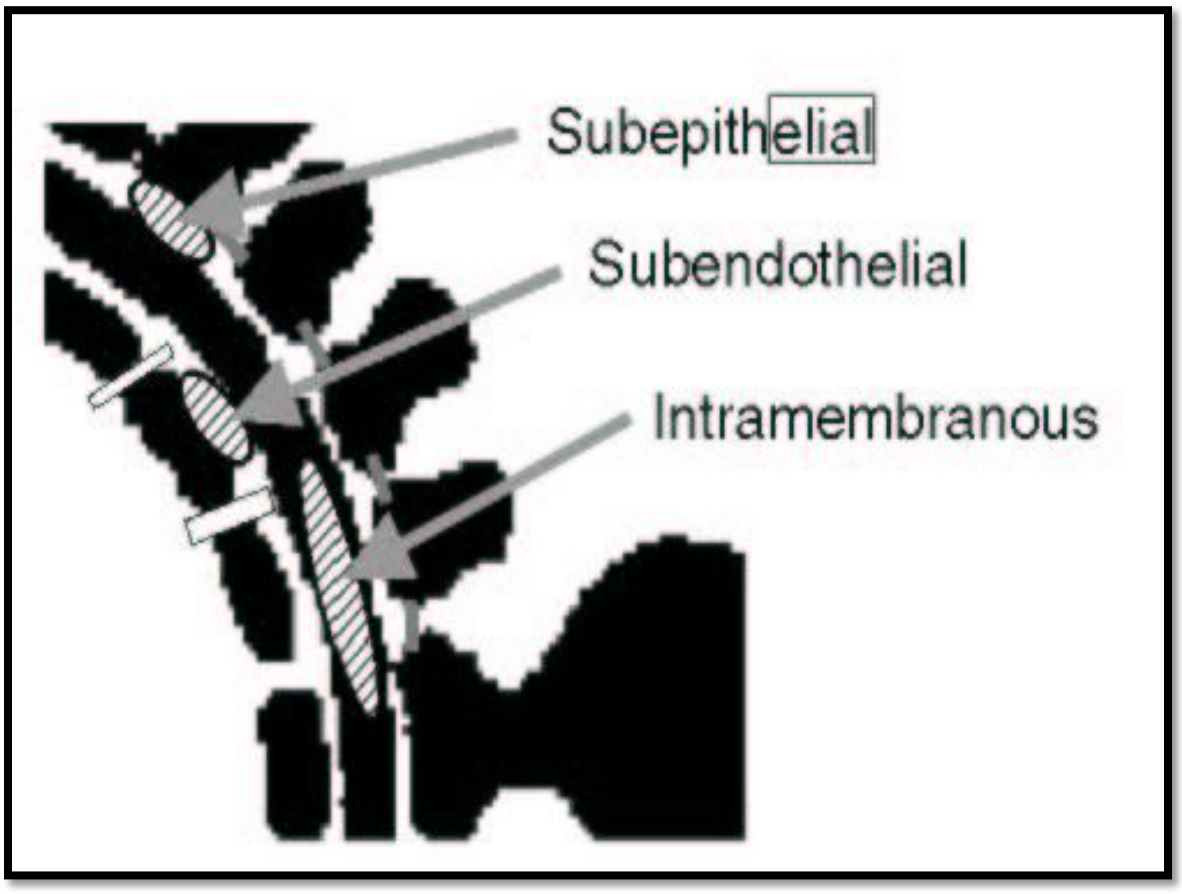
Complexes accumulate in tissues where filtration of plasma occurs.
(The reasons why those diseases occure)

Glomerulonephritis	**deposition in the kidney**
Vasculitis	**deposition in the arteries**
Arthritis	**deposition in the synovial joints**

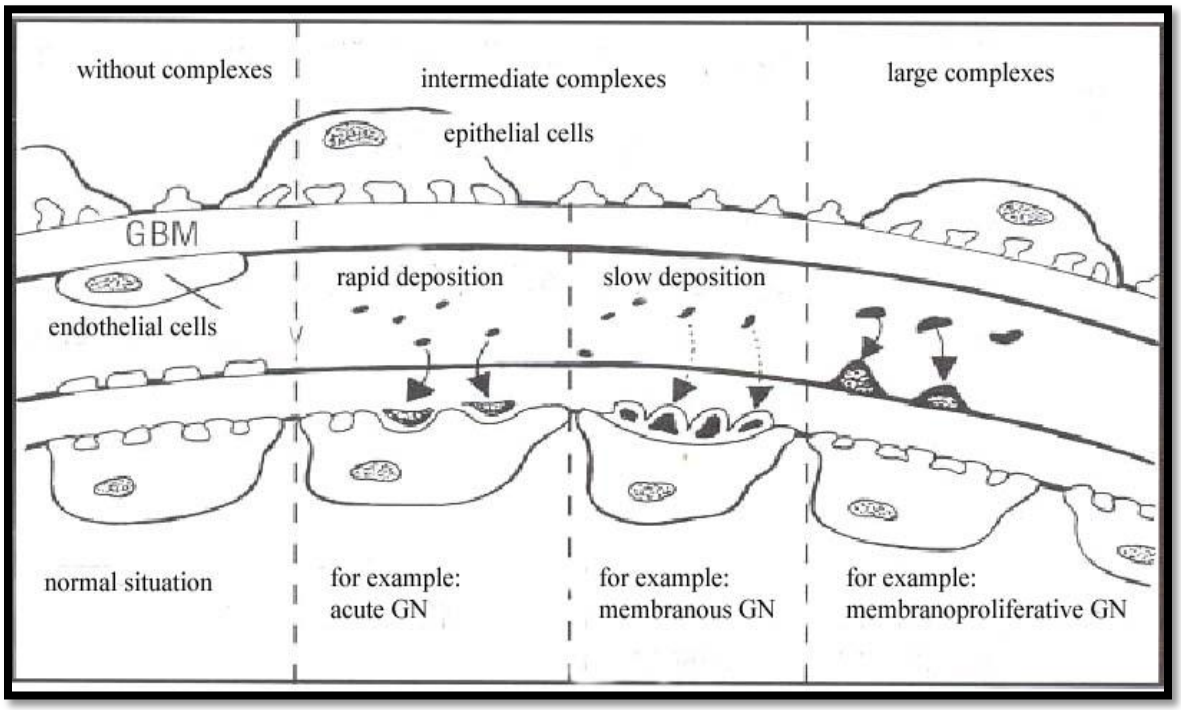
Situations that occur with different complexes:

Without complex	Endothelial cells	Normal situation
Intermediate soluble Immune complex	Rapid deposition→ Acute GN	Slow deposition→ Membranous GN
Large insoluble Immune complex	Membranoproliferative GN	

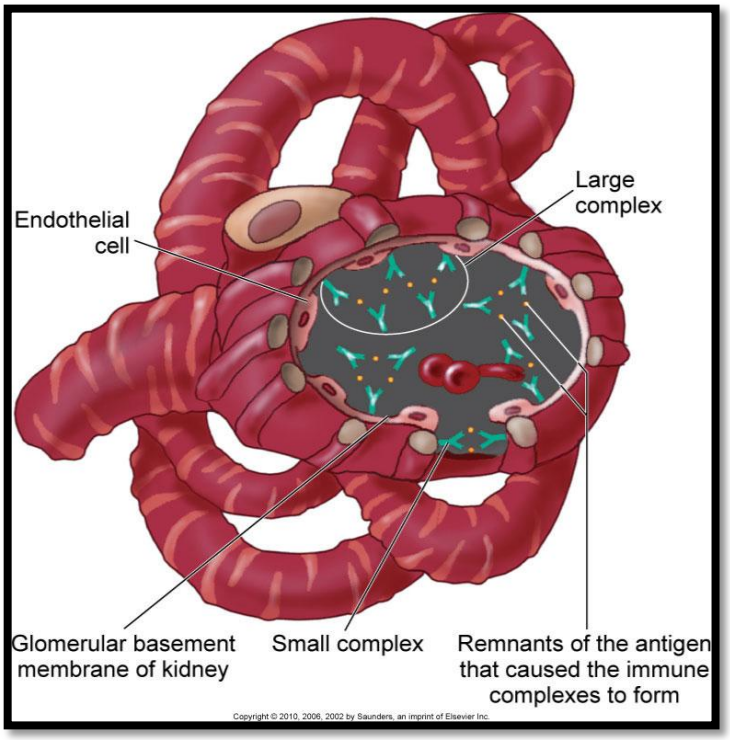
Location of immune deposits in the glomerular capillary wall :



The extent of the reaction depend on the size ,the site and rate of deposition of the immune-complexes :



Immune Complex in a Type III Hypersensitivity Reaction:



Antibodies may interact with:

- Intrinsic components of the glomerular basement membrane (from inside the glomerular)
- Antigens on glomerular cells. (Antigens of the glomiruli itself)
- Exogenous antigens planted within the glomerulus (foreign antigens).
- Glomerular deposition of circulating immune complexes.

Types of immune-mediated renal injury:

- Antibody- Mediated Injury :

  - Membranous glomerulonephritis.
  - IgA nephropathy.
  - Membranoproliferative glomerulonephritis.
  - Post infectious glomerulonephritis
  - Antiglomerular basement membrane disease.

1. Post Infectious GN

Duration	**7-14 days after pharyngitis** **14-21 days after (skin infection ,impetigo)**
Action	**Strep antigens trigger antibodies that cross-react with glomeruli → activate complement system**
Site	**immune complexes during filtration in the glomerulus deposit in the kidney**
Diagnosis	**In most of the children bacteriological cultures are negative** **anti-streptolysin-O antibodies (ASO) are the only evidence of a previous Strep infection.**
Other	**generalized damage to glomeruli** **Known nephritic strains include M types 1, 2, 4, 12, 18, 25, 49, 55, 57, 60.**

Features of acute glomerulunephritis

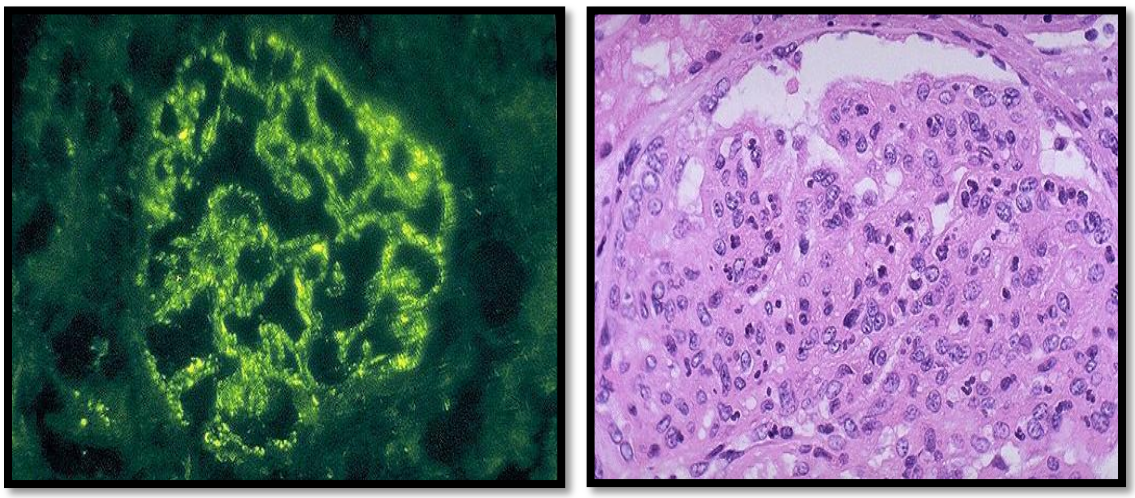
- Diffuse Proliferative GN (PGN)
- Proliferation of cells within the glomeruli, accompanied by leukocyte infiltrate
- Typical features of immune complex disease :

  - Hypocomplimentemia. (Less complements in blood)

  - Granular deposits of IgG & complement on GBM

Poststreptoccal GN (nephritic strains)

- Known nephritic strains include M types 1, 2, 4, 12, 18, 25, 49, 55, 57, 60.
- In most of the children bacteriological cultures are negative
- The only evidence of previous strep infection is the detection of anti-streptolysin-O antibodies (ASO)
- Post streptococcal GN. Diffuse Proliferative GN . (generalized damage to glomeruli).



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

2.Membranous Glomerulonephritis

Duration	**A slowly progressive disease** **Most common between 30 - 50 years**
Site	**The subepithelial aspect of the capillary loop between the outer aspect of the basement membrane and the podocyte(slow deposition)**
Idiopathic in 85% of cases	**Endogenous antigens.** **Planted glomerular antigens**
In the remainder (15%)	**may be secondary to :** **1. Infections.** **2. Tumors.** **3. Autoimmune disease.** **4. Drugs.**

3.Membranoproliferative Glomerulonephritis

A chronic progressive glomerulonephritis that occurs older children and adults

- **Type I (80%)**

Action	**Circulating immune complexes have been identified**
Site	**sub-endothelial deposits**
Related Disease	**hepatitis B&C antigenemia, extra-renal infections or SLE**

- **Type II (dense deposit disease)**

Characteristic	**excessive complement activation (not involving antibody)**
Site	**by intramembranous dense deposits(endothelial cell)**
Other	**Some patients have autoantibody against C3 convertase called C3 nephritic factor**

4.IgA Nephropathy (Berger disease)

*Is the most common from of primary glomerulo-nephritis in the world

Affect	children and young adults
symptoms	hematuria that occurs within 1-2 days of a non specific upper respiratory tract infection
Site	the deposition of IgA in the mesangium
Diagnosis	of abnormal production and clearance of IgA and activation of complement by the alternative pathway
Related Disease	Some consider IgA nephropathy as a localized variant of Henoch-Schonlen purpura

Henoch- Schonlen purpura

A systemic syndrome involving the :

- Skin (purpuric rash)
- Gastrointestinal tract (abdominal pain)
- Joints (arthritis)
- Kidneys

5. Rapidly Progressive (Cresentic) Glomerulonephritis

- RPGN is a clinical syndrome and not a specific form of GN
- In most cases the glomerular injury is immunologically mediated
- A practical classification divides CrGN into three groups

Type I (anti-GBM antibody) (Cresentic GN)

- Idiopathic: Characterized by linear deposition of IgG and C3 on the GBM
- Goodpasture syndrome : Antibodies also bind pulmonary alveolar capillary basement membranes

Type II (immune-complex)

(immune complex - mediated Cresentic GN)

This may occur as a complication of:

- Post infectious
- SLE
- IgA nephropathy
- Characteristic granular (lumpy-bumpy) pattern of
- Staining of the GBM for immunoglobulin & complement

Type III (Pauci-immune)

Cresentic GN

*Characterized by the lack of anti-GBM antibodies

Most cases are associated with:

- Anti-neutrophil cytoplasmic antibodies in the serum (ANCA) and systemic vasculitis.

Chronic Glomerulonephritis

Represents the end stage of a variety of entities:

- Cresentic Glomerulonephritis
- Focal segmental glomerulosclerosis
- IgA nephropathy
- Membranoproliferative Glomerulonephritis

- Among all individuals who require chronic hemodialysis or renal transplantation, 30% to 50% have the diagnosis of chronic GN.
- 20% of cases may arise with no history of symptomatic renal disease
- Chronic GN may develop at any age, but it is usually noted in young and middle aged adults.