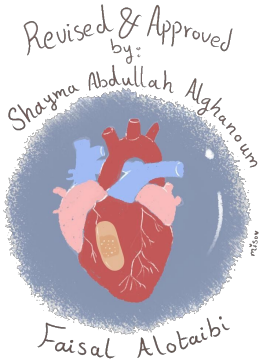


Immune-Complex Nephritis

Color index

Important

Extra information

Notes

Slide reference

IMMUNOLOGY
TEAM 439

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.

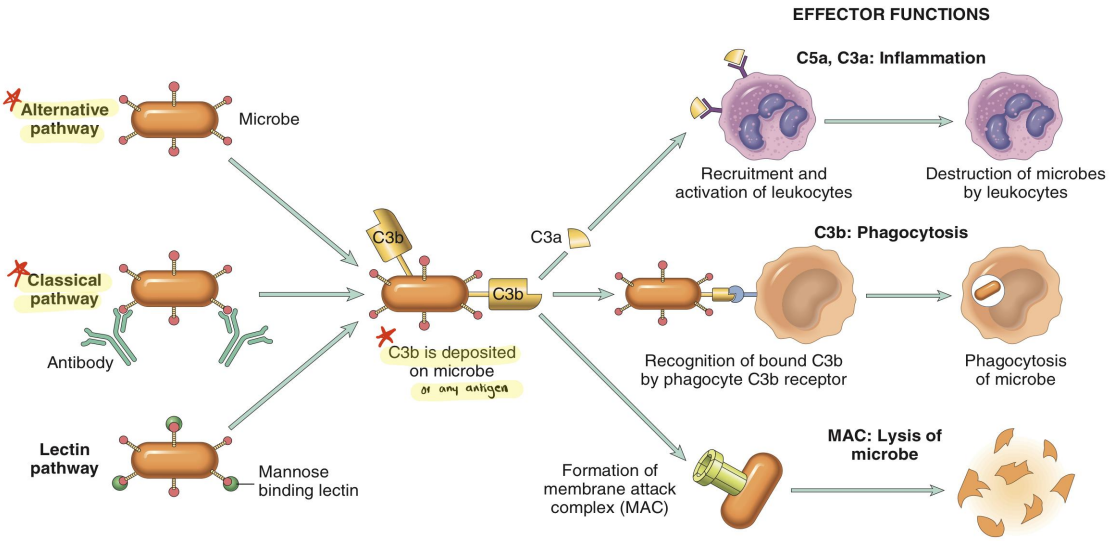
Editing File

Click here!
Please check frequently

Please do not be frightened by the slide number or notes. The lecture is easy and simple. We did our best to explain it in the clearest way possible.

GOOD LUCK!

Complement System Recap



One of the regulatory functions of complement system is the **clearance of immune complexes** and apoptotic cells without causing harm to tissue (Physiological, may become pathological when it causes harm).

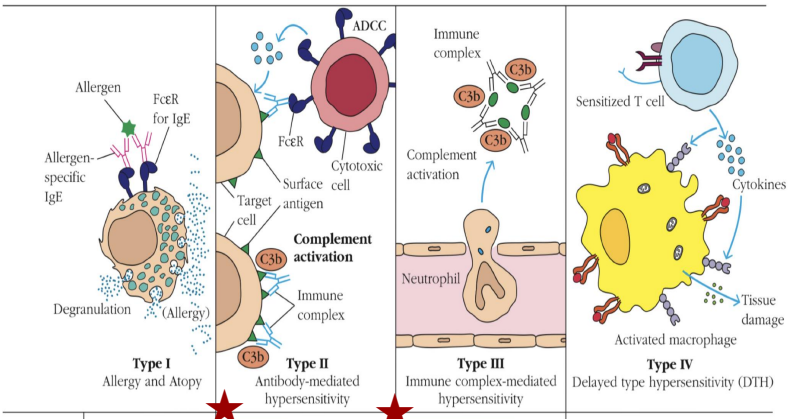
Normally, insoluble immune complexes that are formed are cleared by the phagocytic cells of the immune system, but when an **excess** of antigen–antibody are present, the immune complexes are often deposited in tissues, where they can elicit complement activation, localised inflammation resulting in the generation of tissue lesions in a variety of autoimmune diseases, exacerbating disease pathology. Binding of immune complexes to Fc receptors on leukocytes also may contribute to activation of the cells and injury.

One of the important complement proteins is C3. It's normal function is to opsonizes microbial cells and immune complexes, rendering them suitable for phagocytosis.

The binding of antibody to antigen activates a certain pathway. **IgA** activates the **alternative** pathway while **IgG** and **IgM** activate the **classical** pathway.

This introduction was given as we'll be discussing a number of diseases causing disruption in renal function because of the inflammatory process in relation to immune complexes.

Hypersensitivity Reactions



Immune mediator	IgE	IgG or IgM	Immune complexes	T cells
Mechanism	Ag induces cross-linking of IgE bound to mast cells and basophils with release of vasoactive mediators.	Ab directed against cell surface antigens mediates cell destruction via complement activation or ADCC.	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils.	Sensitized T cells (T_H1, T_H2 and others) release cytokines that activate macrophages or T_C cells which mediate direct cellular damage.
Typical manifestat-ions	Includes systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema.	Includes blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia.	Includes localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus.	Includes contact dermatitis, tubercular lesions, and graft rejection.

Type II

Antigens are fixed in the membrane of any tissue. The antibodies (IgG or IgM) will come to the tissue and bind to its antigen (forming an immune complex), which activates the complement system which will initiate an inflammatory response resulting in tissues damage or destruction (associated to autoimmunity).

Type III

The antigens are circulating in the blood (floating antigens) and the antibodies (IgG) bind to them and forming an immune complex. These complexes will be circulating in the blood and could be deposited in tissue where they can also induce an inflammatory response.

Terminology

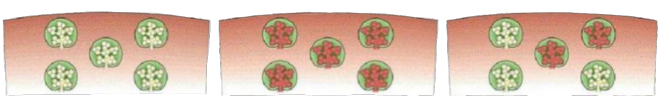
1 Describing to what extent the glomerulus is affected

Normal

Global
If the whole glomerular tuft is involved

Segmental
Only a part of the glomerulus is affected

2 Describing the number of affected glomeruli



Normal

Diffuse
Most of the glomeruli (>75%) contain the lesion

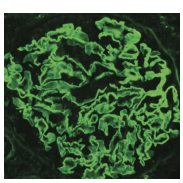
Focal
Some but not all the glomeruli contain the lesion

3 Describing conformational changes in the glomerulus

- **Proliferation:** Hyperplasia of one of the glomerular cell types, with or without inflammatory cell infiltration
- **Membranous changes:** Capillary wall thickening due to immune deposits or alterations in basement membrane.
- **Crescent formation:** parietal epithelial cell proliferation and mononuclear cell infiltration forming a crescent-shape (هلال) in Bowman's space.

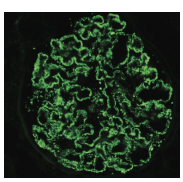
4 Linear Pattern

- IF microscopy reveals well-defined lines, characteristic of anti-GMB GN



5 Granular Pattern

- IF microscopy reveals what is called as "bumps and humps" or "lumpy-dumpy", characteristic of circulating and in situ immune-complex deposition



Pathogenesis of Immune Complex Nephritis

Spectrum of Glomerular Diseases

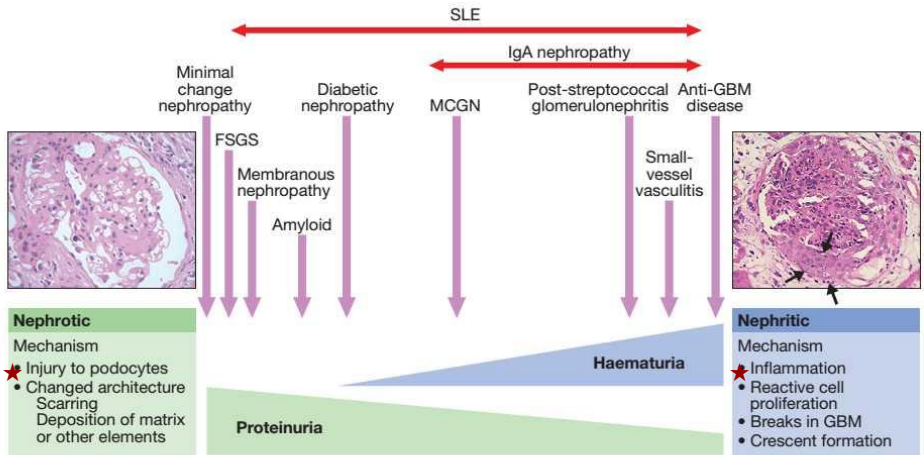


Fig. 17.21 Spectrum of glomerular diseases. At one extreme, specific injury to podocytes or structural alteration of the glomerulus affecting podocyte function (for example, by scarring or deposition of excess matrix or other material) causes proteinuria and nephrotic syndrome (see Box 17.11, p. 475). The histology to the left shows diabetic nephropathy. At the other end of the spectrum, inflammation leads to cell damage and proliferation, breaks form in the GBM and blood leaks into urine. In its extreme form, with acute sodium retention and hypertension, such disease is labelled nephritic syndrome. The histology to the right shows a glomerulus with many extra nuclei from proliferating intrinsic cells, and influx of inflammatory cells shows crescent formation (arrows) in response to severe post-infectious glomerulonephritis. (FSGS = focal and segmental glomerulosclerosis; MCGN = mesangiocapillary glomerulonephritis)

The figure lists some diseases caused by hypersensitivity reactions (type II and III) in the kidney induced by complexes made of **antibodies** with various microbial (nonself) antigens or self **antigens**. The severity of the reaction depend on the **size**, the **site** and **rate** of deposition of the immune complexes. Figure plots the diseases on a spectrum that fits how close the histopathology of the disease relates to either nephrotic syndrome (Characterized by **injury to renal tissue** causing heavy **proteinuria**) or nephritic syndrome (Characterized by **inflammation** of region causing **hematuria** mainly microscopic that can be visible or not).

*Types of Immune-Complexes in Circulation
(Induce Type III Hypersensitivity)

Small, soluble immune-complexes

Very small, not noticed by immune system, therefore cause no disease. Won't cause serious injury and will end up filtered by the glomerulus.

(Excreted in urine)

Intermediate, soluble immune-complexes

Not effectively picked up by macrophages. They're able to deposit in tissue. Deposition on the basement membrane of the capillaries which triggers activation of complement system (inflammatory response), then cause renal damage.

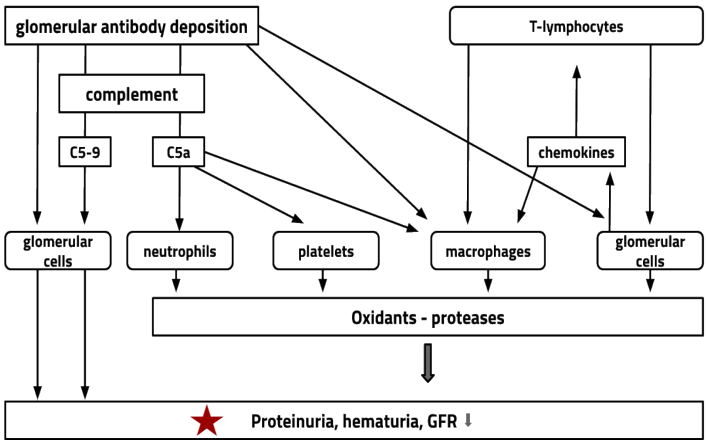
(The ones causing trouble)

Large, insoluble immune-complexes

Eliminated by phagocytosis. They will aggregate and become recognized to the phagocytic cells such as macrophages and be phagocytosed. However, when they increase in number, it will exceed the rate of phagocytosis to clear them and they will be deposited and cause trouble.

*Our bodies normally produce immune-complexes on a daily basis to get rid of the bacteria and viruses. They're cleared by Reticuloendothelial system in the liver. Macrophages of the liver (kupffer cells), engulf them and remove them to keep us healthy. Then, why are there diseases because of these complexes? The problem that the body might face, is when the size of these immune complexes are too big, or when the rate of immune complex formation is overwhelming the ability of the immune system to get rid of them (they're forming faster then they're cleared). -Team 432

Immune- Mediated Glomerular Injury



Mechanism of Glomerular Injury

Initiated by deposition of immune complexes in tissue (glomeruli) → activates complements (C5-9/C5a) → infiltration of different cells (neutrophils/ macrophages/ platelets/ glomerular cells) and **activation of T cells** lead to the release of chemokines and **more** inflammatory cells aggregation → Destruction of the tissue (glomeruli)

This leads to: decrease in GFR, proteinuria and hematuria.

- **Team 434**

Site of Deposition

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

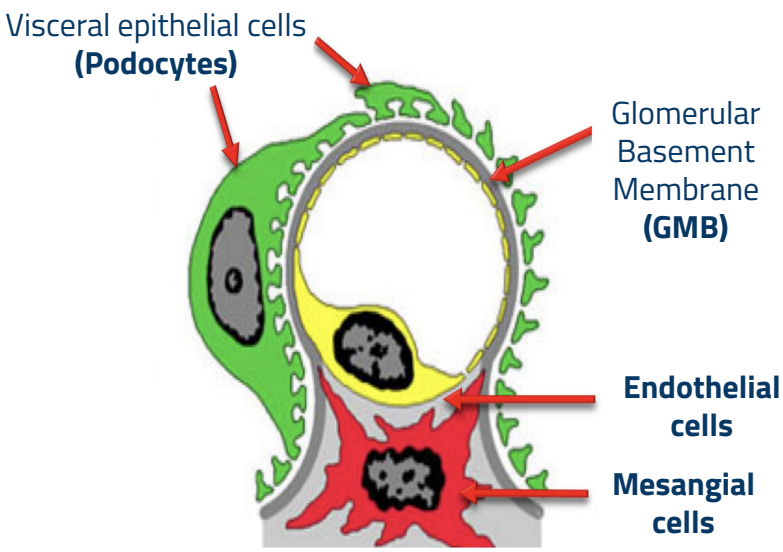
Glomerulonephritis
(Deposition in Kidney)
Most common

Vasculitis
(Deposition in Arteries)
Especially small vessels

Arthritis
(Deposition in Synovial joint)

Where in the kidney do immune-complexes deposit?

★ Glomerular injury is determined by the location of immune complex deposits. And so are the clinical symptoms of the disease.



Normal histology of Glomerulus

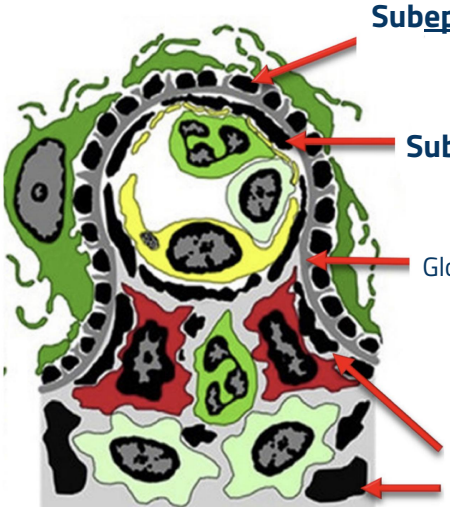
Types of Immune-Mediated Renal Injury

This lecture covers 5 of antibody-mediated renal diseases:

- **Post Infectious Glomerulonephritis** (Post Streptococcal, PIGN)
- **Membranous Glomerulonephritis** (Membranous Nephropathy)
- **Membranoproliferative Glomerulonephritis** (MPGN)
- **IgA Nephropathy** (Berger disease)
- **Anti-Glomerular Basement Membrane Disease** (Type I RPGN)

Overview: Site of Deposition

	Types of Antibody-Mediated Renal Diseases							
Disease	Post-Infectious GN	Membranous GN	Membranoproliferative GN		IgA Nephropathy	Rapidly Progressive GN		
Subtype			Type I MPGN	Type II MPGN		Type I (Anti- GBM)	Type II (immune-mediated Crescentic GN)	Type III (Pauci-immune)
Site	Diffused deposits (everywhere) Usually subepithelial & in GMB	Primary MGN: Subendothelial deposits	Subendothelial & mesangial deposits	Intramemb-ranous **d**ense **d**eposits	Mesangial deposits	GMB	GMB	GMB



Deposits in Glomerulus (in Black)

Subepithelial deposits

Nephrotic range proteinuria, non- inflammatory lesions

Subendothelial deposits

Hematuria, loss of GFR, **non-nephrotic range proteinuria**, inflammatory lesions

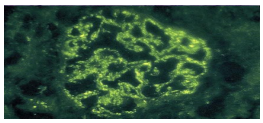
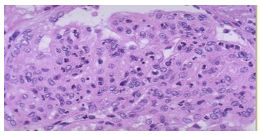
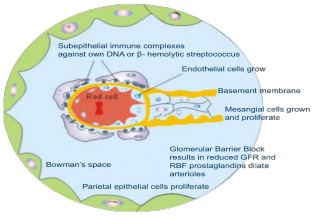
Glomerular Basement Membrane **(GMB)**

Mesangial & Paramesangial deposits

Asymptomatic proteinuria, microscopic hematuria

1. Post-Infectious Glomerulonephritis (GN)

(Post-streptococcal)

Onset	➢ Abrupt onset of disease (after an infection is over, **post-infectious**) ➢ 7-14 days **after** pharyngitis ➢ 14-21 days **after** skin infection Manifests **after** the episode of infection is over. There will be no symptoms of infection, no organisms growing with culture. Occurs following resolution of the infection, and there's an infection-free latent period that occurs after 1-3 weeks. The disease spontaneously resolves in a month.	
Etiology	Caused by antibodies formed against a strain of streptococcal organisms known as **nephritic strain**.	
Mechanism	Circulating immune-complexes that will deposit in the glomerulus during filtration **(Type III HS)**, sometimes some of the strep. antigens will deposit in the glomeruli and antibodies (IgG) will cross-react to form immune-complex there → Activation of complement → Generalized damage to glomeruli due to inflammation (Team 434)	
Diagnostic Tests	Culture	In most children (more susceptible), bacterial culture will be **negative.** Why Because the infection is gone, therefore culture is not useful to diagnose post-infectious GN.
	Serology These tests detect antibodies against enzymes produced by streptococci. They help to establish **prior** infection, not acute streptococcal infections.	**Anti-streptolysin O titer (ASO)** ➢ Only evidence (number one choice) ➢ Not best indicator of streptococcal skin infection because the cholesterol and lipids in the skin **suppress** ASO antibody response **Anti-DNAse B titre (ADB)** ➢ More sensitive indicator of streptococcal skin infection ➢ Not suppressed by skin lipids
	Microscopy	 IF: Immune deposits are distributed in the capillary loops in a **granular, bumpy pattern** because of the focal nature of the deposition process.  LM: Dense cell proliferation seen with marked infiltration
Characteristic	➢ It is a type of acute diffuse proliferative GN (all glomerulus affected). Diffuse proliferation of glomerular cells and frequent infiltration of leukocytes, especially neutrophils. (hyperplasia of cells with inflammatory infiltrate). ➢ One of the nephritic syndromes (Clinical features will be hematuria etc). ➢ Typical features of immune complex disease: ○ Hypocomplementemia C3, C4 levels in serum are **low**. Why? they got consumed in the immune response, inflammation. ○ Renal biopsy shows **Granular deposits of IgG & complement on GBM** 	

2. Membranous Glomerulonephritis

(Membranous Nephropathy)

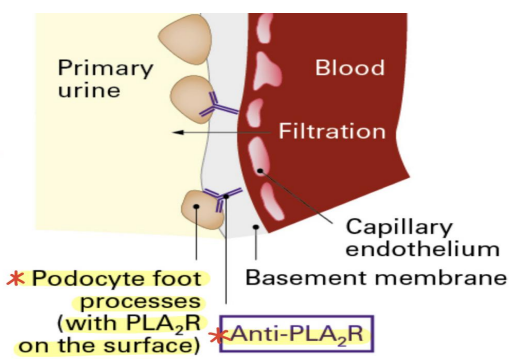
Overview

- Slowly progressive disease, a form of **chronic** immune-complex nephritis (like MPGN, and unlike post-infectious which is **acute**)
- Its a type of nephrotic syndromes (unlike post-infectious which is nephritic)

Epidemiology

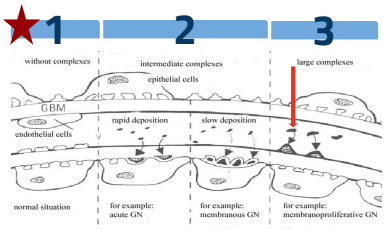
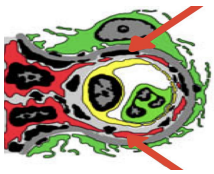
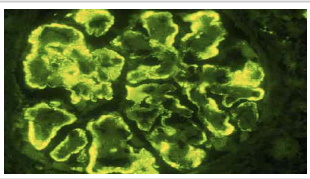
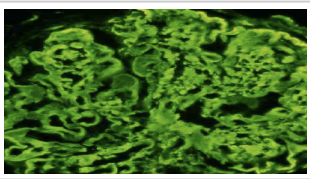
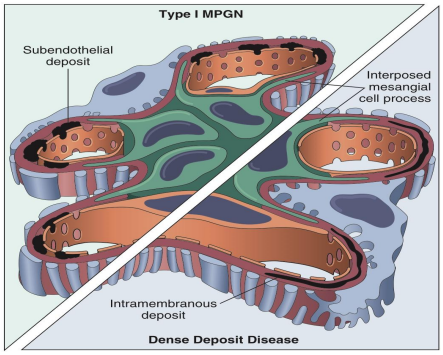
- Most common between 30-50 years but rare in children.
- Most common cause of primary nephrotic syndrome in Caucasian adults above 40. *Which means when a Caucasian patient came with a primary nephrotic syndrome the first type we think of is membranous GN.

	Primary MGN 60% of cases, more common	**Secondary MGN**
Etiology	Majorly due to autoantibodies directed against M-type phospholipase A2 receptor 1 (PLA2R) which are found on the surface of podocytes (subepithelial immune deposits) (Type II Hypersensitivity). It's unknown why these autoantibodies are formed. However, not all patients with Primary MGN will have these autoantibodies (only 70%-80% of patients have anti-PLA2R) as there could be other antigens targeted in this disease (watch osmosis for more).	Disease develops as a results of another condition, autoantibodies formed in response to the following could cause this disease: 1. Cancer (lung carcinoma) 2. Infections (hepatitis B) 3. Drugs



Subepithelial deposition "Under the podocytes"

3. Membranoproliferative Glomerulonephritis (MPGN) or (Mesangiocapillary GN)

Definition	➢ It is a **chronic** progressive glomerulonephritis that occurs in older children and adults. ➢ It can manifest as either nephrotic **or** nephritic syndrome.	
Types	**Type I**	**Type II**
Etiology	**In blood:** Antigen (ex. Antigen of hepatitis B, chronic infection) + Antibody = Circulating **large** immune complexes that will deposit in the glomerulus. (Type III Hypersensitivity)  More common (**80%** of cases are type I)	The fundamental abnormality is: ➢ Excessive complement activation by the alternative pathway (abnormal activation). ➢ C3 Nephritic Factor is an autoantibody **against C3 convertase**, which causes uncontrolled cleavage of C3 by the alternative pathway [Robbins]. *The autoantibody (Abnormal IgG) will recognize and stabilize the C3 convertase enzyme, meaning it will exist for a longer period than usual & will continue to cleave C3 into C3a + C3b.
Pathogenesis	Immune-complex deposits (Large)	Alternative pathway (complement deposits)
Site	 Sub**endothelial** & mesangial deposits	Intramembranous dense deposits. *formed by C3. **Also known as, Dense Deposit Disease.**
Complement Pathway	Deposition triggers activation of the complement system by the **classical pathway**. How do we know its the classical pathway? By detecting **C2, C4, and C3** we will find that their levels in the plasma have **decreased**. Proteins involved: (C1,**C4,C2,C3**,C5,C6,C7,C8,C9)	Autoantibody triggers activation of the complement system by the **alternative pathway**. How do we know its the alternative pathway? By detecting **C2 or C4 and C3** we will find that: ➢ C2 and C4 levels are **normal** in plasma as they're not involved in alternative pathway. ➢ C3 level is highly **decreased** in plasma as its the first protein to be activated Proteins involved: (**C3**,C5,C6,C7,C8,C9), no C2 or C4
IF		
Associated diseases	1. **Hepatitis B&C** antigenemia (presence of antigen in the blood) 2. Extra-renal infections 3. **SLE** *It can be associated with the immune-complexes which are generated in either autoimmune diseases such as SLE or in viral or bacterial infections especially hepatitis B&C.	**Extra** 

4. IgA Nephropathy
(Berger Disease)

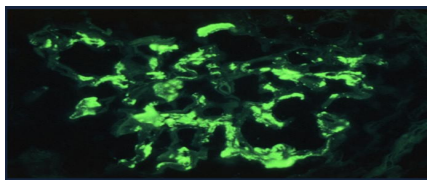
Overview

- One of the most common causes of recurrent microscopic or gross hematuria [Robbins]
- **Most common** form of **primary** glomerulonephritis (kidney disease) in the world.
- It manifests as nephritic syndrome (*Hematuria)
- Some experts have considered IgA nephropathy to be a localized variant of Henoch-Schönlein purpura (Recall, Vasculitis lecture) [Robbins].
  IgA nephropathy: Affects only kidneys.
  Henoch-Schönlein purpura: Affects Kidneys and other tissue (skin, joint, etc)(a systemic syndrome).

Epidemiology

- Affects children and young adults, **typically during an infection**

Etiology	Formation of underglycosylated IgA and its deposition in glomerulus. Why is this type of IgA formed? It's unknown.
Clinical Manifestation	Begins as an episode of gross hematuria that occurs within **1-2 days** of a nonspecific **upper respiratory tract infection**. Unlike Post-Infectious GN, which appears after weeks.
Site	Deposition of IgA* (can only activate the alternative pathway) & complement C3 (inflammatory proteins) in the mesangium
Mechanism	Pathogenic hallmark: * **Antigen** (**underglycosylated IgA in serum) + **Antibody** (Anti-underglycosylated IgA) **=** Circulating immune-complex which **deposits in mesangium** (Type III Hypersensitivity) *The structure of the IgA in the nephropathy is abnormal (underglycosylated), it will be recognized by the body as foreign and act as an antigen to induce antibody production, then the abnormal IgA antibody and anti-IgA antibody will form a complex and deposit in the **mesangium**. **What does "underglycosylated" mean? Usually antibodies have a hidden region from the immune system. This region is kept hidden by sugars and what is noticed here is that these sugars are either **missing** or they are **present** but not in the same amount that covers the underlined part of the antibody. So when this region is exposed to the immune system, it starts behaving as an antigen and the inflammatory processes begins.
Complement Pathway	**When immune-complexes deposit, which pathway is activated?** **There is evidence of** activation by the **alternative pathway** as the serum of complement protein C1, **C2,** and **C4** will be **normal**. Why? These complements are part of the **classical** pathway which can't be activated by IgA. However, **C3** level will be **low** since its part of the alternative pathway.



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

5. Rapid Progressive GN

(Crescentic GN)

Overview

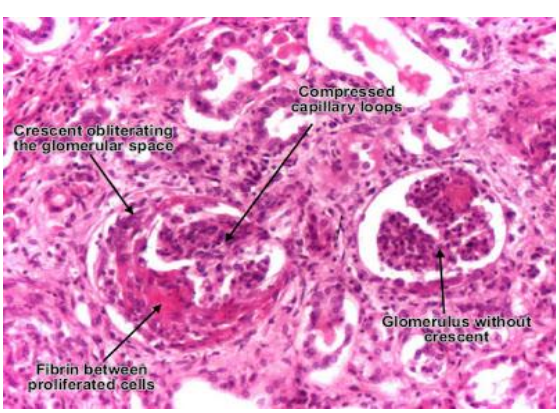
- RPGN is a clinical syndrome and not a specific form of Glomerulonephritis. (All what we discussed are immune-mediated GN that could show RPGN syndrome which would be the end result of these disease) Why did we say end result? Because Its Very serious condition which may lead to complete renal damage if untreated (Poor prognosis). Patient could need a kidney transplant.
- In most cases, glomerular injury is **immunologically mediated**.

Characteristics

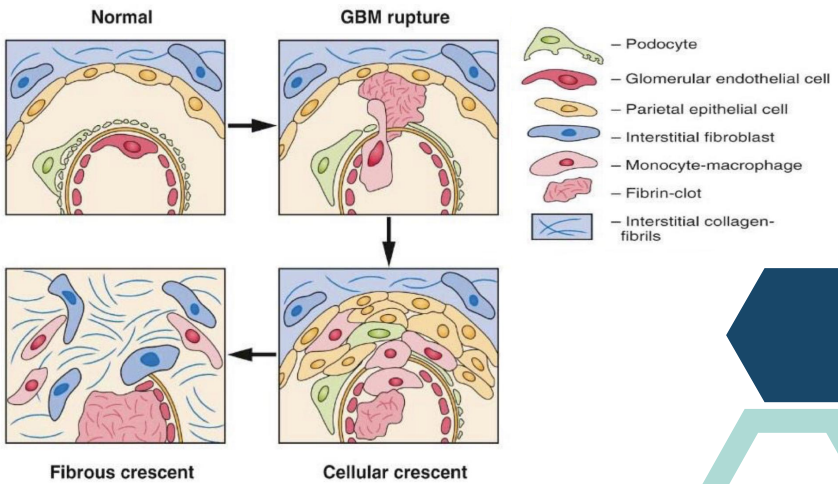
- **Crescents** are defined as the presence of **2 or more** layers of cells in the Bowman space. Presence of crescents in the glomeruli is a **marker of severe injury**. Causes irreversible injury, therefore it's important to detect it in time so the rest of the kidney could be saved.

Mechanism

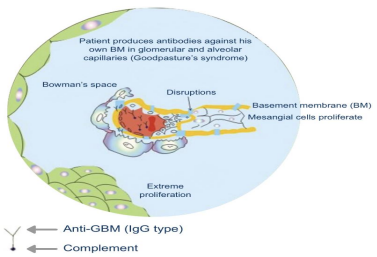
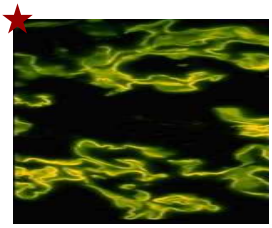
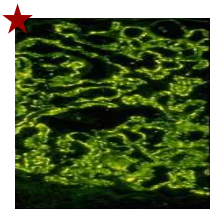
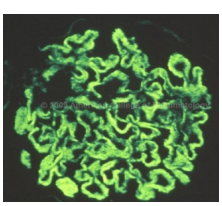
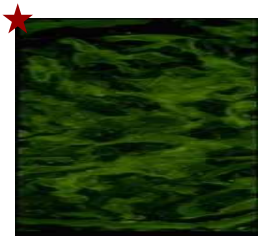
- The initiating event is the development of a physical disruption in the GBM (physical disruption by the "extra" parietal epithelial cells present in the area that have reached GMB and are compressing it).
- The lesions (crescents and other histopathological manifestations) are mediated by processes involving macrophages and cell-mediated immunity.
- Following disruption of the glomerular capillary and its GMB, substances such as circulating cells, inflammatory mediators, and plasma proteins will pass through the capillary wall into the Bowman space creating the crescent and fibrin will be deposited in the bowman's space once the healing process begins.



Histopathology of RPGN Syndrome



A practical classification divides crescentic glomerulonephritis into three groups on the basis of immunologic findings:

Type	Type I (Anti-GBM Antibody Crescentic GN)	Type II (Immune Complex-Mediated Crescentic GN)	Type III (Pauci-immune Crescentic GN)
Overview	➢ It's due to autoantibodies directed against the basement membrane of the glomerulus (Anti-GMB). ➢ **Type II** Hypersensitivity (antigen on GMB).  **Diagram:** Destruction of the membrane leads to leakage of blood components (fibrin), causing rapid multiplication of cells at Bowman's capsule and infiltration of the macrophages and the lymphocytes into the space forming the crescents.	➢ May occur as a **complication** of any of the immune complex nephritides (any immune mediated renal disease that shows crescents could fall under this category), it is not a primary disease of its own, it's a severe form of other diseases. Results from renal damage due to other conditions such as: 1. Post Infectious GN 2. **SLE** (also mentioned as an associated disease with MGN) 3. IgA nephropathy ➢ **Type III** Hypersensitivity (circulating antigens).	Pauci= Poor (قليل). Called pauci-immune because when we examine the glomerulus there is no evidence of anti-GBM antibodies. Its renal damage is defined by the **lack** of anti-GBM antibodies. No antibodies or complements are found. ➢ It's due to **A**nti-**N**eutrophil **C**ytoplasmic **A**ntibodies in serum
Associated diseases	➢ **Goodpasture syndrome:** is a rare autoimmune disease in which Anti-GBM antibodies attack the basement membrane of **both** the **lungs** & **kidneys**, leading to hematuria because of the damaged blood vessels in the lungs and kidney. If somebody is presented with **Hematuria** & **Glomerulonephritis** then you should look for anti-GBM antibody to confirm diagnosis for this syndrome.		➢ **Systemic vasculitis** (diseases we took in cardio block like: Granulomatosis with polyangiitis), affects the **small** vessels
Microscopy	Characterized by linear deposition of IgG and C3 on the **GBM**. This type is recognized by taking renal biopsy and staining it for antibodies against C3 and IgG.  **Linear staining (Anti-GBM)**	Characteristic granular, lumpy-bumpy pattern of staining of the GBM for immunoglobulin (commonly IgG) & complement.  Granular staining (Immune Complex)  A lumpy-bumpy pattern of staining of the GBM	ANCA **not detected** by the stain because it's not directed against the renal tissue. No antibody staining.  **No antibody staining** (Pauci associated with vasculitis)

Take home messages

Immune complexes underlie the pathogenesis of many of the glomerulo-nephritides.

Activation of the complement system (classical, alternative, or both) is an integral part of the process, and measurement of the complement proteins (C3,C4) help in diagnosis and follow- up of patients.

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

Extra

- Type II Hypersensitivity
- Type III Hypersensitivity
- Post-infectious GN
- RPGN (osmosis)
- MGN
- MPGN
- IgA Nephropathy (osmosis)

Summary

Types of Immune-Complexes in Circulation -Depending on complex size- (Induce Type III Hypersensitivity)

- **Small, soluble immune-complexes:** Very small will not be noticed by immune system, therefore not deposited (excreted in urine).
- **Intermediate, soluble immune-complexes:** Not effectively picked up by macrophages. (deposit in tissue).
- **Large, insoluble immune-complexes:** Eliminated by phagocytosis (through specialized macrophages).

Mechanism of Glomerular Injury

Deposition of immune complexes in glomeruli → Activation of complements (C5-9/C5a) → Infiltration of different cells (neutrophils/ macrophages/ platelets/ glomerular cells) + activation of T cells (lead to the release of chemokines and more inflammatory cells aggregation) → Destruction and disease which leads to: decreased GFR, proteinuria and hematuria.

Diseases

Post Infectious Glomerulonephritis (Post Streptococcal)		➔ An example of nephritic syndromes, onset is sudden, **acute** glomerulonephritis. **Etiology:** Antibodies formed against streptococcal organisms (nephritic strain). **Diagnostic test:** Anti-streptolysin, and Anti-DNAse B (in case of skin infection). +Remember that Culture is negative. **Characteristics:** Acute diffuse proliferative GN & frequent infiltration of leukocytes (especially neutrophils). **IF characteristics:** Hypocomplementemia & Granular deposits of IgG & complement on GBM.
Membranous Glomerulonephritis (Membranous Nephropathy)		➔ A form of **chronic** immune-complex nephritis. (chronic GN), onset is slow. ➔ Most common cause of primary nephrotic syndrome in Caucasian adults. **Etiology:** - Primary MGN (60%): antibodies against antigen of the M-type phospholipase A2 receptor 1 (PLA2R). - Secondary MGN: conditions such as cancer, infection, and drugs.
Membranoproliferative Glomerulonephritis (MPGN)		A **chronic** progressive glomerulonephritis, can manifest as either nephrotic or nephritic syndrome. has two types:
	Type I (More prevalent) 80% of cases	**Etiology:** Circulating immune complexes. **Pathway:** Activates the complement system by the classical pathway. **Characteristics:** subendothelial and mesangial deposits. **Associated diseases:** Hepatitis B&C antigenemia, extra-renal infections, and SLE.
	Type II	**Etiology:** Excessive complement activation. **Pathway:** Activates the complement system by the alternative pathway. **Characteristics:** intramembranous dense deposits. * Some patients have autoantibody against C3 convertase called: **C3 nephritic factor.**
IgA Nephropathy (Berger disease)		➔ It manifests as **nephritic syndrome** (*Hematuria), Affects **children and young adults.** **Clinical manifestations:** Gross hematuria that occurs within 1-2 days of a nonspecific upper respiratory tract infection. **Mechanism:** Production of abnormal glycosylated IgA and development of autoantibodies against them. **Pathway:** Activation of complement by the alternative pathway (serum complement C2, and C4 will be normal, C3 will be low). **Characteristics:** Deposition of IgA & complement C3 in the mesangium.
Rapid Progressive Glomerulonephritis (RPGN) Or **Crescentic Glomerulonephritis** (CGN)		➔ A clinical syndrome and not a specific form of Glomerulonephritis. ➔ **Characteristics:** Crescents (2 or more layers of cells) in Bowman space (presence in the glomeruli = severe injury). ➔ **Mechanism:** Development of a physical disruption in the GBM → substances such as circulating cells, inflammatory mediators, and plasma proteins will pass through the capillary wall into the Bowman space → crescent is created.
	Type 1	- **Characterized by** linear deposition of IgG and C3 on the GBM. (Anti-GBM antibody). - Associated with Goodpasture syndrome.
	Type 2	- **Characteristized by** granular (lumpy-bumpy) pattern of staining of the GBM for immunoglobulin commonly IgG & complement. - May occur as a complication of immune complex nephritides.
	Type 3	- **Characterised by** a renal damage that lacks anti-GBM antibodies. - Most cases are associated ANCA and systemic vasculitis.

QUIZ

Q1) The site of immune complexes deposition in Membranous glomerulonephritis is:							
A	Mesangium	B	Basement membrane	C	Visceral epithelial	D	Parietal epithelial
Q2) Which glomerular disease would you suspect most in a patient with linear pattern of immune complex deposition:							
A	Goodpasture syndrome	B	Berger's disease	C	Membranous glomerulonephritis	D	Lupus nephritis
Q3) Which of the following may occur as a complication of Systemic Lupus Erythematosus?							
A	Type I RPGN	B	Type II RPGN	C	Type III RPGN	D	All the above
Q4) Which of the following may occur with hepatitis B or C?							
A	MGN	B	IgA nephropathy	C	MPGN	D	RPGN
Q5) Which one of the following requires C3 Nephritic Factor for its pathogenesis?							
A	MGN	B	MPGN	C	IgA Nephropathy	D	RPGN
Q6) Immune complex nephritis is considered to be which type of hypersensitivity?							
A	Type I	B	Type II	C	Type III	D	Type IV
Q7) Poststreptococcal GN is caused by known streptococcal types called:							
A	Nephritic strains	B	Nephrotic strains	C	Both a & b	D	None
Q8) Post Infectious Glomerulonephritis occurs 7-14 days after which of the following?							
A	Nephritic Syndrome	B	Pharyngitis	C	Skin infection	D	Anti-GBM disease
Q9) Which one of the following is associated with Berger's disease?							
A	IgA	B	IgG	C	IgM	D	IgE
Q10) A patient diagnosed with Type III RPGN, immunofluorescence will reveal							
A	Linear Pattern	B	Granular Pattern	C	No staining	D	Lumpy bumpy Pattern

Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
B	A	B	C	B	C	A	B	A	C

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