Renal Block

Lecture Four & Five

Nephrotic & Nephritic Syndromes

Important notes & MCQs

Objectives:

- Recognize the five major renal clinical syndromes.
- Describe the main differential pathological diagnosis for each syndrome.
- Perform a clinico-pathological correlation.
- Describe the patterns of injury of each syndrome.

Nephrotic syndrome:

Clinical presentation: **Heavy proteinuria (3.5+g)**

It is important to differentiate between clinical syndromes (which are basically a set of symptoms) and the underlying pathology (i.e. the cause of the syndrome)

You have to differentiate between those two terms:

- When we speak of blood vessels or glomeruli fibrosis we say **(Sclerosis)**
- But when we speak of the interstitium we call it **(Fibrosis)** only

Nephrotic Syndrome is a clinical syndrome not a pathological one, including:

- Heavy proteinuria
- Hypoalbuminemia
- Hypercholesterolemia

Those patients are prone (susceptible) to infections.

Nephrotic syndrome is a clinical syndrome but when we do a biopsy there will be different diseases and **different pattern of injuries causing it.**

Nephrotic Syndrome causes:

Diseases intrinsic to the Kidney (Mainly from the Kidney):

- Minimal Change Disease
- Focal Segmental Glomerulosclerosis
- Membranous Glomerulopathy

Diseases systemic (they affect the kidney):

- Diabetes Mellitus
- Amyloidosis
- SLE

Minimal Change Disease

The patient (usually children) present with heavy proteinuria that's abundant in albumin (selective proteinuria). Further investigations reveal the following:

- It's a diffuse epithelial cell disease. (Epithelial cell injury)
- In the biopsy under the microscope (LM) and Immunofluorescence the glomeruli is normal (Hence, 'minimal change')
- But on the Electron Microscope there is a **diffuse** effacement of the podocytes
- No inflammation
- Microvillus transformation/ degeneration
- This disease could be due to a Circulating Cytokine or Post Bee Sting

Glumerulonephritis is a misnomer, as there is no inflammation in minimal change disease.

Focal Segmental Glomerulosclerosis

Glomerulosclerosis that affects parts of some glomeruli

We can do a biopsy and see:

- Some glomeruli are abnormal and some are normal we call the disease **(FOCAL).**
- If one specific glomerulus is half normal and half abnormal we call the disease **(SEGMENTAL).**
- If there was fibrosis in the glomerulus we call it **(GLOMERULOSCLEROSIS)**

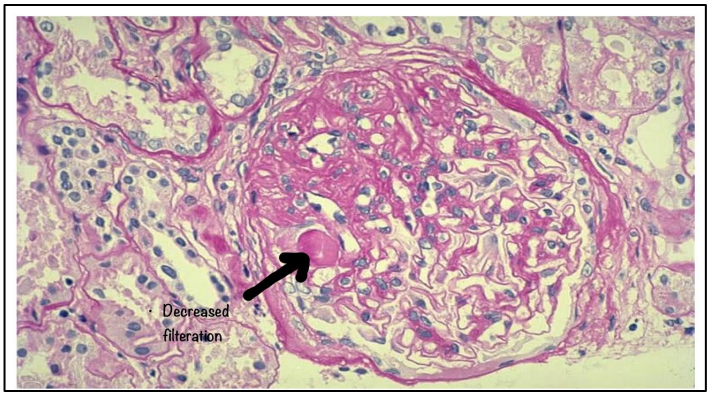
Characterized by:

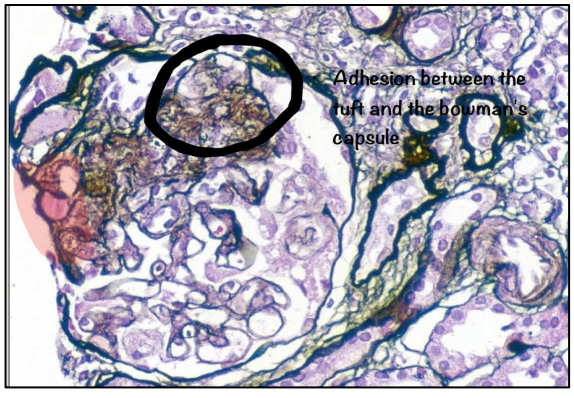
- Increase matrix
- Obliteration of capillary lumina.
- Hyalinosis
- Adhesions

- Can be primary familial.
- Could be caused by circulating cytokines.

It is important to distinguish between focal/diffuse and global/segmental.

- Focal (some) and diffuse (all) are used to describe all the glomeruli.
- Global (entire) and segmental (part) are used to describe one glomerulus.





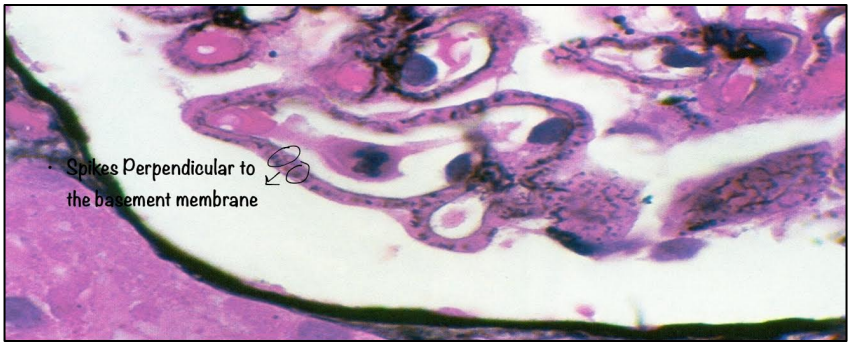
Membranous Glomerulopathy

We see under the microscope:

- A very thickened basement membrane
- Spikes.

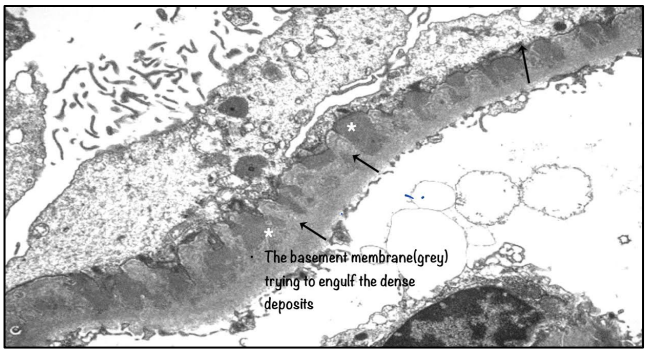
  Spikes are projections of the basement membrane that appear on either side of the subepithelial deposits, to engulf them. Observed as black dots under the LM + silver stain and light spikes under the EM

  The silver stain stains the basement membrane showing the spikes perpendicular to the basement membrane
- The dense deposits (stained pink) came and sat on the basement membrane forming basement membrane material on both sides of the deposits (stained black) to try to engulf it and stop it from entering.



- The immunofluorescence stains the dense deposits **(diffused highly granular deposition of IgG and C3 along the glomerular capillary wall)**
- The electron microscopy shows the basement membrane as light grey trying to engulf the dense deposits
- **So what can we see?**

  - Dense subepithelial deposits:
    Observed in pink under the LM + silver stain
    Observed as dark segments under the EM
  - Deposits injured the podocytes (causing nephrotic syndrome and proteinuria)
  - Immune complex (IgG and C3)
    Showing a granular pattern immunofluorescence



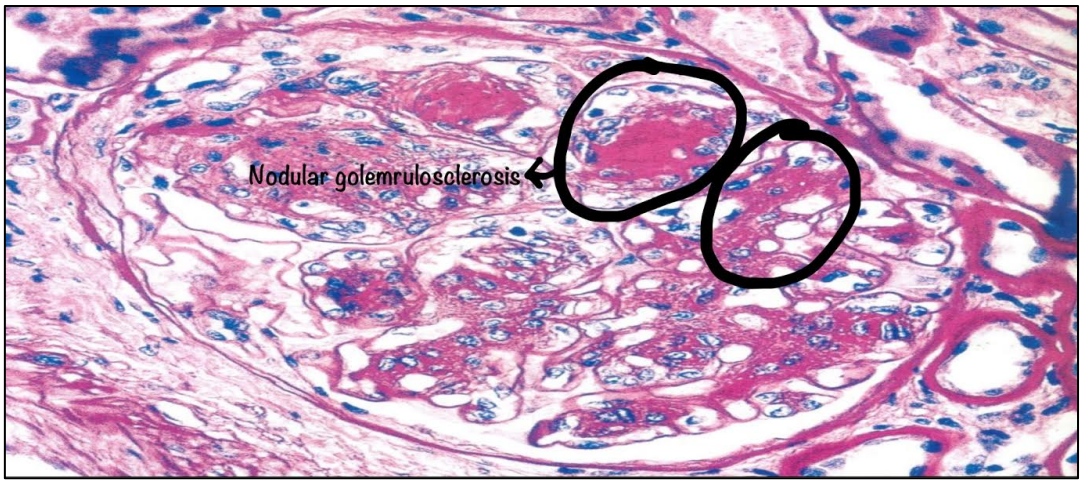
Diabetic Nephropathy

Diabetes is characterized under the microscope by:

- Arterial Hyalinization.
- Increase in the mesangial matrix
- Thickening of the glomerular capillary wall
- Formation of sclerosis (Nodular Glomerulosclerosis).

The Nodular Glomerulosclerosis are called **KIMMELSTIEL-WILSON NODULES**

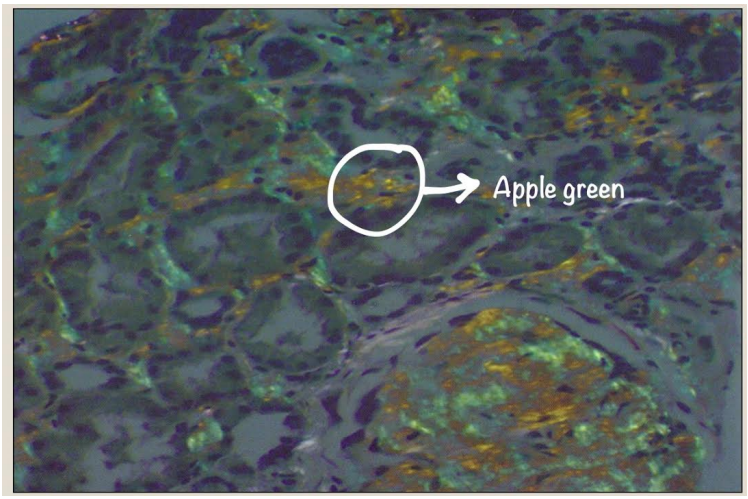
Kimmelstiel-Wilson nodules = Diabetic Nephropathy



Amyloidosis

Amyloidosis is stained with Congo-red stain, showing the amyloidosis as orange red.

- Amyloid deposits seen under the LM (Congo red stain)
- Also seen as apple-green birefringence under polarized light.
- Fibrils of amyloid are randomly oriented and 8-10 nm.



Lupus Nephritis

SLE might give membranous nephropathy meaning that Membranous nephropathy can be intrinsic (primary) or secondary to a systemic disease

Class 5 SLE looks exactly like the membranous nephropathy under the microscope showing subepithelial deposits under the electron microscope and spikes under the silver stain

The difference between normal Membranous nephropathy and Membranous nephropathy secondary to SLE is that **SLE is an autoimmune disease** thus containing **more immune-complex** on the membrane also might be showing in the mesangium and para-mesangium but you wont see it on the subendothelial

If the immune-complex is shown on the subendothelial that means that this is nephritic syndrome NOT nephrotic

****NephrOtic with an O= Zero (0) increase cellularity**

So what do we see?

Presents as membranous nephropathy a systemic form of membranous nephropathy secondary to SLE

- Subepithelial deposits
- Spikes are observed
- Moth eaten appearance the capillary wall

Because spikes show holes once cut (Spike-dome pattern) under silver methanamine (Jones) stain.

Nephrotic syndrome

Intrinsic

Minimal Change

- Normal immunofluorescence
- Normal light microscopy
- Diffuse effacement of podocyte foot processes

Focal Segmental

- Increased matrix
- Obliteration of capillary lumina
- Hyalinosis

Membranous Nephropathy

- Thickening of basement membrane
- Spikes
- Subepithelial deposits

Systemic

SLE class V

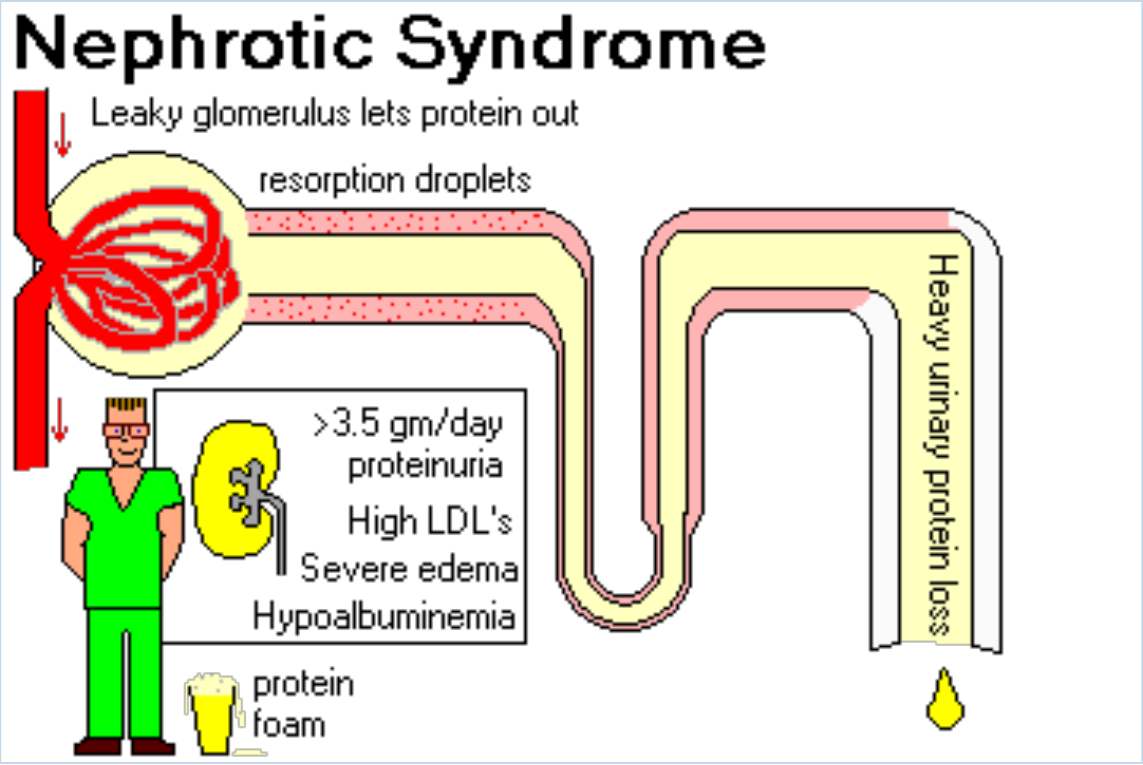
- Subepithelial deposits
- Spikes are observed

Diabetic Nephropathy

- Arterial hyalinization
- Increased mesangial matrix
- thickening of the capillary wall
- Kimmelstiel-Wilson nodule

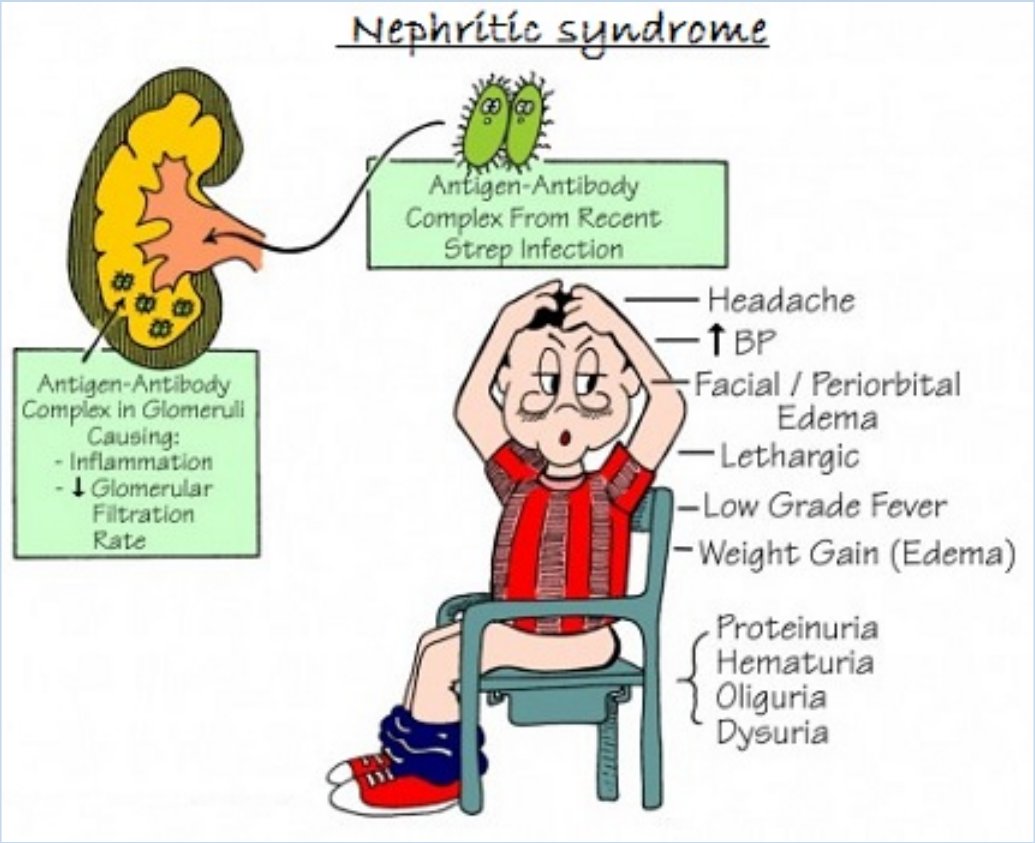
Amyloidosis

- Amyloid deposits seen under the LM
- Apple-green birefringence under polarized light



Nephritic syndrome:

Increased cellularity



Clinical presentation:

- Gross hematuria
- Edema
- Hypertension
- Mild-moderate proteinuria (not heavy)

Polymorphonuclear infiltration is seen in:

1. Acute post-infectious glomerulonephritis
2. Membrano-proliferative GN

Lets say a child has a little bit of every one of these, when we do a biopsy for it in nephritic syndrome we will see:

- Increased cellularity.
- First thing we do is ask about history.

Classification:

A. Intrinsic:

- **Acute post-infectious glomerulonephritis:**
  It's important to look into the history of the patient
  - Post group A β hemolytic strept. (Pharyngitis and cellulitis)
    Increased ASO titer, although sometimes title is negative
  - **Polymorphonuclear infiltration (most imp)**
  - Endocapillary proliferation
  - IgG and C3 under immunofluorescence
  - Subepithelial humps under EM (large)
  - Diffused acute inflammation
  - Nephrogenic the bacteria.

- **Membrano-proliferative glomerulonephritis:**
  - **GBM splitting and proliferation (double contouring)**
    Due to the sub endothelial deposits
  - Circulating immune complex
  - Endothelial injury
  - Polymorphonuclear infiltration
  - Subendothelial deposits

Membranous vs. membranoproliferative (MP):
1. MP is proliferative (polymorphs)
2. MP has subENDOTHELIAL deposit, compared to the sub epithelial deposits of membranous

Divided into:

I. **Type I**
   - IgG and C3
   - Lobular uniform appearance of glomeruli
   - Possibly associated with hepatitis C

II. **Type II (dense deposit disease)**
   - AKA C3 glomerulopathy
   - C3 mainly!
   - Thickening of the GBM
   - GBM appears dark in color

B. Systemic

- **SLE class III**
- **SLE class IV**

Nephrotic syndrome/ glomerulonephritis: →There is no cellularity

Rapidly progressive:

Crescentic glomerulonephritis:

Can be a complication of any of the diseases (especially acute post-infectious glomerulosclerosis) as soon as they form crescents (seen under the microscope).

Crescents are seen in all of the following:

- **Anti- GBM antibodies:**

  Crescents are quick to appear, more common among men

  - Circulating anti-GBM antibodies
  - AKA Goodpasture syndrome
  - Affects alveolar basement membrane (causing hemoptysis)
  - Segmental necrosis
  - GBM breaks
  - Linear pattern immunofluorescence
- **Immune complex:**

  Seen in children mostly, as crescentic post-streptococcal infection.
  Start as nephritic and progress to rapidly progressive when crescents are formed

- **Pauci immune:**

  - Nothing is observed under immunofluorescence
  - Acute and fibrinoid necrosis
    Crescents are quick to appear

Vasculitis:

- Wegener's granulomatosis
- Microscopic polyangiitis
- Churg Strauss

Asymptomatic hematuria/Proteinuria:

- ### IgA nephropathy:

  IgA nephropathy + skin lesions = Henoch-Schönlein purpura

  - Focal necrotizing lesion
  - IgA seen under immunofluorescence
  - AKA Berger disease
  - Disease of the mesangium
  - Mesangial deposits
  - Increase in mesangial matrix
  - Mesangial proliferative
  - Most common cause of primary GN worldwide

- ### Alport syndrome

  The disease begins with a thin basement membrane (i.e. a benign asymptomatic disease of its own) that progress to Alport syndrome (a genetic abnormality in the gene encoding collagen IV) showing alterations of thin and thick GBM. More common in men (X-linked).

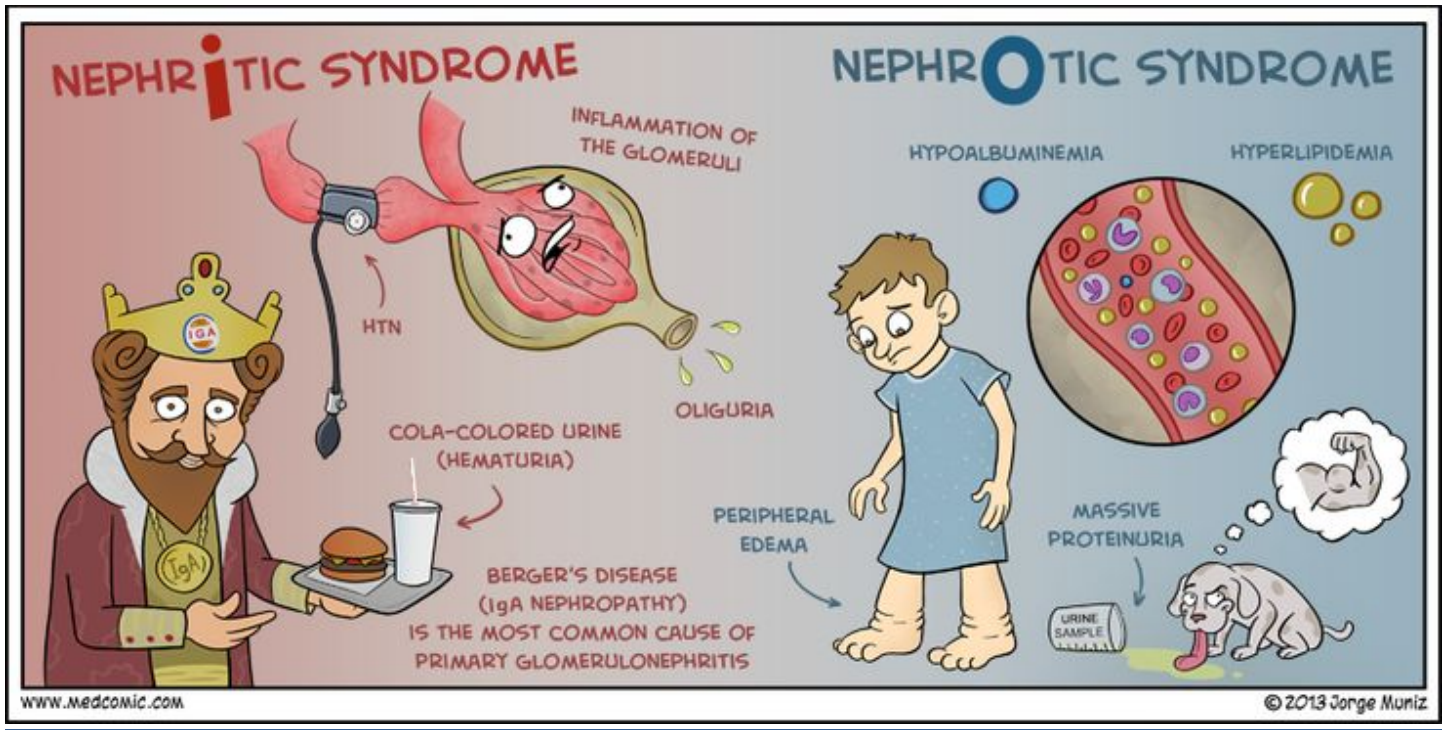
  - GBM abnormality
  - Hearing problems
  - Lamellated appearance (light and dark alterations)
  - Slight podocyte injury (insignificant proteinuria)

Chronic renal failure:

- Fibrosis of the interstitium
- Sclerosis of vessels
- Azotemia
- Hypertension
- Active urine sediment (variable)
- Variable proteinuria
- Shrunk kidneys

Biopsies are performed to know the cause and assess transplant (since some diseases, like FSGS, reoccur after transplantation)

Types	Morphologic findings
A. Disorders manifest by the nephrotic syndrome	
Minimal change disease (lipid nephrosis)	Not visible basement membrane changes, fused epithelial foot process, lipid accumulation in the renal tubular cells.
Focal segmental glomerulosclerosis	Not visible basement membrane changes, segmental sclerosis of scattered juxtamedullary glomeruli
Membrane Glomerulonephritis	Basement membrane markedly thickened by intramembranous and epimembranous (subepithelial) immune complex deposits, granular immunofluorescence, "Spike and dome" appearance.
Diabetic nephropathy	Basement membrane markedly thickened, diffuse or Nodular mesangial accumulations of basement membrane like material
Renal amyloidosis	Amyloid protein identified by specified stains (e.g. Congo Red) with birefringence under polarized light, or electron microscopy “crisscross” fibrillary pattern.
Lupus nephropathy	Immune complex deposition in subendothelial location may manifest as membranous glomerulonephritis.
B. Disorders manifest by nephrotic syndrome	
Post-streptococcal glomerulonephritis rapidly progressive (crescentic) glomerulonephritis	Subepithelial electron dense “humps”; “lumpy bumpy” immunofluorescence, crescents formation, antineutrophil cytoplasmic antibody (ANCA) – negative forms with immune complexes or antiglomerular basement membrane antibodies; ANCA-positive (pauci-immune) form with Wegener granulomatosis
Goodpasture syndrome	Linear immunofluorescence antibody deposition caused by antiglomerular basement membrane antibodies
Alport syndrome	Split basement membrane due to hereditary nephritis
C. Other glomerular disorders	
IgA nephropathy	Mesangial IgA deposits (Berger Disease)
Membranoproliferative Glomerulonephritis	Tram-track appearance; deposits of C3 and dense deposits in one variant.



Summary of the Nephrotic Syndrome:

- Characterized by proteinuria, which results in hypoalbuminemia and edema.
- Podocyte injury is an underlying mechanism of proteinuria, and may be the result of nonimmune causes (as in minimal-change disease and FSGS) or immune mechanisms (as in membranous nephropathy).
- *Minimal-change disease:* The most frequent cause of nephrotic syndrome in children; it is manifested by proteinuria and effacement of glomerular foot processes without antibody deposits; the pathogenesis is unknown; the disease responds well to steroid therapy.
- *FSGS:* May be primary (podocyte injury by unknown mechanisms) or secondary (e.g., as a consequence of previous glomerulonephritis, hypertension, or infection such as with HIV); glomeruli show focal and segmental obliteration of capillary lumina, and loss of foot processes; the disease often is resistant to therapy and may progress to end-stage renal disease.
- *Membranous nephropathy:* Caused by an autoimmune response, most often directed against the phospholipase A2 receptor on podocytes; it is characterized by granular subepithelial deposits of antibodies with GBM thickening and loss of foot processes but little or no inflammation; the disease often is resistant to steroid therapy.
- *MPGN and dense deposit disease* Are now recognized to be distinct entities. MPGN is caused by immune complex deposition; dense deposit disease is a consequence of complement dysregulation. Both may present with nephrotic and/or nephritic features.

Summary of Nephritic syndrome: (pg. 531)

- The nephritic syndrome is characterized by hematuria, oliguria with azotemia, proteinuria, and hypertension.
- The most common cause is **immunologically mediated glomerular injury**; lesions are characterized by proliferative changes and leukocyte infiltration.
- *Acute postinfectious glomerulonephritis*:

  Typically occurs after streptococcal infection in children and young adults but may occur following infection with many other organisms; it is caused by deposition of immune complexes, mainly in the subepithelial spaces, with abundant neutrophils and proliferation of glomerular cells. Most affected children recover; the prognosis is worse in adults.
- *IgA nephropathy:*

  Characterized by mesangial deposits of IgA-containing immune complexes, is the most common cause of the nephritic syndrome worldwide; it is also a common cause of recurrent hematuria; it commonly affects children and young adults and has a variable course.
- *Hereditary nephritis* (*Alport syndrome*):

  Caused by mutations in genes encoding GBM collagen; it manifests as hematuria and slowly progressing proteinuria and declining renal function; glomeruli appear normal by light microscopy until late in the disease course.

Summary of Rapidly Progressive Glomerulonephritis:

- RPGN is a clinical entity with features of the nephritic syndrome and rapid loss of renal function.
- RPGN is commonly associated with severe glomerular injury with necrosis and GBM breaks and subsequent proliferation of parietal epithelium (crescents).
- RPGN may be immune-mediated, as when autoantibodies to the GBM develop in anti-GBM antibody disease or when it arises consequent to immune complex deposition; it also can be pauci-immune, associated with antineutrophil cytoplasmic antibodies.

	Clinical Signs	Serology	Biopsy
Immune Complex	Infection, lupus or IgA Nephropathy history	Decreased C3 (except in IgA nephropathy) - ANA + if lupus.	IgG and C3 deposits (or IgA deposits in IgA nephropathy)
Anti-GBM	Pulmonary hemorrhage (Goodpasture syndrome)	Anti-GBM antibody	Linear IgG deposits
Pauci-immune	Skin rash, pulmonary hemorrhage, upper respiratory granuloma (Wegener's (GPA))	ANCA antibody	No immune deposits

Recap of some of what we took previously: (Mentioned in Dr. Rikkabi's notes)

Major clinical characteristics of uremia

(1) **Azotemia** (elevated urea and creatinine)

(2) **Acidosis** resulting from the accumulation of sulfates, phosphates and organic acids.

(3) Hyperkalemia

(4) Abnormal control of fluid volume:

(a) An early characteristic is the inability to concentrate urine; a later manifestation is the inability to dilute urine.

(b) Sodium and water retention can result in congestive heart failure.

(5) **Hypocalcaemia** caused by failure to synthesize the active form of Vitamin D, hypocalcaemia can lead to renal osteodystrophy.

(6) **Anemia** caused by decreased secretion of erythropoietin.

(7) **Hypertension** caused by hyperproduction of rennin.

Other clinical characteristics of uremia include:

Anorexia, nausea and vomiting; neurologic disorders, ranging from diminished mental function to convulsions and coma; bleeding caused by disordered platelet function; accumulation in the skin of urochrome and other urinary pigments and fibrinous pericarditis.

Non-Renal Causes Of Azotemia:

Pre-renal azotemia:

This condition results from decreased renal blood flow due to blood loss, decreased cardiac output, systemic hypovolemia (as in massive burns), or peripheral pooling of blood due to marked vasodilatation (as in gram- negative sepsis).

It is characterized by increased tubular reabsorption of sodium and water, resulting in oliguria, concentrated urine and decreased urinary sodium excretion.

(1) Measurement of urinary sodium is diagnostically significant in the delineation of the **oliguria of shock.**

(a) Oliguria may be caused by **decreased renal blood flow with consequent decreased glomerular filtration rate,** in which case tubular reabsorption of sodium is maximally increased and urinary sodium is low.

(b) Oliguria may be a manifestation of **acute tubular necrosis**, in which case tubular reabsorption is greatly impaired and urinary sodium is not decreased.

(2) **The BUN:**

Creatinine ratio is characteristically greater than 15 due to a combination of both decreased glomerular filtration and increased tubular reabsorption of urea.

Post-renal azotemia:

Results from mechanical blockage (obstruction) of urinary flow.

- BUN is an abbreviation of Blood Urea Nitrogen.

Now Check Your Understanding:

1) **A 5 years old boy present with hematuria. His mother states that he has had a sore throat for the past 2 days and that he has had hematuria a few times in the past, also associated with a sore throat. She states that his urine usually returns to a normal clear, yellow color after a few days. She denies any history of rash , abdominal pain , or GI bleeding with the hematuria. Which of the following is the most likely diagnosis?**

   A. Henoch-Schonlein purpura
   B. Alport syndrome
   C. IgA nephropathy
   D. Goodpasture syndrome
   E. Poststreptococcal glomerulonephritis

2) **An 11 years old present to clinic two weeks after recovery from a skin infection of the lower cheek that was characterized by multiple small honey crusted lesion. Her mother brought her to clinic because she is worried about the acute onset of malaise, nausea, headache," puffiness " around her daughter's eyes, and odd "coke-colored" urine. Her PMH is insignificant, but her mother is very worried. Which of the following finding is expected?**

   A. Granular "full house" standing in the mesangium
   B. Effacement of visceral foot processes
   C. "Tram-track" appearance of the GMB with silver staining
   D. Active hepatitis C infection
   E. Large electron dense subepithelial deposits

3) **LM: glomeruli enlarged and hypercellular, neutrophils, "lumpy-dumpy". EM: subepithelial humps .IF: granular pattern, most frequently seen in children?**

A) Membranoproliferative glomerulonephritis

B) IgA nephropathy (Berger's disease)

C) Acute poststreptococcal glomerulonephritis

D) Good pasture's syndrome

4) **A patient, who is known to have hepatic failure, came to the clinic complaining from hematuria after she getting a respiratory infection. During investigation after taking a renal biopsy, the lab found a deposition of IgA antibody with other immune complexes, what is most likely the diagnosis?**

A) Nephritic syndrome

B) Glomerulonephritis

C) Renal failure

D) IgA nephropathy

5) **IgA nephropathy is associated with a vasculitis disease, which is:**

A) Churg-Strauss syndrome

B) Buerger disease

C) Henoch-Schönlein purpura

D) Polyarteritis Nodosa

1. E	2. E	3.C	4. D	5. C

6) In IgA nephropathy under the immunofluorescence, we see a deposition of IgA in the mesangium, often with an immune complex which is:

A) C1a

B) C2b

C) C3

D) C4

7) In the diagnosis of malignant renal hypertension, which of the following statements is CORRECT?

A) The morphology picture of onion skinning is proportional to the degree of renal failure

B) Due to kidney dysfunction, there is decreased levels of renin

C) Malignant hypertension only occurs in patients with previous hypertension

D) Occurs in 5-10% of individuals with an elevated blood pressure

8) A relatively uncommon form of acute glomerulonephritis that results in damage within the glomerulus of the kidney. There is rapid loss of kidney function with the formation of crescents on microscopic analysis (kidney biopsy). This disorder may result in acute glomerulonephritis or nephrotic syndrome, but ultimately results in renal failure and end-stage renal disease.

A) Crescentic glomerulonephritis

B) Membranous glomerulonephritis

C) Membranoproliferative glomerulonephritis

D) Anti-GBM disease

E) Focal segmental glomerulonephritis

9) Which of the following is not a 'renal' cause of acute renal failure?

A) SLE

B) Drugs or poisoning

C) Ischemia

D) Prostatic cancer

E) Acute glomerulonephritis

10) Which of the following is not a post renal cause of renal failure?

A) Benign prostatic hyperplasia

B) Urethra obstruction

C) Prostatic cancer

D) Congestive cardiac failure

E) Urolithiasis

11) Which of the following is histological hallmark for the diagnosis of RPGN

A) Crescents within the glomeruli

B) Fibrinoid necrosis of efferent arteriole

C) Fibromuscular hyperplasia of afferent arteriole

D) Spike and dome appearance of glomerular basement membrane

6. C	7. A	8. A	9. D	10. D	11. A

12) A 7-year-old child presents with hypoalbuminemia, edema, hyperlipidemia, and proteinuria. The edema is in the periorbital region initially and eventually spreads to the rest of the body. The patient is given steroid therapy and the disease goes away. What is a key morphological feature of the patient's disease?

A) Fusion of the foot processes

B) Destruction of the basement membrane

C) Destruction of the glomerulus

D) Hemosiderin laden macrophages in the kidney

E) None of the above

13) A 26 year old African American diagnosed with AIDS, and also a heroine abuser, presents with hypertension, microscopic hematuria, and renal insufficiency. The disease does not go away with steroid therapy. What is a key feature on immunofluorescence?

A) IgG and C4 deposition

B) IgM and C3 deposition

C) IgM only

D) IgG only

E) None of the above

14) A patient presents with symptoms of nephrotic syndrome. The disease is immune complex mediated and is known to create an increase in glomerular basement membrane size. IgG and C3 levels are deposited along the basement membrane. Which of the following would best describe the morphology of the disease?

A. Proliferation of new basement membrane between complexes

B. Spike and dome pattern

C. Infiltration of the area with lymphocytes

D. A and B

E. B only

15) A diabetic patient presents with macroalbuminuria that was once microalbuminuria. He also has hypertension and his GFR has decreased a lot. He has retinopathy. His kidney glomerular basement membrane is thickened and there appears to be sclerosing. What is a key feature of his syndrome?

A. Kimmelstiel-Wilson nodules

B. Haberden Nodes

C. Bouchard nodes

D. All of the above

16) A patient presents with proteinuria, edema, and symptoms of renal insufficiency. There appears to be hyaline masses in the glomerulus of the kidney. Tests indicate that the organ has enlarged. The disease with the most similar presentation would be?

A. Diabetic Nephropathy

B. IgA Nephropathy

C. Osteomyelitis

D. Membranoproliferative glomerulonephritis

E. All of the above.

17) A 25-year-old Asian male is notices to have gross hematuria. Upon returning, there appears to be no great symptoms, however, after taking a sample of the urine, there appears to microscopic hematuria, hence hematuria between recurrences. The patient has cirrhosis and fatty stools, indicating some sort of malabsorption syndrome. He sometimes has arthritis. What is deposited in the mesangial matrix?

A. IgA

B. C3

C. IgM C3

D. A and B

E. None of the above

12. A	13. B	14. D	15. A	16. A	17. D

18) A child after a strep infection presents 10 days later with hypertension, hematuria, edema, and sometime oliguria. There appears to be elevated titers of anti-streptolysin O antibodies. What is a key morphological feature of his disease?

A. Spike and dome appearance

B. Humps

C. Deposition of IgG and C3

D. Deposition of IgM and C3

E. B and C

19) A patient presents with hematuria, proteinuria on urinalysis, edema and recurrent episodes of gross hematuria. C3 levels are low and examination of the basement membrane reveals thickening of the glomerular loop or tram-tracking. He is diagnosed with the rare form of the disease. Electron dense deposition is most commonly seen in:

A. The subepithelial area

B. Glomerular basement membrane

C. Mesangium

D. The loops of henle

E. None of the above

20) A patient presents with malar rash, photosensitivity, oral ulcers, arthritis, and signs of nephritic syndrome. Upon examination of his kidney, there appears to be crescent formation. Test samples reveal antibodies against DNA, ANA, and snRNA. What is the pathogenic mechanism of the disease?

A. Immune complex mediated

B. Infection

C. Tumor

D. None of the above

E. All of the above

21) A patient presents with hypotension, low urine output, uremic signs like pericardial friction rub, asterixis and confusion. Laboratory findings indicate elevated serum creatinine and BUN levels, hyperkalemia, hyperphosphatemia, and metabolic acidosis. Urinary findings would indicate:

A. Muddy brown granular casts
B. Epithelial cell casts
C. Rbc casts
D. A and B
E. A and C

22) A patient presents with fever, flank pain, dysuria, costovertebral angle tenderness, papillary necrosis, pyonephrosis and perinephric abscess. Laboratory findings indicate elevated creatine and BUN levels. Laboratory findings will also reveal:

A. WBC casts
B. RBC casts
C. Granular casts
D. No casts
E. None of the above

23) A patient with a history of gout experiences abrupt onset of flank pain extending to the groin, nausea, vomiting, and microscopic hematuria. All of the following are related to his condition except:

A) Renal colic
B) UTI
C) Calcium oxalate
D) Increased fluid intake
E) All are related

24) The tram- track appearance is a characteristic feature of which of these:

A) Nephritic syndrome
B) MPGN
C) Chronic renal failure
D) Minimal change renal disease

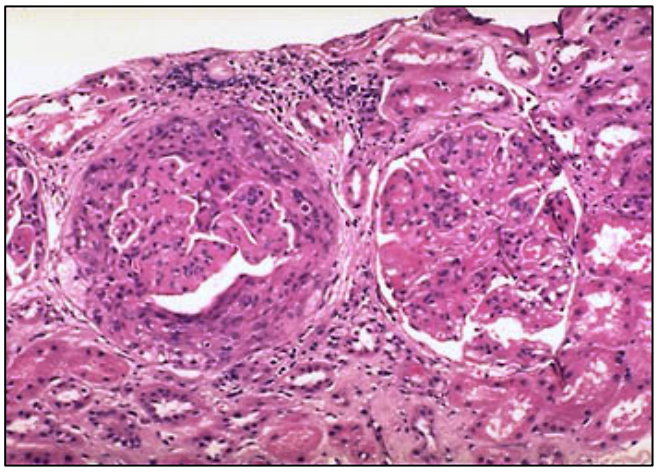
18. E	19. A	20. A	21. D	22. A	23. E	24. B

SAQs:

A 27-year-old white man who was previously in good health presented to his family physician with increasing fatigue and red urine. There was no history of previous illness, and review of systems was negative. Physical examination was negative except for hypertension (165/110 mm Hg). Urinalysis revealed 2+ protein and 2+ blood; his serum creatinine was 1.8 mg/dL.

A week later, the patient continued to have intermittent bouts of hematuria and began to notice ankle swelling and generalized malaise, nausea and vomiting, and decreasing urine output. He presented to a hospital emergency department and was noted to be almost anuric. On physical examination, his blood pressure was 170/110 mm Hg. An abdominal sonogram showed kidneys of normal size with no evidence of hydronephrosis. Laboratory examination revealed:

Urinalysis:	Protein 2+ **Blood 4+** Glucose negative
Microscopy:	>40 RBCs/HPF (0-2 RBCs/HPF) 10 WBCs/HPF (0-2 WBCs/HPF) 5-10 RBC casts/LPF (0 casts/LPF)
Hematocrit	**38%**
Creatinine	**3.9 mg/dL**
BUN	**102 mg/dL**
Liver serology	Normal
ANCA, ANA, HIV	Negative



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The patient was admitted to the intensive care unit with acute renal failure and fluid retention. An emergency renal biopsy was performed. Based on the light microscopic and immunofluorescence findings, plasmapheresis was begun. Over the ensuing 2 weeks, the patient's creatinine decreased to 1.7 mg/dL with a reduction in peripheral edema and resolution of hematuria.

1. **Name the lesion in the picture, what is it composed of, what does it lead to and what is it a result of?**

   Name: Kidney, crescentic glomerulonephritis. The glomerulus on the *left* shows a crescent.

   Composed of: The crescent is composed of parietal epithelial cells that have proliferated and some mononuclear cells derived from blood.

   Leads to: The crescent distorts and compresses the glomerulus

Result of: The crescent is a result of severe glomerular injury, but it tells little about the pathogenesis of the injury.

2. **What kinds of tests will you need to confirm pathogenesis?**

   Immunofluorescence (IF), electron microscopy (EM), and serologic tests are required to determine the cause of injury

3. **With what renal syndrome did this patient present? What is the most common cause of this entity?**

   This patient presented initially with two of the three symptoms associated with acute nephritic syndrome (hypertension, hematuria, and evidence of renal failure, [i.e., increased creatinine]. The most common cause of acute nephritic syndrome is poststreptococcal (postinfectious) glomerulonephritis. This is an immune complex mediated disease with IgG and C3 visible along the glomerular basement membrane by IF ("lumpy-bumpy pattern") and large, subepithelial humps visible by EM

4. **How would immunofluorescence (IF) help in the diagnosis?**

   IF findings can help classify rapidly progressive glomerulonephritis (RPGN) into three categories: type I RPGN (anti-GBM) has a linear pattern; type II RPGN is caused by immune complexes and has a granular pattern; type III RPGN is defined by lack of anti-GBM or immune complex etiology, so IF is normal

- **Rapidly progressive glomerulonephritis is a group of disorders associated with severe oliguria and death from renal failure within weeks and is commonly associated with _____ formation. Formation of what?**

  Crescent, nodule, membrane, immune complex

- **Obstructive uropathy will cause dilation of renal pelvises and calyces also known as:**

  Hydronephrosis, gallstone disease, pyelonephritis

- **Mention three of the histological findings which you can see in the MPGN.**
  1. The glomeruli are large, with an accentuated **lobular appearance**
  2. **Proliferation of mesangial and endothelial cells**
  3. Infiltrating leukocytes
  4. **GBM is thickened**
  5. Glomerular capillary wall often shows a double contour, or "tram track," appearance.

Contact us: Pathology435@gmail.com

Team Members

Nouf Altwaijri

Aljohara Almazroua

Amjad Alduhaish

Budoor Julaidan

Deema Alfaris

Kayan Kaaki

Khawla Alammari

Lamees Altamimi

Nojood Alhaidri

Noura AlBulushi

Noura AlKharraz

Nouf Alabdulkarim

Reem AlAqeel

Khalid Aburas

Ahmad Taha Alkhiary

Ammar Saleh Almansour

Anas Baleegh Mohammad Ali

Faris Ibrahim Alwarhi

Hamzah Abdullah Alfiar

NaiF MoHaMMeD AlHaDi

Qusai Abdulbaqi Ajlan

Rayan Abdulrahman Almuneef

Zeyad Abdulaziz Alsalem

قال صلى الله عليه وسلم: (من سلك طريقًا يلتمس فيه علمًا سهّل الله له به طريقًا إلى الجنة).

دعواتنا لكم بالتوفيق.