L20: Glomerular diseases

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MEDICINE 433

objectives

1. Classify Glomerular diseases.
2. Understand the pathophysiology is correlated with the clinical manifestation in Glomerular diseases.
3. Recognize the clinical manifestations in Glomerular diseases.
4. Recognize the most common causes of Nephritic glomerular disease.

Color index: Step up to medicine , slide , Doctor's note , Davidson , Extra Explanation

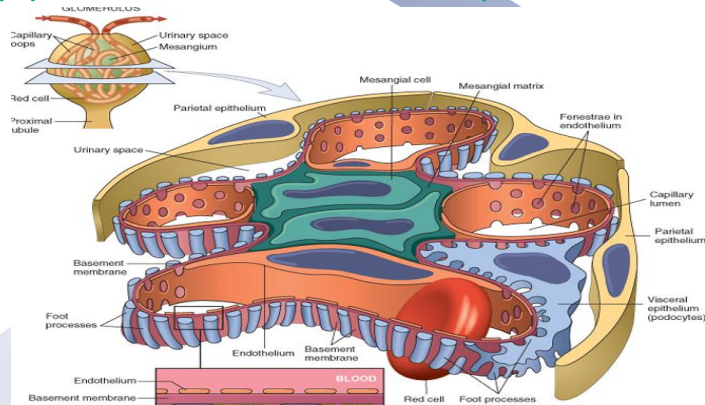
Normal Glomerular structure is needed to:

- Keep the glomerular filtration normal, thus maintains normal kidney function.
- keeps the urine volume maintained; so preventing fluid retention in the body which causes edema and high blood pressure. (maintaining normal Bp)
- Prevents the blood components (cells, proteins) from leaving the blood stream and appearing in the urine. (maintain the electrolyte balance)

The most important part of the kidney is the **Cortex**.

So normal urine will have:

- No protein. (if present proteinuria)
- No red blood cells (accept: <2 rbcs/high power field) (if >2RBCs : haematuria)
- No heme.
- No cellular casts.
- No fat (if present lipiduria)
- No sugar (if present glycosuria)



Glomerular diseases

Possible presentations of glomerular disease
- Isolated proteinuria
- Isolated hematuria
- Nephritic syndrome—hematuria, HTN, azotemia
- Nephrotic syndrome—proteinuria, edema, hypoalbuminemia, hyperlipidemia

General characteristics	Causes	Clinical features	Diagnosis	Treatment
1. Glomerular disease can be **primary (intrinsic renal pathology) or secondary (to a systemic disease).** Two important categories of glomerular pathology are diseases **that present with nephrotic syndrome and those that present with nephritic syndrome.** Many conditions have features of both. 2. There is a wide range in the rate of disease progression, varying from days to weeks in the acute glomerular diseases, to years in the chronic disorders.	1. GN is usually caused by immune-mediated mechanisms. 2. Other mechanisms include metabolic and hemodynamic disturbances.	1. Glomerular disorders are characterized by impairment in selective filtration of blood, **resulting in excretion of larger substances such as plasma proteins and blood cells. As disease advances, GFR decreases proportionately, leading to renal failure** and the possible need for dialysis and/or transplantation. 2. The classic features of glomerular disease are **proteinuria, hematuria, or both.** Nephrotic range proteinuria is pathognomonic for glomerular disease.	1. **Urinalysis** (hematuria, proteinuria, RBC casts) 2. **Blood tests** (renal function tests) 3. **Needle biopsy** of the kidney	depends on the disease, but often involves the use of **steroids and cytotoxic agents.**

Clinical and laboratory features of glomerular injury
- Leakage of cells and macromolecules across the glomerular filtration barrier

Proteinuria: characteristic of diseases that affect the podocyte, scarring and deposition of foreign material

Haematuria: characteristic of inflammatory and destructive processes
- Impaired renal function and reduced GFR
- Hypertension

Rapid progressive glomerulonephritis is a clinical syndrome that includes any type of GN in which rapid deterioration of renal function occurs over weeks to months, leading to renal failure and ESRD.

5

Glomerular diseases

TABLE 7-5 Nephritic Versus Nephrotic Syndrome

	Nephritic Syndrome	Nephrotic Syndrome
Pathogenesis	Inflammation of glomeruli due to any of the causes of glomerulonephritis	Abnormal glomerular permeability due to a number of conditions
Causes	Poststreptococcal glomerulonephritis is the most common cause, but may be due to any of the causes of glomerulonephritis	Many conditions. Membranous glomerulonephritis is the most common cause in adults. Other causes include diabetes, SLE, drugs, infection, glomerulonephritis (focal segmental and others) Minimal change disease is the most common cause in children
Laboratory findings	Hematuria AKI—azotemia, oliguria Proteinuria, if present, is mild and not in nephrotic range	Urine protein excretion rate >3.5 g/24 hr Hypoalbuminemia Hyperlipidemia, fatty casts in urine
Clinical findings	HTN Edema	Edema Hypercoagulable state Increased risk of infection

How glomerular diseases start?

- A lot of times the exact cause is not really clear, but the result of the damage in the glomerulus is telling how immune system is playing an important rule.
- Here we are talking about ***primary* glomerular diseases** that are mostly caused by ***immune system dysfunction***. :

  1- Auto-antibodies targeting glomerular structure or

  2- Immune-complexes (antigen-antibody) depositing and traumatizing the glomerular components.
- The manifestations of a glomerular disease are *usually indicative of which components of glomerular capillary wall was affected* at the most.

Affected glomerular component	Manifestation	Syndrome caused	Glomerular filtration status	Notes
Podocytes (foot processes)	Proteinuria only	Nephrotic Syndrome	Normal	No blood components in the urine
Endothelial cells, GBM or Mesangial cells	•Heamaturia •Proteinuria •Abnormal renal function	Nephritic Syndrome	Abnormal	Blood components appear due to disruption of glomerular filtration wall

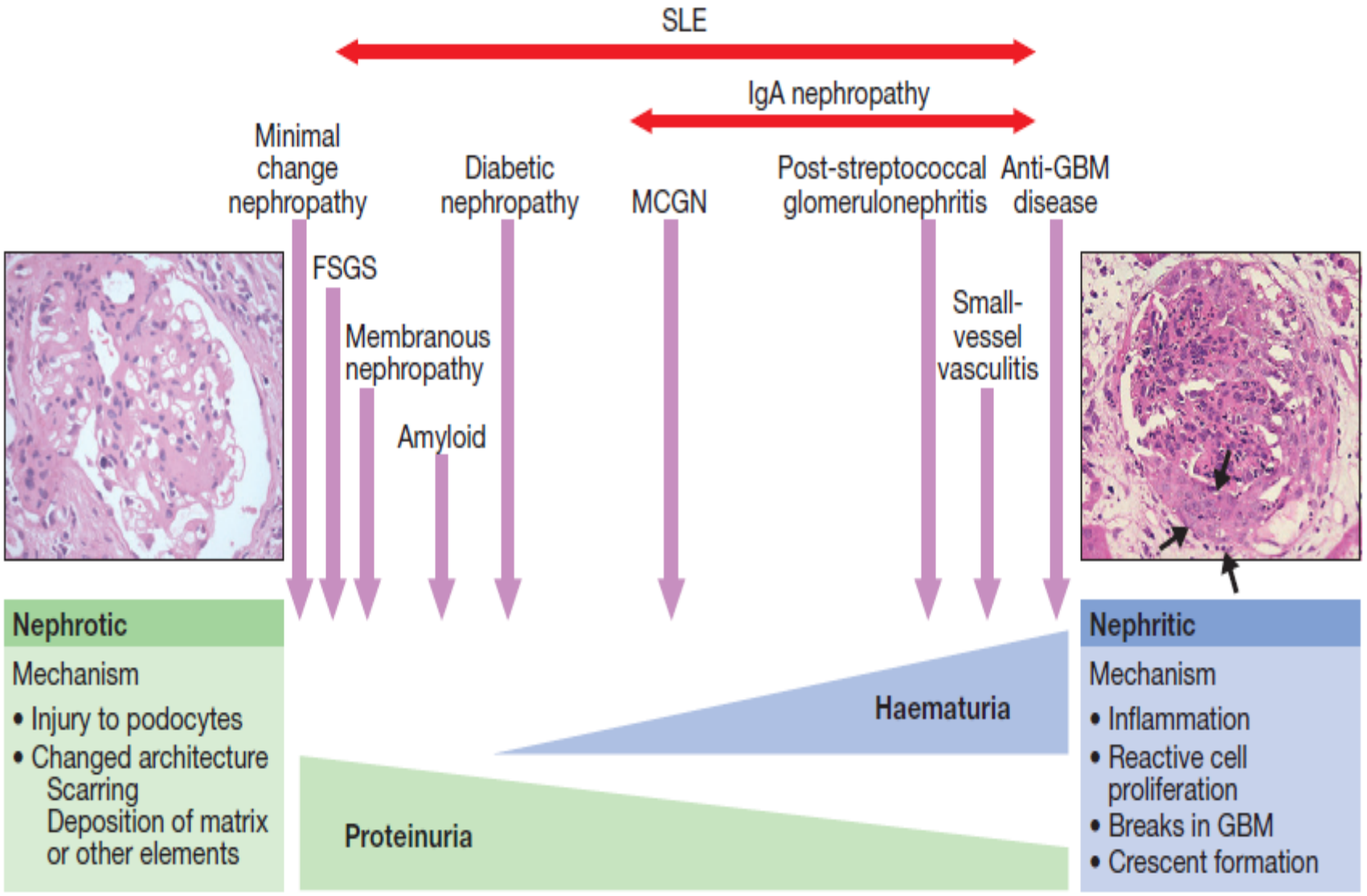
How glomerular diseases start?

- Mesangium is very sensitive. It starts to proliferate when anything “not part of it” attached to it “e.g. IgA” or when the glomerulus is irritated > disruption of capillaries > protein and RBCs in urine.
- However, when podocyte dysfunction occurs >>its digitations(foot processes) disappear “effacement”>> but that doesn’t cause blood components appearance in the urine because podocytes are away from the blood stream >>so mainly proteinuria occurs.

- **Primary glomerular diseases are diagnosed by : *Kidney biopsy***

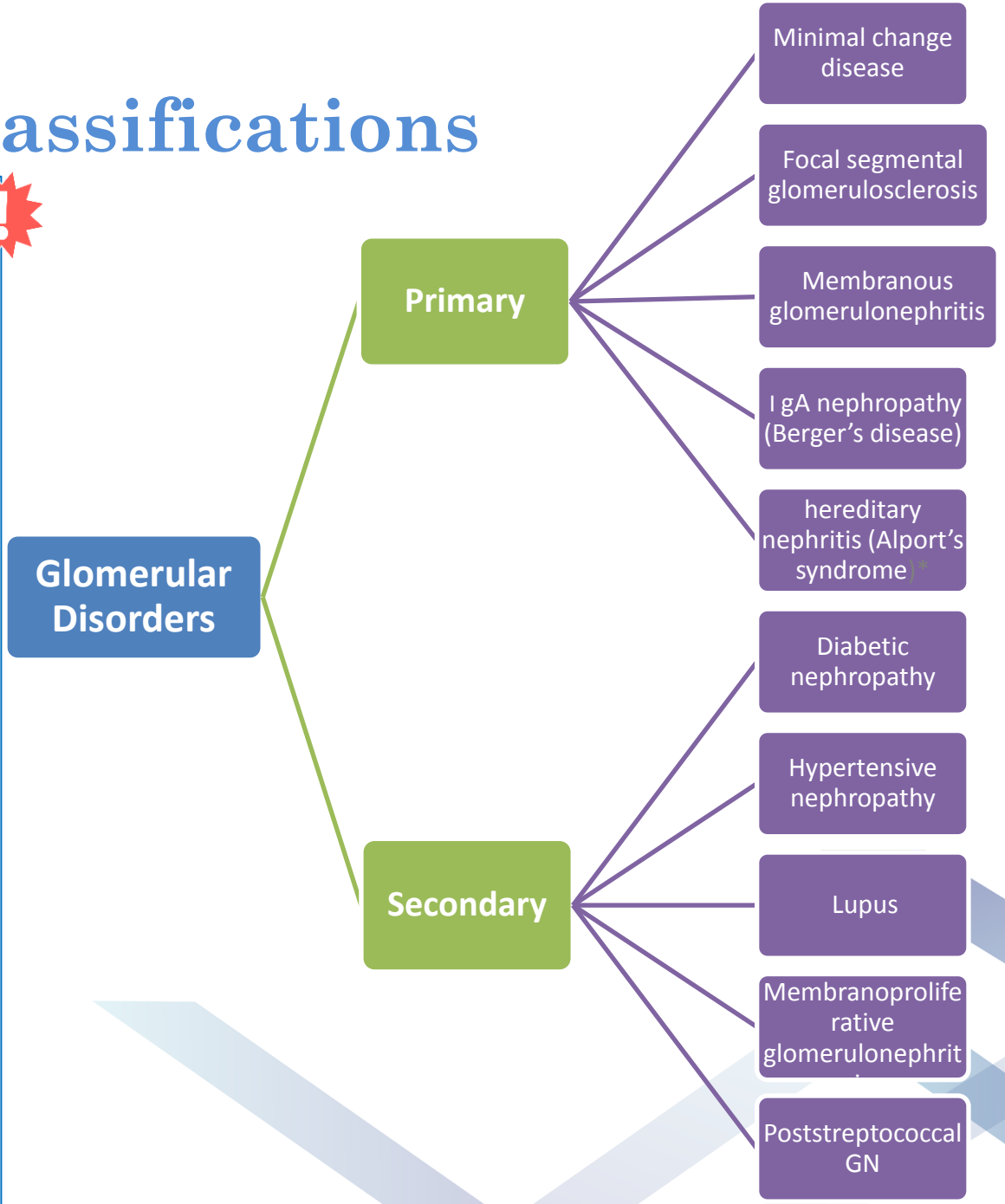
Why?! *Because*: Glomerular diseases are *named* based on their ***histo-pathological characteristics*** seen under the microscope.

- When mesangial cells gets irritated it multiply, thus it damages the kidney.
- It is important to recognize that the manifestation of glomerular disease depends on where the mechanism happened; if endothelial cells, glomerular basement membrane and mesangial cells were damaged, the results will be **hematuria, proteinuria** and **dysfunction of the glomerulus**, because there is no filtration ability. However, if epithelial cells were only damaged the integrity of the basement membrane will remain the same, so there will be no **hematuria**, but **proteinuria** will be present


SLE
IgA nephropathy
Minimal change nephropathy
Diabetic nephropathy
MCGN
Post-streptococcal glomerulonephritis
Anti-GBM disease
FSGS
Membranous nephropathy
Amyloid
Small-vessel vasculitis
Nephrotic
Mechanism
• Injury to podocytes
• Changed architecture
Scarring
Deposition of matrix or other elements
Haematuria
Proteinuria
Nephritic
Mechanism
• Inflammation
• Reactive cell proliferation
• Breaks in GBM
• Crescent formation

Classifications

*Most cases arise from a mutation or deletion of the *COL4A5* gene on the X chromosome, which encodes type IV collagen, resulting in inheritance as an X-linked recessive disorder. Mutations in *COL4A3*or *COL4A4* genes are less common and cause autosomal recessive disease. The accumulation of abnormal collagen results in a progressive degeneration of the GBM. Affected patients progress from haematuria to ESRD in their late teens or twenties. Female carriers of *COL4A5* mutations usually have haematuria but less commonly develop significant renal disease. Some other basement membranes containing the same collagen isoforms are similarly involved, notably in the cochlea, so that Alport's syndrome is associated with sensorineural deafness and ocular abnormalities.



Nephrotic Syndrome

- **Podocytes abnormality** is the primary finding in NS.
- Podocytes will sustain a *structural dysfunction*; making them **lose their Foot-processes (effacement).**
- This will lead to significant amount of protein appearing in the urine (**Proteinuria**).

Clinical and laboratory features:

- Hypoalbuminemia (serum Albumin <30 g/L) Normal serum Alb: 35-55g/L
- Heavy proteinuria (> 3.5 g/24 hours of urine collection)
- Peripheral or generalized edema (Low oncotic pressure and problem in regulating salt within that makes water retention).
- Hyperlipidemia (Liver will try to synthesize lipoprotein, to composite for the low albumin).

Complications:

- Infections & sepsis. (due to loss of immunoglobulins in the urine)
- Thrombosis. (due to loss of the anticoagulant factors)
- Acute kidney injury. (BC nephrotic syndrome pt. have problems in regulating their body fluids (Salt-Water retention), so when seeking medical help doctors prescribe diuretics to them >> this will cause hypovolemia (kidneys become hypoperfused)>> AKI)
- End stage kidney disease (ESRD) if heavy proteinuria not going into remission (BC the untreated nephrotic syndrome will cause chronic passage of protein/albumin in the renal tubules , and the tubules are sensitive to protein ; they can't tolerate its passage, so this will cause tubular injury then fibrosis thus causing CKI and if severe enough ESRD)

Nephrotic Syndrome

- **In nephrotic syndrome patients generalized edema occurs due to the following reasons:**

1- decreased oncotic pressure (hypoalbunemia >> fluid is shifted from the capillaries to the interstitium)

2- Salt-Water retention (Nephrotic syndrome pt. have problems in regulating their body fluids, because their kidneys reabsorb salt again)

- **Why hyperlipidemia occurs in the nephrotic syndrome?**

Due to **hypoalbuminemia >> serum albumin <30 g/L** (It is well known that liver is the main factory for albumin synthesis with a capacity of 10 g/day , and normally the average albumin in the body is ***40mg***, so if the albumin levels in the blood **decreased to 30 g/L** the liver will be able to compensate the loss by the 10 g that he normally synthesizes, but if the serum albumin **decreased to less than 30g**, unfortunately the liver will **not be able to compensate by the 10 g of albumin** that he synthesizes so instead the liver will produce **lipoproteins in large quantities** to compensate for the albumin loss , but since these lipoproteins *carry cholesterol* this will cause hyperlipidemia).

Nephrotic Syndrome

Proteinuria:

How many mgs of proteins are normally secreted in the urine per-day?

< 150 mg/day of all kinds of proteins including on **average 4-7mg/day** of Albumin that are secreted in the urine.

Urine Analysis in Nephrotic Syndrome:

- Heavy protein (Proteinuria) or called Nephrotic range proteinuria.
- No RBCs (few are occasionally seen).
- No RBCs casts.
- Lots of fat (Lipiduria) (Fatty casts, oval fat bodies & fat droplets).
- No WBCs (few may be seen).

Nephrotic Syndrome

Clinical Presentation

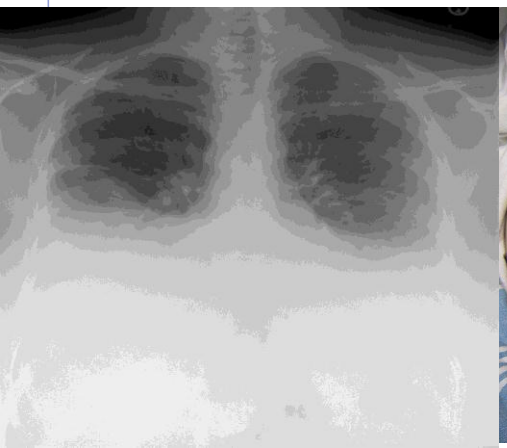
- Generalized edema " also called anasarca" due to :

1- Low serum albumin (low oncotic pressure)

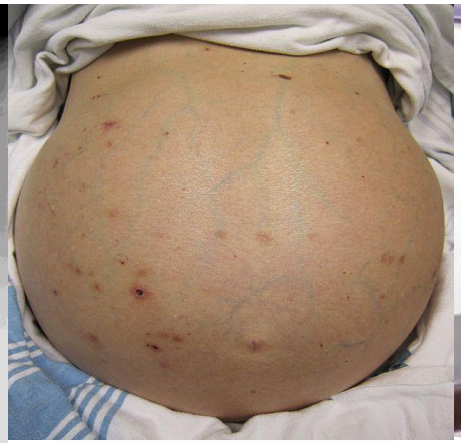
2-Increase Renal sodium retention Because of uncontrolled activation of the epithelial sodium channels (ENaC channels in the renal tubules)

- Fatigue
- Frothy urine (froth persists for long time after voiding)
- Anorexia
- Nausea and vomiting
- Abdominal pain
- Weight gain due to fluid retention
- Shortness of breath if having pleural effusion
- Signs and symptoms of DVT and PE

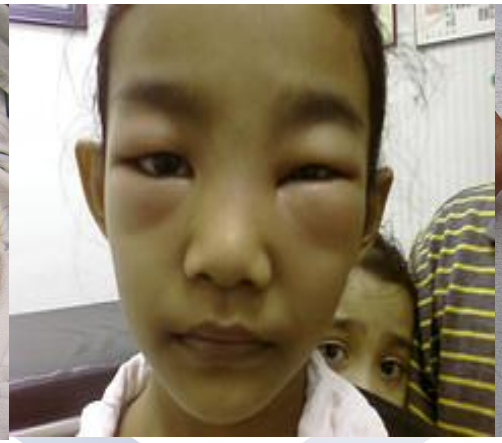
In the nephrotic syndrome the periorbital edema appears in the **MORNING** but then it disappears when the patient starts walking due to the gravity



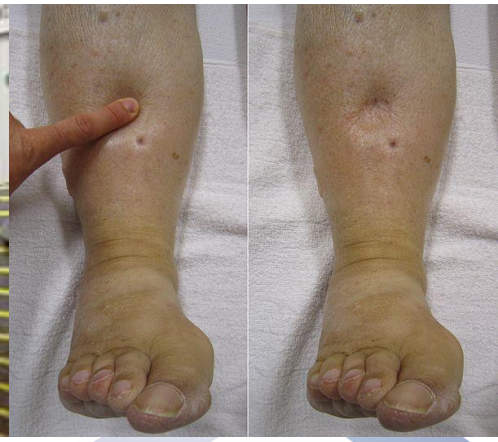
Pleural effusion



Ascites



Periorbital edema



Pitting edema

Glomerular Diseases present as Nephrotic Syndrome

1-**F**ocal **S**egmental **G**lomerulo**S**clerosis (**FSGS**)

2- **M**inimal **C**hange **D**isease (**MCD**)

3- **M**embranous **N**ephropathy (**MN**)

1-Focal Segmental GlomeruloSclerosis (FSGS)

The primary variant on **light microscopy**:

which may also show positive staining for deposits of C3 and IgM on immunofluorescence

Focal: some glomeruli are affected by sclerosis but the rest of them look normal.

Segmental: *only a segment* of the affected glomeruli is sclerosed

A ***common cause*** of Nephrotic syndrome in ***adults*** (12 – 35 %)

NB. **All the glomeruli (whether sclerosed or normal) will have a *diffuse foot processes effacement* (thus Nephrotic syndrome appears)**

Types of FSGS:

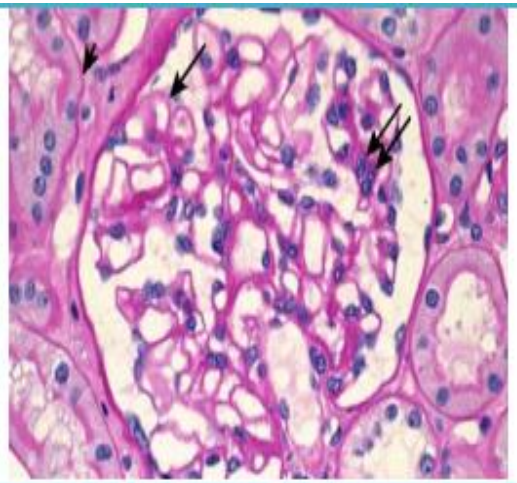
1-Primary FSGS

2-Secondary FSGS

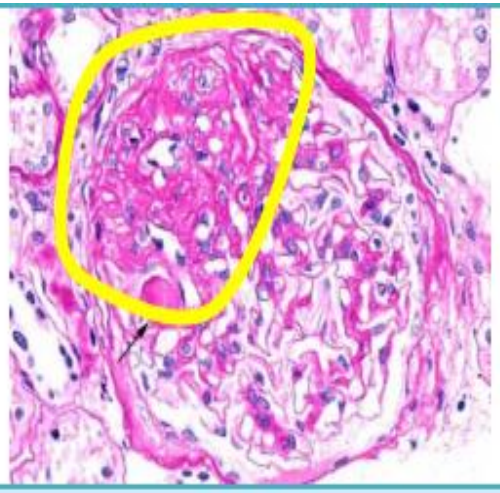
1. This accounts for 25% of cases of nephrotic syndrome in adults and is more common in blacks. Hematuria and HTN are often present.
2. It has a fair to **poor prognosis**. It is generally resistant to steroid therapy—patients develop renal insufficiency within 5 to 10 years of diagnosis. The course is progressive.
3. The treatment regimen is controversial, but remission has been achieved in 50% of patients with the use of **cytotoxic agents, steroids, and immunosuppressive agents. ACE/ARBs are also commonly indicated.**

1-Focal Segmental GlomeruloSclerosis (FSGS)

LM

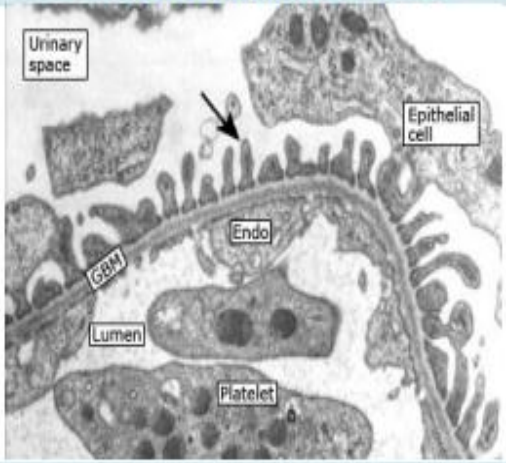


Normal Glomerulus

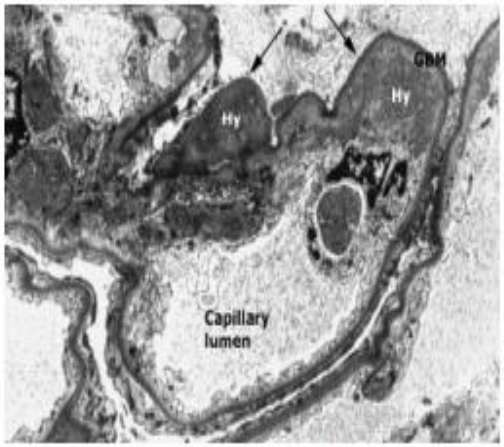


FSGS

EM



Normal Glomerulus



FSGS, like minimal change disease, diffuse foot process effacement but with segmental sclerosis

Primary FSGS:

Sudden onset of proteinuria and other manifestations of nephrotic syndrome (i.e. anasarca, periorbital edema,….)

Secondary FSGS:

It gradually happens (slowly over years) and its progressive (it causes slow irreversible destruction to the kidney unlike the primary FSGS)

Laboratory signs:

-Proteinuria is less heavy than other causes of nephrotic syndrome.

-Serum Albumin is not very low like the primary type.

-**Renal impairment is commonly seen with the secondary FSGS and this is not a good prognostic sign**

Treatment:

Primary FSGS: *Immunosuppressive therapy*

1st line: corticosteroids

2nd line: cyclosporins / tacrolimus

Secondary FSGS: Not typically treated with immunosuppression.

We treat the underlying cause (if obesity then reduce weight , if HTN the lower BP…) + *Supportive measurements* to protect the kidney i.e keeping the BP well controlled with ACEi

Possible causes of secondary FSGS:

-Long standing hypertension

-Massive obesity

-Nephron loss (> 75% of renal mass) e.g renal agenesis

-Reflux nephropathy

-Healing of prior GN (IgA, Lupus etc)

-Anabolic steroid abuse

-Severe preeclampsia (in pregnant ladies)

-Drugs: Interferon, Pamidronate, Heroin

-Infections: HIV

2- Minimal Change Disease (MCD)

- No glomerular sclerosis (the most important difference between MCD and the FSGS)

Called minimal because:

- **light microscopy:** is typically showing normal glomeruli. So called: nil disease.

BUT:

- **electron microscopy**: shows diffuse effacement of the epithelial cells' foot processes only.

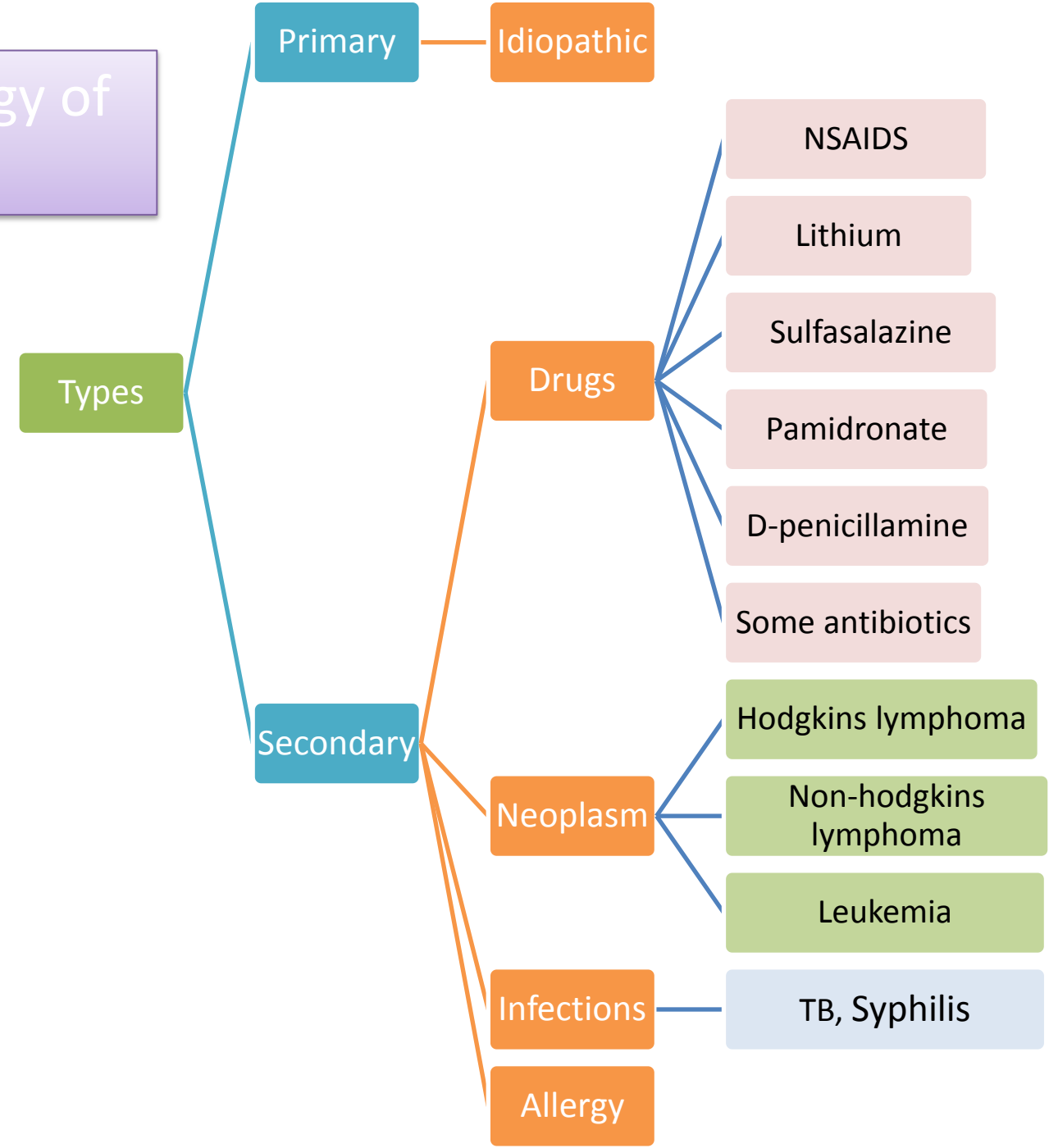
- **It is the main cause of nephrotic syndrome in children**
  - **-90 % of cases in children < 10 years old**
  - **-> 50 % of cases in older children**
- It **causes 10-25** % of Nephrotic syndrome **in adults**

In children with nephrotic syndrome manifestations, **kidney biopsy is not needed** because they are mainly having MCD and the treatment is given **empirically** for such cases.

But in adults kidney biopsy is very important to role out other causes.

1. Nephrotic syndrome—most common presentation
2. Most common in children—hodgkin's disease and non-Hodgkin's lymphoma have been associated with minimal change disease.
3. No histologic abnormalities on light microscopy; **fusion of foot processes on electron microscopy**
4. Excellent prognosis; responsive to steroid therapy (4 to 8 weeks), although relapses may occur
5. Current evidence points to systemic **T cell dysfunction as the most likely root cause of MCD.**

Etiology of MCD



2- Minimal Change Disease (MCD)

- **Clinical presentation of MCD:**

➢Typically has a sudden onset Edema
➢BP may be normal or slightly elevated
➢Heavy proteinuria (Nephrotic range)
➢ Lipiduria
➢Hypoalbuminmia (usually very low serum Albumin)
➢Hyperlipidemia
➢Creatinine is always within the normal range or slightly elevated and normalizes with remission

- **Diagnosis:**

Must do **kidney biopsy** in adult patients with this presentation
Diffuse effacement of foot process.

- **Treatment:** (only for primary MCD , if secondary MCD then treat the underlying cause")

***First line*: Corticosteroids,** given x 3-4 months then taper over 6 months (1 mg/kg **prednisolone** for 6 weeks)
***Second line*:** oral Cyclophosphamide, Cyclosporin

3- Membranous Nephropathy (MN)

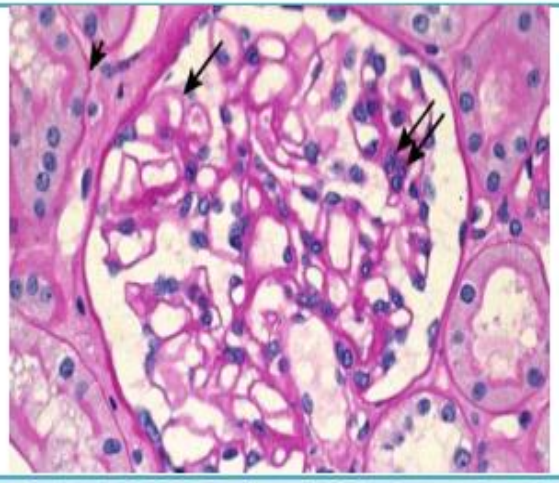
- **Most common cause of nephrotic syndrome in adults (15% and 33%)**
- Mostly **secondary in children** (hepatitis B antigenemia)
- Presentation: slowly developing nephrotic syndrome and Usually presents with nephrotic syndrome; glomerular capillary walls are thickened.

	Primary (Commonest in adults)	Secondary (common in children)
Etiology	Idiopathic It is caused by antibodies (usually autoantibodies) directed at antigen(s) expressed on the surface of podocytes. Recent studies suggest that one such antigen is the M-type phospholipase A_2 receptor 1.	Secondary: causes of MN: ➢Systemic lupus erythematosus (SLE) Class V Lupus Nephritis (10-20%) ➢Drugs: penicillamine, gold, high dose Captopril, and NSAIDs, Anti-TNF. ➢Infections: Hepatitis B, Hepatitis C, syphilis ➢Malignancy: solid tumors prostate, lung, or GI track (undiagnosed)
Treatment	-Corticosteroids plus -Cyclophosphamide or cyclosporine -May be Rituximab	Mainly **target the primary disease** that caused MN, and treat the Nephrotic syndrome manifestations.

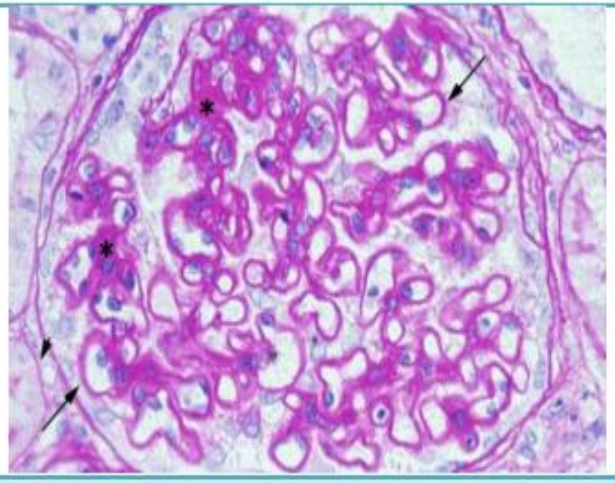
The prognosis is fair to good. The course is variable; remission is common (in40% of cases), but renal failure develops in 33% of patients. Steroid therapy does not change the survival rate.

3- Membranous Nephropathy (MN)

LM



Normal Glomerulus



Diffuse **thickening** of the glomerular capillary **wall** throughout all glomeruli (**IgG and C3 deposition**)

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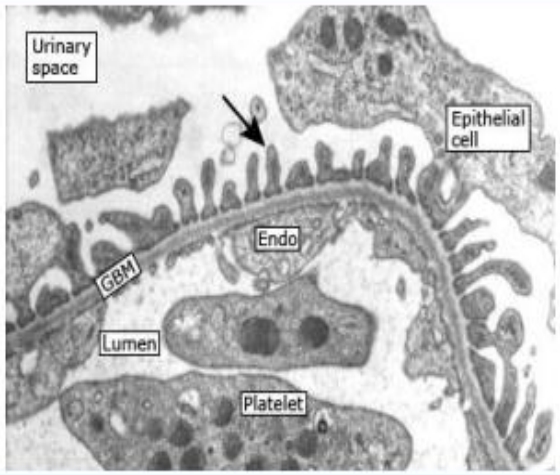
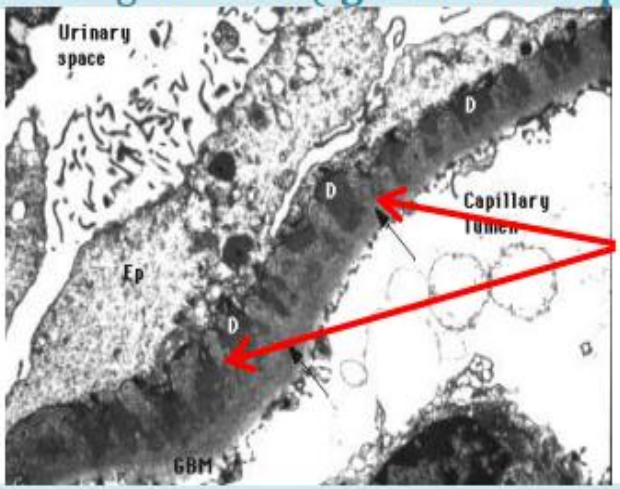


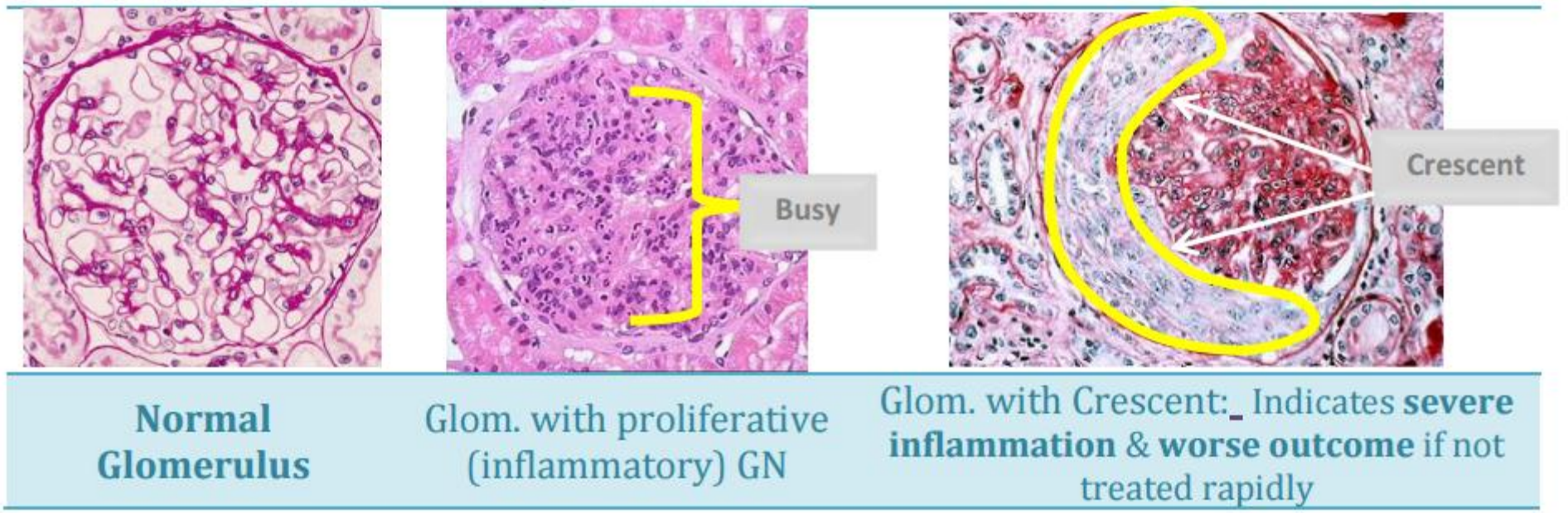
Normal Glomerulus



MN

Nephritic Glomerular diseases

- When we say Nephritic; it means a clinical pattern of presentation for a group of GNs, and not a syndrome like what we saw in Nephrotic causes.
- The Nephritic pattern is **always indicative of underlying inflammatory process in the glomeruli**; causing inflammatory modulators attraction, cellular proliferation and eventually glomerular permanent dysfunction if left untreated.
- The GLomerular mesangium, endothelium and GBM components of the Glomerulus are likely going to be targeted because of their proximity to blood circulation.

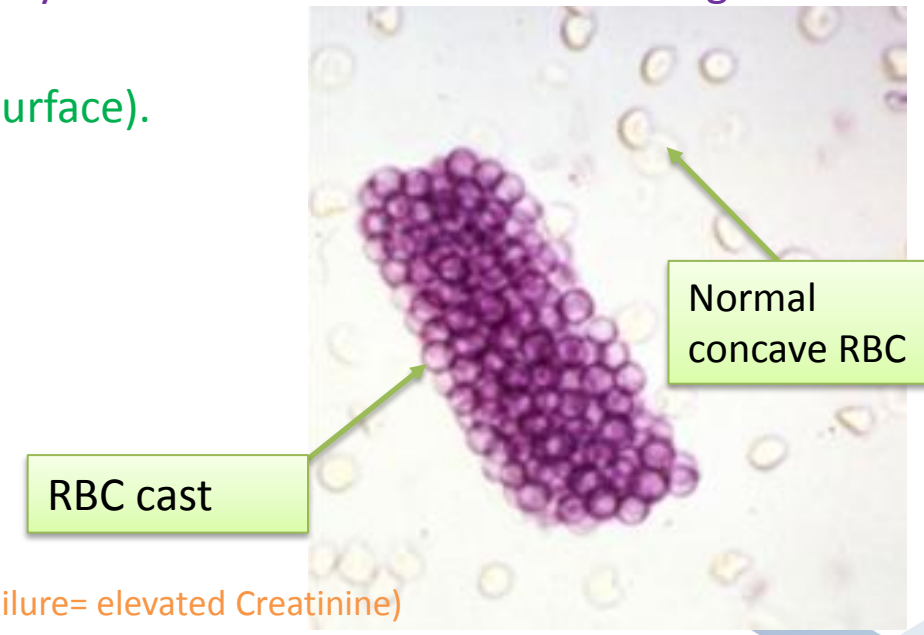


Nephritic Glomerular diseases

Nephritic urine analysis shows:

- Red Blood Cells (RBCs) (dysmorphic RBCs "normally they look concave")
- RBCs casts *, or cellular casts. "formed by naturally occurring TammHorsfall mucoprotein in the distal tubules & collecting ducts when they become loaded with RBCs coming from the Glomerulus (due to GN)."
- Dysmorphic RBCs (RBCs lose their smooth surface).
- Protein (at variable amount).
- They are called Active Urinary Sediments.

(Active = is indicative of underlying glomerular inflammatory process; requiring urgent medical attention).



clinical manifestations:

- AKI (Acute Kidney Injury) =Acute Renal impairment or Failure= elevated Creatinine)
- Decreased Urine output
- Edema
- High Blood Pressure "always high in nephritic, normal or slightly high in nephrotic"
- May have other manifestations of systemic vasculitis since some GN types are actually vasculitis (e.g. skin rash, pulmonary hemorrhage, etc)
- Positive immune markers: ANA, Anti-DNA, low complements, +ve ANCA (depends on the cause)

Glomerular Diseases present as Nephritic Syndrome

1- IgA Nephropathy / HSP (Henoch-Schönlein purpura)

2- Post streptococcal glomerulonephritis (PSGN)

3- Lupus Nephritis

4- Anti-GBM (Goodasture's disease)

5- ANCA vasculitis (e.g. Wegner's Granulomatosis)

6- Membranoproliferative GN (MPGN)

Important secondary causes of nephrotic syndrome:

- Diabetes mellitus.
- Amyloidosis.

1- IgA Nephropathy

- **Renal function is usually normal.**
- Mesangial deposition of **IgA and C3** are seen on electron microscopy.
- **The prognosis in most patients is good** with preservation of renal function (renal
- insufficiency may develop in 25%).

- History of **upper respiratory tract infection (< one week)**
- Most common type of 1ry GN in developed countries.
- crescent formation may be seen.
- Patient presents **with dark urine (hematuria) and hypertension+/- proteinuria** (1-3 days after URTI) Found incidentally
- Diagnosed incidentally by **renal biopsy** that is done for other reason
- It has a chronic course that can **progress to ESRD.**
- **Pathology: IgA deposit abnormally in the glomeruli**; hence triggering a local inflammatory response in the Glom mesangium (mesangial expansion)
- **Treatment:**

No effective immunosuppressing therapy except in severe cases where it can be tried.

Most important treatment is to ***control the blood pressure*** which also decreases the proteinuria.

1- Henoch-Schönlein purpura

- This condition most commonly occurs in children but can also be observed in adults.
- It is characterised by a systemic vasculitis that often arises in response to an infectious trigger.
- The presentation is with a characteristic petechial rash typically affecting buttocks and lower legs, and abdominal pain due to the occurrence of vasculitis involving the gastrointestinal tract.
- The presence of glomerulonephritis is usually indicated by the occurrence of haematuria.
- Renal biopsy shows mesangial IgA deposition and appearances that are indistinguishable from acute IgA nephropathy.
- Treatment is supportive in nature; in most patients,
- the prognosis is good, with spontaneous resolution, but some, particularly adults, progress to develop ESRD.

2- Post streptococcal glomerulonephritis (PSGN)

- History of :
  1. Sorethroat infection with Gram positive cocci (Group A beta-hemolytic Streptococcus (GAS).
  2. Soft tissue or bone infection in adults caused by Staphylococcus
- Patients present with frank hematuria *gives the urine a red or smoky appearance* usually **after one week** and up to 3 weeks from the start of infection.
- Serum will show positive Antistreptolysin-O (ASO) titer.
- Low C3, Normal or slightly low C4 in the serum. (C3 will be consumed in the immuneocomplex, that's why the patients with PSGN will have low C3)
- May have positive throat culture.
- It is much more common in children than adults.
- Children have better and faster recovery than adults.
- Treatment is usually supportive= wait and see.

antihypertensives, loop diuretics for edema; the use of antibiotics is controversial. Steroids may be helpful in severe cases.

- Remarkably, the renal lesion in almost all children and many adults seems to resolve completely

- **most common cause of nephritic syndrome**
- Features include **hematuria**, edema, HTN, low complement levels, and proteinuria.
- **It is self-limited** (usually resolves in weeks to months) with an **excellent prognosis**. Some cases develop into rapidly progressive GN (more commonly in adults).

3- Lupus Nephritis

- Usually in young females with SLE and they present with haematuria and proteinuria
- SLE patients
- Diagnosed by kidney biopsy
- Low complements (C3, C4) level along with the positive Lupus markers, abnormal urine analysis & abnormal renal function
- **Treatment:** high degree of immunosuppressing medications.

Causes of glomerulonephritis associated with low serum complement

- Post-infection glomerulonephritis
- Subacute bacterial infection: especially endocarditis
- Systemic lupus erythematosus
- Cryoglobulinaemia
- Mesangiocapillary glomerulonephritis, usually complement type

4- Anti GBM antibody disease

- Clinical features include rapidly progressive renal failure, hemoptysis, cough, and dyspnea.
- Lung disease precedes kidney disease by days to weeks. It is associated with a variable course.

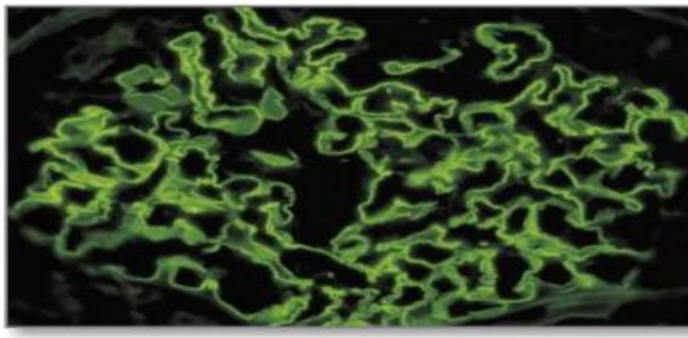
- Due to autoantibody against (alpha-3 chain) of type IV Collagen; found in Glomerular & alveolar basement membrane.
- The manifestations will be: -

1. **proliferative GN** (usually crescentic) (can be the only presenting finding).
2. **Pulmonary hemorrhage** causing hemoptysis (if with GN; it is called: Goodpasture's disease). "With smoking"
3. **Positive test for Anti-GBM antibodies in the serum.**

- Kidney biopsy shows the diagnostic Immunofluorescence pattern: **Linear stain of IgG and C3.**
- **Treatment:** is always started immediately by

  1.Plasmapheresis (a process of removing the plasma from the blood which has the autoantibodies)
  to remove the antibodies

  2.Giving heavy immunosuppression that includes corticosteroids and cyclophosphamide << to prevent further antibodies production



Linear **Anti-GBM** staining by Immunofluorescence is a *Diagnostic test.* ***Linear*** *means taking the same shape of smooth capillary walls.*

5- ANCA Vasculitis

- Autoimmune disease that involves the presence of Neutrophils adhesion enhancing molecule called ANCA=Anti-neutrophil cytoplasmic antibody (its an autoimmune molecule that triggers neutrophils to attack blood vessels)

	C-ANCA	P-ANCA
	Cytoplasmic type	**P**erinuclear type
Associated disease	Granulomatous Polyangiitis= old name *Wegner's Granulomatosis*	Microscopic Polyangiitis & Churg-Strauss syndrome

- They may present with hemoptysis+ hematuria+ high creatinine levels
- Diagnosis is made by kidney biopsy and positive ANCA titer in the serum.
- Crescent sign on renal biopsy
- **Treatment:** potent immunosuppressing medications (high dose corticosteroids & cyclophosphamide).

6- Membranoproliferative GN (MPGN)

- It is a pathological description & has multiple causes.

- is characterised by an increase in mesangial cellularity with thickening of glomerular capillary walls and subendothelial deposition of immune complexes and/or components of the complement pathway
- **It can be classified into two main subtypes.**

1. is characterised by deposition of immunoglobulins within the glomeruli. This subtype is associated with chronic infections, autoimmune diseases and monoclonal gammopathy.
2. is characterised by deposition of complement in the glomeruli and is associated with inherited or acquired abnormalities in the complement pathway. Within this category is so-called 'dense deposit disease', which is typified by deposition of electron-dense deposits within the GBM.
3. is recognised, in which neither immunoglobulins nor complement are deposited in the glomeruli. This is associated with healing following thrombotic microangiopathies, such as HUS and TTP.

- It may present with Nephritic picture or Nephrotic syndrome

- The primary (idiopathic) MPGN is mainly seen in children.
- The secondary type is seen in adults due to:
- **Hepatitis B and C**
- Endocarditis
- **Lupus** and Sjogren's syndrome
- Cancer
- Complement deficiency

- Common association with **cryoglobulinemia**
- The prognosis is poor. **Renal failure develops in 50%** of patients. Treatment is rarely effective.

MCQs

Q1-Which glomerular disease would you suspect most in a patient with the following findings? Anti-GBM antibodies, hematuria, hemoptysis:

A)Post streptococcal glomerulonephritis (PSGN)
B) Lupus nephritis c)
C) Wegner's Granulomatosis
D) Goodpasture syndrome

Q2- 5-year-old boy is noted to have increased puffiness around his eyes for the past week, and he has been less active than normal. On physical examination he has periorbital edema. Vital signs include T 37 C, P 75/minute, RR 18/minute, and BP 140/90 mm Hg. A urinalysis reveals sp. gr. 1.010, pH 6.5, no glucose, 4+ protein, no blood, no casts, and no ketones. Microscopic urinalysis reveals oval fat bodies, but no WBC's or RBC's. He improves following a course of corticosteroid therapy.

Which of the following renal lesions is most likely to have been present in this boy?

A) Glomerular crescents
B) Fusion of podocyte foot processes
C) Patchy tubular necrosis
D) Hyperplastic arteriolosclerosis
E)Mesangial immune complex deposition

MCQs

Q3-clinical study is performed involving subjects with glomerulonephritis. One group of subjects has a diagnosis of crescentic glomerulonephritis and another group has membranous glomerulonephritis.
Which one of the following laboratory findings is most likely to be found in the absence of other findings in subjects with membranous glomerulonephritis?

A) Rapid onset
B) Red blood cell casts
C) Oliguria
D) Albuminuria
E) Hypertension

Q4- 60-year-old man was diagnosed last year with adenocarcinoma of the lung, and he underwent right lower lobectomy. For the past 3 weeks he has had increasing malaise. On physical examination he has pitting edema to his knees and presacral edema. Abdominal and chest CT scans show scattered hepatic mass lesions and hilar lymphadenopathy. A urinalysis reveals 4+ proteinuria, and his 24 hour urine protein is 2.7 gm. His serum urea nitrogen is 55 mg/dL with creatinine of 6.1 mg/dL. A renal biopsy is performed, and there is focal deposition of IgG and C3 with a granular pattern.
Which of the following forms of glomerular disease is he most likely to have?

A) Membranous glomerulonephritis
B) Rapidly progressive glomerulonephritis
C) Nodular glomerulosclerosis
D) Goodpasture syndrome
E) Membranoproliferative glomerulonephritis, type II

MCQs

Q5- 10-year-old girl is brought to the physician because of increasing lethargy and passing dark-coloured urine for the past week. She had a sore throat two weeks prior to this. On physical examination she is afebrile with blood pressure 140/90 mm Hg. Laboratory studies show her serum creatinine is 2.8 mg/dL and urea nitrogen 24 mg/dL. Urinalysis shows 2+ blood, 1+ protein, no glucose, and no ketones. Microscopic urinalysis shows dysmorphic RBC's. A renal biopsy is performed and on microscopic examination shows glomerular hypercellularity, with PMNs present. Electron microscopy shows subepithelial electron dense "humps".

Which of the following laboratory test findings is most likely to be present in this girl?

A) Elevated serum glucose
B) Antibody to double stranded DNA
C) Antiglomerular basement membrane antibody
D) Positive C3 nephritogenic factor
E) Elevated antistreptolysin O titer

Q6-Which of the following is the most common nephrotic syndrome in children?

A) Focal segmental glomeulosclerosi
B) Minimal change disease
C) Henoch-Schonlein purpura
D) Membranous glomerulonephriti

Answers : 1-D 2-B 3-D 4-A 5-E 6-B

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Medicine is a science of uncertainty and an art of probability