Glomerular disease

Objectives:

- To understand the pathophysiology of Glomerular Diseases.
- To be able to correlate between the clinical presentation & the underlying Glomerular pathology.
- To recognize the differences between Nephritic & Nephrotic Glomerular diseases. The most important objective
- To recognize the important features of Nephritic & Nephrotic renal diseases.
- To be able to recognize the early features of Glomerular diseases before it's too late!
- To learn the common causes of Nephrotic & Nephritic renal diseases.

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Resources: 436 slides + 435 team + Davidson + kumar + Recall questions step up to medicine.

- Editing file
- Feedback

Dr.Saad: This lecture has a lot of information and details, the most important things that I want you to focus on are (1) How to differentiate between Nephrotic and Nephritic syndromes. (2) Urinalysis in both (3) disease that cause them

Introduction (Anatomy and Physiology)

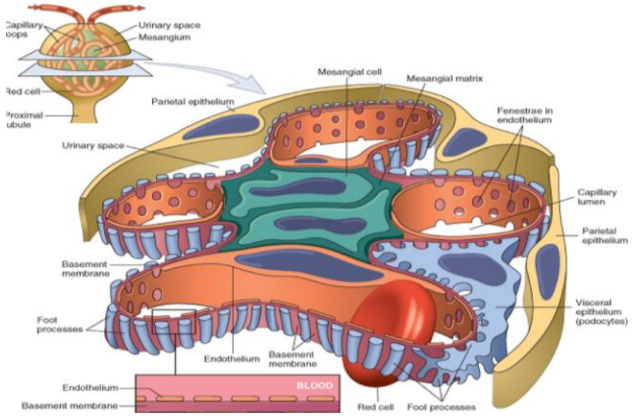
- **Renal cortex** is the most important functional part of the kidney, because it has the **Glomeruli**.
  In chronic kidney diseases their cortex shrinks and become fibrosed, so that's why we see a smaller kidney and in US it appears whitish and atrophied
- The Glomerular Capillary wall has **3 layers**, through which filtration occurs: You must know them because they keep fluids states maintained and any disruption in any of them will cause the kidney function to decline and blood components will appear in urine (Hematuria, proteinuria)

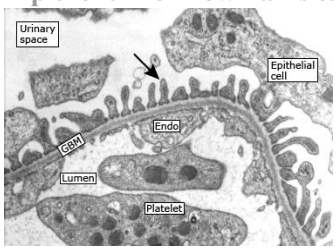
1) Fenestrated endothelium. **2)** Glomerular Basement Membrane. **3)** Podocyte (Away from blood components, WHY IT'S IMPORTANT TO KNOW THIS? SEE NEXT SLIDE regarding how glomerular diseases start)

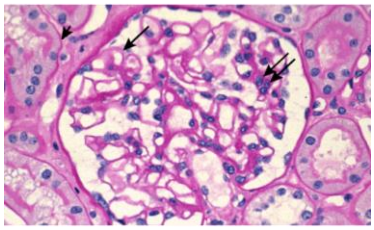
Recall:

- The glomerulus is a network of capillaries enclosed by Bowman's capsule, which marks the beginning of the proximal convoluted tubules.
- On its journey to Bowman's capsule, the filtrate passes through:

1. **Fenestrated endothelium**
2. **Glomerular Basement Membrane (GBM):** Made up of type IV collagen fibers synthesized by the supportive mesangial cells found in between capillaries.
3. **Podocytes:** Which are structurally complex cells with multiple foot processes, the space between the foot processes create slit diaphragms that act as a barrier to the passage of plasma proteins.
4. **Epithelium of Bowman's capsule**







This is a normal glomerulus under light microscope (right) and electron microscope (left)

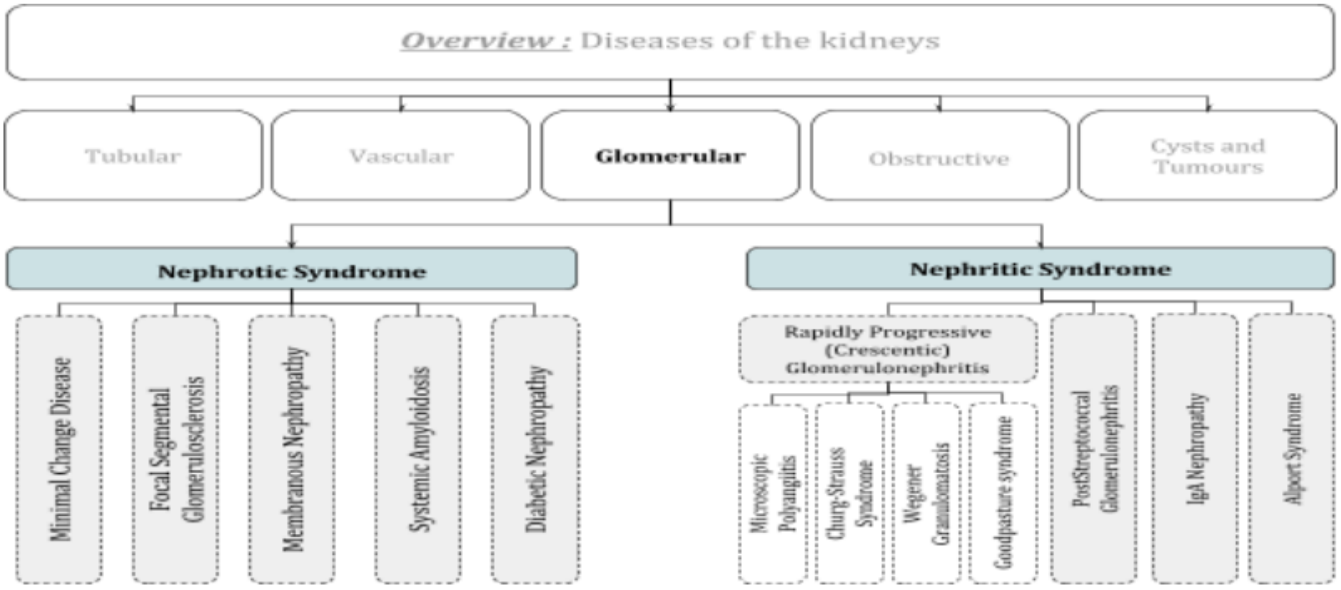
★ Normal glomerular structure is needed to:

1. Keep the glomerular filtration normal, to maintain normal kidney function.
2. Maintain urine volume and hence, preventing fluid retention in the body which causes edema and high blood pressure.
3. Prevents the blood components (cells, proteins) from leaving the blood stream and appearing in the urine. Urine is bland which means it has nothing – no cell components

Normal Glomerular Capillary Wall Filtrate	Disrupted Glomerular Capillary Wall
• **Devoid** of protein • **Devoid** of RBCs (Accept: <2 RBCs/High power field) • **Devoid** of heme • **Devoid** of cellular casts • **Devoid** of fats • **Devoid** of sugar	Depending on the site and type of damage: • **Proteinuria** caused by either structural (like podocyte effacement) or physiochemical (alterations in the anionic molecules within the GBM) changes • **Hematuria** a glomerular cause of hematuria is either inflammation or breaks in the GBM Glomerular hematuria is coming from the capillaries unlike hematuria which could be from from bladder, RCC)

Glomerular Diseases

Key findings in nephrotic syndrome (highly recomended)



- There is something autoimmune where the body targets any component of the capillary wall or there is an antigen antibody reaction somewhere else that gets filtered and trapped into the kidney and attacks the glomeruli creating a local inflammatory stage
- We will be talking about primary glomerular diseases that are mostly caused by immune system dysfunction How? Auto-antibodies targeting glomerular structure or immune-complexes (antigen-antibody) depositing and traumatizing the glomerular components. The pathology will depend on the targeted area of the glomerulus. (basement membrane, msesengium) by the immune system.
- *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.*

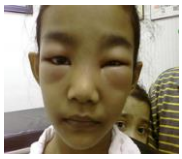
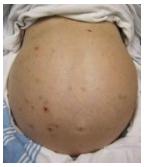
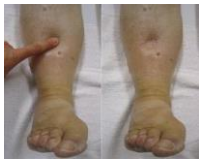
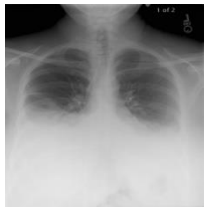
How do glomerular diseases start?

Any insult will cause inflammation (Recruitment of inflammatory cell) and if this happened to the mesangial cell they will start to proliferate and compress the surrounding cells leading to glomerulonephritis and blood compartments will be shown in urine.

- The manifestations of a glomerular disease are usually indicative of which components of glomerular capillary wall was affected at the most, examples include:
- if **Podocytes** are the main target of the disease process → mainly **proteinuria** (at large amount) will manifest; thus **Nephrotic Syndrome** will be the main finding. **Podocytes are outside the capillary** basement membrane, so when they are affected there will not be any inflammation because it is far from the blood compartment and the inflammatory markers are prevented from reaching that area so there will only be irritation. **That's why we only see protein in the urine and no blood.**
- if **endothelial** cells, **Mesangial** cells or **GBM** are affected → mainly hematuria and abnormal renal function will manifest because of disruption in glomerular filtration wall; thus **Nephritic pattern** of renal disease will manifest. *(Note that Proteinuria is always present in this kind of glomerular injury as well).*
- Glomerular diseases are named based on their **histo-pathological characteristics** seen under the microscope. So, almost always a kidney biopsy is needed to diagnose any suspected primary glomerular disease.

Nephrotic Syndrome

★ **Clinical categories of glomerular diseases:** **it is important to differentiate between nephrotic and nephritic syndrome** because the approach, the treatment and the urgency of treatment is different. If A patient presents with a nephritic picture then we have to act quickly otherwise they will lose part of their kidney.

Definition	Nephrotic syndrome is a measure of the severity of proteinuria in association with any form of glomerular disease. It occurs when proteinuria is so massive that the liver can no longer increase the production of albumin to compensate for urinary loss.
Causes/association	Overall, diabetes and hypertension are the most common conditions associated with nephrotic syndrome. In addition to systemic diseases, there are a number of diseases limited to the kidney that produce nephrotic syndrome. It is better to describe "associations" rather than "causes" since we do not know what exactly causes nephrotic syndrome.
Clinical presentation	**Signs and symptoms? A picture of anasarca[1]** • **Edema** Caused by: • Low serum albumin (↓ oncotic pressure) • Increased renal sodium retention Because of uncontrolled activation of the epithelial sodium channels (ENaC channels in the renal tubules)    Preorbital edema, seen in early morning bec there's no oncotic pressure so fluids redistribute with gravity.  ★ **Patients with nephrotic syndrome get** pleural effusion but are protected from pulmonary edema because cardiopulmonary circulation depends on hydrostatic pressure and not on the oncotic pressure! otherwise even us normal people will get pulmonary edema occasionaly. **Patients may also present with:** • Fatigue • Frothy urine (froth persists for long time after voiding) • **Anorexia** • Nausea & vomiting because there is edema in their bowels as well and this constricts their bowel movement and produces GI symptoms. • they don't get pulmonary edema. why? because pulmonary circulation depends on hydrostatic pressure not oncotic pressure • Abdominal pain • Weight **gain** due to fluid retention • Shortness of breath if having pleural effusion • Signs & symptoms of **DVT**, PE Urineanalysis will show: IMPORTANT! • Heavy proteinuria (>3.5g "nephrotic range" per 24 hrs. of urine collection) Daily, < 150 mg/day of all kinds of proteins. Including on average 4-7 mg/day of Albumin that are secreted in the urine normally. we should never neglect proteinuria because when protein (albumin, specifically) passes through the tubules all day long it will lead to tubular fibrosis and eventually chronic kidney failure.

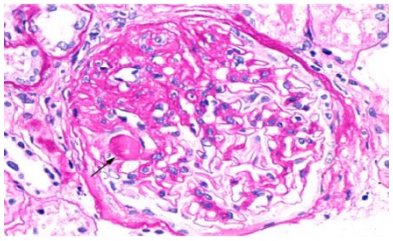
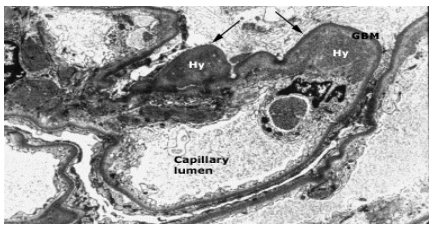
[1] a condition that causes a general swelling of the body.

	• Hypoalbuminemia (<30 g/L) by losing albumin till the point where liver can't compensate by producing more albumin! "Normal serum Alb: 35-55g/L" • Peripheral or generalized edema[2] • NOTE : No RBCs because there is no destruction of capillary loop!, RBCs casts or WBCs (few may be seen) are seen here. tubules). • Fat (Lipiduria) : Fatty casts, oval fat bodies & fat droplets. A lot of fats in blood which will escape to the glomeruli • Hyperlipidemia[3] (Hyperlipidemia and hypercholesterolemia are caused by increased hepatic lipoprotein synthesis.) In nephrotic syndrome there is loss of albumin in the urine and this will lead to a decrease in oncotic pressure, the liver reacts to this by synthesizing more albumin to compensate but further down the line it can't produce anymore albumin so it starts producing other proteins (including LIPOPROTEIN) which carry lipids into the blood leading to hyperlipidemia
Pathological findings	• Podocytes abnormality is the primary finding • Podocytes will sustain a structural dysfunction; making them lose their Foot-processes They disappear and the basement membrane will be uncovered but the good thin here is that when they are treated these foot will appear again (effacement), but the cells bodies are intact. • This will lead to significant amount of protein appearing in the urine (Proteinuria). Normally the podocytes and the albumin are both negatively charged so this prevents the albumin from passing through but in case of podocyte destruction the albumin will be free and it will be released in the urine
Complications	In Nephrotic patients die due to complications unlike Nephritic which u have to act quickly to save them from death. • Infections and sepsis because of protein loss • Thrombosis Loss of anti-thrombotic proteins: Proteins S and C and antithrombin. (Can cause renal vein thrombosis) • Acute Kidney injury due to low oncotic pressure • End Stage Renal Disease (ESRD) if proteinuria does not resolve Central tubules don't like any proteins to bass thru them! So they get scaring -> shrinking -> fibrosis -> ESRD. This is why we give them immunosuppressants, ACE1 or ARB. the longer it goes on the more damage leading to shrinkage of the kidney.
Glomerular diseases with the presentation of nephrotic syndrome	1. Focal Segmental Glomerulosclerosis (FSGS) 2. Minimal Change Disease 3. Membranous Nephropathy Will talk in more details about each in next slides!

[2] CHF leads to edema of dependent areas like the legs. Nephrotic patients are edematous everywhere

[3] Hyperlipidemia and hypercholesterolemia are caused by increased hepatic lipoprotein synthesis.

★ Glomerular diseases with the presentation of nephrotic syndrome:

<table>
<tr><th colspan="3">1. Focal Segmental Glomerulosclerosis (FSGS): some glomeruli are affected, and others are not</th></tr>
<tr><td>General Info</td><td colspan="2">A common cause of Nephrotic syndrome in <u>adults</u>.
Causes 12 – 35 % of the cases in adults
More common among people of African descent</td></tr>
<tr><td>On microscopy</td><td colspan="2"> 
 

FSGS, like minimal change disease, diffuse foot process effacement but with segmental sclerosis</td></tr>
<tr><td>Types</td><td>1. Primary FSGS:</td><td>2. Secondary FSGS (not autoimmune related): very common in adults</td></tr>
<tr><td>Clinical feature:</td><td>• Has sudden onset of heavy proteinuria and other manifestations of nephrotic syndrome.
Autoantibody affecting <u>podocyte</u>
Autoimmune related so treat with immunosuppressants</td><td>• patients progress slowly to ESRD
• Proteinuria is less heavy than other causes of nephrotic syndrome. Functional problems.
• 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</td></tr>
<tr><td>Diagnosis:</td><td>Seen on light microscopy as <u>focal</u>: some glomeruli are affected by sclerosis (the rest of them look normal) and <u>segmental</u>: sclerosis only involves a segment of each glomerulus that is affected.
But most importantly, all glomeruli (the ones affected by sclerosis and the ones that are not affected) will have a diffuse foot processes effacement (thus Nephrotic syndrome appears)
Mostly it’s a podocyte disease</td><td></td></tr>
<tr><td>Possible causes</td><td>Autoimmune related</td><td>A number of conditions which include:
1. Diabetes mellitus causes nodular sclerosis.
2. Obesity, anabolic steroid abuse
3. Nephron loss (>75% of renal mass e.g renal
4. agenesis).
5. Reflux nephropathy.
6. Healing of prior GN (e.g IgA).
7. Severe preeclampsia.
8. Drugs : Interferon, Pamidronate[4], Heroin.
9. Anabolic steroid abuse.
10. Infections : HIV</td></tr>
</table>

[4]Nitrogen-containing bisphosphonate used to prevent osteoporosis.

		11. Sickle cell anemia
Treatment (Not Important)	First line: corticosteroids Second line: cyclosporine or tacrolimus ACE Is/ARBs are commonly indicated	Not typically treated with Immunosuppression **treat the primary cause and add supportive measures to protect the kidneys,** e.g. keeping blood pressure well controlled with **ACE inhibitors.**

2. Minimal change disease

General Info

The older the child gets the less likely to have MCD In children we immediately start treatment in the ER, no need for biopsy

It's called minimal change because:

Light microscopy: is typically showing normal glomeruli (so called: nil disease).

Electron microscopy: shows diffuse effacement of the epithelial cells' foot processes only.

The most important difference between MCD and the FSGS is the presence of glomerular sclerosis in FSGS (there's no sclerosis in MCD)

Hodgkin disease and non-hodgkin lymphoma have been associated with minimal change disease (StepUp)

Current evidence points to systemic T cell dysfunction as the most likely root cause (StepUp)

It is the main cause of Nephrotic syndrome in children: so common in children that when a child presents with nephrotic syndrome we usually **don't do a biopsy**, **we treat as minimal change.**

- The cause in 90 % of cases in children < 10 years old.
- > 50 % of cases in older children

It causes 10-25 % of Nephrotic syndrome cases in adults

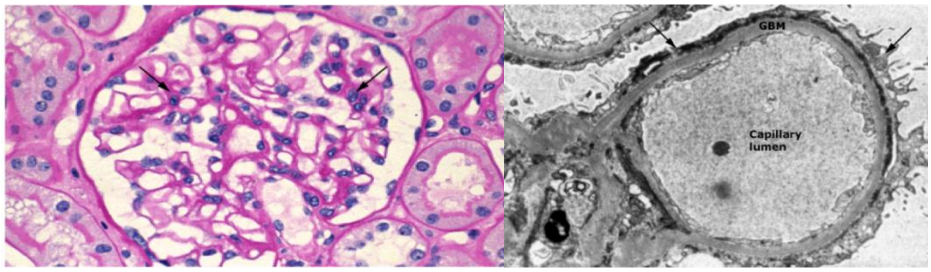
Types

1-Primary (Idiopathic).

2-Secondary (less common) in adults:

- Drugs (NSAIDs, Lithium, Sulphasalazine, Pamidronate, D-Penicillamine, some antibiotics)
- Neoplasm (Hodgkin lymphoma, non-hodgkin lymphoma and leukemia)
- Infections (TB and syphilis)
- Allergies

On microscopy

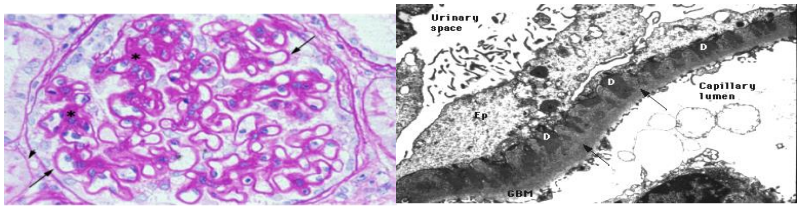


MCD (nothing can be seen under light microscope "NILL"), but on Electron microscope we can see diffuse effacement of foot processes

Clinical feature

- Typically has a sudden onset Edema
- BP may be normal or slightly elevated
- Heavy proteinuria (Nephrotic range)

They are full & blown	• Lipiduria • Hypoalbuminemia (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, It shows diffuse effacement of foot process. • Kidney biopsy is not done on children, usually nephrotic syndrome in a child < 10 years old is MCD until proven otherwise.
Treatment	• In children; typically is corticosteroid responsive in > 90%, treatment is given empirically. • First line: Corticosteroids, given x 3-4 months then taper over 6 months (90%+ responsive) • Second line: oral Cyclophosphamide, Cyclosporine

3. Membranous Nephropathy		
General Info	• It's called membranous because the capillary loops get thickened because of immunoglobulin deposits which make them look like membranes. • Most common cause of Primary nephrotic syndrome in adults (15% and 33%) • Mostly secondary in children (hepatitis B antigenemia) Remember: Membranous hepB • Slowly developing nephrotic syndrome There is a change it will be a tumor. Pt. has hidden malignancy somewhere عشان كذا لما نشوفها ندور على كانسر ولو عالجناه بتروح السندروم	
On microscopy	 **Notice the Diffuse thickening of the glomerular capillary throughout all glomeruli (IgG and C3 deposition)** The thickening is because of the autoantibody's immunoglobulins deposited under podocytes food processes the dense deposits outside intact basement membrane look just like this basement membrane	
Possible causes:	Primary MN is idiopathic but secondary is related with a few conditions: • Systemic lupus erythematosus (SLE): Class V Lupus Nephritis (10-20%) • Drugs: penicillamine, IV gold salts, high dose Captopril, and NSAIDs, Anti-TNF. • Infections: Hepatitis B, Hepatitis C, syphilis • Malignancies: solid tumors prostate, lung, or GI tract usually MN in adults is idiopathic but sometimes it is because of underlying cancer, so we have to screen. We do CXR, abdominal CT and colonoscopy	
Types	**1. Primary:**	**2. Secondary**
Clinical feature:	Accounts for 75% of cases in adults.	

Possible causes:	idiopathic	A few conditions: • Systemic lupus erythematosus (**SLE**): Class V Lupus Nephritis (10-20%) • Drugs: penicillamine, IV gold salts, high dose Captopril, and NSAIDs, Anti-TNF. • Infections: Hepatitis B, Hepatitis C, syphilis Malignancies: solid tumors prostate, lung, or GI tract usually MN in adults is idiopathic but sometimes it is because of underlying cancer, so we have to screen. We do CXR, abdominal CT and colonoscopy
Treatment	• Corticosteroids plus Cyclophosphamide or cyclosporine • May be Rituximab	• Mainly target the primary disease that caused membranous nephropathy and treat the Nephrotic syndrome manifestations. • if MN is caused by malignancy you have to look for the cancer and treat it, when you treat it the MN will go away.

★ Other important 2ndary causes of Nephrotic syndrome in adults:

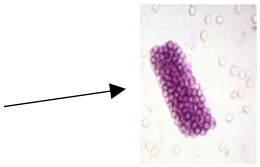
- **Diabetes Mellitus**: just remember DM
  Nephrotic syndrome in a patient with diabetes mellitus (DM) first suggests the diagnosis of diabetic nephropathy. However, glomerular diseases other than diabetic nephropathy have been reported in patients with DM.
- **Amyloidosis** produced in association with myeloma, rheumatoid arthritis, IBDs and chronic infections. Biopsy + Congo Red will show green birefringence. Remember that amyloidosis and DM enlarge the kidneys (along with HIV nephropathy and polycystic kidneys)
- **IgA Nephropathy** :
  Nephrotic syndrome is a rare presentation of IgA nephropathy
- **Membranoproliferative glomerulonephritis (MPGN):**
  It may present with Nephrotic or Nephritic.

Nephritic Syndrome

Clinical presentation

- When we say Nephritic, it means a clinical pattern of presentation for a group of glomerulonephritis, 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 Glomerular basement Membrane components of the Glomerulus are likely going to be targeted because of their proximity to blood circulation

Urineanalysis will show: IMPORTANT!



- Hematuria RBCs
- RBC casts: Formed by naturally occurring. Cylindrical in shape by precipitating in renal tubules
- Tamm-Horsfall mucoprotein in the distal tubules & collecting ducts when they become loaded with RBCs coming from the inflamed Glomerulus (due to GN).

توم هورسفال هو اللي يعطي الشكل مصنوع من جيلاتين

Its very sticky, coming from glomerulus, we'll immediately stick to it, become redundant and flushed

- Dysmorphic RBCs (RBCs lose their smooth surface passing through the cracks in inflamed glomerular basement membrane)
  If we don't see dysmorphic it properly means something else (not glomerular in origin)
- Proteinuria at variable amounts

  Those are called Active Urinary Sediments

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

  Cast & dysmorphic they mean Glomerulitis you have to act quickly! Do biopsy next day.
- Best initial test → Urine analysis
- Most accurate test → Biopsy

Decreased Urine output:

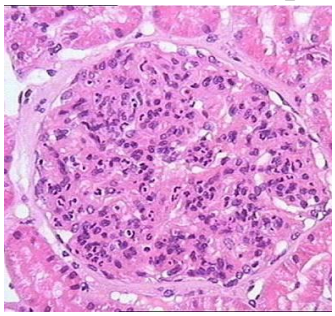
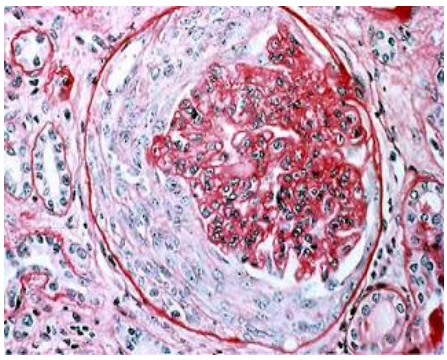
When the filtration barrier is disrupted there will be a Decrease in GFR will lead to increase in RAAS activation which will increase fluid retention and it will cause edema and hypertension.

- Edema Increased volume; the patient can't get rid of high amount of fluid and they drink daily. urea and creatinine will go up. if suspect vasculitis measure for their markers.
- High Blood Pressure
- May have other manifestations of systemic vasculitis

since some glomerulonephritis types are actually

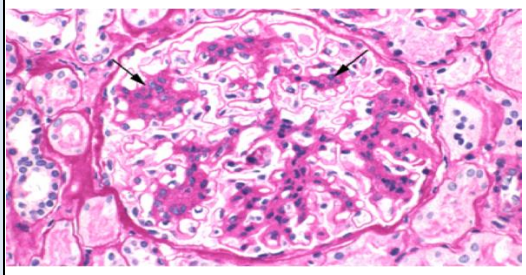
vasculitis (e.g. skin rash, pulmonary hemorrhage, etc)

- Positive immune markers: ANA, Anti-DNA, low complements, +ve ANCA (depends on the cause)

Microscopy	**Glomeruli with proliferative (inflammatory)GN.**  Fully destructed by inflammation **Glomeruli with Crescent[5] (VERY BAD!** Worse GN seen in nephrology**)**  **RBGN: Rapidly progressive glomerulonephritis**
Pathological findings	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
Complications	• AKI (Acute Kidney Injury) =Acute Renal impairment or Failure= elevated Creatinine). • End Stage Renal Disease (ESRD). • Pulmonary edema
Renal diseases that can present with nephritic picture	• IgA Nephropathy / HSP (Henoch-Schönlein purpura) • Post streptococcal glomerulonephritis (PSGN) • Lupus Nephritis • Anti-GBM (Goodasture's disease) • ANCA vasculitis (e.g. Wegner's Granulomatosis) • Membranoproliferative GN (MPGN) Will talk in more details about each in next slides!

[5] indicates severe inflammation & worse outcome if not treated rapidly GN + Crescent indicates very poor prognosis RBGN: when the inflammation is very big even bowman's capsule participate.
If not treated the patient will lose the kidney's function and will go through dialysis

★ Renal diseases that can present with nephritic picture:

1. IgA Nephropathy (Berger's disease)/ HSP (Henoch-Schönlein purpura)	
General Info	• Most common type of Primary GN in developed countries • Can present actively and can be silent. Most common scenario is when an individual applies for a job and we discover that he has microscopic hematuria and proteinuria with normal function, this is most likely IgA nephropathy. • It has a chronic course that can progress to ESRD. • HSP (Henoch-Schönlein purpura) is a systemic vasculitis caused by immune deposition of IgA in different organs; typically skin, bowel and kidneys. Everywhere in the body
On microscopy	 
Possible causes	• It is thought to be secondary to altered mucosal immunity that leads to excessive IgA synthesis followed by deposition in the glomeruli.
Clinical feature	• Can present as dark urine[6] (hematuria) 1-3 days after upper respiratory tract infection . (< one week of URT infection) follows mucosal infections. When there is inflammation of the mucous membrane there will be an increase in IgA(which is abundant in mucosal membranes) and it will lead to deposition in the kidney. • A lot of times it gets picked up incidentally by finding abnormal urine analysis (Hematuria+/- Proteinuria) done for other reasons with no symptoms. • Needs kidney biopsy to reach the diagnosis as IgA levels are elevated in only 50% of patients.
Diagnosis:	• The diagnosis is made by finding abnormal deposition of IgA immunoglobulin in the Glomeruli, it elicits a local inflammatory response in the glomerular mesangium (mesangial expansion) "conclusion : mesangial deposition of IgA and C3 seen in EM" • Needs kidney biopsy to reach the diagnosis as IgA levels are elevated in only 50% of patients . (The most accurate test) • More common among Asians Look for → 1-2 day history of an upper respiratory tract infection
Treatment	• There is really no effective immunosuppressive therapy except in severe cases where it can be tried. 30% will completely resolve • Most important treatment is to control the blood pressure which also decreases the proteinuria. Severe proteinuria is treated with ACEi and steroids . Fish oil is of uncertain benefit.

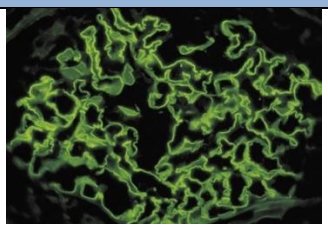
[6] In renal cancer the urine will be bright red and this indicates fresh blood but in IgA the urine will be tea or Pepsi colored

2.Post streptococcal glomerulonephritis (PSGN)	
General Info	• PSGN follows throat or skin infection (impetigo) by one to three WEEKS in contrast to IgA nephropathy which follows an infection by 1-3 DAYS.
Possible causes	• This is a specific subtype of post-infectious glomerulonephritis. It is much more common in children than adults but is now rare in the developed world. The latency is usually about 10 days after a throat infection or longer after skin infection, suggesting an immune mechanism rather than direct infection. Sometimes the patients even forget they had a respiratory infection • Typically caused by throat infection with Gram positive cocci (Group A beta-hemolytic Streptococcus (GAS). • But also can be caused by Staphylococcus soft tissue or bone infection in adults. • Bacterial Antigen cross react with glomerular antigens, or may be an immune-complex (Antigen-antibody) response that is responsible.
Clinical feature	• Patients present with frank hematuria usually after one week and up to 3 weeks from the start of infection. • Dark cola colored urine • Periorbital edema • Hypertension • Oliguria

Diagnosis:	• Serum will show positive Antistreptolysin (**ASO**) titer.
	• Low C3, Normal or slightly low C4 in the serum (Complement levels are low in PSGN).
	• May have positive throat culture.
	  • Confirmed by → AntiStreptolysin O (ASO) titers and anti DNAse antibody
	  • Most accurate test → kidney biopsy (not done routinely)
	  • Look for → A history of URTI or skin infection (impetigo) in the last 1-3 weeks

Treatment	Self-limited, but some are treated through 2 weeks of dialysis • Children have better and faster recovery than adults. • Management of PSGN does not reverse the GN, use supportive therapies(wait and see) such as : Antibiotics / diuretics (to control fluid overload).

3. Lupus Nephritis	
General Info	• could be nephrotic or nephritic because the autoantibodies could target any part of the glomeruli, if it the targets were podocytes then it will cause nephrotic syndrome but if the endothelium, mesengium or basement membrane were affected then it will lead to nephritic syndrome or it could be both simultaneously. • Lupus (SLE): The Disease with a Thousand Faces • Kidneys can be affected by SLE like other organs. • The degree of involvement can be from mild (or even not visible to the physician) to a very severe one causing ESRD in few months. • Most important in dealing with these cases is having high suspicion of its presence and to start immediate workup & referral for diagnosis and treatment
Diagnosis **Not important**	• Kidney biopsy is mandatory to make the diagnosis . It's needed for accessing the stage of involvement (biopsy is not performed to diagnose lupus, but rather to guide intensity of therapy).Long-standing SLE may simply "scar" the kidneys and biopsy will show glomerulosclerosis which has no active inflammatory components and may lead to such damage as to require dialysis. • Low complements (C3, C4) level along with the positive Lupus markers, abnormal urine analysis & abnormal renal function should make you think of its presence.
Treatment	• Lupus Nephritis treatment depends on the findings in renal biopsy. • We have to treat aggressively • It usually involves high degree of immunosuppressing medications. • Mild inflammatory changes may respond to glucocorticoids.

4. Anti-GBM (Good pasture's syndrome)	
On microscopy	 **We stain it, we find it.**
Possible causes	• Due to autoantibody against (alpha-3 chain) of type IV Collagen that is found in Glomerular and alveolar (lungs) basement membrane. Affects middle aged women and smokers (smoking exposes their lung's collagen into being recognized as an antigen so the body starts to release antibodies against it) this collagen in lungs similar to that in the kidney basmant membrane that's why they have both kidney and lung disease
Clinical feature	• GN (can be the only presenting finding) & Pulmonary hemorrhage (coughing blood) (if with GN; is called Goodpasture's disease = Lungs + renal involvement). • Unlike Wegener granulomatosis there is NO upper respiratory tract involvement. • Goodpasture is limited to the lung and kidney, so signs of systemic vasculitis are absent . There is NO skin, joint, GI, eye or neurological involvement. • Anemia is often present from chronic blood loss from hemoptysis.
Diagnosis:	• Positive test for Anti-GBM antibodies in the serum • Kidney biopsy shows the diagnostic Immunofluorescence pattern: Linear stain of Ig G and C3. • The chest x-ray will be abnormal but it is insufficient to confirm the diagnosis.
Treatment	• Treatment is always started immediately to remove the antibodies by Plasmapheresis and preventing further antibodies production by giving heavy immunosuppression that includes corticosteroids and cyclophosphamide

5.ANCA vasculitis (e.g. Wegner's Granulomatosis)	
General Info	Autoimmune disease that involves the presence of Neutrophils adhesion enhancing molecule called ANCA= anti-neutrophil cytoplasmic antibody We stain it, we don't find it
Types	1. C-ANCA= Cytoplasmic type, more commonly causing Granulomatous Polyangiitis = old name **Wegner's Granulomatosis** (so a granuloma forming disease) Angiitis: means small vessels vasculitis → C-ANCA: if glowed in cytoplasm, more common in wegnas granulomatosis Deposite in the vessel and can't be stained as other antibodies so called ***Pauci-immune***[7]) 2. P-ANCA= Perinuclear type, more commonly associated with Microscopic **Polyangiitis & Churg-Strauss syndrome** P/C-ANCA are named based on the glow in immunofluorescence → P-ANCA: if glowed around the nucleus (perinuclear)
Clinical feature	• Upper airways and lung involvement is common and patients can present with renal and pulmonary manifestations (GN + Pulmonary hemorrhage: hemoptysis). hemoptysis can cause anemia
Diagnosis:	• Diagnosis is made by kidney biopsy and positive ANCA titer in the serum.
Treatment	• It is usually an aggressive disease that should be treated with potent immunosuppressing medications. (high dose corticosteroids & cyclophosphamide).

6. Membranoproliferative GN (MPGN) NOT important	
General Info	It is a pathological description & has multiple causes. It may present with Nephritic picture or Nephrotic syndrome
Types	• The primary MPGN is mainly seen in children. • The secondary
Possible causes	The primary is idiopathic but the secondary is caused by any of these conditions: • Hepatitis B and C • Endocarditis • Lupus and Sjogren's syndrome • Cancer • Complement deficiency

[7] minimal evidence of hypersensitivity upon immunofluorescent

How to approach a patient with glomerulonephritis?

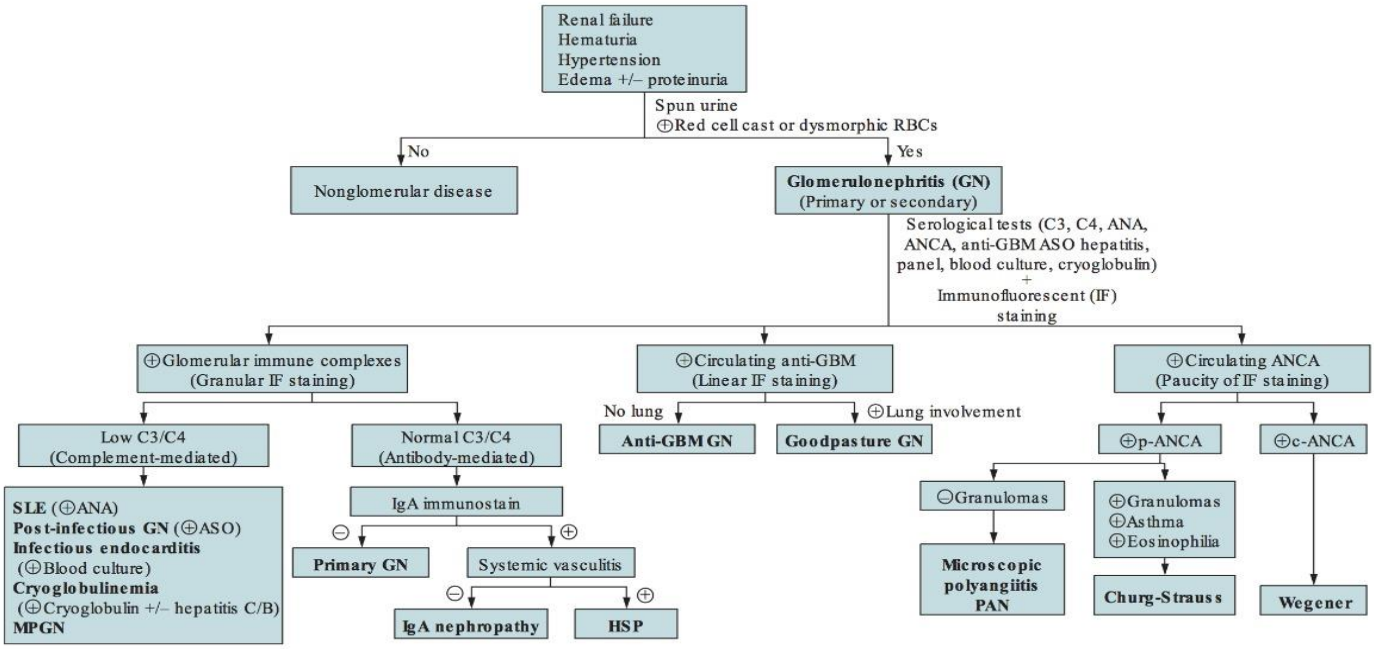


Figure 28–1. Algorithm of approach to the patient with acute glomerulonephritis. Abbreviations: ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; ASO, antistreptolysin-O; c-ANCA, cytoplasmic antineutrophil cytoplasmic antibody; GBM, glomerular basement membrane; HSP, Henoch–Schönlein purpura; MPGN, membranoproliferative glomerulonephritis; PAN, periarteritis nodosa; p-ANCA, perinuclear antineutrophil cytoplasmic antibody; SLE, systemic lupus erythematosus.

SUMMARY

Nephrotic Syndrome (NS) we can wait for more diagnostic value before starting management	
Primary etiology	* Auto-antibodies targeting glomerular structure * immune – complexes deposition
Involvement and pathophysiology	* Podocytes will lose their Foot-processes
Main manifestation	* proteinuria
Criteria of NS	* Hypoalbuminemia (serum Albumin **<30 g/L**) * Heavy proteinuria (**> 3.5 g/24** hours of urine collection) * Peripheral or generalized edema
Complications of NS	* Infections & sepsis * Thrombosis * Acute kidney injury and ESRD
Clinical presentation	* **Edema** (Anasarca) * frothy urine * anorexia * abdominal pain
Urine analysis	* **proteinuria** * No RBCs * No RBCs casts * No WBCs
Glomerular Diseases that present as Nephrotic Syndrome	
FSGS	* Histopathology: diffuse foot **process effacement** but with **segmental sclerosis** * involvement: focal and segmental * in case of primary FSGS: Has sudden onset of heavy proteinuria and Other manifestations of nephrotic syndrome and treated with Corticosteroids and other immunosuppressing medications. * in case of secondary FSGS: Proteinuria is less heavy * examples of secondary causes of FSGS: 1) sever obesity 2) healing of prior GN
MCD	* Histopathology: 1) **no abnormality** is seen on **light microscopy** 2)**EM** shows the **diffuse foot process effacement** *Clinical presentation: 1)sudden onset Edema 2)Heavy proteinuria 3)Lipiduria 4) Hypoalbuminmia 5) Hyperlipidemia * It is the main cause of Nephrotic syndrome in **children** * example of secondary causes of MCD: Drugs (NSAID)
MN	* Histopathology: Diffuse **thickening** of the glomerular capillary wall throughout all glomeruli (IgG and C3 **deposition**) * 75% of cases in adults * example of secondary causes of MN: **Malignancy**: **solid tumors prostate, lung, or GI track**
Important **secondary** cause of nephrotic syndrome	
* Diabetes mellitus is the most common	

Cases from 435 medicine team

Case 1: A 17 year old male presents with generalized swelling of lower limbs and abdomen for 3 days. He also complains that his
urine has bubbles. He has no prior illness. His BP is 110/70 mmHg ,HR is 90, RR is 20 , temp is 36.1. He has puffy eyes, abdominal
swelling lower limb pitting edema. Otherwise his exam is normal.

➔ Serum creatinine (SCr) : 50 umol/L, Lytes are normal, Urinalysis +3 protein, negative glucose, negative blood, urine microscopy : no casts/cells.

➔ 24 hr urine 15 g/day, serum albumin 10 g/L

➔ ANA negative, HepB,HepC,HIV negative. CXR and ECG are normal.

Kidney biopsy will most likely show which of the following pathologic features :

A. Minimal change disease.
B. Focal segmental glomerulosclerosis.
C. Membranous nephropathy.
D. IgA nephropathy.
E. Lupus nephritis.

Case 2: A 70 year old man presenting to your clinic with history of lower limb swelling for 3 weeks.

➔ PMH : Smoker for 50 years, HTN (on amlodipine).

➔ BP : 130/80 mmHg, HR: 90 b.p.m, RR: 18, T: 36.1 C

➔ Serum creatinine (SCr) : 80 umol/L, Lytes N, Urinalysis +3 protein, negative blood, urine microscopy : no cells/casts.

➔ 24 hr urine 4 g/d, serum albumin 20 g/L

➔ ANA negative, HepB,HepC,HIV negative.

➔ A kidney biopsy was performed.

Which of the following is the next step in management ?

A. Start treatment with prednisone
B. Start treatment with cyclosporine
C. Start treatment with rituximab
D. Start treatment with plasmapheresis
E. None of the above

Questions

1-Which one of the following is the most common presentation in patient with nephrotic syndrome ?

A-Proteinurea

B- Hematurea

C-High Blood Pressure

D-Renal impairment

2-In case of nephrotic syndrome, what is the most common site will be affected by the deposition of antigens ?

A-Mesangium

B-Blood compartments

C-Glomerulus

D- Podocytes

3-Which one of the following will be deposited in Membranous Nephropathy under Electronic Microscopy ?

A-IgA

B-IgG + C3

C-Anti-GBM Antibodies

D-IgE

4-Patient presents to the clinic complaining of Blood in the urine

The patient says that I had sore throat 2 weeks ago after that I felt that my joints hurts me then today's morning I saw blood in the urine , which one of the following you suspect the patient has ?

A-Membanous Nephropathy

B-IgA Nephropathy

C-Post Streptococcal Glomerulonephritis

D-ANCA Vasculitis

5-Linea Anti-GBM staining in the glomerulus is diagnostic test for which of the following?

A-Good Pasture Syndrome

B-MPGN

C-Lupus Nephritis

D-Minimal Change Disease

Answer:

1-A

2-D

3-B

4-C

5-A