Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Glomerular diseases

Objectives :

1- To understand the pathophysiology of Glomerular Diseases.
2- To be able to correlate between the clinical presentation & the underlying Glomerular pathology.
3- To recognize the differences between Nephritic & Nephrotic Glomerular diseases.
4- To recognize the important features of Nephritic & Nephrotic renal diseases.
5- To be able to recognize the early features of Glomerular diseases before it is too late!
6- To learn the common causes of Nephrotic & Nephritic renal diseases.

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Resources :

- Doctor ‘s slides - Team 436

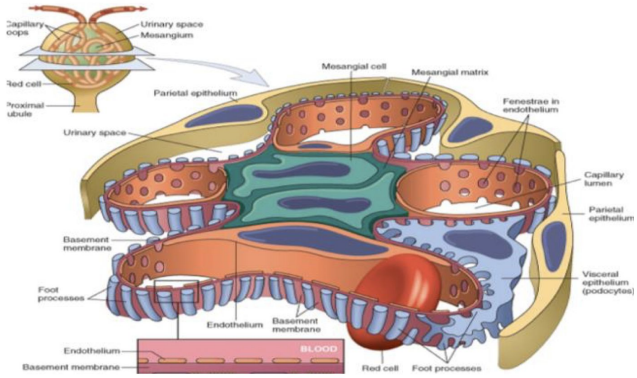
  Lecturer: Dr. Saad Alobaili

  Same 436 lecture Slides: Yes

Introduction (Anatomy and Physiology)

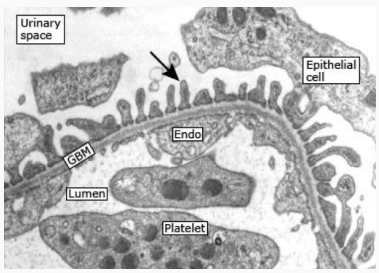
- Renal cortex is the most important functional part of the kidney, because it has the **Glomeruli** (The cortex shrinks and becomes fibrosed in CKD, which explains why the kidneys become smaller in US)

- The Glomerular Capillary wall has **3 layers**, through which filtration occurs (Any disruption here leads to decrease in kidney function and blood components will appear in the urine)
  1) Fenestrated endothelium. 2) Glomerular Basement Membrane. 3) Podocyte[1]
- The Nephritic pattern is always indicative of underlying inflammatory process in the glomeruli; causing 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

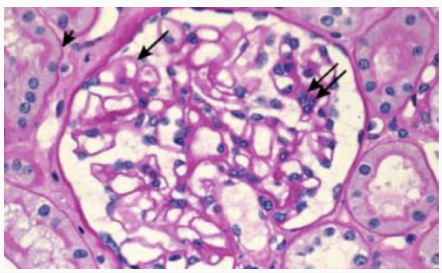


Recall:

- 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



Normal glomerulus under **electron** microscope



Normal glomerulus under **light** microscope

[1]Podocyte is away from blood components (damage here will not lead to blood components in urine)

Normal glomerular structure is needed to:

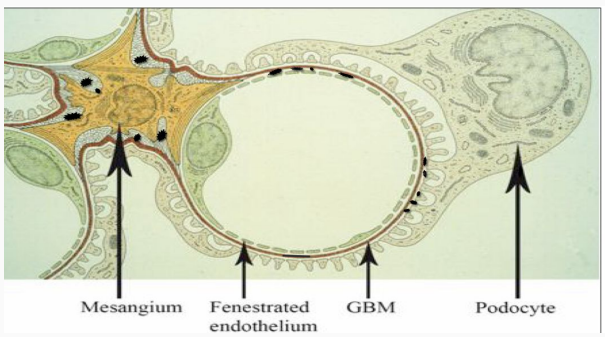
1. Keep the glomerular filtration normal, to maintain normal kidney function.
2. Maintain urine volume and hence, preventing fluid retention in the body which causes edema and high blood pressure.
3. Prevents the blood components (cells, proteins) from leaving the bloodstream and appearing in the urine. Urine will appear normal (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 **physicochemical** (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 usually due to disruption of glomerular capillaries (Normal hematuria can be from the bladder

How do glomerular diseases start?

- 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.
  • 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 **histopathological characteristics** seen under the microscope. So, almost always a kidney biopsy is needed to diagnose any suspected primary glomerular disease.

Any inflammation causing injury to the mesangial cells will cause them to proliferate which will compress surrounding cells. (this will lead to Glomerulonephritis and blood components appearing in the urine

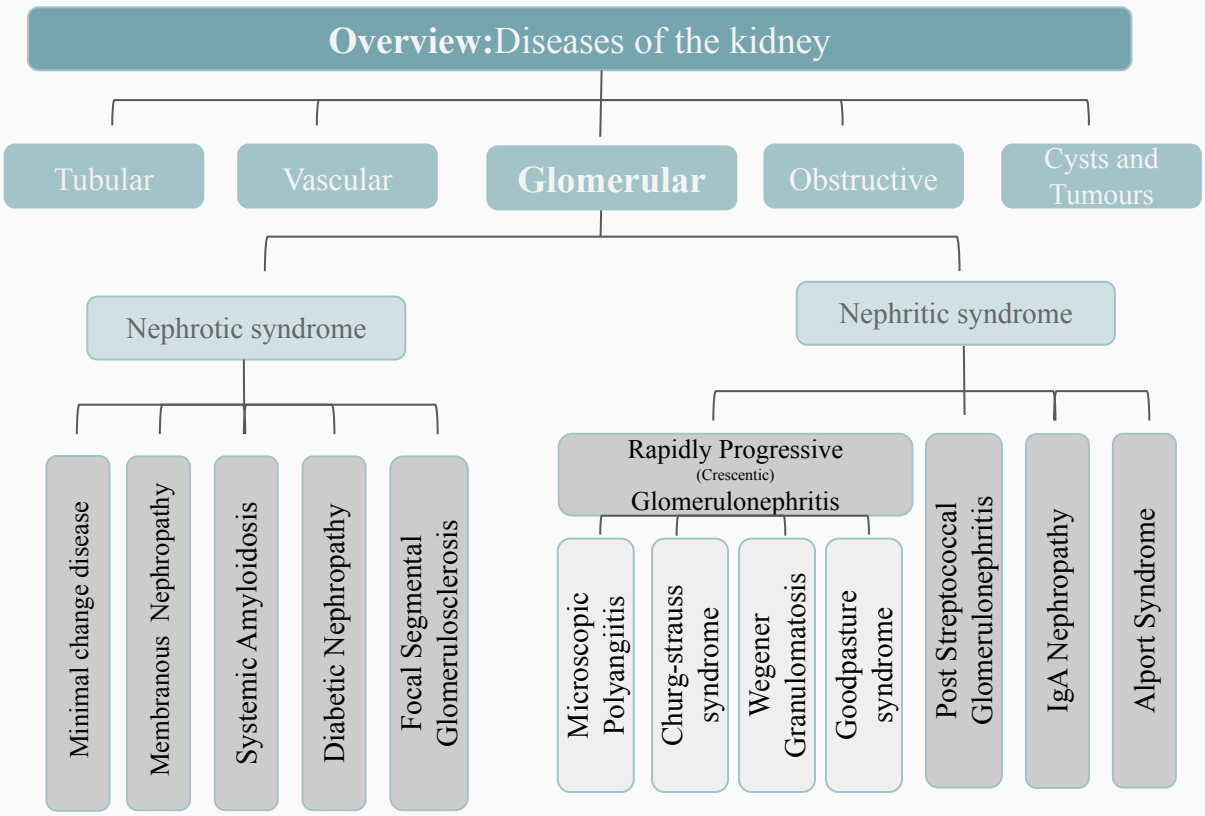


Glomerular Diseases

How glomerular diseases start?
Most important to recognize:

- The manifestations of a glomerular disease are usually indicative of which components of glomerulus structure was affected mainly by the disease process:

- If Podocytes were the main target of the disease process this leads mainly to proteinuria (at large amount); thus Nephrotic Syndrome will be the main finding.
- If endothelial cells OR Mesangial cells OR GBM OR all of them together were targeted; then hematuria, proteinuria and abnormal renal function will manifest because of the disruption in glomerular filtration wall; thus Nephritic pattern of renal disease will be present (Clinically called: Glomerulonephritis or GN)



Key findings in nephrotic syndrome (highly recommended)

- 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.
- 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.

The insult to the glomeruli is either an autoimmune attack or is the result of deposition of antibody-antigen complex in the kidney which will attack the glomeruli which will lead to a local inflammation there. The pathology depends on the component of the glomeruli that is affected (basement membrane, mesangium…)

Nephrotic Syndrome

it is important to differentiate between **nephrotic** and nephritic syndrome

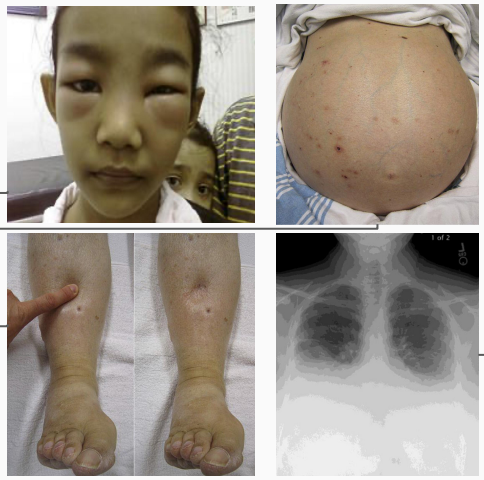
PDF

Clinical Presentation:

Signs and symptoms:

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)

Anasarca: A condition that causes general swelling of the body



Patients may also present with:

- Fatigue
- Frothy urine (froth persists for long time after voiding)
- Anorexia
- Nausea & vomiting (edema will cause restriction of movement in the GI)
- Abdominal pain due to bowel edema
- Weight **gain** due to fluid retention
- Shortness of breath if having pleural effusion
- Signs & symptoms of **DVT**, PE as complications

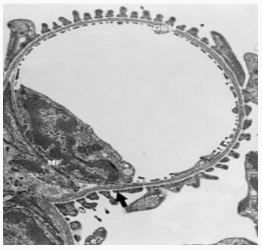
Patients with nephrotic syndrome get pleural effusion but are protected from pulmonary edema because cardiopulmonary circulation depends on hydrostatic pressure and not on the oncotic pressure! otherwise even us normal people will get pulmonary edema occasionally .

Urine analysis will show: **IMPORTANT**

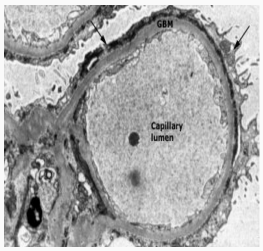
- Heavy proteinuria (>3.5g "nephrotic range" per 24 hrs. of urine collection)
  Daily, < 150 mg/day of all kinds of proteins. Including on average 4-7 mg/day of Albumin that are secreted in the urine normally. Proteinuria should never be ignored since it might lead to tubular fibrosis
- Hypoalbuminemia (<30 g/L) "Normal serum Alb: 35-55g/L" (Loss of albumin > Production by liver)
- Peripheral or generalized edema
- No RBCs (some times few RBCs are occasionally seen)
- No RBCs casts
- Fat (Lipiduria) : Fatty casts, oval fat bodies & fat droplets. A lot of fat will be excreted because a large amount goes to kidney
- Hyperlipidemia (Hyperlipidemia and hypercholesterolemia are caused by increased hepatic lipoprotein synthesis.) at some point, the Liver will not be able to produce enough albumin so it will switch to making other types of proteins (Lipoproteins) which carry lipids into the blood and as a result, cause hyperlipidemia
- No WBCs (few may be seen)

Pathological findings:

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



Normal Foot Processes



Diffuse Foot Processes Effacement

Complications:

- Infections and sepsis
- Thrombosis Loss of antithrombotic proteins (Protein S,C and anti-thrombin)
- Acute Kidney injury Low oncotic pressure
- End Stage Renal Disease (ESRD) if proteinuria does not resolve Central tubules can't tolerate letting proteins pass through them so the become scarred, shrinked, and fibrosed with time. So we use immunosuppressants, ACE, and ARBs. Nephrotic patients usually die because of complications

Glomerular diseases with the presentation of :

1. Focal Segmental Glomerulosclerosis (FSGS)
2. Minimal Change Disease
3. Membranous Nephropathy

Will talk in more details about each in next slides!

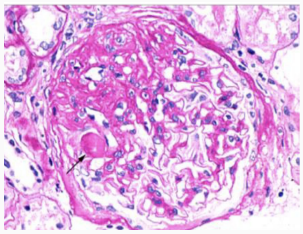
1. Focal Segmental Glomerulosclerosis (FSGS):

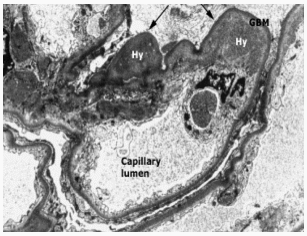
Video

General Info:

- A common cause of Nephrotic syndrome in **adults**.
- Causes 12 – 35 % of the cases in adults
- More common among people of African descent

Microscopy:





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

Types:

1- Primary FSGS:

- **Clinical feature:**

Has sudden onset of heavy proteinuria and other manifestations of nephrotic syndrome. Autoantibody affecting podocyte

- **Diagnosis :**

Seen on light microscopy as **focal**: some glomeruli are affected by sclerosis (the rest of them look normal) and **segmental**: 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)

- **Possible causes:**

Autoimmune related

- **Treatment :** Not important

First line: corticosteroids
Second line: cyclosporine or tacrolimus
ACE Is/ARBs are commonly indicated

2- Secondary FSGS:

- **Clinical feature:**

-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
Patients slowly progress to ESRD

- **Possible causes:**

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 agenesis).
4. Reflux nephropathy.
5. Healing of prior GN (e.g IgA).
6. Severe preeclampsia.
7. Drugs : Interferon, Pamidronate, Heroin.
8. Anabolic steroid abuse.
9. Infections : HIV
10. Sickle cell anemia

- **Treatment :** Not important

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

Video

General Info:

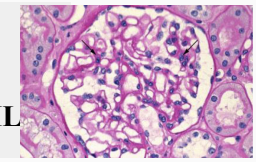
- It's called minimal change because:
- **-Light** microscopy: is typically showing normal glomeruli (so called: nil disease)
- **-Electron** microscopy: shows diffuse effacement of the epithelial cells' foot processes only.
- The most important difference between MCD and the FSGS is the presence of glomerular sclerosis in FSGS (there's no sclerosis in MCD) It is the main cause of Nephrotic syndrome in children (Suspected children are treated immediately, there is no need for a biopsy): 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 Older children are less likely to get MCD. We immediately start treatment for children

Types :

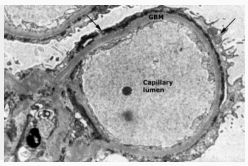
1. Primary (Idiopathic).
2. Secondary (less common) in adults:
   - Drugs (NSAIDs, Lithium, Sulphasalazine, Pamidronate, D-Penicillamine, some antibiotics)
   - Neoplasm (Hodgkin lymphoma, non-hodgkin lymphoma and leukemia)
   - Infections (TB and syphilis)
   - Allergies

Microscopy:

MCD, basically no abnormality is seen on light microscopy (NIL



MCD, EM shows the diffuse foot process effacement



Clinical Features:

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

- First line: Corticosteroids, given x 3-4 months then taper over 6 months (90%+ responsive)
- Second line: oral Cyclophosphamide, Cyclosporine

3. Membranous Nephropathy:

Video

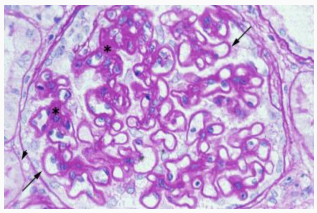
General Info:

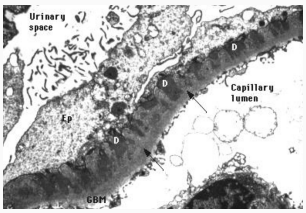
- Most common cause of Primary nephrotic syndrome in adults (15% and 33%)
- Mostly secondary in children (hepatitis B antigenemia) Remember: Membranous hepB
- Presentation: slowly developing nephrotic syndrome (few weeks)

It's called membranous because the capillary loops are so thickened they look like membranes, Closely associated with malignancy (Look for cancer in these patients)

Microscopy:

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





The dense deposits outside intact basement membrane look like this

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 It might be idiopathic but it is sometimes caused by cancer that is why screening (CXR, abdominal CT and colonoscopy is important)

Types:

1- Primary:

- **Clinical feature:**

Accounts for 75% of cases in adults.

- **Possible causes:**

idiopathic

- **Treatment :**

-Corticosteroids plus Cyclophosphamide or cyclosporine membranous nephropathy and treat the Nephrotic
-May be Rituximab

2- Secondary:

- **Possible causes:**

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

- **Treatment :**

-Mainly target the primary disease that caused membranous nephropathy and treat the Nephrotic syndrome manifestations.
Treat cancer first if present

Other important 2ndary causes of Nephrotic syndrome in adults:

- Diabetes Mellitus
- Amyloidosis
- IgA Nephropathy
- MPGN

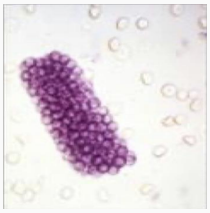
Nephritic Syndrome

PDF

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(A patient presenting with nephritic clinical picture should be treated immediately).

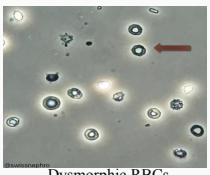
- Cylindrical in shape by precipitating in renal tubules



RBC casts

Urine analysis will show:

- Hematuria RBCs
- RBC casts: Formed by naturally occurring
- Tamm-Horsfall mucoprotein in the distal tubules & collecting ducts when they become loaded with RBCs coming from the inflamed Glomerulus (due to GN).
- Dysmorphic RBCs (RBCs lose their smooth surface passing through the cracks in inflamed glomerular basement membrane) (No dysmorphic proteins excludes nephritis



Dysmorphic RBCs

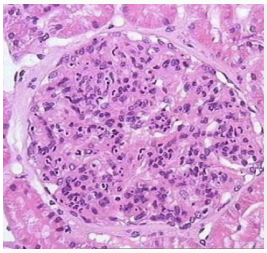
- Proteinuria (at variable amounts from subnephrotic to nephrotic range)
  - Those are called Active Urinary Sediments (Active = is indicative of underlying glomerular inflammatory process; requiring urgent medical attention)

Tamm horsfall mucoproteins look like their made from gelatin it is very sticky . it comes from the glomerulus so RBC's will stick to it easily.

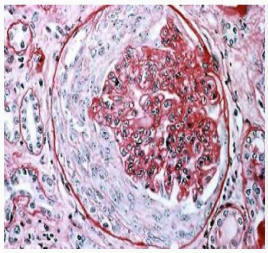
Nephritic clinical manifestations:

- **AKI** (Acute Kidney Injury) =Acute Renal impairment or Failure= elevated Creatinine) & electrolytes imbalance.
- **Decreased Urine output**
- **Edema** **Filtration barrier disrupted--->decrease in GFR---->RAAS activation--->Fluid retention.**
- **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 (VERY BAD! Worse GN):
- Indicates severe inflammation & worse outcome if not treated in a short time from presentation

When the inflammation is this large even bowman's capsule participates

Pathological findings:

The Nephritic pattern is always indicative of underlying inflammatory process in the glomeruli ; causing Pathological inflammatory modulators attraction, cellular proliferation and eventually glomerular permanent dysfunction if left findings 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 (Goodpasture's disease)
- ANCA vasculitis (e.g. Wegener's Granulomatosis)
- Membranoproliferative GN (MPGN)

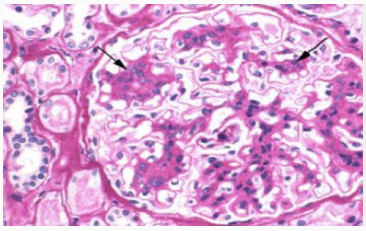
1. IgA Nephropathy (Berger's disease)/ HSP (Henoch-Schönlein purpura)

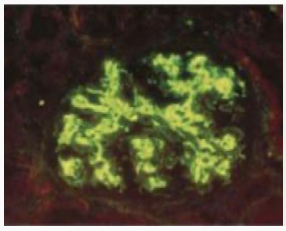
Video

General Info:

- Most common type of Primary GN in developed countries
- Can present actively and can be silent. Commonly detected on pre-occupational testing
- It has a chronic course that may or may not worsen.
- HSP (Henoch-Schönlein purpura) is a systemic vasculitis caused by immune deposition of IgA in different organs; typically skin, bowel and kidneys.

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 Features:

- Can present as dark urine (hematuria) 1-3 days after upper respiratory tract infection. (< one week of Clinical URT infection) When there is inflammation of the mucous membrane there will be an increase in IgA which will lead to it being deposited 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; e.g. pre-employment investigations.
- Needs kidney biopsy to reach the diagnosis

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)
- Needs kidney biopsy to reach the diagnosis (The most accurate test)
- 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.
- Most important treatment is to control the blood pressure which also decreases the proteinuria. Severe proteinuria is treated with ACEi or ARB.

2. Post streptococcal glomerulonephritis (PSGN)

Video

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 causes 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.
- 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 Features:

- 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.
- May have positive throat culture.

Treatment:

- Treatment is usually supportive = wait and see.
- 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

3. Lupus Nephritis

Video

General Info:

- 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
- Could be nephrotic or nephritic depending the structure targeted by the antibodies. (if they target the podocytes its nephritic, if it targets the endothelium, mesangium, or basement membrane it is nephritic

Diagnosis:

- Kidney biopsy is mandatory to make the diagnosis
- Low complements (C3, C4) level along with the positive Lupus markers (ANA, Anti DNA), abnormal urine analysis & abnormal renal function should make you think of its presence.

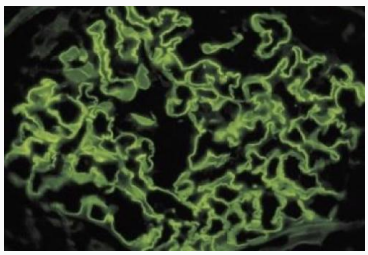
Treatment:

- Lupus Nephritis treatment depends on the findings in renal biopsy
- It usually involves high degree of immunosuppressive medications. We treat aggressively.

4. Anti-GBM (Goodpasture's syndrome)

Microscopy:

Linear Anti-GBM staining in the Glomerulus by Immunofluorescence is a Diagnostic test



Possible Causes:

- Due to autoantibody against (alpha-3 chain) of type IV Collagen that is found in Glomerular and alveolar (lungs) basement membrane. Specifically targets smoking middle aged smokers (smoking exposes their lungs collagen as an antigen, so antibodies will be released against it) this collagen is similar to the kidney basement membrane)

Clinical Features:

- GN (can be the only presenting finding)
- Pulmonary hemorrhage(disease is called Goodpasture's disease if Lung vasculitis + GN)

4. Anti-GBM (Goodpasture's syndrome)

Video

Diagnosis:

- Positive test for Anti-GBM antibodies in the serum
- Kidney biopsy shows the diagnostic Immunofluorescence pattern:
- Linear stain of IgG and C3.

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. Wegener's Granulomatosis)

General Info:

- Autoimmune disease that involves the presence of Neutrophils adhesion enhancing molecule called ANCA= anti-neutrophil cytoplasmic antibody, This molecule establishes vascuilitis cascade

Types:

1. C-ANCA= Cytoplasmic type, more commonly causing Granulomatous Polyangiitis = old name Wegener's Granulomatosis (so a granuloma forming disease) Angiitis: means small vessels vasculitis
2. P-ANCA= Perinuclear type, more commonly associated with Microscopic Polyangiitis & Churg- Strauss syndrome

Clinical Features:

- Upper airways and lung involvement is common and patients can present with renal and pulmonary manifestations (GN + Pulmonary hemorrhage: hemoptysis).

Diagnosis:

- Diagnosis is made by kidney biopsy and positive ANCA titer in the serum.
- Kidney pathology will show sever Glomerulonephritis; maybe RPGN; but all starting with immunofluorescence for immunoglobulins is NEGATIVE; hence the name Pauci- Immune vasculitis or GN (Pauci = little or non)

Treatment:

- It is usually an aggressive disease that should be treated with potent immunosuppressive medications. (high dose corticosteroids & cyclophosphamide).

6. Membranoproliferative GN (MPGN)

Video

General Info:

- It is a pathological description & has multiple causes.
- It may present with Nephritic picture or Nephrotic syndrome

Types:

1. The primary MPGN is mainly seen in children.
2. 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

	NS	Nephritic (GN)
Pathology	- Mainly a Podocytes disease present with foot process effacement +++ - Usually No Glomerular inflammation	Is an inflammatory disease involves any or all of Glomerular elements: Base Membrane, Endothelium or mesangium. Foot Proce effacement ++
Proteinuria	> 3.5 g/Day	Variable amount from few 100s mg to grams / day
Urine Microscopy	- No hematuria - + Lipids (Lipiduria)	+ RBCs, + dysmorphic RBCs, + RBC casts (active sediments)
Labs	- Low serum Alb < 30 gm/L - High Cholesterol	- Low GFR (Renal impair) - Electrolytes imbalance
Clinical	- Edema ++++ - BP maybe high	- Edema ++ High BP ++ - Symptoms & signs of renal impairment or vasculitis
Complications (Acute)	- Thrombosis - Infection	- RPGN - AKI
Complications (Chronic)	- Atherosclerosis - Tubular atrophy & Fibrosis then CKD	- Glomerular sclerosis then CKD (chronic Kidney disease) to ESRD

How to approach a patient with glomerulonephritis?

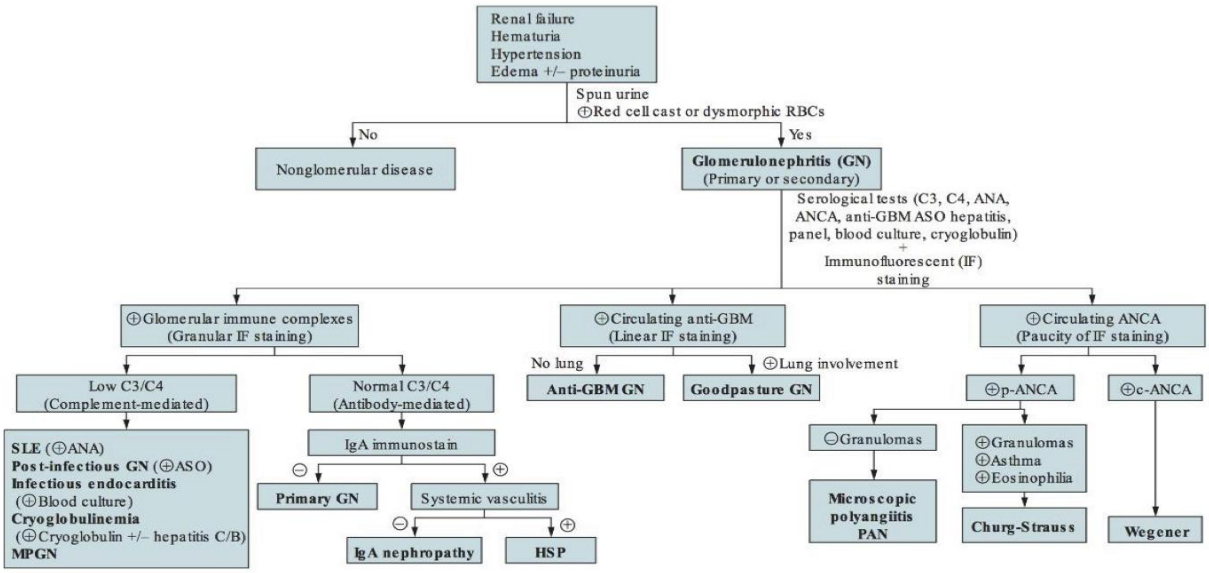


Figure 28–1. Algorithm of approach to the patient with acute glomerulonephritis. Abbreviations: ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; ASO, antistreptolysin-O; c-ANCA, cytoplasmic antineutrophil cytoplasmic antibody; GBM, glomerular basement membrane; HSP, Henoch–Schönlein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

Nephrotic Syndromes	
FSGS	Primary (Autoimmune): sudden onset of heavy proteinuria and other manifestations of nephrotic syndrome. Treatment: corticosteroids Secondary: Proteinuria is less heavy than other causes of nephrotic syndrome. Associated with Sickle Cell Anemia, Steroids & Obesity. Treatment: Treat underlying cause Diagnosis: focal: some glomeruli are affected by sclerosis (the rest of them look normal) and segmental: sclerosis only involves a segment of each glomerulus that is affected. But most importantly, all glomeruli will have diffuse foot processes effacement (Nephrotic syndrome)
MCD	Primary: Idiopathic. Secondary: Drugs (NSAIDs) Light microscopy: normal glomeruli Electron microscopy: 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 It is the main cause of Nephrotic syndrome in children. Nephrotic syndrome in a child < 10 years old is MCD until proven otherwise. Clinical features: Heavy proteinuria (Nephrotic range), Lipiduria, Hypoalbuminemia, Hyperlipidemia Treatment: Corticosteroids
MN	Most common cause of Primary nephrotic syndrome in adults Primary: Idiopathic Secondary: SLE, Solid tumors Diagnosis: Diffuse thickening of the glomerular capillary throughout all glomeruli (IgG and C3 deposition) Treatment: Primary: Corticosteroids Secondary: Treat the underlying cause
Secondary causes of Nephrotic Syndrome: **Diabetes Mellitus**	

Nephritic Syndromes Glomeruli with Crescent is VERY BAD	
IGA/HSP	Most common type of Primary GN in developed countries Can present actively and can be silent. The diagnosis is made by finding abnormal deposition of IgA in the Glomeruli. Can present as dark urine (hematuria) 1-3 days after upper respiratory tract infection HSP (Henoch-Schönlein purpura) is a systemic vasculitis caused by immune deposition of IgA in different organs; typically skin, bowel and kidneys. There is really no effective immunosuppressive therapy
PSGN	Typically caused by throat infection with Gram positive cocci (Group A beta-hemolytic Streptococcus (GAS). Patients present with frank hematuria usually after one week and up to 3 weeks from the start of infection Serum will show positive (ASO) titer
Anti-GBM	Due to autoantibody against (alpha-3 chain) of type IV Collagen that is found in Glomerular and alveolar (lungs) basement membrane Clinical Features: GN + Pulmonary hemorrhage (collectively known as goodpasture's disease Diagnosis: Linear stain of IgG and C3 under IF
ANCA vasculitis	Autoimmune disease that involves the presence of Neutrophils adhesion enhancing molecule called ANCA= anti-neutrophil cytoplasmic antibody C-ANCA= Cytoplasmic type, more commonly causing Granulomatous Polyangiitis = old name Wegener's Granulomatosis P-ANCA= Perinuclear type, more commonly associated with Microscopic Polyangiitis & Churg-Strauss syndrome Upper airways and lung involvement is common and patients can present with renal and pulmonary manifestations (GN + Pulmonary hemorrhage: hemoptysis). Kidney pathology will show sever Glomerulonephritis; maybe RPGN; but all staining with immunofluorescence for immunoglobulins is NEGATIVE; hence the name Pauci- Immune vasculitis or GN (Pauci = little or non)

Questions

1-Which one of the following is the most common presentation in patient with nephrotic syndrome ?
A-Proteinuria
B- Hematuria
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-Membranous Nephropathy
B-IgA Nephropathy
C-Post Streptococcal Glomerulonephritis
D-ANCA Vasculitis

5-Linear 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