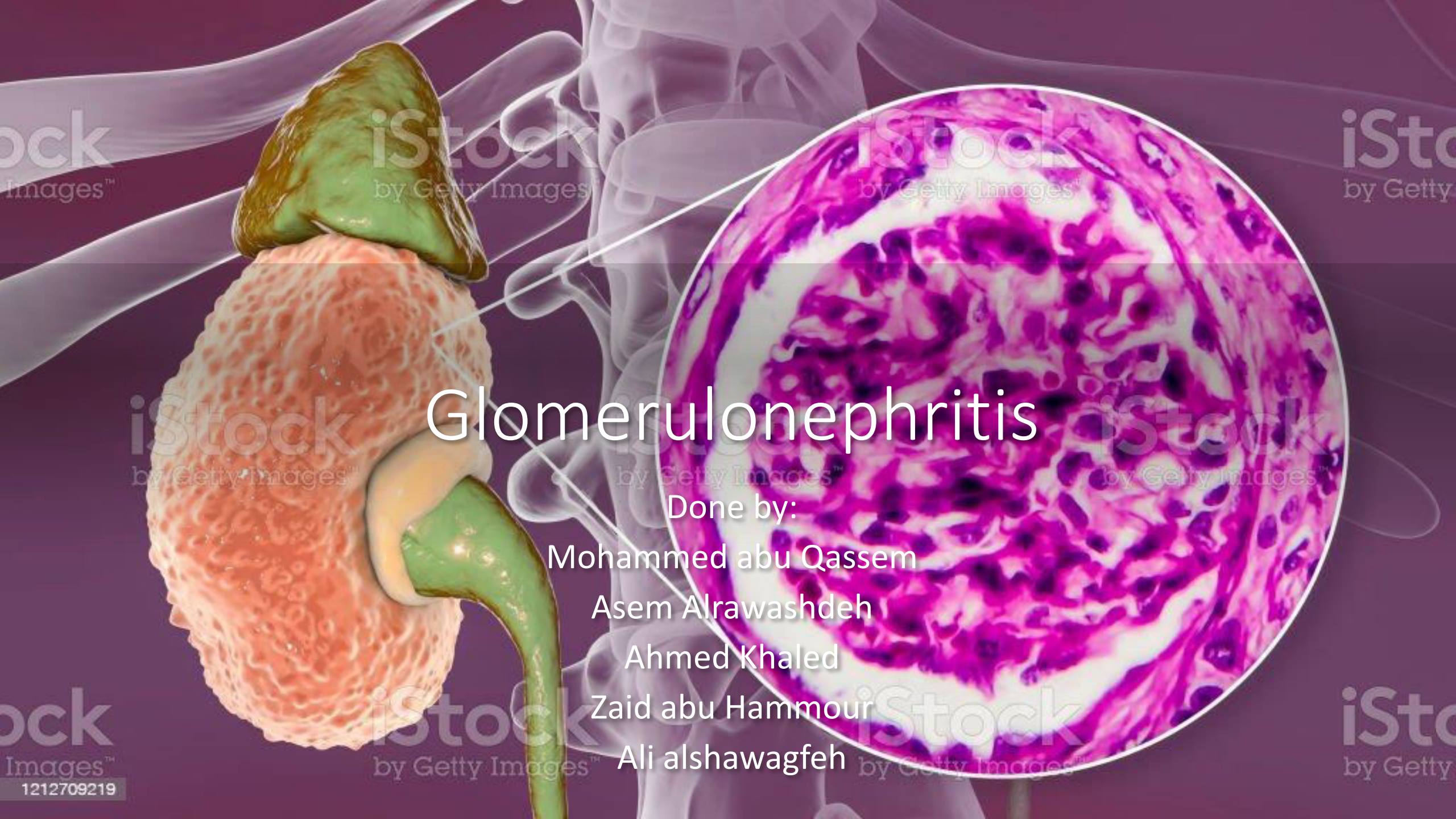

Glomerulonephritis

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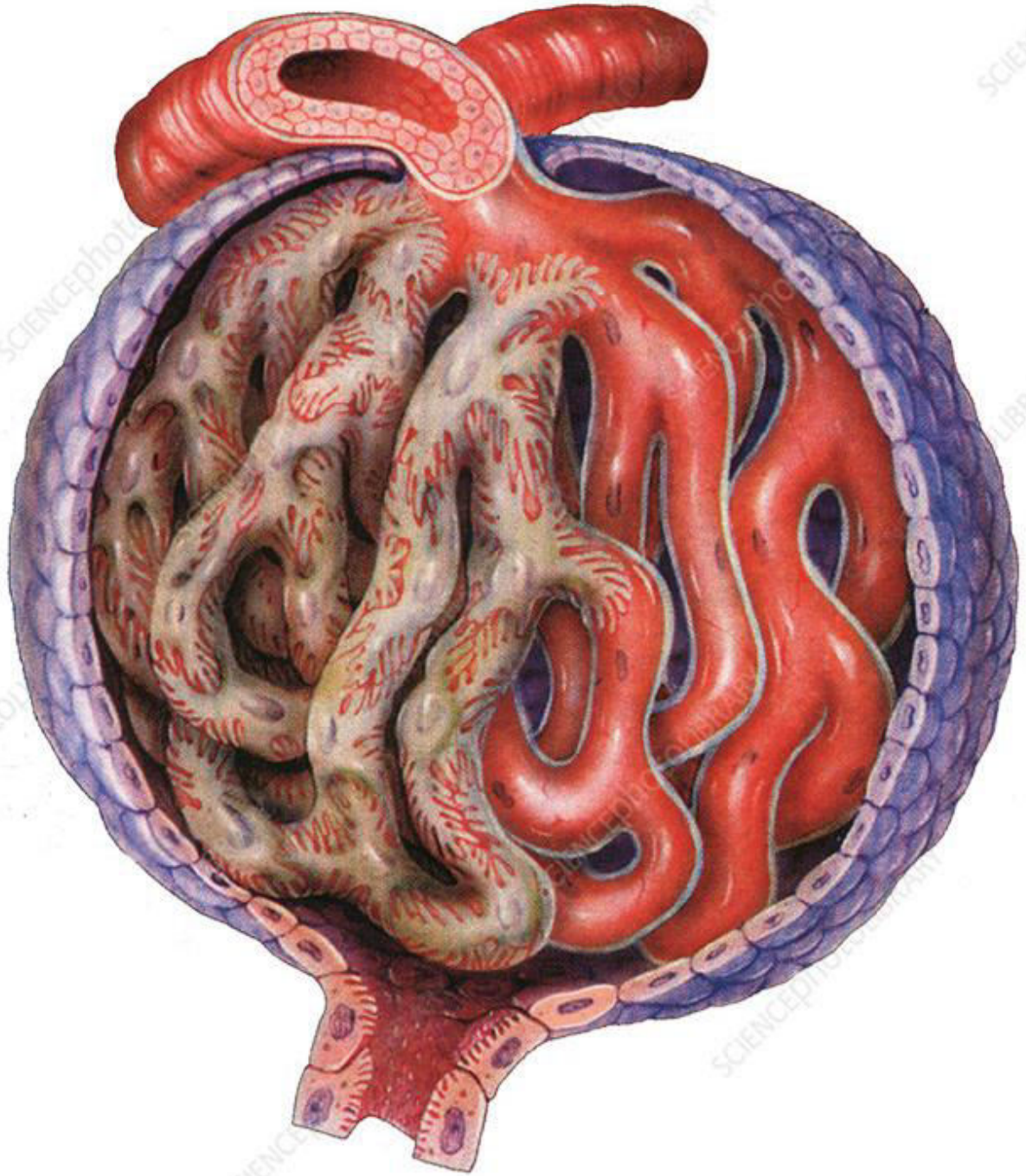
We’ll be talking about:

- Introduction
- Definition
- Types
- PSCG(case)
- Presentation
- Investigations and diagnosis
- Treatment and prognosis

The glomerulus:

- It’s a TUFT OF CAPILLARIRES.
- The capillaries have three main layers.
- 3 layers:

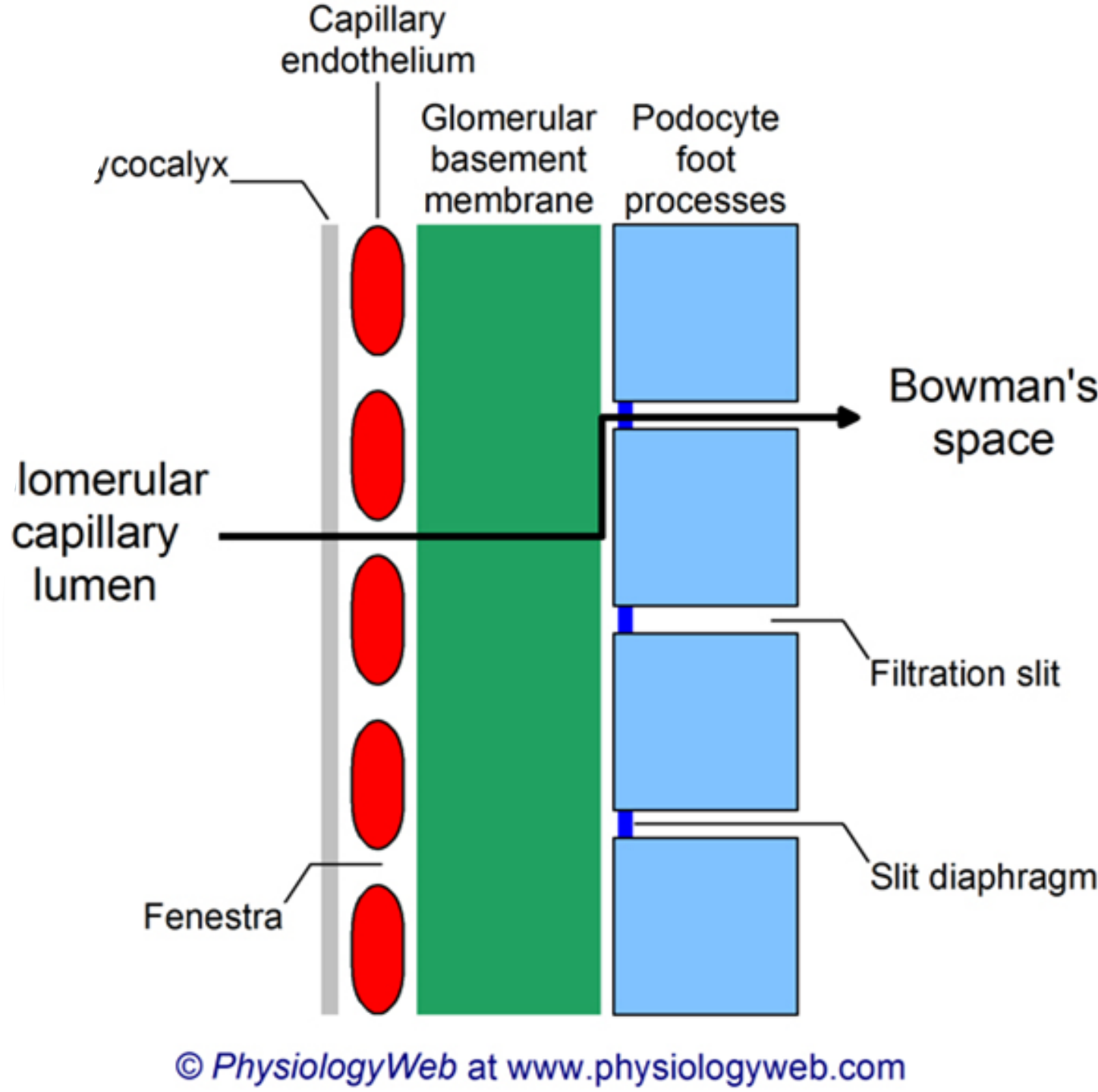
1. Endothelium
2. GBM
3. Podocytes



Three layers:

1. Endothelium
2. GBM
3. Podocytes

Mesangial cells



Glomerular disease:

Nephrotic syndrome

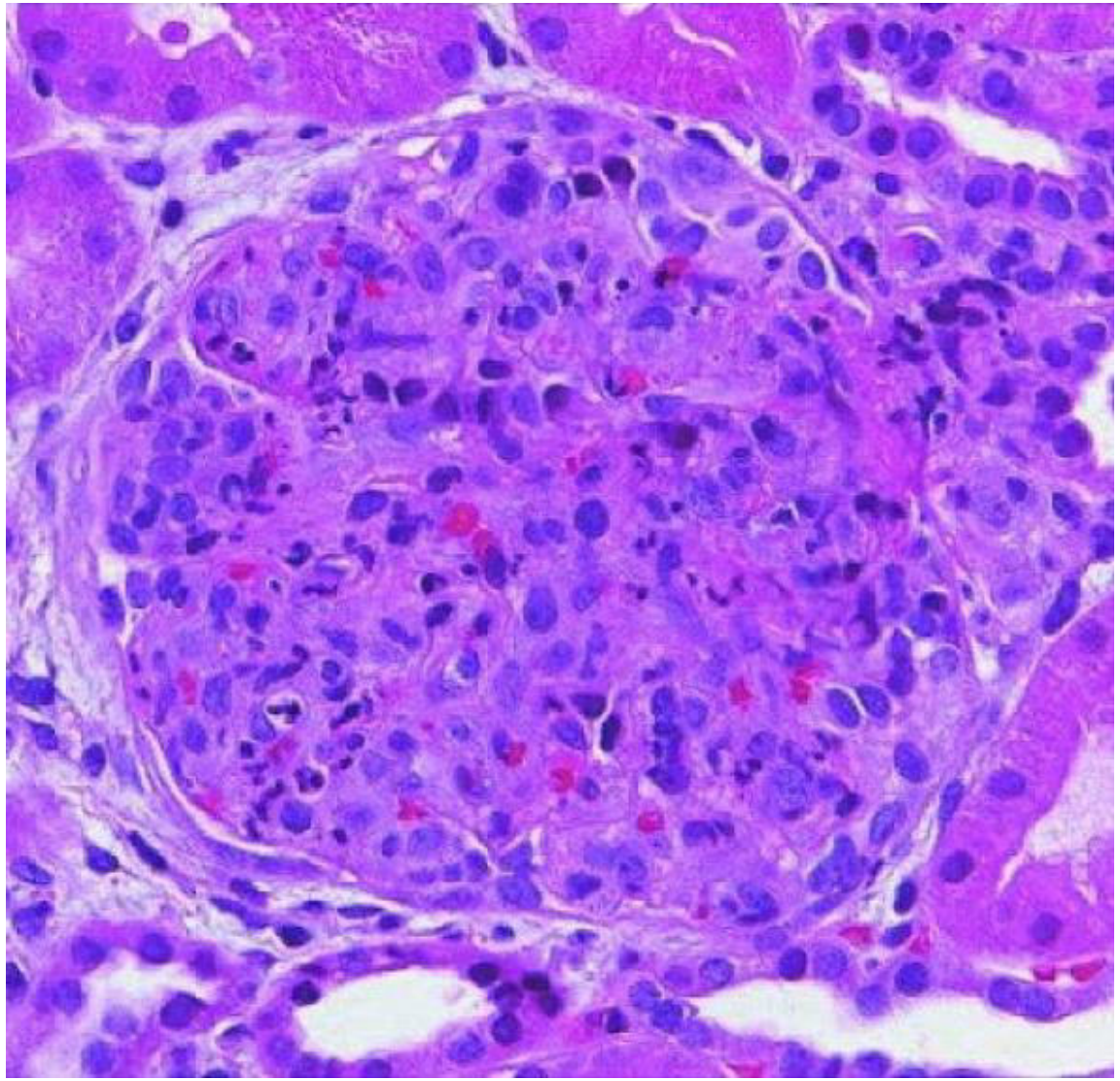
- More than 50 mg/kg body weight/day.
- Urine Protein/Creatinine ratio more than 2

Glomerulonephritis (nephritic syndrome)

- Usually P/Cr less than 2 (could be in nephrotic range)

Definition : glomerulonephritis

- It is an inflammation of the glomeruli.
- Immune mediated, immune complexes or vasculitis.
- Causing damage to the capillary endothelium, GBM, podocytes or the mesangial cells.
- (hypercellularity)



What happens in GN?

Low GFR

- High Cr/BUN (azotemia)
- Fluid overload (HT)

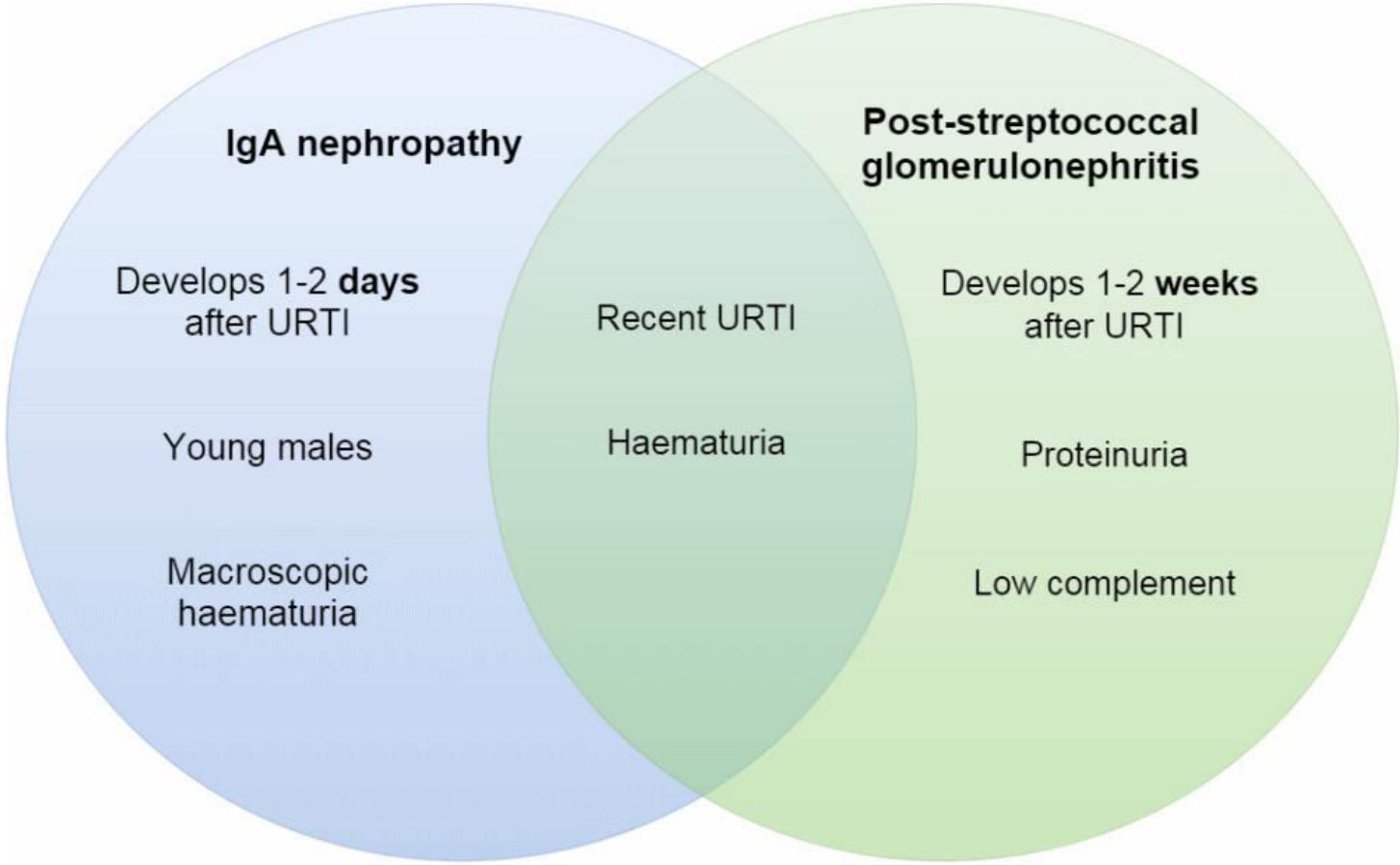
Disruption of the filtration barrier.

- proteinuria
- Hematuria
- Edema

Types:

- The most common types are:

1. PSGN in children
2. IgA nephropathy in adults



GN Types:

1

Primary

- IgA nephropathy
- PSGN
- Minimal change disease
- FSGS
- Membranous nephropathy
- Membranoproliferative GN
- Mesangial nephropathy

2

secondary

- Good pasture syndrome
- Wenger granulomatosis*
- Microscopic polyangiitis*
- Allergic polyangiitis*
- Polyarteritis nodosa*
- HSP*
- Lupus nephritis
- Cryoglobulinemia

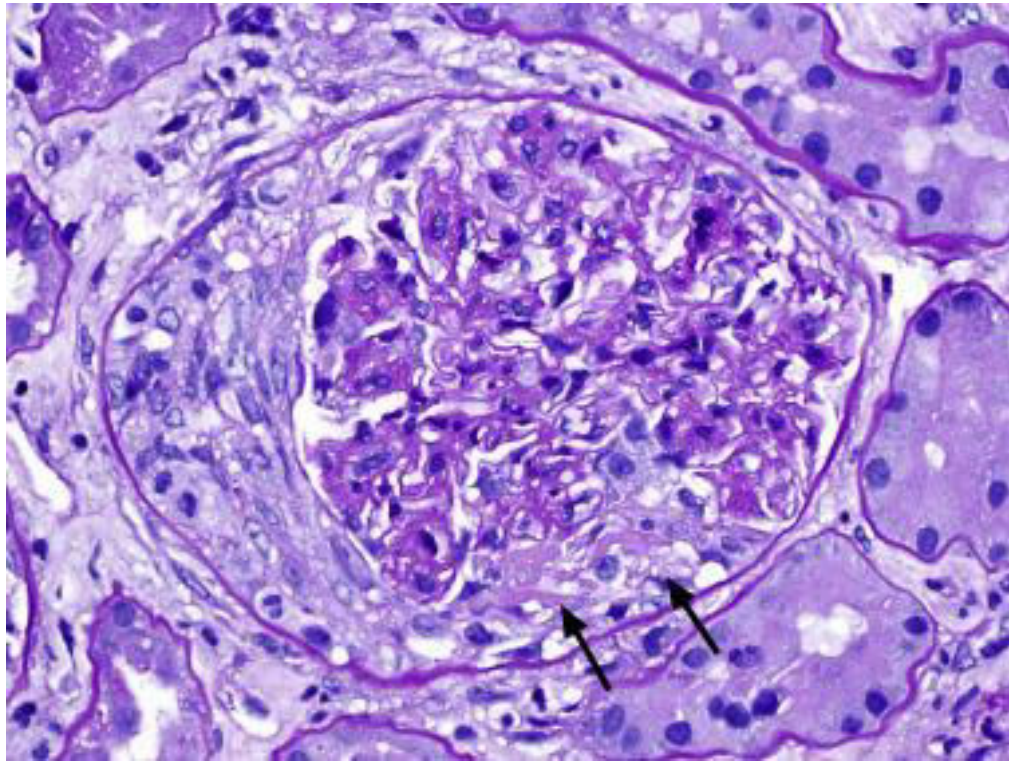
3

Hereditary

- Alport syndrome

RPGN

- Rapidly progressive glomerulonephritis (RPGN) is not a separate disease.
- It's when nephritic syndrome progress into acute renal failure.
- RPGN refers to the most severe and rapidly progressive form of GN. The terms RPGN and "crescentic glomerulonephritis" are essentially interchangeable.
- Some diseases like Goodpasture (anti-GBM disease) frequently become rapidly progressive. Some, like PSGN, rarely become progressive.



GN may progress to:

- Rapidly progressive GN.
- End stage renal disease.
- Damage to the glomerular wall may lead to nephrotic range proteinuria (P/Cr urine more than 2 with hypoalbuminemia).

Post-streptococcal Acute Glomerulonephritis (PSAGN)

- Case scenario:
- Kasap B, Çarman KB, Yiş U. A case of acute post-streptococcal glomerulonephritis that developed posterior reversible encephalopathy syndrome. Turk Pediatri Ars. 2014 Dec 1;49(4):348-52. doi: 10.5152/tpa.2014.430. PMID: 26078688; PMCID: PMC4462310.

Presentation(history and physical examination)

- A 10-year old male patient presented with facial puffiness, leg and scrotal edema. He was treated with a diagnosis of tonsillitis 8 days before his complaints started, had diarrhea (up to 3–4 times a day) a few days before his presentation and his urinary output was reduced. On physical examination, his body weight and height were in the 25–50th percentile, his blood pressure was 135/80 mmHg (the 95th percentile for age height & gender is 121/80), he had pretibial 2+ edema and diffuse edema in the palpebraes, pubic region and scrotal region.

investigations

1 Urinalysis revealed:

- Protein 3+
- Erythrocytes 3+
- leukocytes 1+
- urinary microscopic examination: abundant erythrocytes, 4–5 leukocytes.

Investigations

2 KFTs showed:

- Urea: 195 mg/dL
- Serum creatinine: 2.58 mg/dL (N: 0.3-0.7 mg/dl)

3 24 hour urine protein: 256 mg/m^2/h (> 6 g/d) (nephrotic range)

4 Anti-sterptolsine O antibody: 586 IU/mL (upper limit of normal=276 IU/ML)

5 C3 20.1 mg/dL (N: 83–177) & C4 23.5 (n: 15–45).

Investigations

6 CBC:

- hemoglobin: 11.1 g/dL
- hematoctrit: 37%
- white blood cells: 10,700/mm^3
- platelets: 115 000/mm^3

APSGN was considered in the patient, but biopsy was planned, since he had nephrotic range prpteinuria .

The result was interpreted to be compatible with PSAGN.

Complications

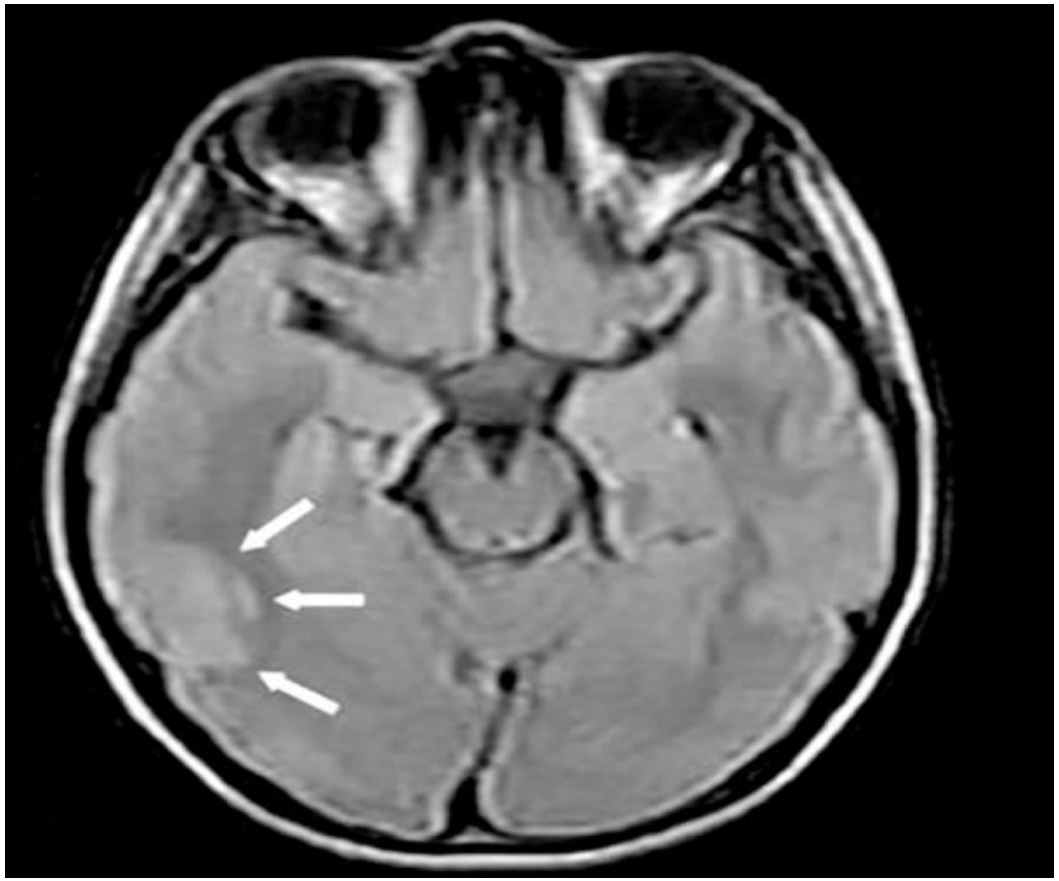
- On the sixth day of follow-up, severe headache and vomiting started from the morning hours while he was receiving antihypertensive treatment (Calcium channel blocker) and diuretic treatment, and BP was under control. The BP values during this period were found to be 120/80 mmHg.

At the noon hours, convulsions occured. At this time, the BP was 130/80 mmHg.

complications

- MRI was done → revealed Posterior reversible encephalopathy syndrome (PRES)

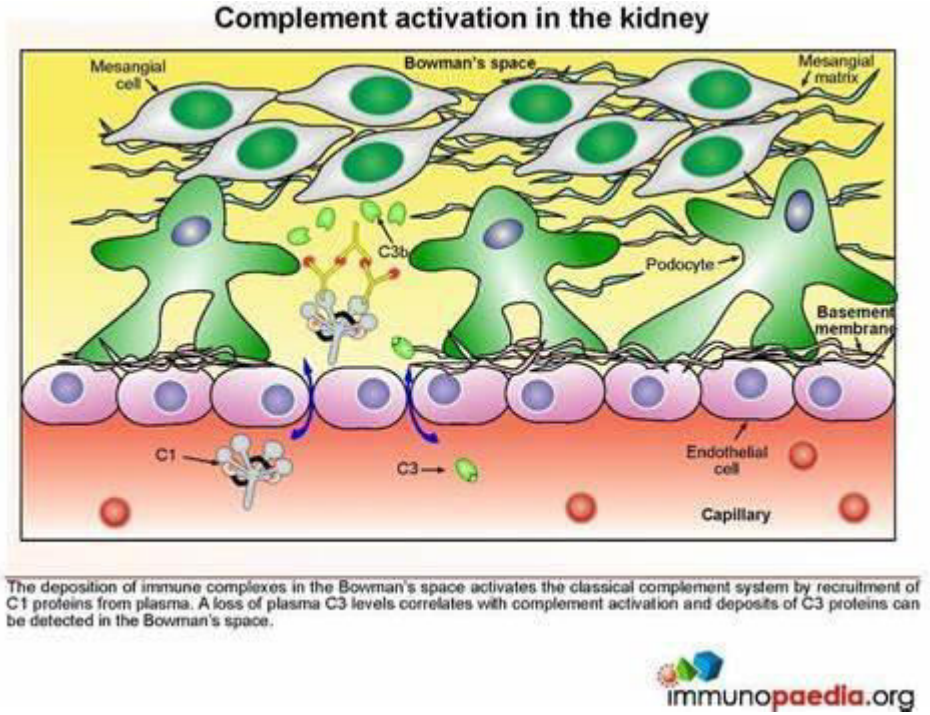
- EEG was done → normal



PSAGN

- Definition:
  it's a type of GN caused by deposition of immune-complexes after a history of strep infection.
- Type A beta-hemolytic streptococcus.
- M protein in strep is the

nephrogenic antigen.



Presentation

- Usually gross hematuria occurs, but occasionally It may be in the form of asymptomatic microscopic hematuria.
- In some cases it may progress to acute renal failure (RPGN)
- Especially in older adults

Presentation

- Patients usually present with: (nephritic syndrome)

  Dark (cola-colored) urine.

  Edema that is often periorbital.

  Hypertension.

  Oliguria.

  Proteinuria (may be in the nephrotic range – 20% of cases)

- Symptoms are preceded by Streptococcal infection whether:

  - Strept. pharyngitis (1-2 weeks) OR

  - Impetigo or scarlet fever (4-6 weeks)

PSAGN vs Rheumatic fever (RF)

- RF - only preceded by strep pharyngitis (6 weeks)
- PSAGN can be preceded by pharyngitis, impetigo (and scarlet fever).

- Early antibiotic treatment may prevent RF but doesn’t prevent PSAGN.

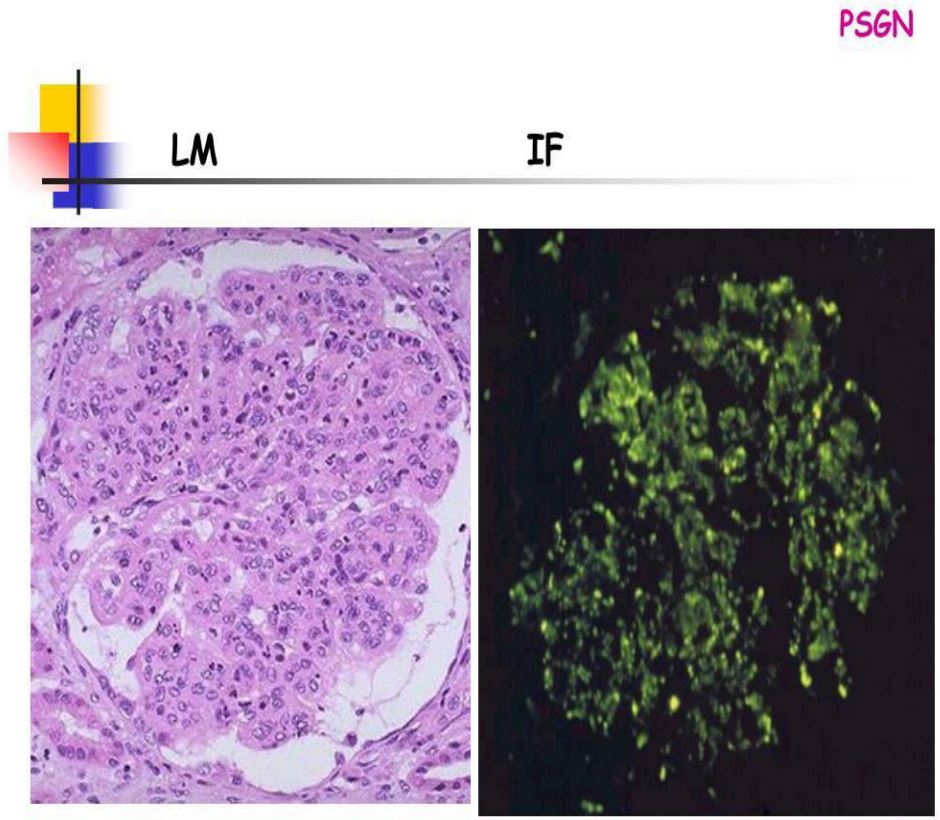
Diagnosis

- **Urialysis** : proteinuria, hematuria (microscopic ± RBC casts).

- Evidence of strep infection (swab culture, ASO titers, anti-DNAse antigen which is the best single test)

- Low C3

- Usually renal biopsy is not required in PSGN



Renal biopsy may be considered in PSGN

- In Nephrotic range proteinuria.
- Progressive decline in the renal function (Crescentic-RPGN).
- If there is no latent period between the acute GN and streptococcal infection.
- If the complement levels are normal.
- When there is no rise in anti-streptococcal antibodies.

Treatment

- Management of PSAGN does not reverse the glomerulonephritis.
- It resolves spontaneously in most cases
- Use supportive therapies such as: Antibiotics.
- Diuretics to control fluid overload. (loop diuretics)
- Less than 5% of those with PSAGN will progress (may require dialysis).
- Anti-hypertensive meds (ACE inhibitors or ARBs), why?

Complications

- HTN
- Acute renal failure (Acute kidney injury)
- Congestive heart failure / pulmonary edema due to fluid overload.
- Electrolyte abnormalities.
- Seizures (uremic/hypertensive encephalopathy, PRES)
- Most patients begin to improve after 1 week and the edema usually resolves in 1-2 weeks.
- Recovery usually occurs within 6-8 weeks.

Presentation

- General symptoms:

1. Edema (preorbital initial site, worse during mornings)
2. Hematuria (dark/red urine)
3. Proteinuria.
4. Oliguria
5. Elevated blood pressure
6. Decreased renal function

History

Propre history shows group of general and cause-specific symptoms that vary with the cause of GN.

- General symptoms:

1. Age (congenital, primary, secondary)
2. Onset/duration (acute vs chronic)
3. Urinary symptoms present (color, amount, quality)
4. SOB (in patients with heart failure or pulmonary edema; it is usually uncommon)
5. Possible flank pain (rare)
6. Headache/confusion (This may occur secondary to hypertension)

History

Cause specific symptoms:

- Infection; Recent fever, sore throat, joint pains, hepatitis, travel, heart valve replacement, and/or intravenous drug use.

- SLE; skin rash (malar/discoid), Serositis, Oral ulcers, Arthritis, Photosensitivity, Neurologic (seizure/psychosis), Hematologic disorder, +ANA, history of Immunologic disorder, history of renal problem)

History

- Wegener granulomatosis; Triad of sinusitis, pulmonary infiltrates, and nephritis granulomatosis with polyangiitis
- HSP; nausea and vomiting, arthralgia, abdominal pain, and purpura commonly present.
- Goodpasture syndrome or idiopathic progressive glomerulonephritis; hemoptysis
- hypersensitivity vasculitis; skin rash

Acute vs Chronic GN

- Chronic glomerulonephritis develops over a long time, often without obvious symptoms. However, complete kidney failure can occur with time.
- Symptoms;
- high blood pressure (more common than acute)
- swollen ankles or face, because of water retention (compared to puffiness of the face on waking up in acute)
- urinating frequently during the night
- bubbles or foam in the urine, caused by excess protein (more noticeable)
- uremic symptoms; poor appetite, nausea, and vomiting. They may feel tired due to disruptions to their sleeping pattern, with muscle cramps occurring during the night. The skin might feel dry and itchy.

Clinical examination

A complete physical exam should be conducted, with focus on these findings for better diagnosis;

- Signs of fluid overload;
  - Periorbital and/or pedal edema
  - Crackles (ie, if pulmonary edema)
  - Elevated jugular venous pressure
  - Ascites and pleural effusion
- Rash (as with vasculitis, HSP, or lupus nephritis)

Clinical examination

- Abnormal neurologic examination or altered level of consciousness (from malignant hypertension or hypertensive encephalopathy).
- Renal angle (ie, costo-vertebral) fullness or tenderness, joint swelling, or tenderness
- Pallor
- Arthralgia / Arthritis

Clinical examination

Other signs include the following:

- Pharyngitis sings
- Oral ulcers
- Impetigo
- Respiratory infection signs (hemoptysis)
- Heart murmur (possibly indicative of endocarditis)
- Scarlet fever signs
- Anorexia signs
- Abdominal pain
- Back pain
- Weight gain

Complications

- Progression to glomerulo-sclerosis/
- Pulmonary edema and hypertension (may develop)
- Generalized anasarca and hypoalbuminemia (secondary to sever proteinuria)

Complications

- Patients with severe hypertension, encephalopathy, and pulmonary edema may develop:
  - Hypertensive retinopathy
  - Hypertensive encephalopathy
  - Rapidly progressive glomerulonephritis
  - Chronic kidney disease
  - Nephrotic syndrome
  - Heart failure

Diagnosis

Post-streptococcal Acute Glomerulonephritis (PSAGN)

Based on clinical findings and evidence of recent Group-A strept. infection:

- Renal function: Variable decline in GFR, can see rise in serum Cr.
- Positive throat cultures or antibody titers to streptococcal antigen.
- Urinalysis : RBC casts, RBCs, varying amounts of protein, sometimes pyuria.
- Serum complement: Low C3 in first 2 weeks of illness, resolves within 4–8 weeks.
- Renal biopsy: Typically not needed as PSAGN tends to begin to resolve within 1 week of presentation.

Membranoproliferative Glomerulonephritis

- Renal biopsy is required.
- Serum C3 complement levels often low, and persisting.

IgA Nephropathy

- Suspicion generally based on clinical history and lab data.
- Can only be confirmed with renal biopsy with immunofluorescence studies for IgA deposits.
- Identical to renal biopsy findings seen in Henoch-Schönlein purpura , since both have IgA deposition.
- Biopsy only performed if signs of more severe or progressive disease (excessive proteinuria, elevated creatinine).

Alport Syndrome

- Generally suspected from family history of deafness and renal failure.
- Can be confirmed by skin or renal biopsy or molecular genetic testing.

Goodpasture syndrome

- A-Labs :

 - Nephritic sediment-Microhematuria (acanthocytes, RBC casts)
 - Non-selective glomerular proteinuria.
 - Pyuria.
 - Rapid rise of BUN and creatinine.

- B-Serology:

 - Anti-glomerular basement membrane antibodies

Membranous Nephropathy

- The diagnosis can only be established by renal biopsy.
- No serologic test is specific for MN, but finding an active carrier state for hepatitis B or congenital syphilis would make the diagnosis probable in the appropriate clinical setting.
- Common indications for renal biopsy leading to the diagnosis of MN include presentation with nephrotic syndrome in a child > 10 yr or unexplained persistent hematuria with significant proteinuria.

Lupus nephritis

- A-Laboratory findings :

-↑ serum creatinine

-Urinalysis: proteinuria, hematuria, cellular casts (RBCs, hemoglobin, granular, tubular, or mixed)

-Spot urine protein:creatinine ratio: proteinuria ≥ 0.5 g/g

- B-Kidney biopsy:

-Indicated in patients with either:

1-Unexplained ↑ creatinine

2-Proteinuria ≥ 1.0 g/g

3-Proteinuria ≥ 0.5 g/g and hematuria or cellular urinary casts

-Findings: immune complex-mediated glomerulonephritis

Management

Done by : Ali Al-shawagfih

IgA nephropathy

Once kidneys have been damaged, they can not be repaired.

So the treatment is focused on preventing further damage and avoiding end-stage kidney disease.

We have two types of treatment :

- Non-immunosuppreseive medication :

- ACE inhibitors
- ARBS

These meds help by reducing the pressure of blood flowing into the kidney and decreasing the inflammatory damage to glomeruli.

As a result, the amount of blood protein loss in the urine decreases and thus slows the progression of the disease

- Immunosuppressive

- Corticosteroid (Prednisone)

Reduced the inflammatory damage in glomeruli

But due to potentially serious side effects, this treatment is reserved for patients with severe inflammatory damage and rapidly declining kidney function

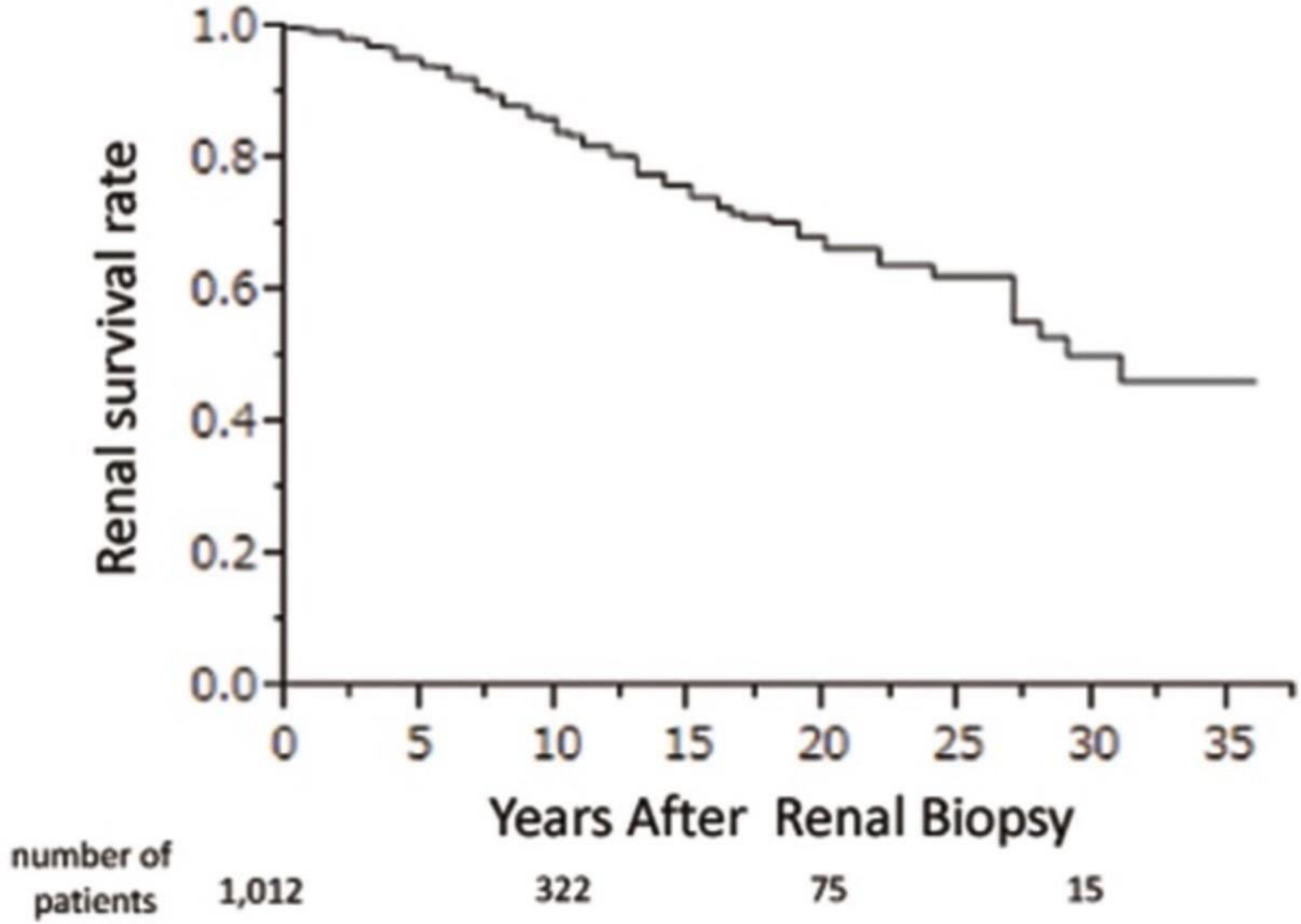
Prognosis :

The cumulative survival rate from renal biopsy to ESRD is

10 years => 84.3%

20 years => 66.6%

30 years =>50.35


Renal survival rate
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
35
Years After Renal Biopsy
number of patients
1,012
322
75
15

Lupus nephritis

the pharmacotherapy for lupus nephritis based on stages seen on biopsy :

1) minimal mesangial lupus nephritis (class 1) :

Requires no specific therapy

2) mesangial proliferative lupus nephritis (class 2) :

May require treatment if proteinuria is greater than 1g/day.

Prednisone in low to moderate dose (1mg/kg/day) for 1-3 month with subsequent taper.

3) focal lupus nephritis (class 3) and diffuse lupus nephritis (class 4) :

These patients are at high risk of progressing to ESRD and thus require aggressive therapy.

Prednisone 1 mg/kg/day for at least 4 weeks, then taper it gradually to a daily maintenance dose of 5-10 mg/day for 2 years.

In severe cases, we can add Iv methylprednisolone up to 1g/day for 3 days .

+ Cellcept

+ Imuran

+ Cyclophosphamide.

- 4) membranous lupus nephritis (class 5)

Patients with membranous lupus nephritis are generally treated with prednisone for 1-3 months, followed by tapering for 1-2 years if a response occurs. If no response occurs, the drug is discontinued.

+ Cellcept

+ Imuran

+ Cyclophosphamide.

- Belimumab (new therapies) ;

Anti-B lymphocyte stimulator monoclonal antibody.

Used for treating active lupus nephritis in children aged 5-7 years.

Prognosis :

5-30% of patients developed end-stage kidney disease despite the treatment

HSP nephritis

- there is no treatment for HSP nephritis and the most effective treatment remains controversial
- Oral steroids may be used.

- prognosis :

Children with mild to moderate HSP nephritis generally achieve full recovery and have minimal risk of permanent kidney injury

Goodpasture syndrome

The mainstay of treatment for Goodpasture syndrome nephritis involves a combination of immunosuppressive medications and supportive measures. It's crucial to start treatment promptly to prevent further kidney damage.

- Immunosuppressive Medications :
- **Corticosteroids**: High doses of corticosteroids, such as prednisone, are often prescribed initially to rapidly suppress the immune system.
- **Cyclophosphamide or Rituximab**: These drugs are often used in combination with corticosteroids to further suppress the immune system and prevent further damage.

- Plasma Exchange (Plasmapheresis):

Plasma exchange is a procedure where the liquid part of the blood (plasma) is removed and replaced with a substitute or donor plasma. This helps remove circulating antibodies that are attacking the kidneys and lungs.

- Supportive care :

-Blood pressure control

-Diuretics

-Dialysis (in severe cases)

Prognosis :

5 years survival rate is 80 % and fewer than 30 % of affected individuals require long dialysis

(Wegener granulomatosis)

- Corticosteroids (prednisone).
- Cyclophosphamide , azathioprine , mycophenolate , methotrexate , rituximab ,

These drugs are often combined with corticosteroids

- Plasma exchange

- Prognosis :

With early diagnosis and appropriate treatment, you might recover from granulomatosis with polyangiitis within a few months.