Letuda's Nephrology Note

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Chronic kidney disease (CKD)

Definition:

Presence of any of the following for at least 3 months:

1. Evidence of kidney damage with/ without reduced GFR

OR

2. GFR ≤60 ml/min/1.73 sq.mt body surface area.

Evidence of kidney damage:

1. Biochemical abnormalities: Urea↑ Creatinine↑
2. Urinary abnormalities: Proteinuria/ sediment/ cast
3. Radiological evidence: Bilateral small kidneys
4. Histopathological abnormalities.

Stages of CKD:

Stage	***GFR (Normal: ≥90)***	***Description***
1	Evidence of kidney damage +Ve when GFR ≥90	Minor kidney damage
2	60-89	Mild
3	30-59	Moderate
4	15-29	Severe
5	<15	Kidney failure/ end stage renal disease*

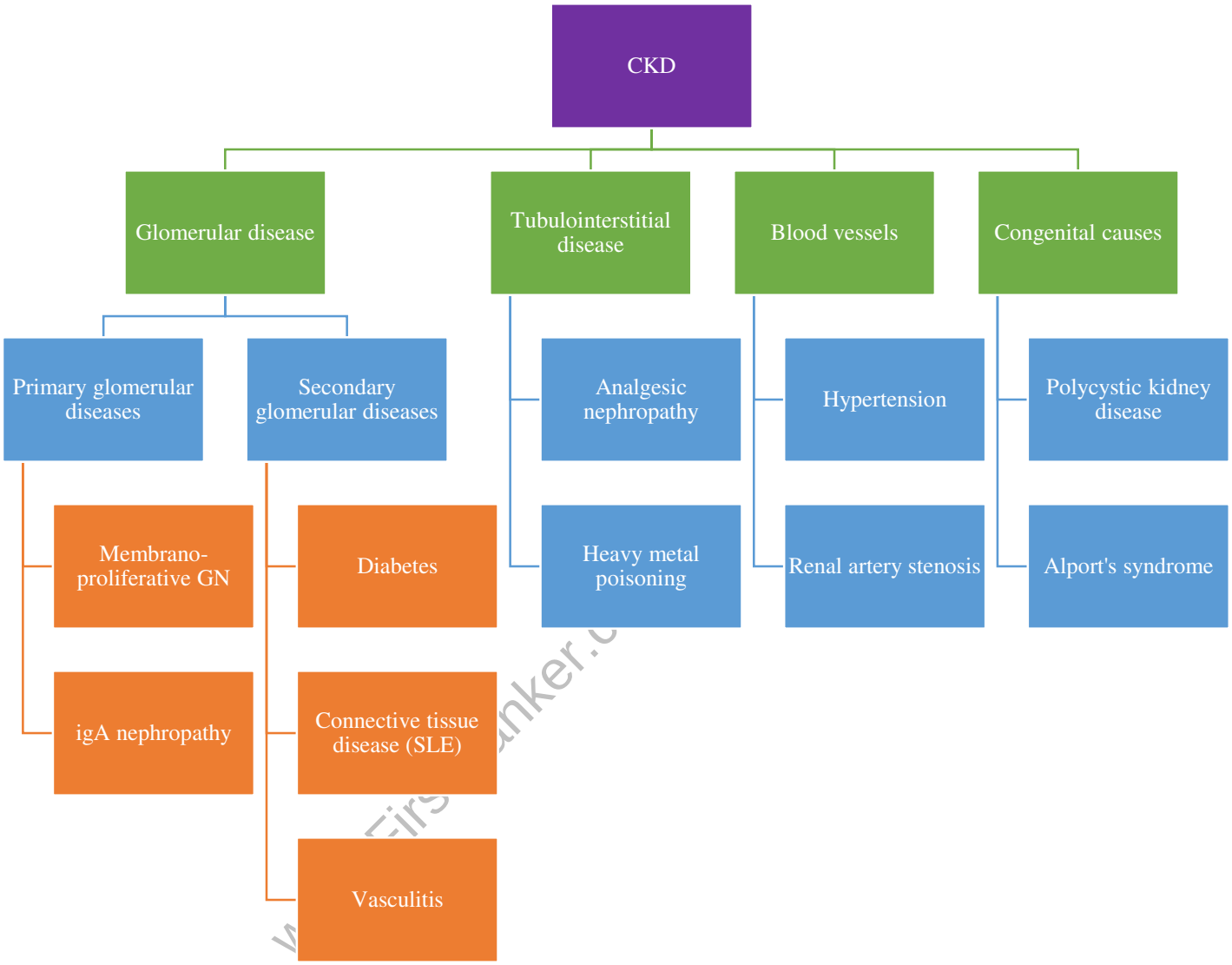
*It is a condition where without renal replacement therapy (dialysis/ renal transplantation), patient will not survive.

Azotemia and uremia

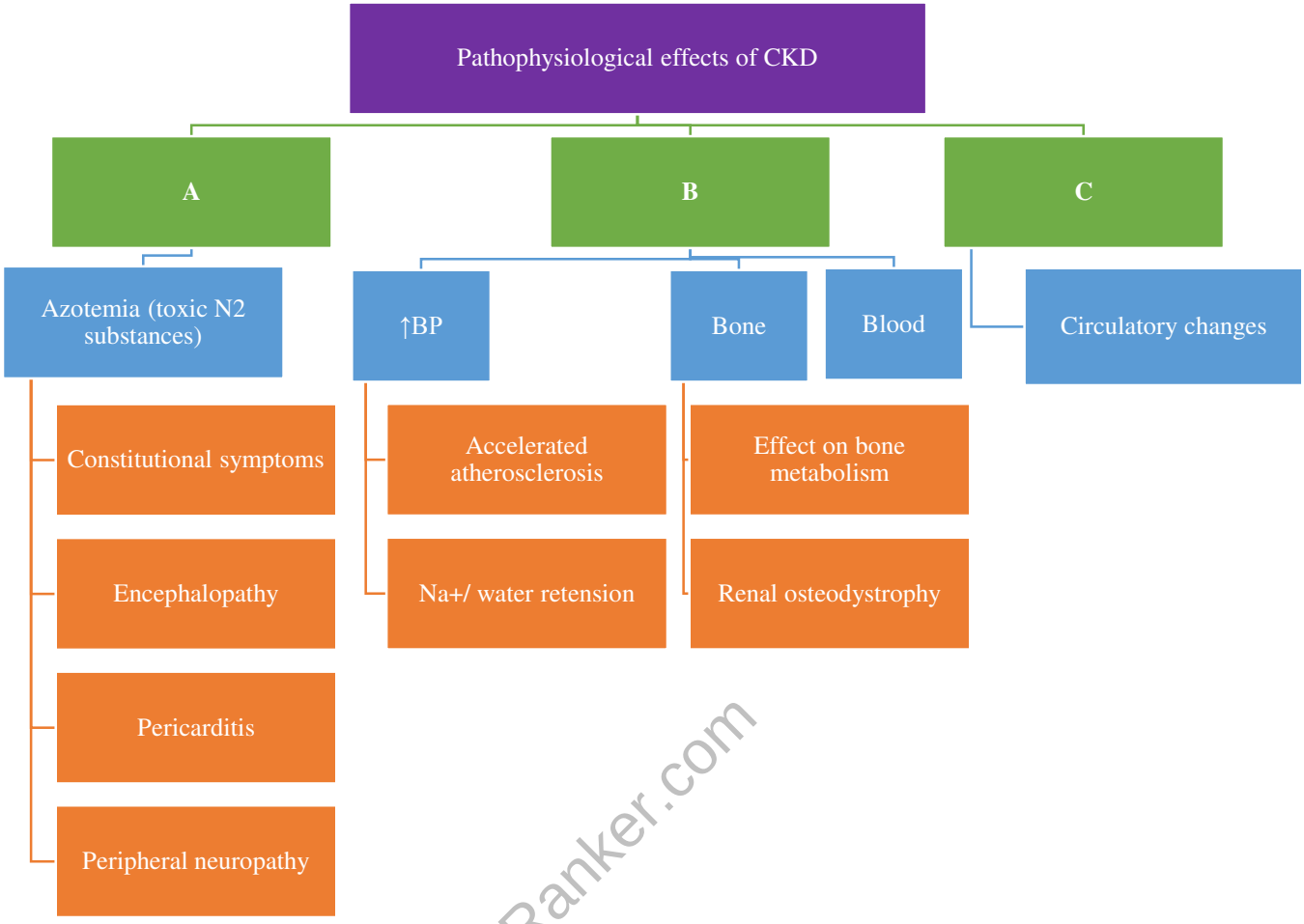
Azotemia: Accumulation of nitrogenous substance in the blood due to defective renal clearance.

Uremia: Clinical manifestations due to azotemic condition.

Causes of CKD:



Pathophysiological effects of CKD:

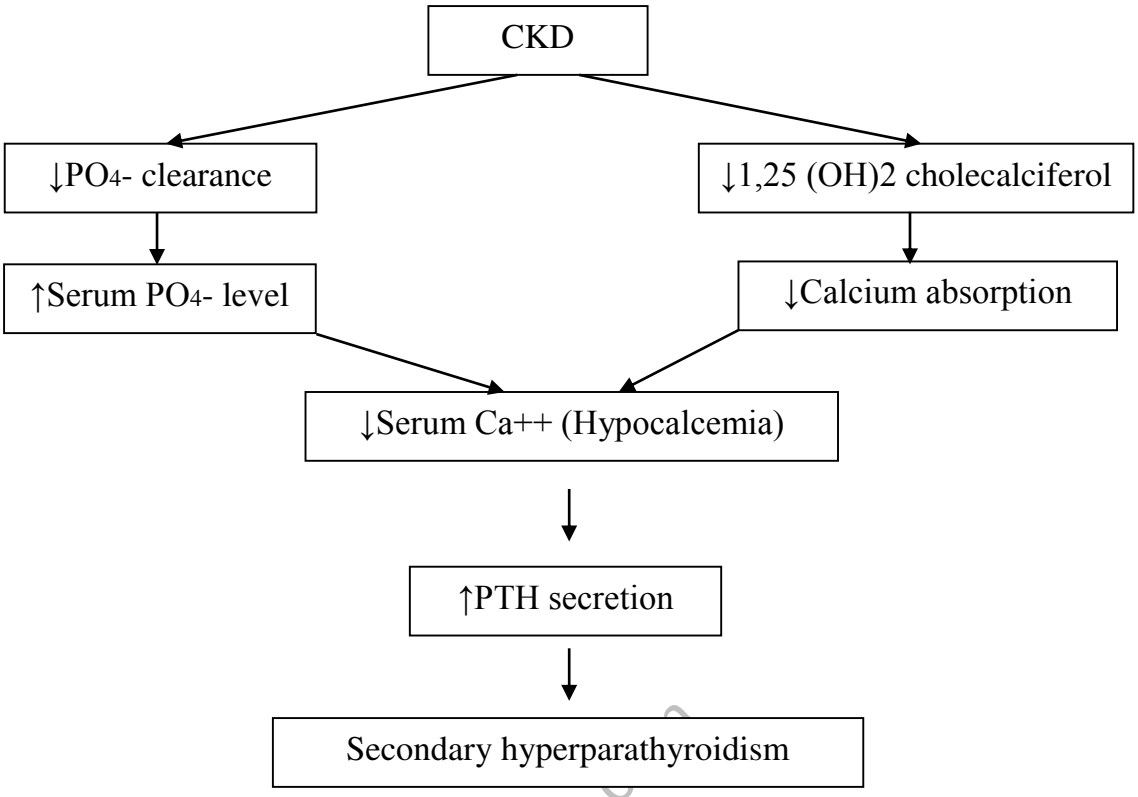


Effects of CKD on bone:

Effect on bone mineralization

1. De-mineralization
2. Osteitis fibrosa cystica.

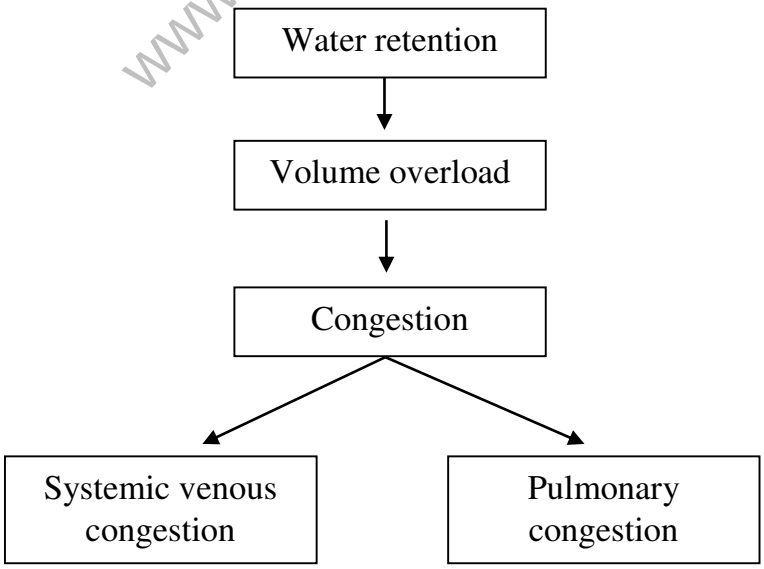
Renal osteodystrophy



Effect of CKD on blood picture:

1. ↓Erythropoietin synthesis --→ Anemia
2. ↑Toxins--→ Platelet dysfunction.

Circulatory effect:



Clinical features

1. Constitutional symptoms:
   - ✓ Anorexia
   - ✓ Nausea
   - ✓ Refractory hiccup
   - ✓ Metallic taste in mouth
   - ✓ Wasting of the muscles.
2. CNS (symptoms of uremic encephalopathy):
   - ✓ **A**ltered sensorium
   - ✓ **B**ehavioral disturbances
   - ✓ **C**onfusion; in severe cases: convulsion and coma may occur
   - ✓ **D**elirium
   - ✓ **F**lapping tremor
   - ✓ ↓**G**CS.
3. Circulatory/ CVS:
   Symptoms and signs are mainly due to volume overload and may resemble heart failure.
   Symptoms:
   - ✓ Progressive swelling
   - ✓ Pulmonary congestion: Shortness of breath, orthopnea, PND

   Signs:
   - ✓ Signs of systemic venous congestion: Edema, ↑JVP
   - ✓ Signs of pulmonary congestion: Bilateral crepitations.
4. Kidney:
   Features due to kidney dysfunction: ↓Urine output
   Note that urine output often remains normal till significant renal dysfunction develops.
5. Disease:
   Features of the underlying disease, ***which must be looked for***.
6. Features due to disturbed bone metabolism:
   - ✓ Bone pain: Spontaneous/ after trivial trauma
   - ✓ Proximal myopathy (due to vitamin D deficiency).

Investigation

Principles:

1. To look for different biochemical and systemic effects of CKD
2. To detect the underlying cause.

Preliminary investigations

A. *Blood biochemistry*:

- Urea creatinine: ↑
- Na+: Normal/ ↓ (due to dilutional hyponatremia)
- K+: Normal/ ↑
- Ca++: Normal/ ↓
- PO_4-: Normal/ ↑

- ABG: pH↓ (due to ↓HCO_3-)
- Vitamin D level: Normal/ ↓
- PTH level: Normal/ ↑
- Uric acid: Normal/ ↑
- Hb level: Normal/ ↓

- Special note: Blood glucose in diabetic patients:
  Often glucose control becomes better/ patient may develop recurrent hypoglycemia due to delayed excretion of insulin which in turn prolongs half-life of insulin. Therefore in diabetic patients, once CKD develops, dose of medications often needs to be decreased.

B. Calculating creatinine clearance:

$$Creatinine\ clearance = \frac{(140 - Patient's\ age) \times Patient's\ body\ weight\ (in\ kg)}{Serum\ creatinine\ level\ (in\ mg/dl) \times 72} = x$$

For females, $Creatinine\ clearance = x \times 0.85$

C. Urine (microscopic examination):
To look for biochemical abnormalities:

- ✓ Proteinuria
- ✓ Any cast (particularly RBC case, tubular cast): May give an idea about the underlying disorder.

24 hour urine for albumin: creatinine/ microalbumin: creatinine ratio.

D. Kidney-ureter-bladder (KUB) USG:

- ✓ Bilateral small kidneys (seen in CKD)
- ✓ Unilateral small kidney (seen in renal artery stenosis).

E. Chest X-Ray, ECG, Echo:
To look for any cardiac pathology.

F. Renal biopsy:
In selected cases only: confirms the underlying type of kidney disease: which in most cases are: unexplained glomerulonephritis and nephrotic syndrome.

G. Relevant investigation(s) to detect the cause.

Treatment

General treatment

R:

1. **R**egular monitoring of urine output: particularly in significant CKD
2. **R**egular monitoring of volume status, i.e. regular monitoring of body weight
3. **R**egular monitoring of blood biochemistry.

E:

Treatment of the underlying **e**tiology.

N:

Maintenance of **n**utrition:

Dietary modification

- ✓ Fluid and salt restriction
- ✓ Dietary protein restriction
- ✓ In presence of associated DM: Restriction of carbohydrate
- ✓ Restriction of K+:
  - Parboiling of rice (to discard water after boiling)
  - Avoid juicy food.
- ✓ Avoid beverages (as they are rich in phosphates).

A:

1. **A**void all nephrotoxic drugs
2. **A**djust the dose of drugs according to creatinine clearance.

L:

Look for common complications:

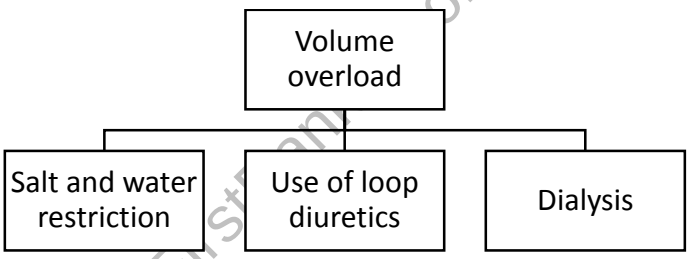
- ✓ Features of dehydrations (due to diuretics + fluid restriction)
- ✓ Features of dyselectrolytemia
- ✓ Features of infection.

Specific treatment

F:

Fluid balance

There may be 3 sources of volume overload:



Often these patients will come with dehydration due to overdiuresis which should be treated with *IV fluid cautiously.*

A:

1. Acidosis:
   Mild to moderate: $NaHCO_3$ if required
   Severe: Dialysis.
2. Anemia:
   - ✓ Blood transfusion if required
   - ✓ Correct any underlying iron deficiency
   - ✓ Long term erythropoietin therapy.

I:

Infection: Treat with appropriately adjusted dose of antibiotics.

L:

Loss of blood due to associated coagulopathy: Treat with blood transfusion.

U:

- ✓ Treat uremic encephalopathy
- ✓ Treat uremic pericarditis
  - By dialysis.

R:

Treatment of **r**enal osteodystrophy, if present:

The underlying biochemical abnormalities are: ↑ PO_4-, ↓Vit-D, ↓Ca, ↑PTH.

- ✓ ***↑ PO_4-:***
  1. PO_4- restriction
  2. PO_4- binding agents:
     - Calcium agents (Ca-carbonate/ Ca-acetate)
     - Non-calcium agents (Sevelamer).
- ✓ ***↓Vit-D:***
  Cholecalciferol/ Calcitriol.
- ✓ ***↓Ca:***
  Ca-salts
- ✓ ***↑PTH:***
  Calcimimetics: Cinacalcet.

E:

1. Treat any **e**lectrolyte imbalance:

Electrolyte imbalance	***Treatment***
↓Na+	Fluid restriction

	Diuretics	
↑K+	Restriction of dietary K+ intake Regular monitoring of serum level	
Severe ↑K+	IV Ca-gluconate Counteract cardiac toxicity	
	IV Dextrose + Insulin OR Nebulized salbutamol	Shifts extracellular K+ to intracellular compartment
	Dialysis	

2. Treatment of **e**nd stage renal disease:
   a. Dialysis:
      - Hemodialysis
      - Peritoneal dialysis.
   b. Kidney transplantation.

Anemia in CKD

Pathogenesis/ mechanism:

1. ↓Erythropoietin (EPO) synthesis
2. Marrow suppression by azotemic toxins
3. ↓RBC life span
4. Coexistent iron deficiency
5. ↑Loss of folic acid (particularly in patients on dialysis)
6. Blood loss due to coagulopathy.

Clinical features:

A. Asymptomatic
B. If symptomatic:
   A. Anemic look
   B. Breathlessness
   C. Cardiac palpitation
   D. Dizziness
   E. Exercise intolerance
   F. Fatigue.

Investigation:

1. Full blood count:
    - Hb: ↓
    - Normochromic anemia.
2. Serum iron/ ferritin/ B12/ folic acid should be checked to rule out any coexisting deficiency.

Treatment:

Symptomatic treatment:

1. Packed cell transfusion
2. Correct any underlying iron deficiency: Usually IV iron supplementation is given
3. Long term s.c. EPO injection
4. Look for any other causes of anemia.

Acute kidney injury (AKI)

Definition:

Any 1 of the following:

1. Serum creatinine increases by ≥0.3 mg/dL in 48 hours
2. Serum creatinine increases by ≥1.5 times of baseline in last 7 days
3. Urine output ≤0.5 mg/kg/hr for 6 consecutive hours.

Stages:

Stage	***Increase in serum creatinine***	***Urine output***
1	1.5 times of baseline	≤0.5 ml/kg/hr for 6-12 hr
2	1.5-2.9 times of baseline	-Do- for ≥12 hr
3	≥3 times of baseline	-Do- for ≥24 hr

Oliguria:

- ✓ Urine output 100-500 ml in 24 hours
- ✓ Urine output ≤0.5 ml/kg/hr for at least 6 hours.

Anuria:

Urine output <100 ml in 24 hours.

Causes of AKI:

1. ***Pre-renal causes***:
   - Hemorrhagic shock (massive bleeding)
   - Hypovolemic shock (severe dehydration)
   - Cardiogenic shock (MI, acute LVF, acute RVF)
   - Fluid sequestration (septicemic shock, acute pancreatitis)
   - Septicemic shock (abnormal peripheral vasodilatation)
   - Severe burn (↑ Insensible loss).

2. ***Intrinsic renal causes***:
   I. Acute glomerular diseases:
      - ✓ RPGN
      - ✓ MPGN
      - ✓ IgA nephropathy.

   II. Acute tubular necrosis:
      - ✓ Ischemic (pre-renal causes)
      - ✓ Toxins (endogenous and exogenous).

   III. Acute interstitial nephritis:
      - ✓ Iatrogenic (β-lactam antibiotics)
      - ✓ Idiopathic
      - ✓ Infection (CMV).

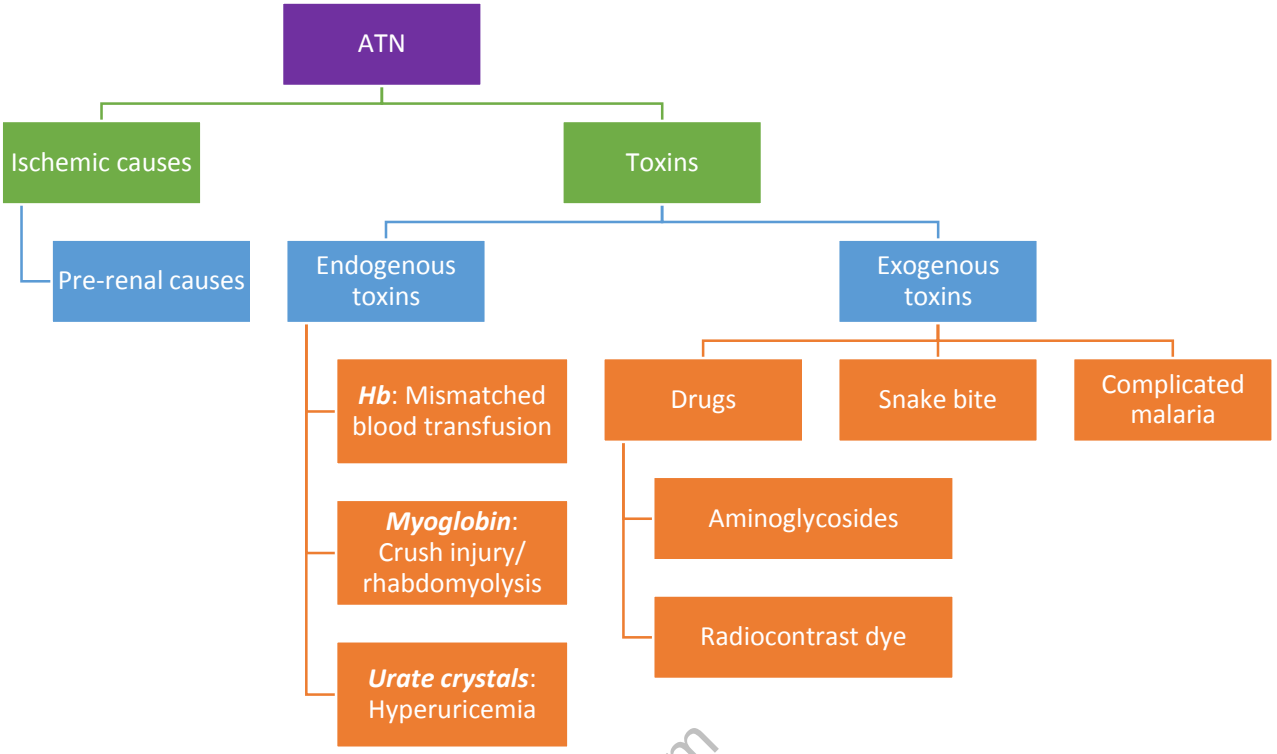
   IV. Renal vasculitis:
      - ✓ Microangiopathic hemolytic anemia
      - ✓ DIC.

3. ***Post-renal causes***:
   An obstructive uropathy can cause AKI, particularly if there is single functioning kidney:
   - Calculus
   - Carcinoma
   - Bladder outlet obstruction
   - Structure.

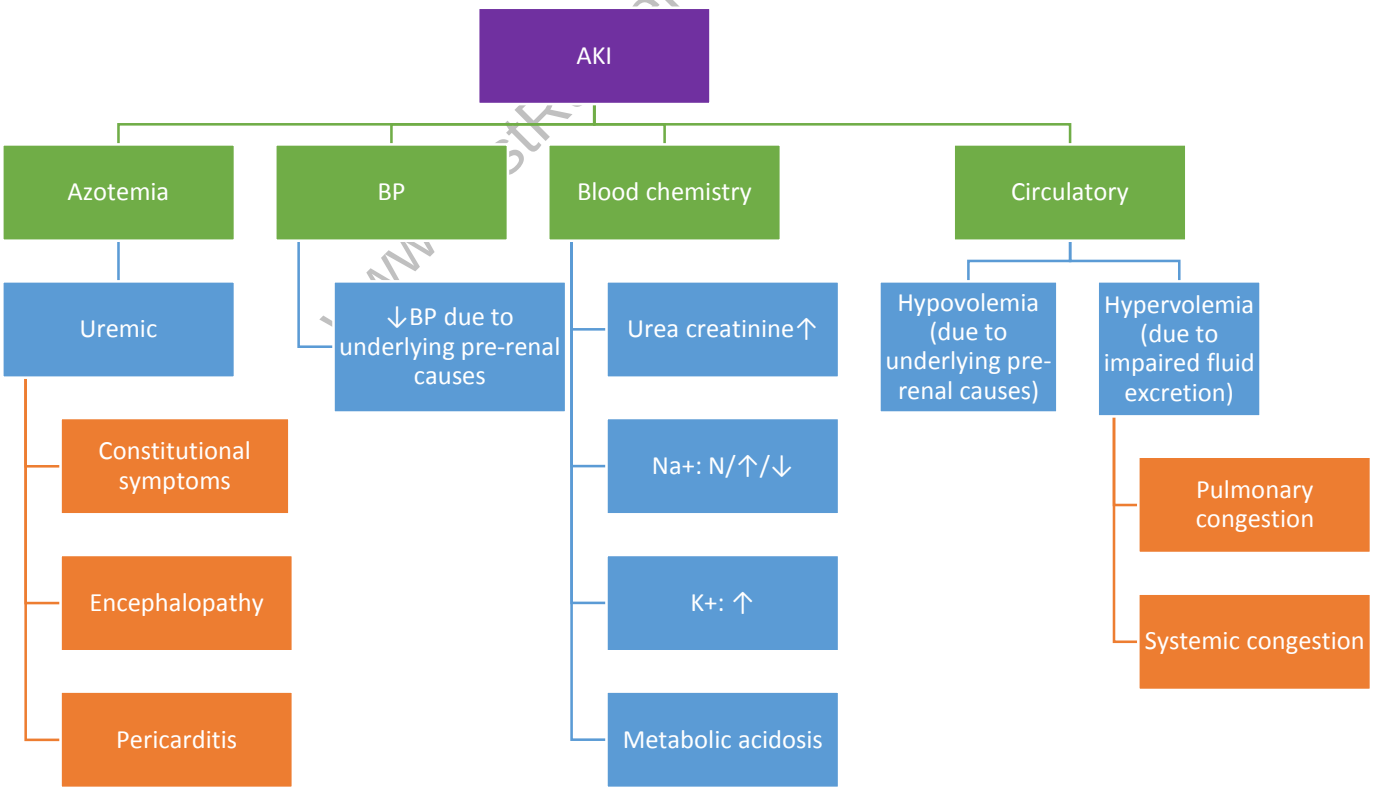
Acute tubular necrosis (ATN)

Acute tubular damage leading to acute malfunctioning of kidney.

Causes:



Pathophysiology:



Clinical features:

Cause	***Clinical features***
Azotemia	1. Constitutional symptoms: ▪ Anorexia ▪ Nausea ▪ Refractory hiccup ▪ Metallic taste in mouth ▪ Wasting of the muscles. 2. Features of encephalopathy: ▪ Altered sensorium ▪ Behavioral changes ▪ Confusion/ convulsion/ coma ▪ Delirium ▪ Flapping tremor ▪ Low GCS. 3. Features of pericarditis: Pericardial rub.
Kidney dysfunction	1. Low urine output: Oliguria/ anuria/ dark coloured urine ***Note:*** Some patients of AKI never develops oliguria/ anuria. They are called *non-oliguric AKI.* Seen in: acute interstitial disease and in some cases, acute tubular disease. 2. Volume status: ▪ Hypovolemia: H/O blood loss/ volume loss/ condition causing fluid sequestration ✓ Dry mucous membrane ✓ ↓ Skin turgor ✓ Hypotension ✓ Tachycardia ✓ ↑ Capillary refill time (≥2 sec). ▪ Hypervolemia: ✓ Symptoms and signs of pulmonary and systemic venous congestion.

Stages of progression of AKI:

Stage	***Description***
Stage of progression	Due to sudden assault on kidney, GFR abruptly decreases which in turn leads to ↓urinary output and accumulation of excessive salt, water and toxins
Stage of maintenance	Falling GFR reaches its lowest limit leading to a full blown picture of AKI
Stage of recovery	With treatment, kidney starts to regain its function. Often in this stage, recovery of tubular function (salt and water retention) lags behind recovery of glomerular function. Patient goes into polyuric phase temporarily.

Investigations of AKI:

1. Full blood count
2. Urea creatinine: ↑

$$BUN = \frac{Blood\ urea}{2.8}$$

$$\frac{BUN}{Creatinine} < 20$$

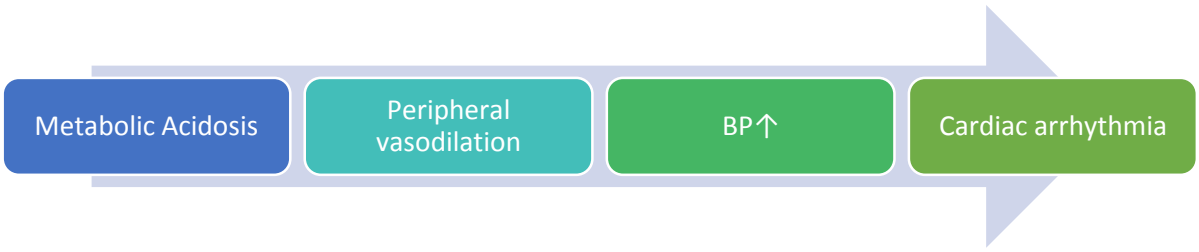
Is ***strongly suggestive of ATN***.

$$\frac{BUN}{Creatinine} > 20$$

May be found in both pre-renal/ post-renal causes of AKI.

3. Electrolyte:
   - Na+: Variable (depends upon the degree of fluid and solute loss)
   - K+: Normal/ ↑ (hypokalemia may occur in diarrhea/ overdiuresis).

4. Blood gas analysis:



5. Urine routine examination/ microscopic examination:
   Often gives vital clue of underlying causes.
   Ex.:
   Tubular cast is suggestive of ***ATN***
   RBC cast ± Dysmorphic RBCs is suggestive of ***GN***.

6. KUB-USG:
   To look for any obstructive uropathy.

7. Chest X Ray:
   To look for any pulmonary edema.

8. ECG:
   To rule out any cardiac pathology due to hyperkalemia.

9. Echocardiogram:
   IVC collapsibility/ fullness indicates volume overload and volume overloaded state respectively.

10. Investigation(s) to assess the underlying disease.
    If cause is not obvious, patients are often investigated for:
    - ✓ Underlying glomerulonephritis: Autoantibody markers
    - ✓ Endogenous toxins: Serum uric acid, Serum + urinary protein electrophoresis
    - ✓ Renal biopsy.

Treatment

General treatment:

1. Absolute bed rest till patient is stable
2. Regular monitoring of volume status:
   a. Urine output [intake-output chart]
   b. Central venous pressure measurement
   c. Echocardiogram: Status of IVC.

C. Treatment of the etiology
D. Nutrition:
   Protein and K+ restriction.
E. Avoid all nephrotoxic drugs
F. Adjust dosage of dugs according to creatinine clearance

G. Look for complications:
   - ✓ Hypo/hyper-volemia
   - ✓ Dyselectrolytemia
   - ✓ Infection.

Specific treatment:

1. Treatment of fluid imbalance:

Hypovolemia

   - ✓ IV fluid resuscitation
   - ✓ If required: Packed cell transfusion
   - ✓ Vasopressor: Noradrenaline/ Adrenaline
   - ✓ Forced diuresis: If urine output does not improve in spite of adequate fluid resuscitation; desperate attempt can be tried by giving *IV Furosemide high dose + Osmotic diuretics (Mannitol)*.

Hypervolemia

   - ✓ Salt and water restriction
   - ✓ Loop diuretics:
     - **IV***: Furosemide*
     - **Oral***: Furosemide/ Torsemide/ Metolazone*.
2. Treatment of acidosis:
   - ✓ Mild to moderate: IV $NaHCO_3$
   - ✓ Severe: Emergency diuretics.
3. Infection:
   Treat with antibiotics.
4. Treatment of uremic complications (if present)
5. Treatment of electrolyte imbalance:
   - ✓ Na+ imbalance: Treatment depends upon the underlying cause
   - ✓ Hyperkalemia:
     - K+ restriction
     - If it becomes dangerous, any of the following may be attempted:
       - ❖ IV Calcium gluconate
       - ❖ IV Dextrose + Insulin
       - ❖ Nebulized salbutamol
       - ❖ Dialysis

         Indications of dialysis:
         i. Uremic manifestations
         ii. Refractory volume overload

iii. Significant acidosis
iv. Severe hyperkalemia.

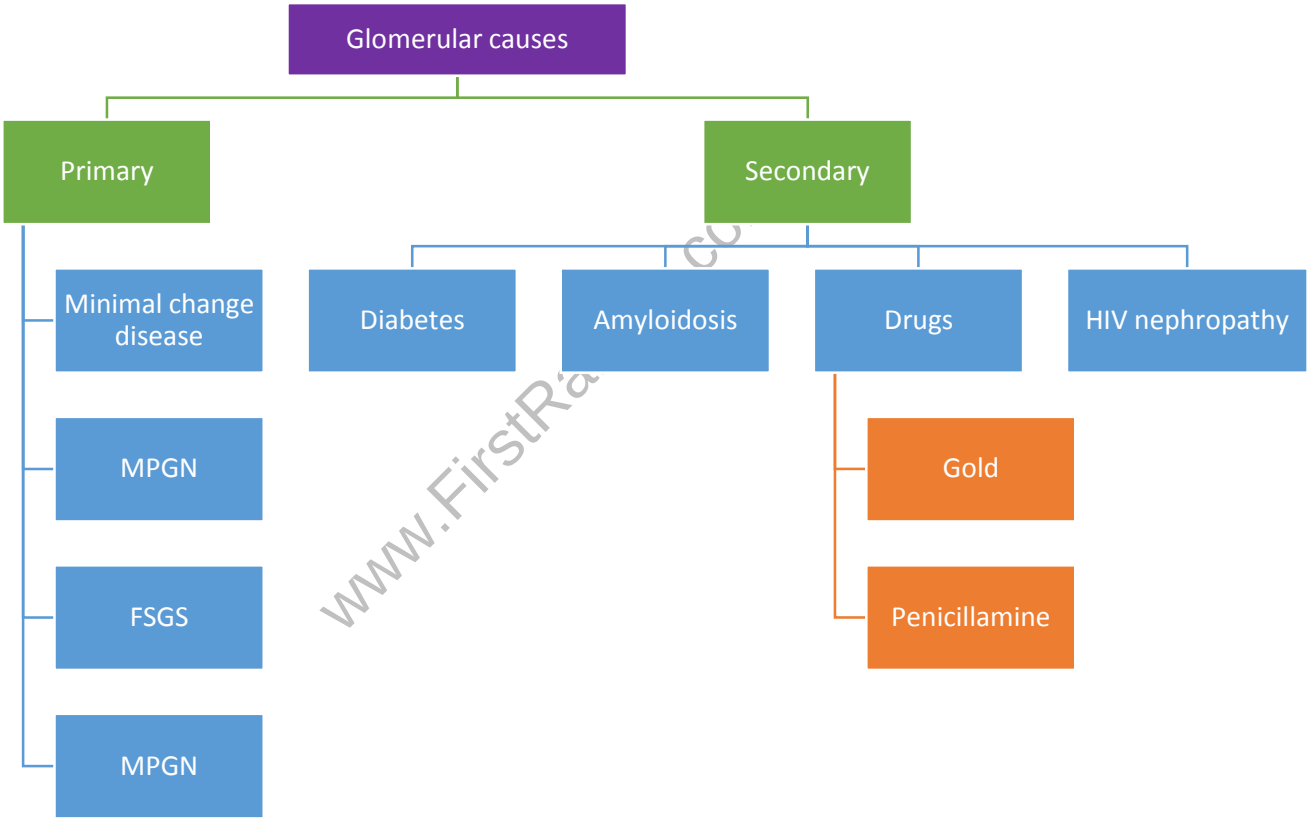
Nephrotic syndrome

Introduction:

It is a condition characterized by:

1. Heavy proteinuria (>3 gm/24 hr)
2. Hypoalbuminemia
3. Hyperlipidemia.

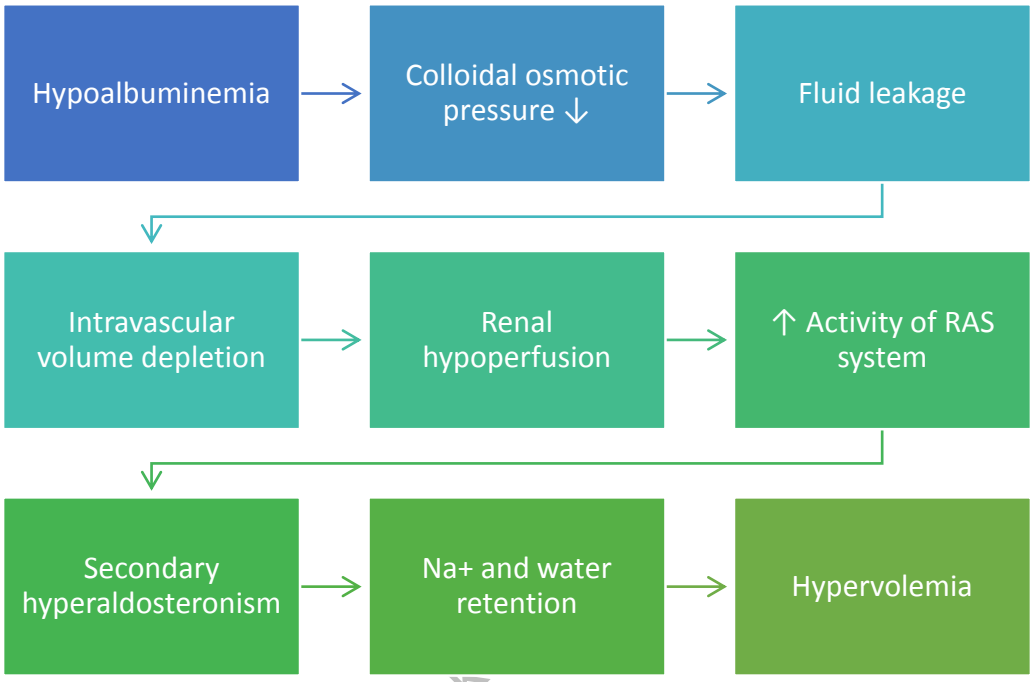
Causes:



Physiological effects:

1. ***Hypoalbuminemia***:
   Due to increased tubular permeability causing heavy proteinuria.

2. ***Hyperlipidemia***:
   I. Accelerated lipid synthesis
   II. Loss of lipid metabolizing protein.
3. ***Hypercoagulability***:
   Due to loss of circulating anticoagulant *antithrombin*.
4. ***Hypervolemia:***



5. ***Hormonal disturbance:***
   Due to loss of hormone binding proteins, causing:
   - ✓ Hypothyroidism
   - ✓ Hypovitaminosis-D.
6. ***Hypo-gamma-globulin-emia:***
   It makes the patient prone to infection.

Clinical features:

Symptoms:

- Progressive swelling of body
- Recurrent infection particularly in children
- Patient may develop unprovoked DVT; particularly *renal vascular thrombosis*, causing acute loin pain ± hematuria.

Signs:

- Edema: ++

Puffy/ swollen face with Periorbital edema.

- Ascites: ++
- Scrotal swelling
- Signs of pleural effusion: Bilaterally seen.
  - Signs and symptoms of underlying disease may be present.

Investigation:

1. ***Blood***:
   - ✓ Full blood count
   - ✓ Urea-creatinine: Derangement in renal function is often absent
   - ✓ Na+: Normal/ ↓ (due to dilutional hyponatremia)
   - ✓ Liver function test:
     - Albumin: ↓
     - Globulin: ↓
     - Liver enzymes: Normal
   - ✓ Fasting lipid profile: May be deranged as a long term complication.

2. ***Urine (routine and microscopic examination):***
   - ✓ Protein: ++
   - ✓ 24 hour urinary albumin: >3 gm.

3. ***ECG and Echocardiogram:***
   To assess cardiac function and status.

4. ***Investigations to diagnose underlying cause:***
   In primary glomerular diseases, renal biopsy confirms the diagnosis.
   However, in clinical life, often diagnosis is presumed to be MCD (minimal change disease) and MPGN (Membranoproliferative glomerulonephritis) in pediatrics and adult age groups respectively.

Treatment:

Supportive treatment:

1. Dietary salt and fluid restriction
2. Protein restriction is not needed unless kidney function is deranged
3. Loop diuretics
4. Prophylactic anticoagulation is often instituted. The agent of choice is *Warfarin*.
5. If dyslipidemia is found: then *statins* are prescribed.

Definitive treatment:

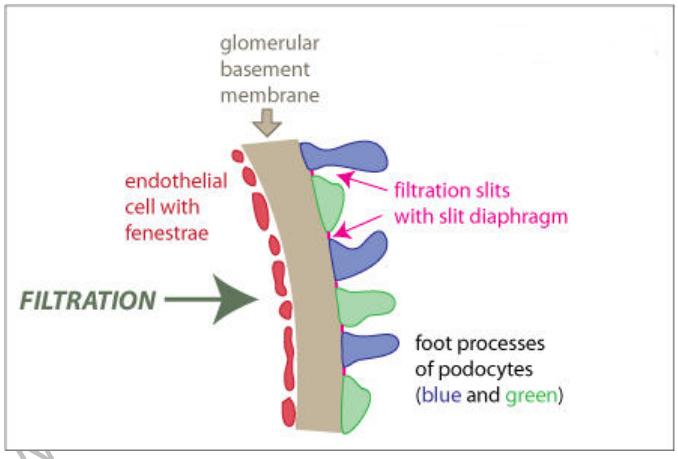
Depends upon the cause. However, in many glomerular diseases, the following drugs may be prescribed:

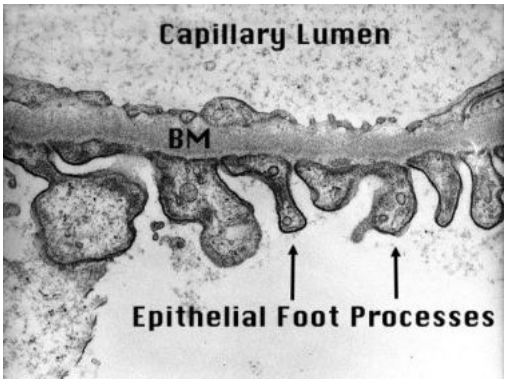
- ✓ Corticosteroid: Often patient needs long term steroid treatment
- ✓ Steroid sparing agents:
  - Mycophenolate mofetil
  - Levamisole
  - Rituximab.

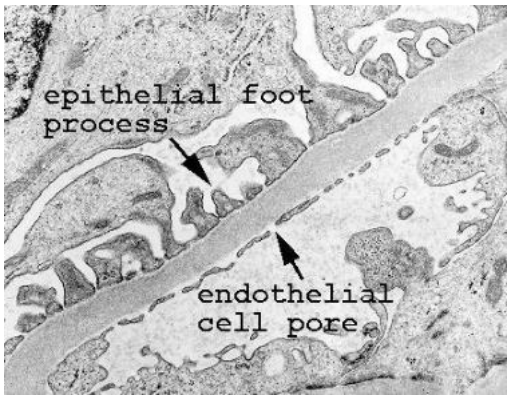
Glomerulonephritis

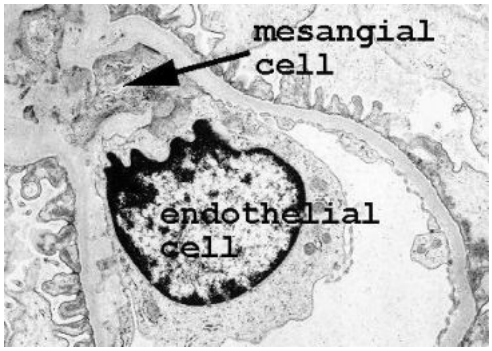
Introduction:

Inflammation of the glomerulus which may affect podocytes/ glomerular basement membrane/ endothelium.

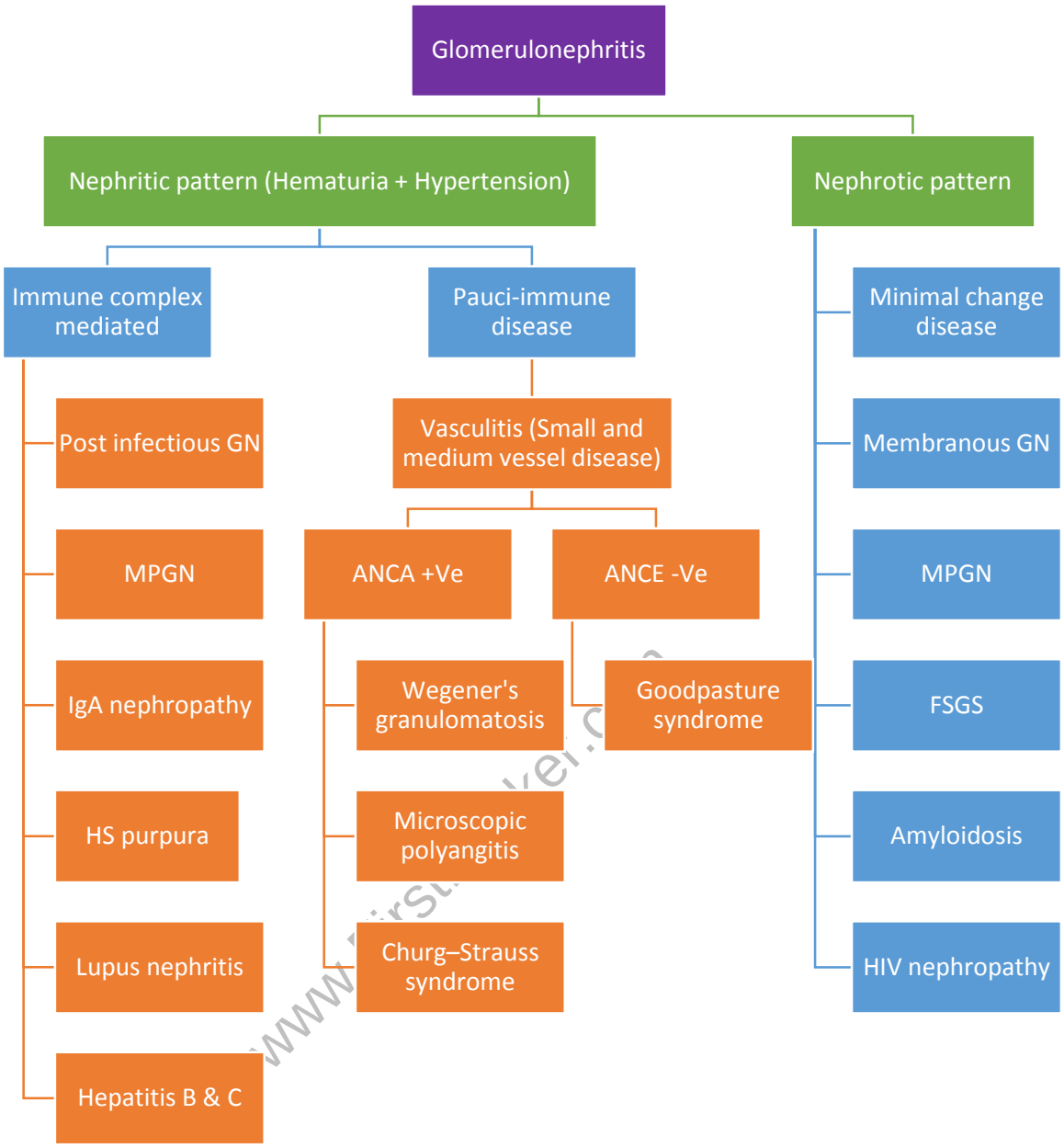








Types:



Clinical features:

Depends upon the predominant pattern:

In case of nephritic pattern

1. Hematuria (may be microscopic)
2. Progressively increasing BP
3. Constitutional symptoms: Fever, malaise, weakness. Weight loss

4. Often anemia is seen
5. AKI/ CKD can occur in some of the underlying types of GN.

In case of nephrotic pattern

1. Progressive swelling
2. Edema +ve , Ascites +ve
3. AKI/ CKD may occur depending upon the underlying lesion.

In all patients of suspected GN, particularly those coming with nephritic pattern, an underlying connective tissue disorder/ vasculitis must to be looked for.

Look for the following symptoms and signs:

1. CNS manifestations: Headache/ focal neurodeficit (suggestive of vasculitis)
2. Eye symptoms: Red/ gritty/ painful eyes (suggestive of connective tissue disorders*)
3. ENT manifestations: Wegener's granulomatosis
4. Lungs: Look for pleurisy/ pneumonitis/ acute shortness of breath (suggestive of Goodpasture syndrome); H/O asthma (suggestive of Churg–Strauss syndrome)
5. Intestinal symptoms: GI bleed, Post-prandial pain (suggestive of ischemia)
6. Vasculitic rash (suggestive of vasculitis)
7. Arthralgic manifestations (suggestive of rheumatoid arthritis).

[* Particularly, Sjogren's syndrome]

Investigations:

A. Blood:

1. Full blood count:
   - ✓ Hb: ↓ (due to hematuria/ chronic inflammation)
   - ✓ WBC: ↑ (due to chronic inflammation)
   - ✓ Platelet: Normal
   - ✓ ESR/ CRP: ↑ (due to chronic inflammation).
2. Renal function:
   Urea creatinine Na+ K+ (to rule out renal derangement)
3. Serum albumin: ↓ (in nephrotic spectrum of diseases)
4. ***Autoimmune markers***:
   - ✓ ANCA: +Ve in:
     i. Wegener's granulomatosis
     ii. Microscopic polyangitis
     iii. Churg-Strauss syndrome.

- ✓ Anti-GBM-antibody: +Ve in: Goodpasture syndrome
- ✓ Antinuclear antibody (ANA): +Ve in: SLE; to confirm: Anti-ds-DNA
- ✓ ASO titre: ↑ in PSGN.

5. Viral serology:
   - ✓ Anti-HCV
   - ✓ Anti-HIV.

B. Urine (routine and microscopic examination):

1. RBC: +Ve
2. RBC cast
3. Dysmorphic RBC
4. Proteinuria: Nephrotic range/ sub-nephrotic range.

C. 24 hour urinary albumin estimation

D. USG kidney: To assess kidney architecture

E. ECG and Echocardiogram: To assess cardiac function

F. Special tests:
Nature of which depends upon preliminary diagnosis.
If the cause of GN is obscure, patient often undergo renal biopsy to find out the exact type of disease.

Treatment:

A. Supportive treatment:
   - ✓ BP control: Antihypertensives
   - ✓ If edema present: Diuretics.

B. Definitive treatment:
Depends on exact type of underlying disease. Many patients are treated with corticosteroid/ cytotoxic/ immunosuppressive drugs.
Ex.:
Mycophenolate mofetil
Rituximab
Azathioprine.

C. Appropriate treatment of AKI/ CKD (if develops).

Post-infectious GN

Glomerulonephritis triggered by an infectious agent.

Causes:

1. β-hemolytic streptococcal infection (LRTI)
2. Staph.aureus (Infective endocarditis/ Lung abscess)
3. Rarely, post-viral/ post-fungal.

Clinical features:

- Preceding/ ongoing features of bacterial infection often present
- In case of PSGN, there is often a recent H/O severe LRTI: sore throat, cough etc.
- GN typically starts with hematuria along with progression hypertension. In PSGN, *there is almost always an asymptomatic period between LRTI and onset of hematuria*.
- Kidney dysfunction very rare.

Investigation:

1. Full blood count
2. Urea creatinine Na+ K+
3. ASO titre
4. ESR/ CRP
5. Urine: Routine and microscopic examination
6. USG KUB
7. Renal biopsy.

Treatment:

Supportive:

1. Salt restriction
2. Control of hypertension
3. Antibiotic to clear any residual infection (although its role is doubtful).

IgA nephropathy/ Berger's disease

Immune complex mediated GN which commonly occurs in children.

Clinical features:

- Recent history of LRTI: Fever, sore throat, cough often present
- GN: Mostly present with hematuria and progressive hypertension. Usually, *no latent period between LRTI and onset of hematuria is present*.
- Renal dysfunction not common.

Investigation:

1. Full blood count
2. Urea creatinine
3. ASO titre (not raised)
4. Urine: R/E and M/E
5. USG KUB
6. Renal biopsy: Shows mesangial IgA deposition.

Treatment:

Supportive: Control of hypertension.

Henoch-Schonlein Purpura (HSP)

It is a type of small vasculitis affecting children.

Clinical features:

- ***H***/O preceding episode(s) of URTI/LRTI
- ***H***ematuria due to GN
- ***S***keletal change: Arthralgia
- ***S***mall bowel ischemia: Leading to abdominal pain and melena
- ***P***urpura: Typically small purpuric spots appear extensively over the buttocks and posterior compartment of lower limb; usually palpable purpura.

Investigation:

A. Blood:
   I. Full blood count
   II. Urea creatinine: Permanent renal dysfunction is rare
   III. ASO titre: Not raised

IV. ESR/ CRP: ↑

B. Urine: R/E and M/E
C. USG
D. Renal biopsy: Typically shows deposition of IgA and C3
E. Skin lesion shows: Leukocytoclastic vasculitis.

Treatment:

- Supportive:
  I. Salt restriction
  II. Control of hypertension
- Definitive: In severe cases; Rituximab/ Plasma exchange may be offered.

Minimal change disease (MCD)

Commonest nephrotic pattern glomerulopathy in children; rarely may occur in adults.

Clinical features:

Typically presents with features of nephrotic syndrome:

- Progressive swelling
- Edema: +Ve
- Ascites: +Ve
- Signs of bilateral pleural effusion: +Ve
- Hypertension may occur.

Investigations:

A. Blood:
   I. Full blood count
   II. Urea creatinine: Mostly normal
   III. Na+ : ↓ (dilutional hyponatremia)
   IV. K+: Normal
   V. Serum albumin: Typically ↓.
B. Urine (R/E and M/E):
   24 hour urinary protein >3 gm
C. Renal biopsy: Typically shows *loss of foot processes (effacement) of podocytes*.
   Rarely required, as mostly the disease is presumed.

Indications of renal biopsy:

I. Steroid resistant cases (proteinuria doesn't significantly decreases even after 4 weeks of corticosteroid)
II. Steroid dependent cases.

Treatment:

A. Supportive: Salt and fluid restriction, Diuretics.
B. Definitive:
   I. Corticosteroids
   II. Steroid sparing agents (Mycophenolate mofetil).

Membranous nephropathy

Commonest nephropathy in adults.

Causes:

1. Mostly idiopathic: Immune complex deposition occurs in glomerular capillary wall
2. Secondary causes:
   I. Malignancy (Lung CA)
   II. Infection (HepB, Syphilis)
   III. Drug induced (Captopril).

Investigation:

Same as above.

Renal biopsy: Shows deposition of IgG + C3.

Treatment:

A. Supportive:
   I. Salt and fluid restriction
   II. Diuretics
   III. Control of hypertension (ACE-I/ ARB).
B. Definitive:
   I. Cyclophosphamide
   II. Cyclosporine
   III. Chlorambucil.

Urinary tract infection (UTI)

Infection anywhere in the urinary passage.

Site of infection:

1. Kidney: Pyelonephritis
2. Urinary bladder: Cystitis
3. Urethra: Urethritis.

Organisms:

- ✓ E.coli
- ✓ Klebsiella
- ✓ Proteus
- ✓ Enterococci
- ✓ Pseudomonas.

Clinical features:

A. ***Constitutive symptoms***:
   - Fever ± chill and rigor, malaise
   - Anorexia + nausea
   - Vomiting (Pyelonephritis -> Fever-> Loin pain + Vomiting)
   - Confusion, drowsiness (particularly in elderly patients).

B. ***Urinary symptoms***:
   - Dysuria: Burning sensation during micturition
   - Mild hematuria
   - Suprapubic pain (cystitis)
   - Symptoms due to prostatitis: Urgency, frequency
   - Kidney: New onset loin pain (pyelonephritis)
   - Urinary incontinence (often occurs in elderly population).

Investigation:

1. Blood:
   - ✓ WBC count: ↑ (predominantly neutrophils)
   - ✓ ESR/ CRP: ↑.
2. Urine analysis (R/E and M/E):
   - ✓ Pus cells: +Ve (it is called significant pyuria when cell count > 7-10/ HPF)
   - ✓ Protein: +Ve
   - ✓ RBC: +Ve

- ✓ Microorganism may be seen.

3. Urine culture and sensitivity:
   Significant bacteruria is said to be present when no. of CFU > 10^5/ml.
   Special note on drug sensitivity:
   I. Usually the organisms are sensitive to ***Cotrimoxazole*/ *Nitrofurantoin***.
   II. **ESBL (Extended spectrum β-lactamase) producing organisms**: These organisms are usually resistant to traditional β-lactams (including fluoroquinolones) and sensitive to Carbapenem.
   III. **Carbapenemase producing organisms:** These organisms are sensitive to Aztreonam.
4. Imaging studies:
   Females with recurrent episodes of UTI/ males after 1st episode of UTI should ideally be investigated for any underlying structural/ functional abnormality of urinary passage. Therefore, they should undergo an USG-KUBP.

Treatment:

Antibiotics:

Empirical antibiotics:

Choice of drug:

Depends upon:

1. Severity of infection
2. Any previous urine culture-sensitivity report.

Any of the following drugs:

1. Fluoroquinolone: Ciprofloxacin/ Levofloxacin/ Ofloxacin
2. Cotrimoxazole
3. Nitrofurantoin.

In severe cases, if there is previously documented result of ESBL +Ve organisms:

1. Ertapenem
2. Meropenem + Imipenem

All empirical drugs administered should be modified according to urine culture-sensitivity report.

Duration of treatment:

Usually 5-7 days, however, in pyelonephritis, at least 10-14 days.

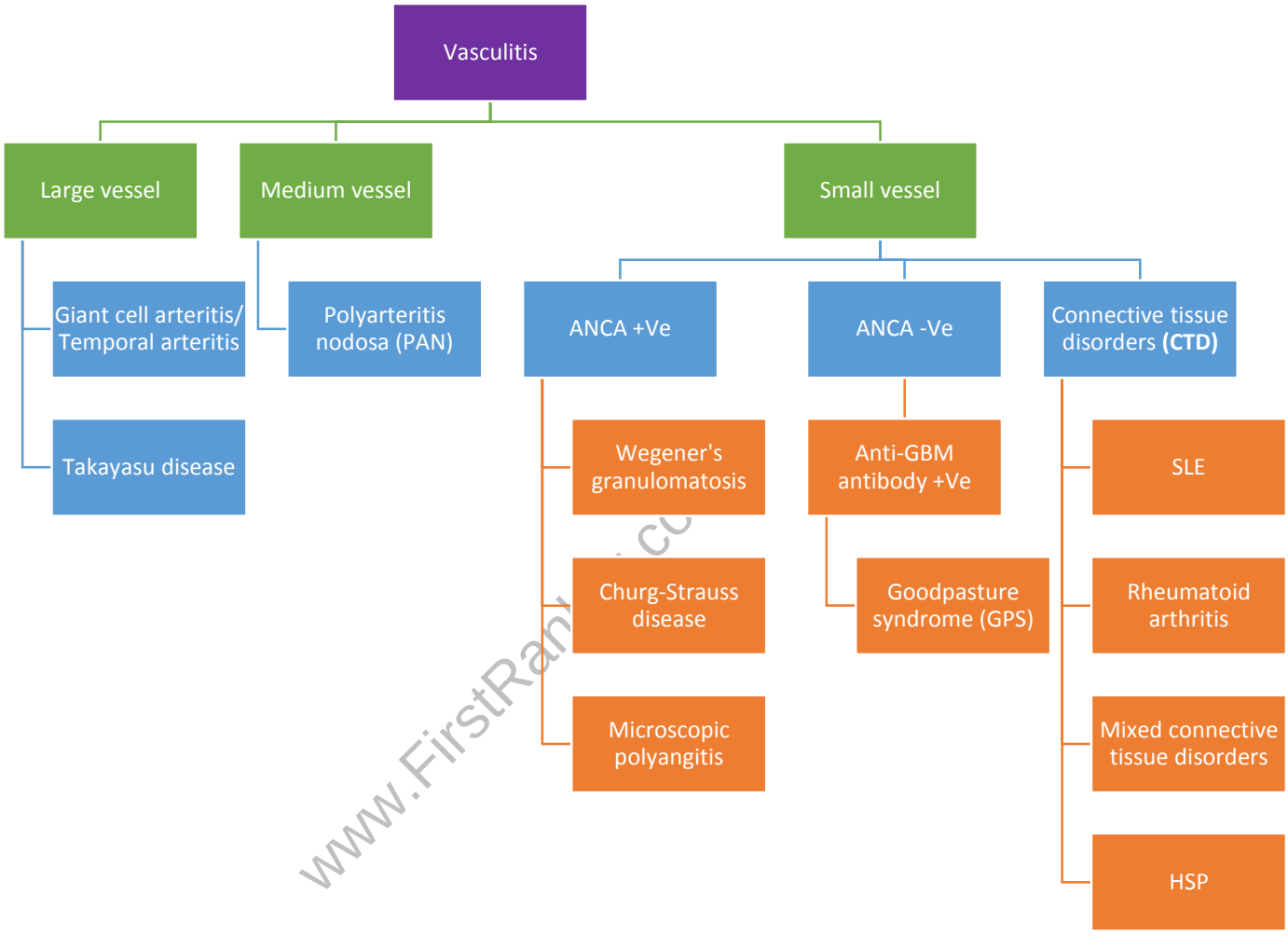
Preventive measures:

- ✓ Personal hygiene
- ✓ Plenty of fluid
- ✓ Any structural/ functional defect should be treated:
  Ex:
  Urethral stricture
  Bladder outlet obstruction
  Vesico-ureteral reflux.

Vasculitis

A group of disorders characterized by inflammation of wall of the vein, arteries and capillaries.

Classification:



A vasculitis can be a primary/ secondary vasculitis due to an underlying connective tissue disorder/ malignancy/ infection/ drug induced.

Approach to a patient of vasculitis

Principle:

1. To suspect vasculitis even if there is no obvious manifestation of it

2. To look for systemic manifestations
3. To look for organ specific manifestations
4. To look for underlying disease.

History:

1. Systemic manifestations:
   - ✓ Low grade fever
   - ✓ Loss of appetite
   - ✓ Loss of weight
   - ✓ Lassitude.
2. Organ damage:
   Look for the following histories:

Organ/ system	***Manifestations of damage***	***Inference***
CNS	Headache/ seizure/ TIA/ stroke*	Stroke in a young patient: always suspect vasculitis
Eye	Red eye/ gritty eye/ painful eye	Connective tissue disorders
ENT	Blocked nose/ epistaxis/ crusting/ ulceration/ ear infection	Wegener's granulomatosis
CVS	Angina (coronary vasculitis)	Takayasu's disease
Respiratory	Asthma	Churg-Strauss disease
	Sudden breathlessness ± Hemoptysis	Goodpasture syndrome
	Recurrent pneumonia	Connective tissue disease
GIT	Melena/ Post-prandial pain	Intestinal ischemia
Renal	Hematuria/ history suggestive of AKI/ CKD	-
Skin	Skin rash	Vasculitic rash
Joint	Joint pain ± Swelling	Rheumatoid arthritis

   - Above questions are asked to screen for any organ involvement. Distribution of organ involvement depends upon the underlying type of vasculitis.
3. Underlying cause:
   - ✓ Infection (infective endocarditis/ meningococcemia/ typhoid fever)
   - ✓ Connective tissue disease
   - ✓ Malignancy
   - To be ruled out if possible.

Examination:

Organ/ system	***Look for:***
Eye	Any evidence of uveitis

ENT	Crusting/ granulations/ septal perforation
Skin	Skin rash: Palpable purpura; Petechiae: suggestive of cutaneous vasculitis. Typical rash for CTDs should be looked for.
CVS	Signs of pericarditis/ pericardial effusion (suggestive of CTD)
Respiratory	1. Pleurisy/ pleural effusion: CTD 2. Widespread crepitations: GPS 3. Focal signs of pneumonia: CTD
Joint	Small joint arthritis: CTD

Investigations:

BLOOD

A. Routine investigations:
   1. Full blood count: Hb↓ (due to chronic inflammation/ ongoing hematuria/ GI bleed/ alveolar hemorrhage)
   2. WBC: ↑ (often ↓ in SLE)
   3. Platelet: Normal
   4. ESR/ CRP: ↑
B. Blood culture:
   To rule out any underlying bacterial infections.
C. Urea-creatinine: To assess any renal derangement
D. Serum auto antibodies:
   - ✓ ANCA (Anti-neutrophil cytoplasmic antibody):
     It is of 2 types:
     I. ***c-ANCA*** (Cytoplasmic pattern):
        Target antigen: Proteinase-3 (PR3)
        +Ve in:
        - ➢ Wegener's granulomatosis.

     II. ***p-ANCA*** (Perinuclear pattern):
        Target antigen: Myeloperoxidase (MPO)
        +Ve in:
        - ➢ Microscopic polyangitis
        - ➢ Churg-Strauss syndrome.
   - ✓ Anti-GBM antibody:
     +Ve in Goodpasture syndrome.

- ✓ Anti-nuclear antibody:
  +Ve in SLE (Confirm with Anti-ds-DNA).
- ✓ Anti-CCP antibody/ RA factor:
  +Ve in Rheumatoid arthritis.

URINE

Routine and microscopic examination of urine: To look for:

- ✓ RBC
- ✓ RBC cast
- ✓ Dysmorphic RBC.

BIOPSY

- To confirm diagnosis.
- Common site of taking biopsy: Kidney, skin.

IMAGING

- Chest X-Ray: To look for nodules/ cavity (suggestive of Wegener's)
- If positive: Do a CE-CT chest.

Echocardiogram

To look for infective endocarditis.

USG-KUB

To look for any structural / functional abnormality of urinary passage.

Treatment:

Specific treatment depends upon the type of vasculitis; however, the mainstay of treatment are:

1. Corticosteroid

2. Immunosuppressants:
   - ✓ Cyclophosphamide
   - ✓ Azathioprine.

Wegener's granulomatosis

Vasculitis characterized by necrotizing granulomatous inflammation of vessels.

Clinical features:

System	***Manifestations***
ENT	• Recurrent episodes of epistaxis/ nasal crusting/ nasal ulceration • Recurrent otitis media • Recurrent septal perforation.
Eye	Uveitis
Lung	Multiple cavitations/ nodules/ cavitary pneumonia May be asymptomatic/ may cause breathlessness/ productive cough.
Kidney	Glomerulonephritis→ Hematuria ± Hypertension
Limbs	Recurrent DVTs

Investigations:

1. Blood:
   - ✓ Hb: ↓
   - ✓ WBC: ↑
   - ✓ ESR/ CRP: ↑
2. Urea creatinine: To rule out renal dysfunction
3. c-ANCA: Characteristically +Ve and a high titre is often a predictor of severe disease.
4. Urine R/E and M/E: Look for RBC cast and dysmorphic RBCs.
5. CXR ± CECT chest
6. Biopsy:
   Site: Lung, kidney.

Goodpasture syndrome

Vasculitis characterized by acute reno-pulmonary involvement.

Clinical features:

1. ***Pulmonar***y: Typically abrupt onset *severe intra-alveolar hemorrhage*; sudden shortness of breath, productive cough; often blood mixed/ frank hemoptysis.
2. ***Renal***: RPGN: Hematuria, hypertension.
3. Often patient becomes significantly anemic.

Investigation:

1. Full blood count:
   - ✓ Hb: ↓
   - ✓ WBC: ↑
   - ✓ ESR: ↑.
2. Anti-GBM antibody: +Ve
3. CXR: Diffuse bilateral alveolar opacities (resembling cardiogenic/ non-cardiogenic pulmonary edema)
4. CECT chest: If possible
5. Urine (R/E and M/E): Look for RBC, RBC cast, Dysmorphic RBC.

Treatment:

1. Supportive: Ventilatory supports
2. Definitive: Corticosteroid, Cyclophosphamide.

Churg-Strauss syndrome

ANCA +Ve small vessel vasculitis.

Clinical features:

1. Background *H/O asthma* often present which is often difficult to control (however, cases may also develop in non-asthmatics)
2. Mononeuritis/ Mononeuritis multiplex: Rapid damage of a motor neurone; causing sudden foot drop/ ocular cranial nerve paralysis
3. Eye: Scleritis/ Episcleritis/ Uveitis
4. Skin: Rash/ vasculitic rash
5. Kidney: Usually spared.

Investigation:

1. Full blood count: Eosinophilia
2. Autoantibody: p-ANCA +Ve.

Treatment:

Corticosteroid ± Cyclophosphamide.

Lupus nephritis (LN)

Renal complication of SLE.

Clinical features:

1. Usually presents with nephritic pattern of disease: hematuria, hypertension
2. Renal dysfunction: Gradual/ rapidly progressive in nature.

Types:

Grade	***Name***
Grade 1	Minimal mesangial
Grade 2	Mesangio-proliferative
Grade 3	Focal
Grade 4	Diffuse
Grade 5	Membranous
Grade 6	Advanced

Each stage can be further divided into:

- Acute (A)
- Chronic (C)
- Acute on chronic (A/C).

Investigation:

1. Urea creatinine
2. Urine (R/E and M/E):
   Look for RBC, RBC cast, Proteinuria, Dysmorphic RBC.
3. Serum autoantibodies:
   - ✓ ANA
   - ✓ Anti-ds-DNA.
4. Renal biopsy.

Treatment:

1. Supportive: For renal dysfunction

2. Definitive:
   - Corticosteroid
   - Immunosuppressants:
     - ✓ Cyclophosphamide
     - ✓ Mycophenolate
     - ✓ Azathioprine
     - ✓ Tacrolimus.

Behçet's disease

Small and medium vessel vasculitis which has no diagnostic test.

Clinical features:

1. Recurrent painful oral aphthous ulcer
2. Recurrent painful genital ulcer
3. Skin:
   - ✓ Erythema nodosum like lesion
   - ✓ Follicular skin rash
   - ✓ Pathergy: Spontaneous blistering of venipuncture site.
4. Eye: Posterior uveitis
5. CNS:
   - ✓ Seizure
   - ✓ Cranial nerve palsy
   - ✓ Meningitis.
6. Recurrent DVT (hypercoagulable state).

Investigation:

No diagnostic test available.

Treatment:

1. Corticosteroid
2. Colchicine
3. Thalidomide
4. Immunosuppressants:
   - ✓ Rituximab
   - ✓ Cyclophosphamide.