Renal Pathology

By Mateusz Gortat

Overview

- Recap of general properties and anatomy of the kidney
- Acute kidney injury and Chronic kidney disease
- Nephrotic and Nephritic syndromes

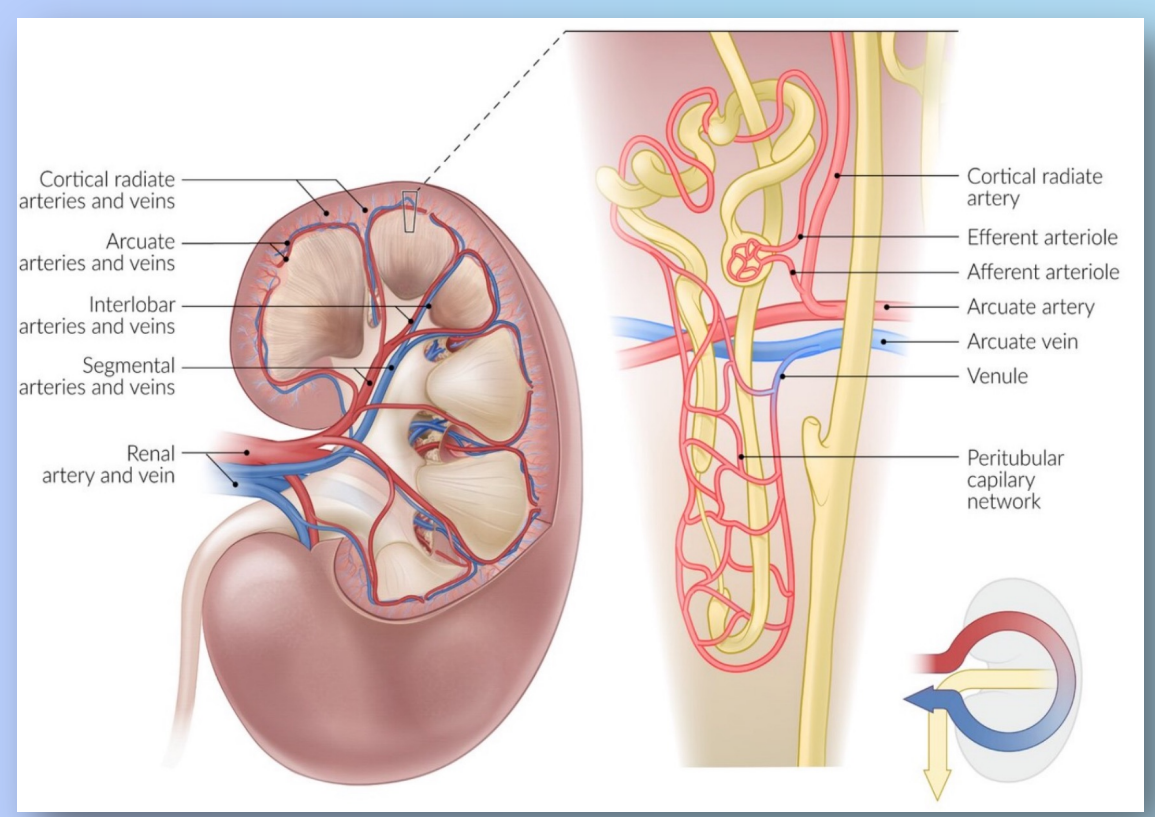
What does the kidney do?

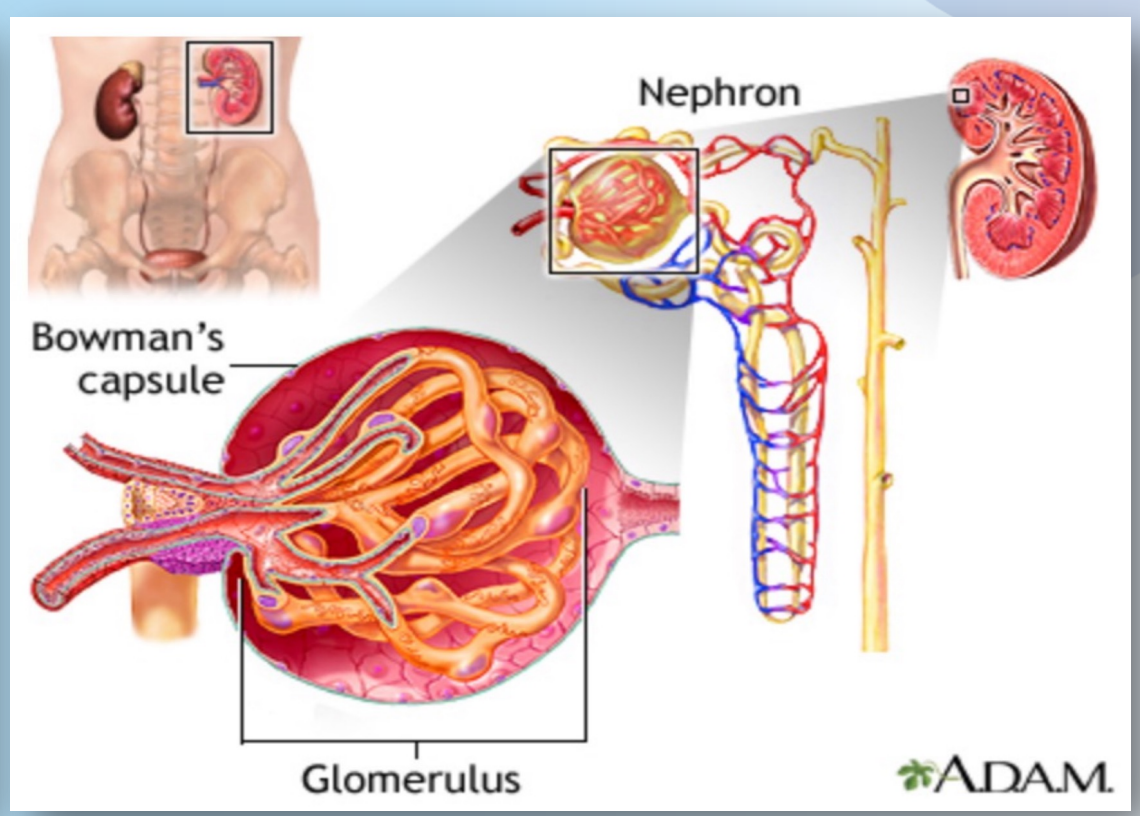
- **Filtration of blood:**
  - Excretes waste products
  - Excessive amounts of electrolytes
- **Homeostasis:**
  - pH
  - Volume
  - Pressure
  - Osmolality
- **Production:**
  - Vitamin D
  - Erythropoietin

Typical signs of renal pathology:

- Increased waste products in serum
  - Azotemia
  - Hyperkalemia
- Oliguria/Anuria
- Proteinuria
- Hematuria

Anatomy recap



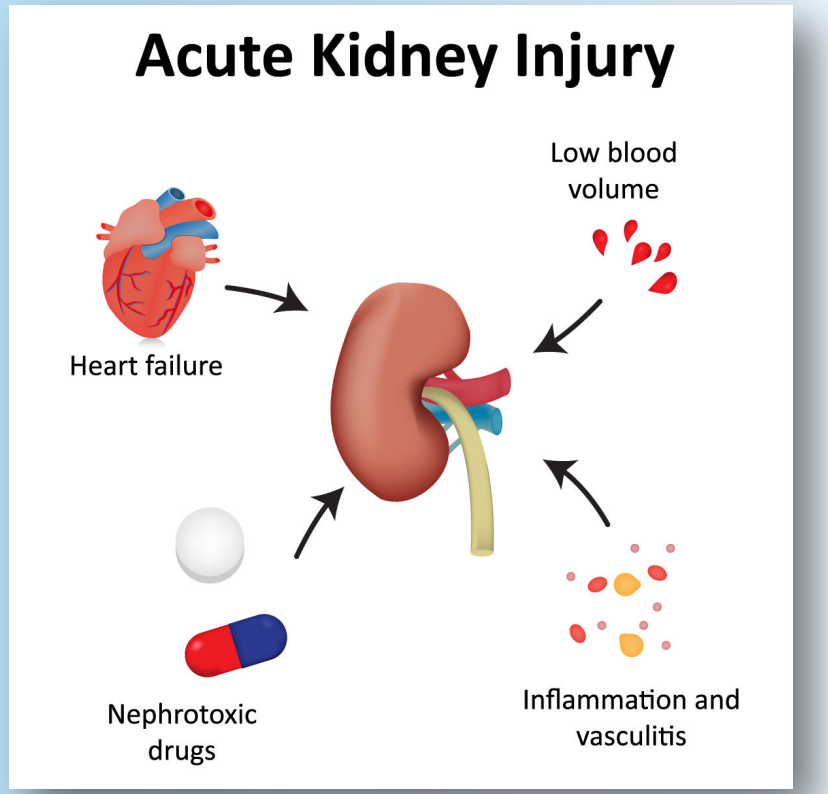


Each kidney consists of millions of nephrons, the functional filtration units, which produce urine

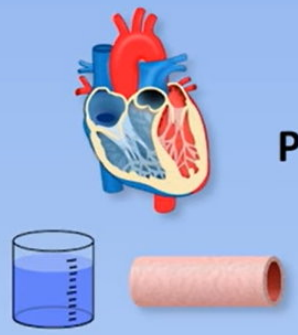
The glomerulus is where the filtration process is initiated and is crucial for the functioning nephron

Acute Kidney Injury

- Sudden and rapid decline in kidney function and filtration
  - Usually within 48 hours of inciting event
- Broken down by underlying cause:
  - Prerenal
  - Intrarenal
  - Postrenal
- Hallmark presentation
  - Azotemia (Usually measured using BUN)
  - Oliguria
- Further injury leads to decrease in endocrine and regulatory functioning

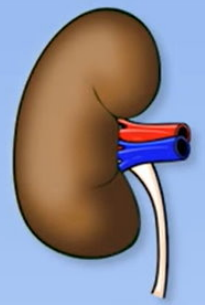


Acute Kidney Injury (AKI)
Prerenal vs. Intrarenal vs. Postrenal Paradigm



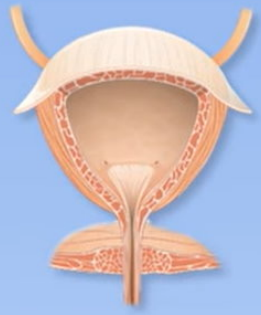
Prerenal

- Dehydration*
- Heart failure
  (a.k.a. cardiorenal syndrome)
- Liver failure
  (a.k.a. hepatorenal syndrome)



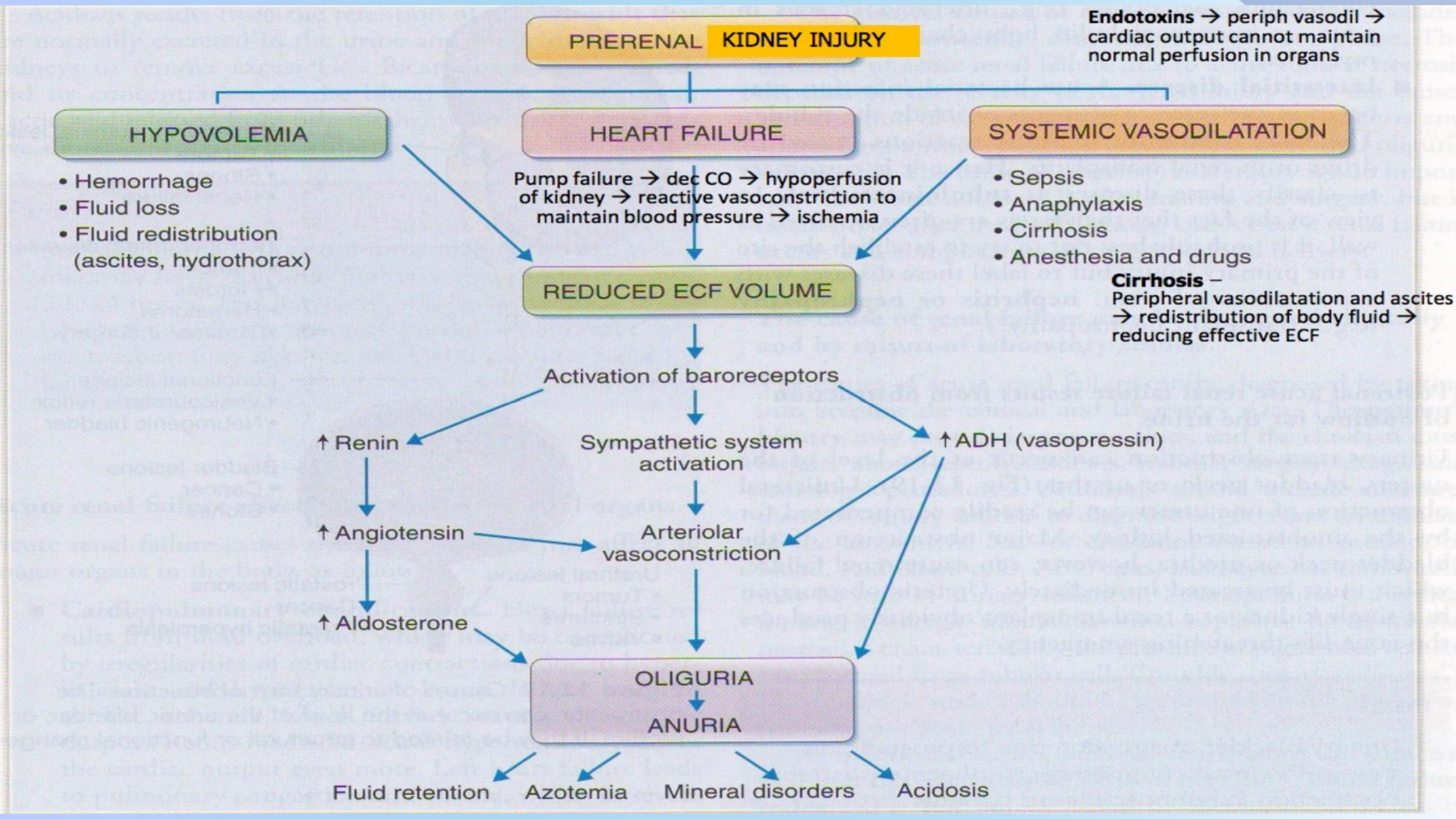
Intrarenal

- Intrinsic renovascular disease
  - Hypertensive emergency
  - Small vessel vasculitis
  - TTP / HUS
- Glomerular disease
  - Post-infectious glomerulonephritis
- Tubulointerstitial disease
  - Acute tubular necrosis (ATN)*
    (causes: sepsis, meds, contrast, rhabdo, prolonged prerenal AKI)
  - Acute interstitial nephritis (AIN)



Postrenal

- Ureteral obstruction
  (usually requires bilateral obstruction)
- Neurogenic bladder
- Urinary tract infection
- Medications
- Benign prostatic hypertrophy (BPH)


PRERENAL KIDNEY INJURY
Endotoxins → periph vasodil → cardiac output cannot maintain normal perfusion in organs
HYPOVOLEMIA
HEART FAILURE
SYSTEMIC VASODILATATION
• Hemorrhage
• Fluid loss
• Fluid redistribution (ascites, hydrothorax)
Pump failure → dec CO → hypoperfusion of kidney → reactive vasoconstriction to maintain blood pressure → ischemia
• Sepsis
• Anaphylaxis
• Cirrhosis
• Anesthesia and drugs
Cirrhosis – Peripheral vasodilatation and ascites → redistribution of body fluid → reducing effective ECF
REDUCED ECF VOLUME
Activation of baroreceptors
↑ Renin
Sympathetic system activation
↑ ADH (vasopressin)
↑ Angiotensin
Arteriolar vasoconstriction
↑ Aldosterone
OLIGURIA
ANURIA
Fluid retention
Azotemia
Mineral disorders
Acidosis

BUN/Cr ratio

Normal

- Creatinine is excreted in PCT
- BUN is reabsorbed
- **Normal BUN:Cr ratio = ~15**

Prerenal

- RAAS activation
- More water reabsorbed
- Therefore, more BUN reabsorbed
- **BUN:Cr ratio >15**

Intrarenal

- Cr isn't excreted well; buildup of creatinine makes **BUN:Cr<15**

Postrenal

- Similar to intrarenal but has progressions
- Early
  - **BUN:Cr>15**
  - Backflow pushes BUN back into the blood
- Late
  - **BUN:Cr<15**
  - Tubular damage

Chronic Kidney Disease

STAGES OF CHRONIC KIDNEY DISEASE		GFR*	% OF KIDNEY FUNCTION
Stage 1	Kidney damage with **normal** kidney function	90 or higher	
Stage 2	Kidney damage with **mild loss** of kidney function	89 to 60	
Stage 3a	**Mild to moderate** loss of kidney function	59 to 45	
Stage 3b	**Moderate to severe** loss of kidney function	44 to 30	
Stage 4	**Severe** loss of kidney function	29 to 15	
Stage 5	Kidney **failure**	Less than 15	

- Clinically defined as 3 months of ↓ GFR (<60ml/hr or Cr ~2)
- Due to abnormal kidney structure or function
- Leads to decreased excretory and regulatory function of the kidney

- Most common causes of CKD include:
  - Diabetes
  - HTN
  - Glomerulonephritis
- Can lead to severe cardiovascular, pulmonological, neurological and hematological conditions

CKD Pathogenesis

Irreversible loss of nephrons

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Normal nephrons compensate for lost nephrons by increasing their filtration

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Increased renal blood flow and hyperfiltration

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Hemodynamic overload of nephrons

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Fibrosis/scarring leads to glomerulosclerosis

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Nephron destruction and loss

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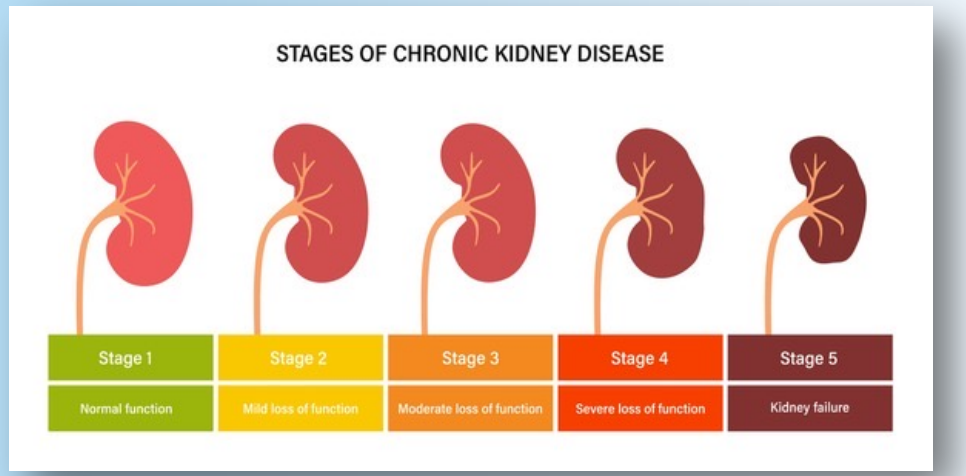
Loss of all kidney function



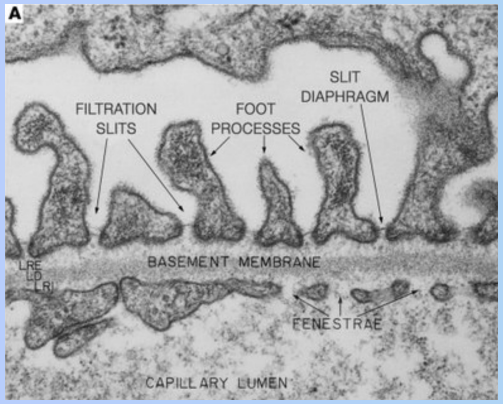
CKD continued

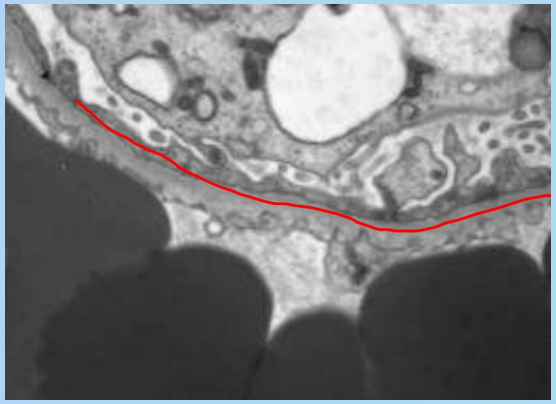
- The consequences of chronic renal failure can be remembered by the mnemonic: **MAD HUNGER**
- **M.A.**: Metabolic Acidosis
- **D**: Dyslipidemia (especially increased triglycerides)
- **H**: Hyperkalemia
- **U**: Uremia
- **N**: Na^+/H_2O retention
- **G**: Growth retardation and developmental delay
- **E**: Erythropoietin failure (anemia)
- **R**: Renal osteodystrophy

Nephrotic vs. Nephritic syndrome

Nephrotic syndrome

- **O** for Pr**O**tein
- Signs and symptoms that indicate damage to the glomerular filtration barrier itself





Nephritic syndrome

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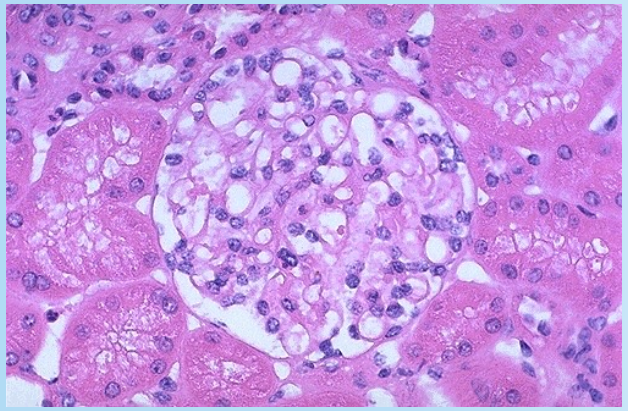
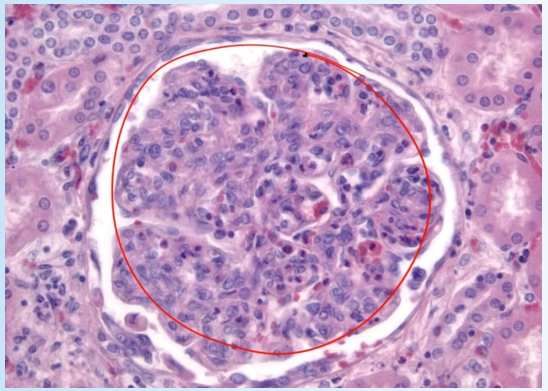
- Signs and symptoms due to glomerular capillary damage due to inflammation





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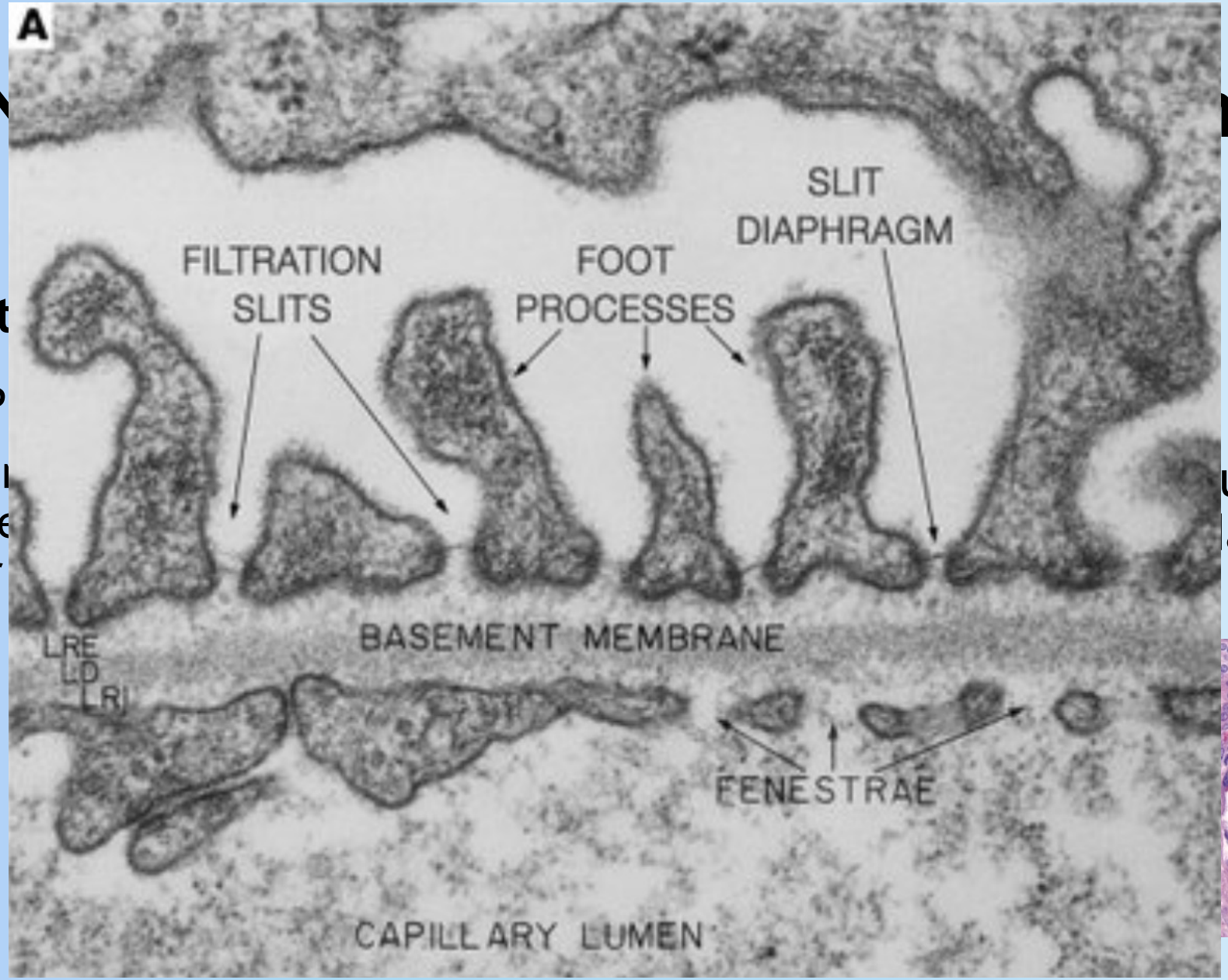
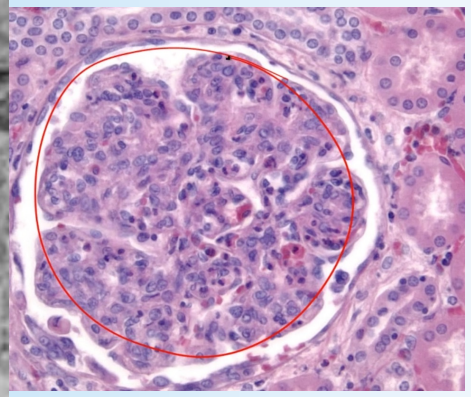
Nephrot

- **O** for P
- Signs a ue to damage amage due barrier





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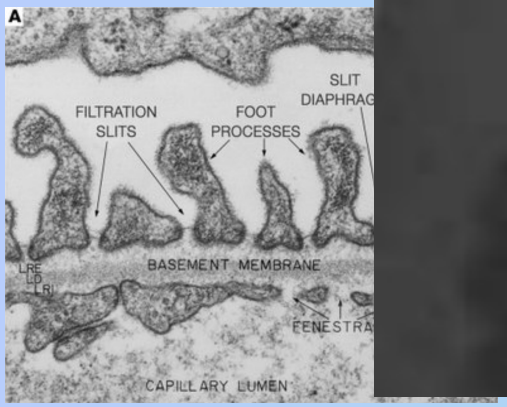

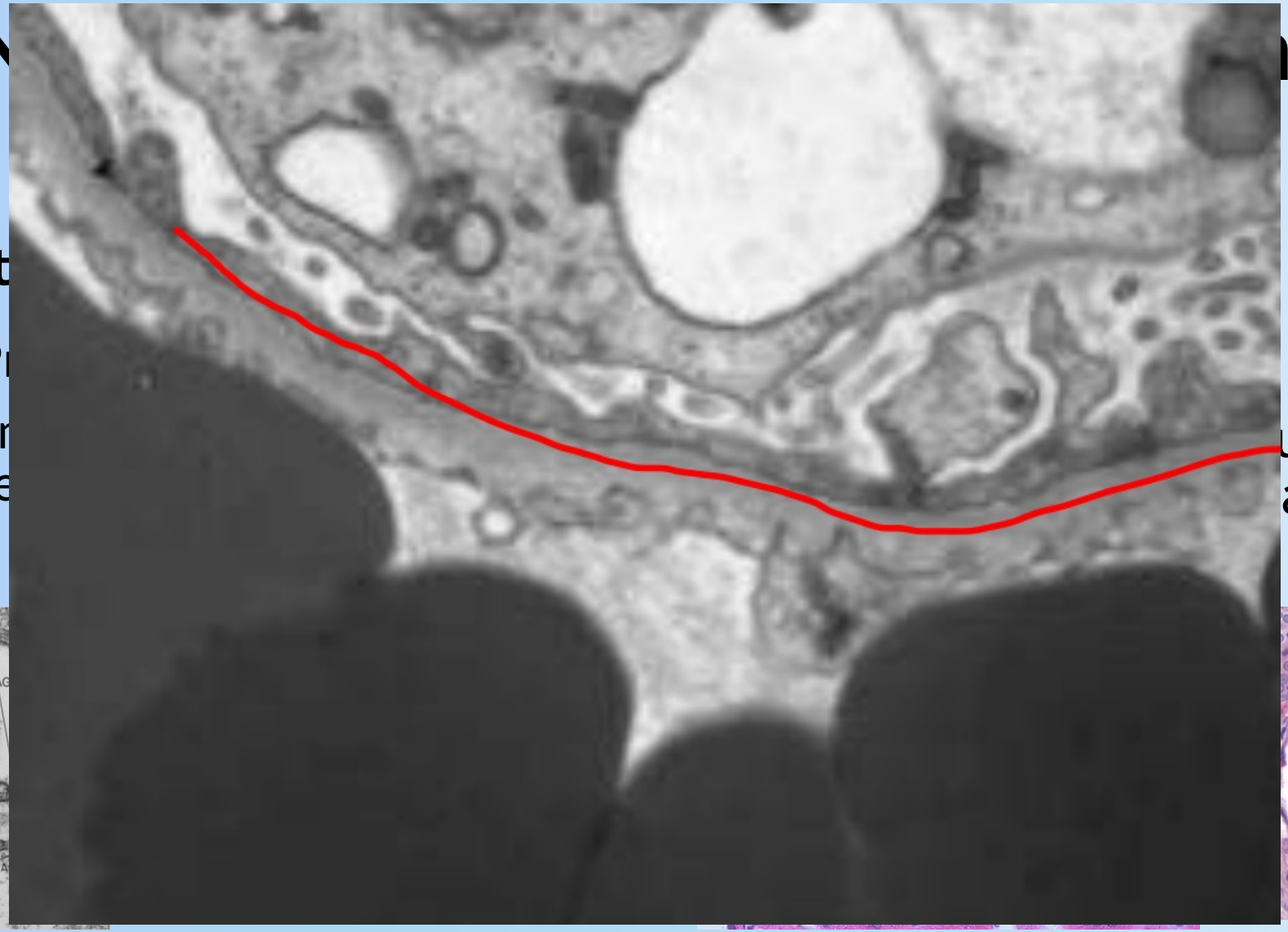

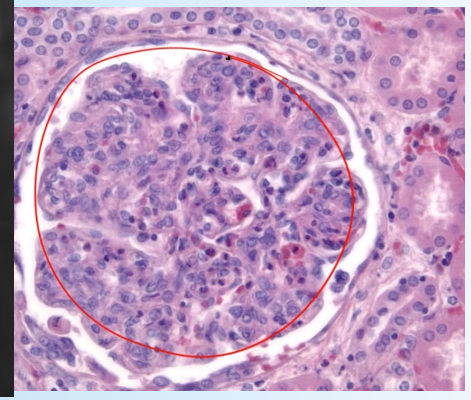

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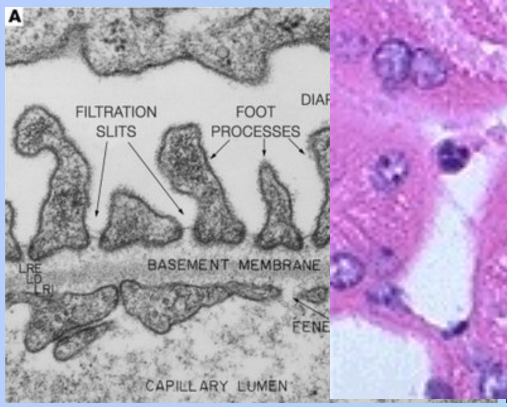

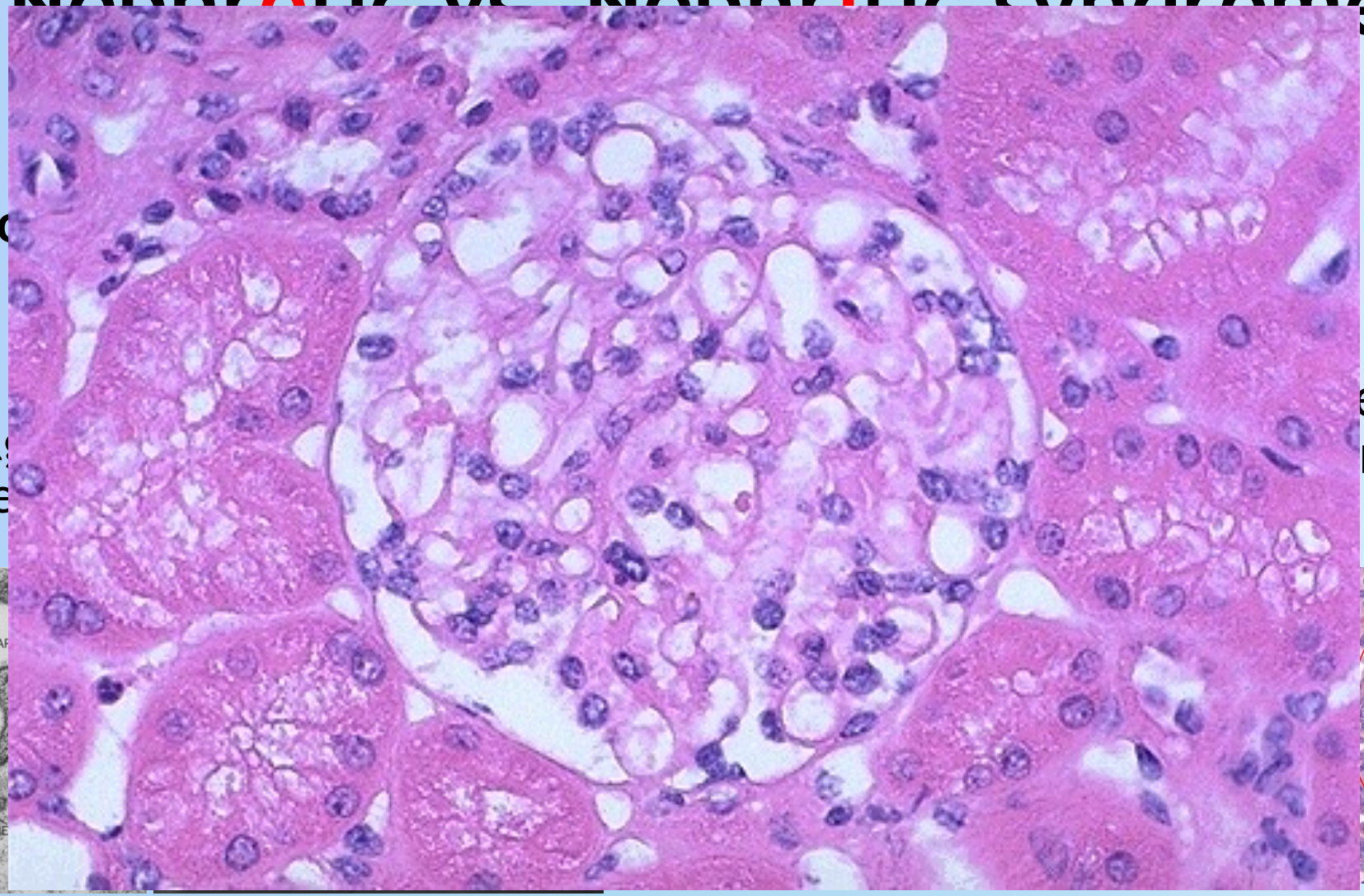

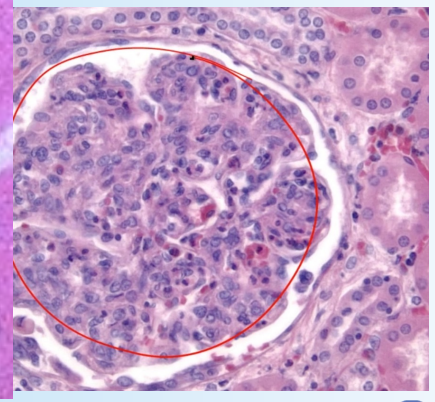

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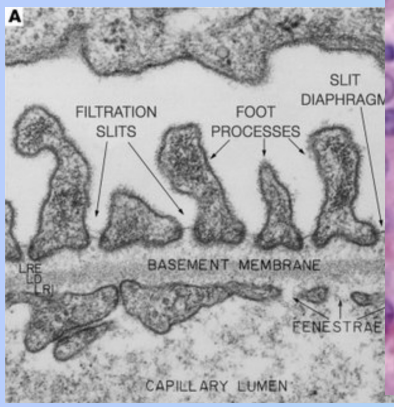

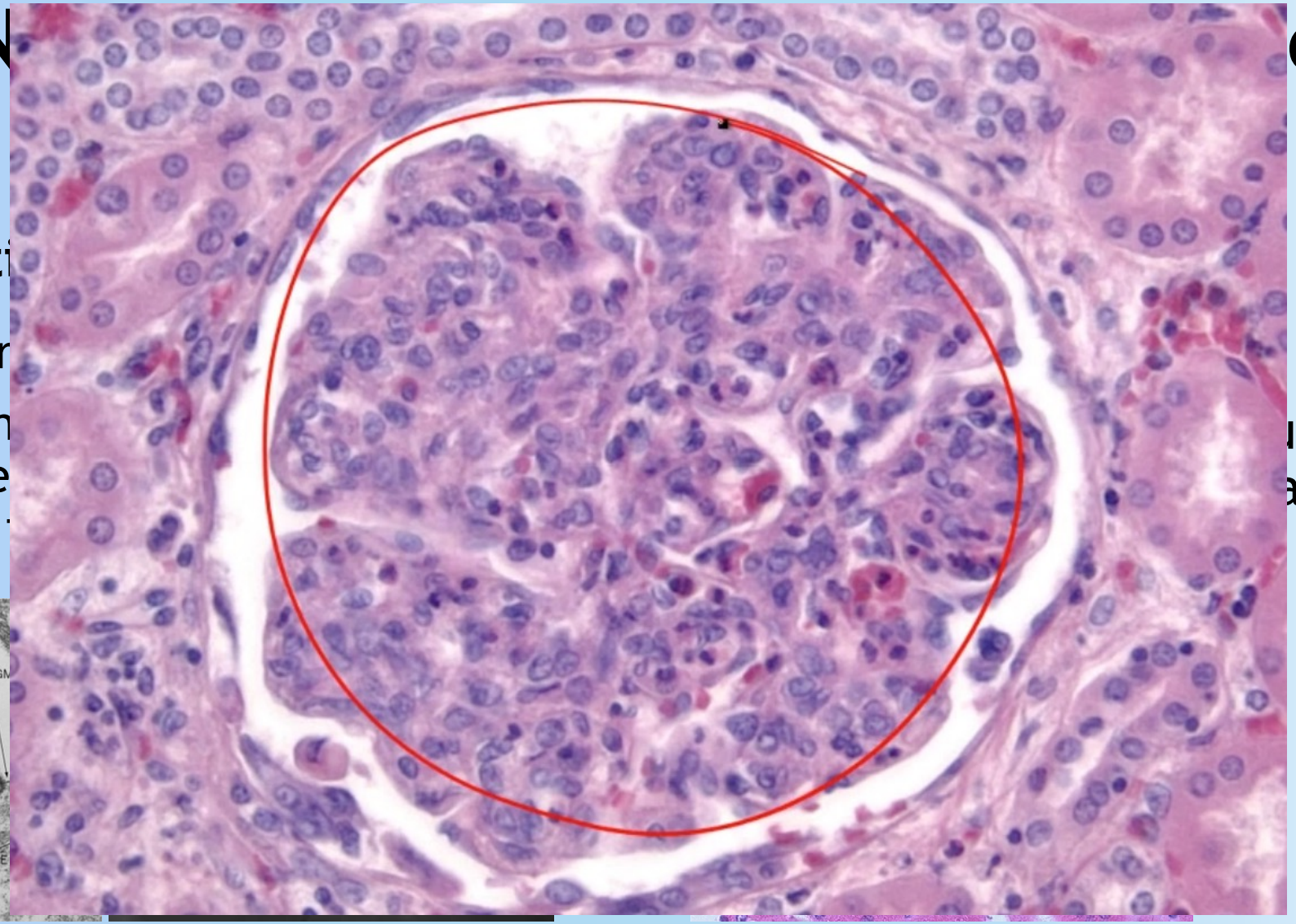

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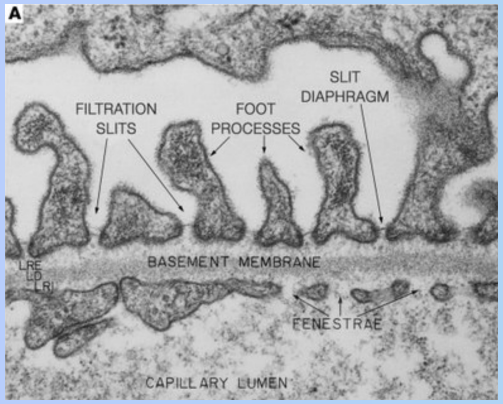

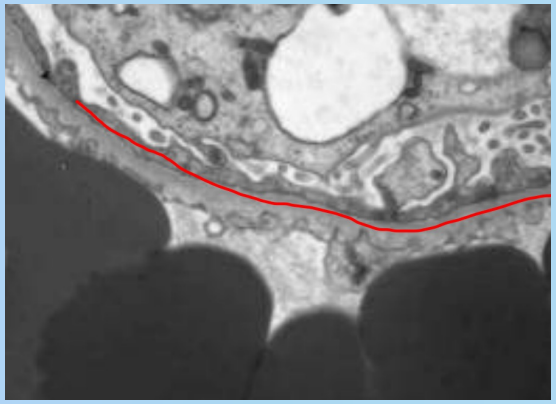

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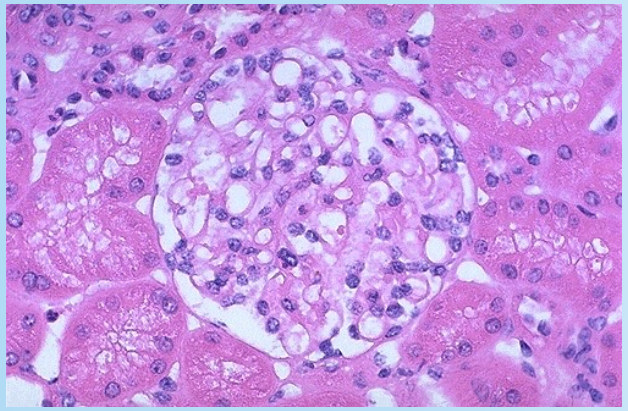

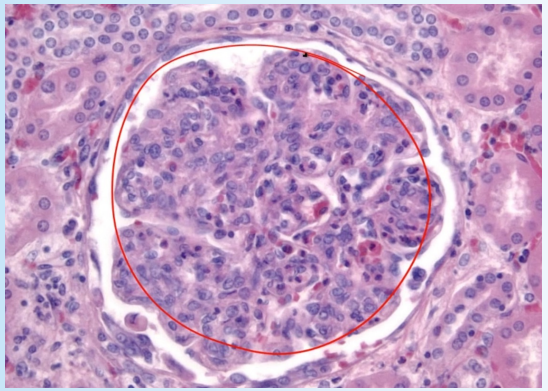

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Nephrotic syndrome pathogenesis

Structural alteration in the glomerular basement membrane

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Increased permeability in glomerulus

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Massive proteinuria and hypoalbuminemia

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Decreased oncotic pressure

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Fluid escapes vessels

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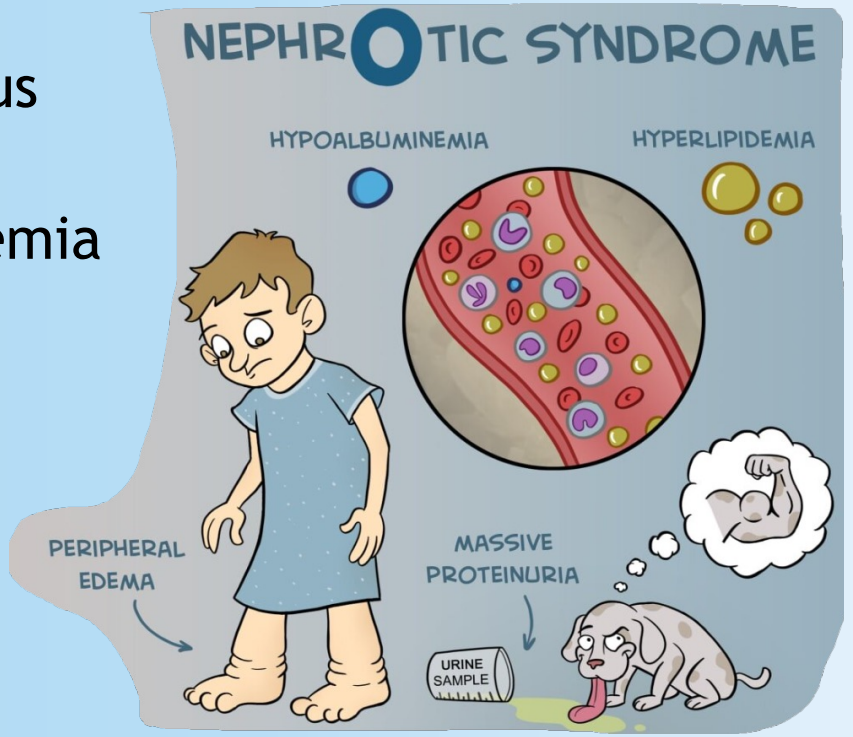
EDEMA



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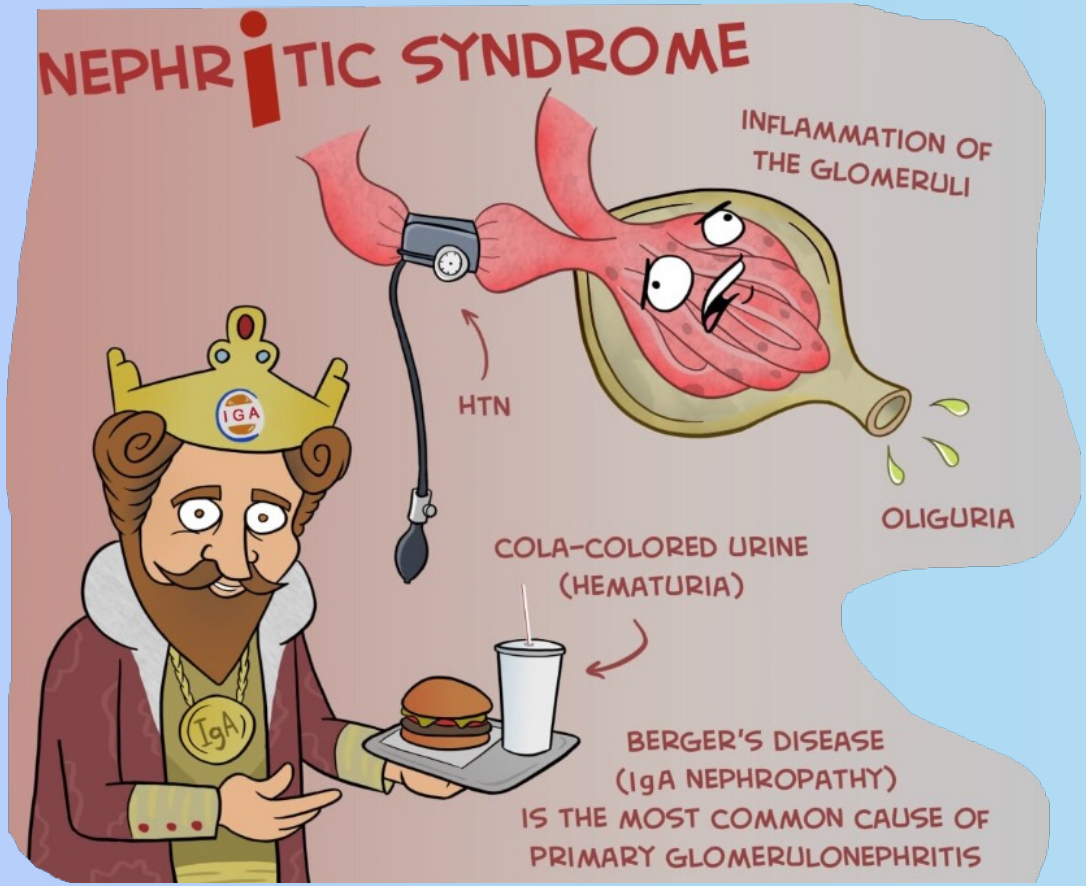

Inflammation in the glomerulus

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Cytokine release

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Capillary damage

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Porous glomerular basement membrane

↓

Leakage of RBC and some protein

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Hematuria

Mild proteinuria

Oliguria

Azotemia

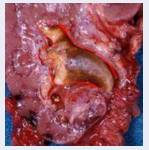
Salt retention (HTN and edema)

Nephrotic vs Nephritic Syndrome

Nephrotic Syndrome		Nephritic Syndrome
• Low serum albumin (<30g/L) • Proteinuria (>3.5g/day) • Oedema • Dyslipidaemia • Hypercoagulability (loss of antithrombin III) • Reduced immunity (loss of immunoglobulins)	**Characteristics**	• Haematuria • Hypertension • Mild proteinuria (<3.5g/day) • Mild oedema • Temporary oliguria and uraemia
Peripheral oedema (adults), facial oedema (children), frothy urine, fatigue, recurrent infections	**Symptoms**	Haematuria (frank/microscopic), mild oedema, oliguria, signs of uraemia (fatigue, pruritus, nausea)
++++	**Proteinuria**	++
May or may not be present	**Haematuria**	+++
Absent	**Red blood cell casts**	Present

• Minimal change disease (most common in children)
• Membranous nephropathy (most common in adults)
• Focal segmental glomerulosclerosis
	Causes	• IgA nephropathy
		• Post-streptococcal glomerulonephritis
		• Rapid progressive glomerulonephritis (RPGN):
		  • Anti-GBM glomerulonephritis
		  • ANCA Vasculitis

Nephrolithiasis

Composition	Frequency	Causes	Treatment	Comments
Calcium phosphate Calcium oxalate	Most common type (usually seen in adults)	Idiopathic hypercalciuria Crohn's disease Ethylene glycol (antifreeze) ingestion	Hydrochlorothiazide	
Ammonium magnesium phosphate (struvite)	Second most common type	Alkilinization of urine by urease positive pathogens (e.g. proteus, klebsiella)	Surgical removal	Staghorn stone 
Uric acid	Third most common (5%)	Gout Hyperuricemia (leukemia and myeloproliferative disorders)	Hydration and alkalinization of urine ($KHCO_3$) Allopurinol for gout	Risk factors: - Hot, arid climates - acidic pH - Low urine volume
Cysteine	Rare; most commonly seen in children	Associated with cystinuria (genetic disorder where there is low reabsorption of cysteine in kidney)	Hydration and alkalinization of urine	Can also cause staghorn stone

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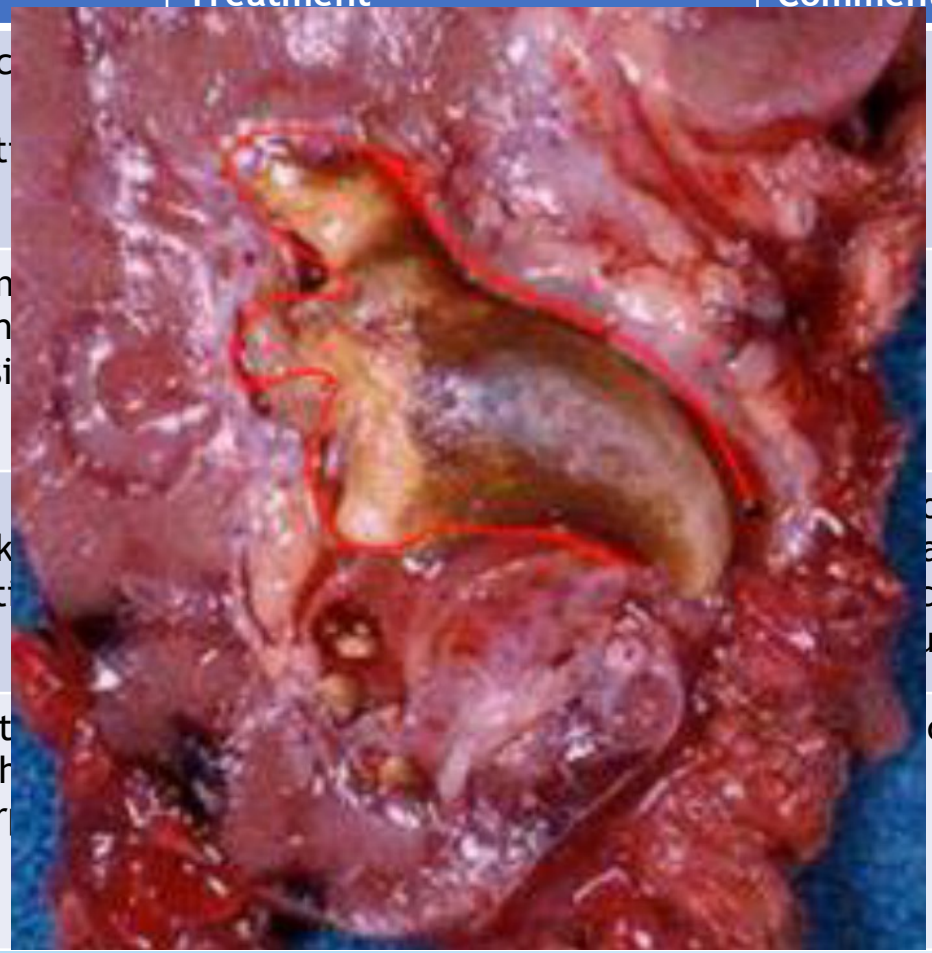

Good luck 👉