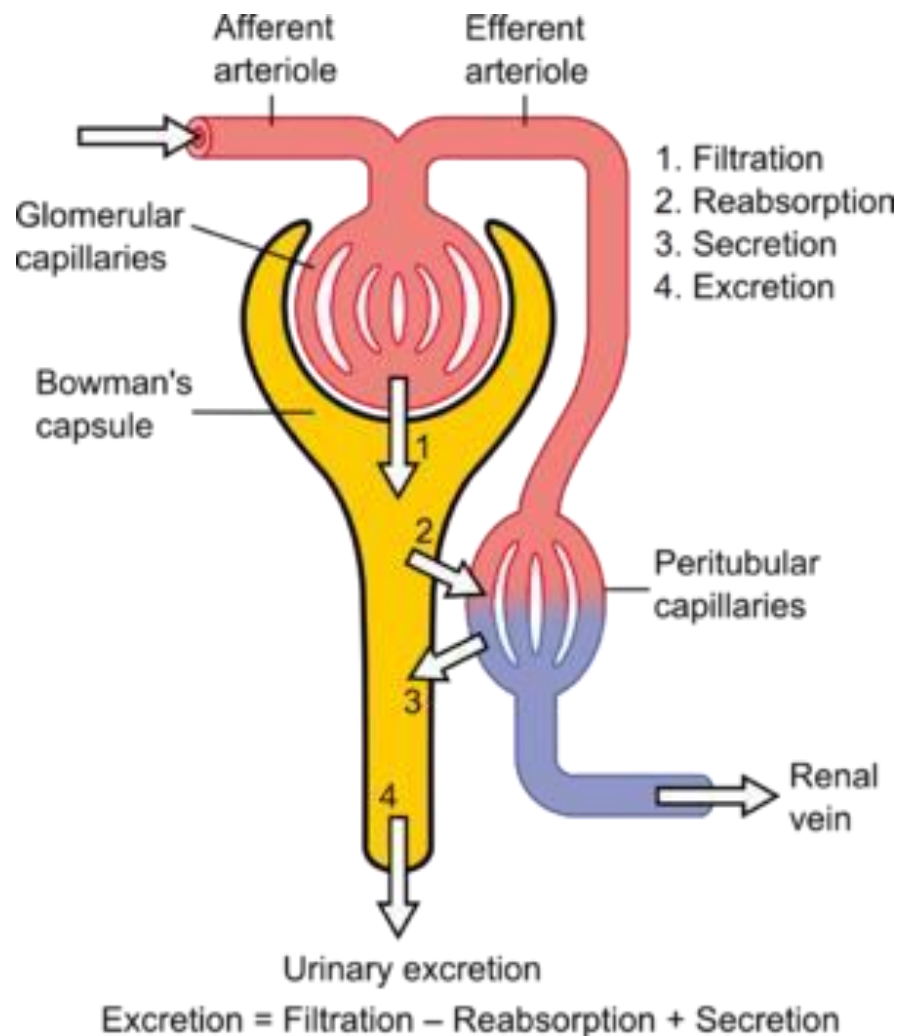


**Pathophysiology**  
**3<sup>rd</sup> stage**  
**Disorders of Renal System**

# Physiologic Concepts

## Renal Clearance

The concentration of a substance totally cleared from the blood into the urine over time is known as the renal clearance.



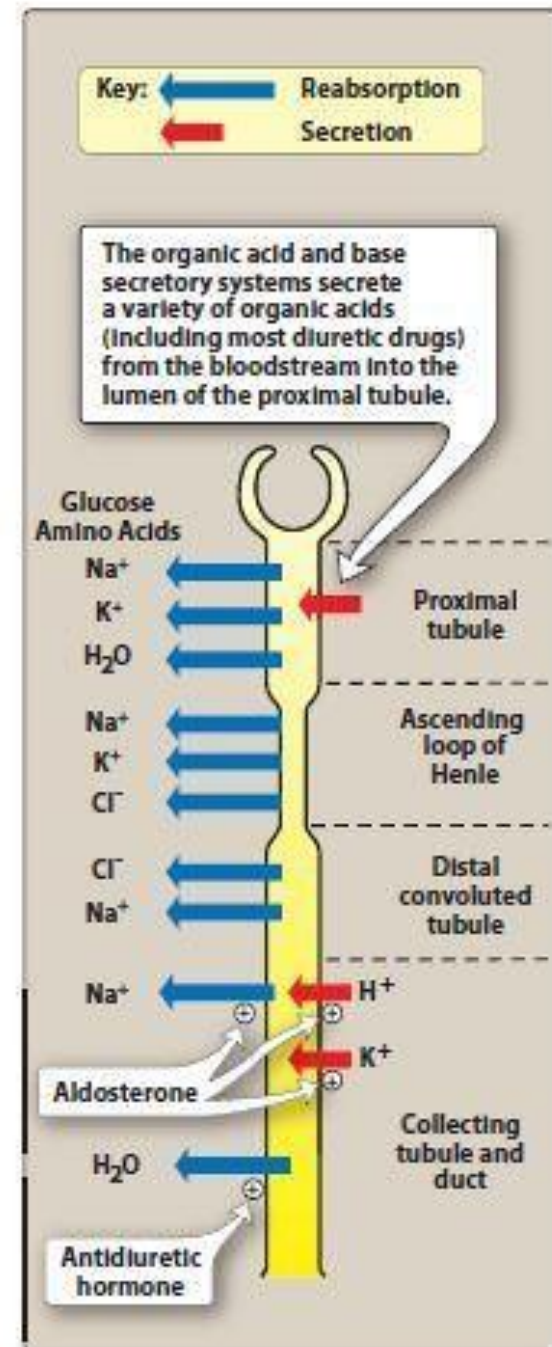
## Glomerular Filtration Rate

The glomerular filtration rate (GFR) is defined as the volume of filtrate entering Bowman's capsule per unit of time.

# Tubular Reabsorption and Secretion

From Bowman's capsule, the glomerular filtrate moves into the tubular segments of the nephron.

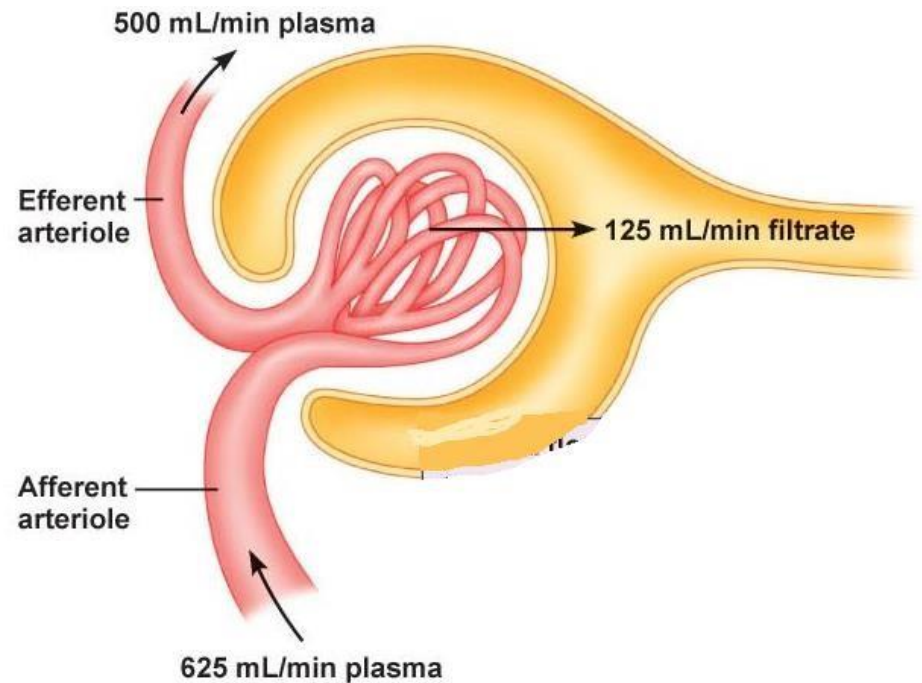
Where the reabsorption of substances have occurred.



## Sympathetic Nervous System

Sympathetic nerves innervate both the afferent and the efferent arterioles of the kidney and can override autoregulation when stimulated and causes constriction of the afferent arterioles .

The net result of sympathetic stimulation to the kidneys is a significant **decrease in renal blood flow**.

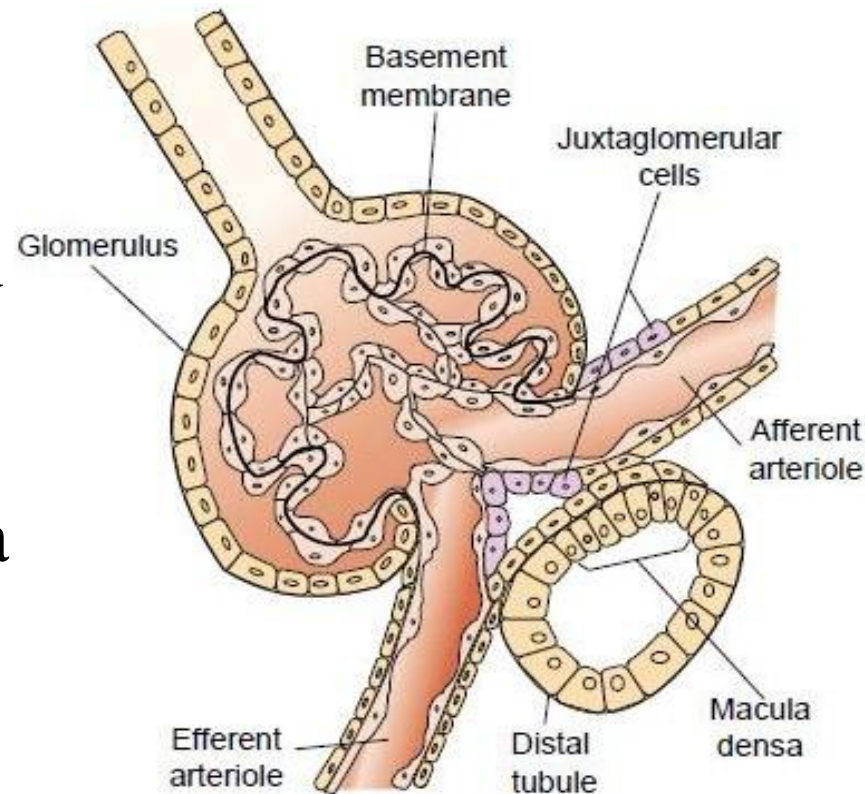


# Renin

Renin is a hormone released from **juxtaglomerular (JG) apparatus of kidney nephrone** in response to either a decrease in blood pressure or a decrease in plasma sodium concentration.

The **smooth muscle** cells synthesize renin and act as baroreceptors monitoring blood pressure.

**Macula densa** cells sense plasma Sodium concentration.



# Renin-Angiotensin-Aldosterone system

## Response to Decreased Sodium

### Angiotensin II

Ang. II is a potent vasoconstrictor that acts throughout the vascular system to increase smooth muscle contraction, thereby increasing systemic blood pressure.

Ang. II induces synthesis of the mineralocorticoid hormone aldosterone by adrenal glands.

### Aldosterone

Aldosterone circulates in the blood and binds to cells of the cortical collecting duct. causing sodium to return into the peritubular capillaries. and water follows sodium movement.

## **Endocrine Functions of the Kidney**

- ❖ Long-term regulation of blood pressure is facilitated through the kidney's activation of the reninangiotensin system and regulation of sodium and water balance.
- ❖ The activation of vitamin D, which is important for intestinal absorption of calcium, occurs in the kidney.
- ❖ The kidney synthesizes erythropoietin, which stimulates bone marrow production of red blood cells.

# DISORDERS OF GLOMERULAR FUNCTION

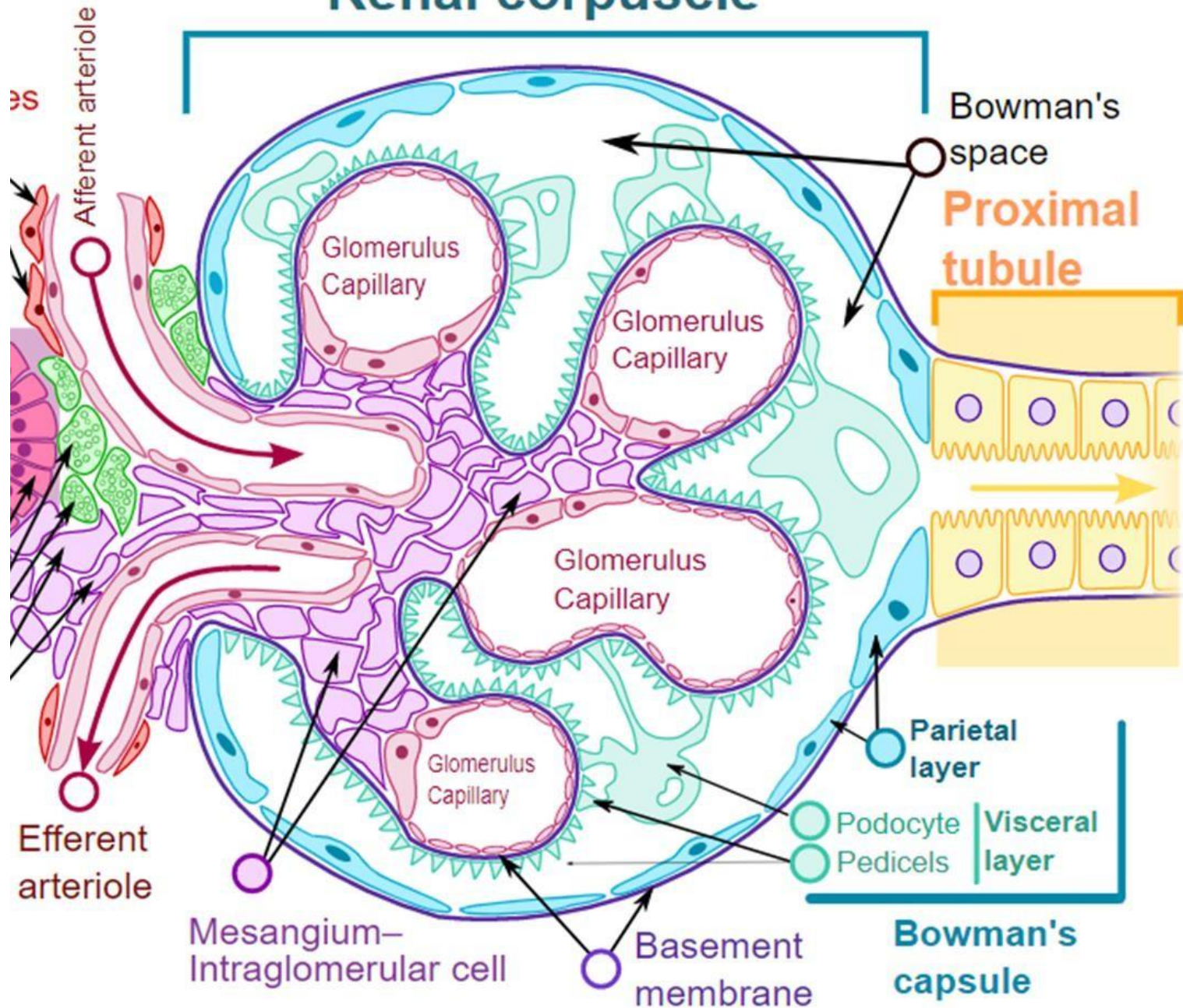
The glomerular membrane is composed of three layers:

- 1- **Endothelial** layer lining the capillary,
- 2 **Basement** membrane, and
- 3 **Layer** of epithelial cells lining Bowman's capsule

The capillary membrane is selectively permeable: it allows **water, electrolytes, and glucose and amino acids**, to leave the capillary and enter Bowman's space and prevents larger particles, such as **plasma proteins and blood cells**, from leaving the blood.



# Renal corpuscle

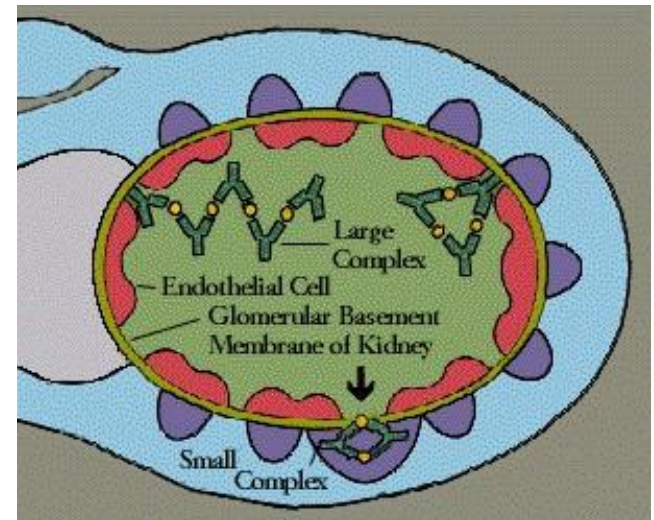
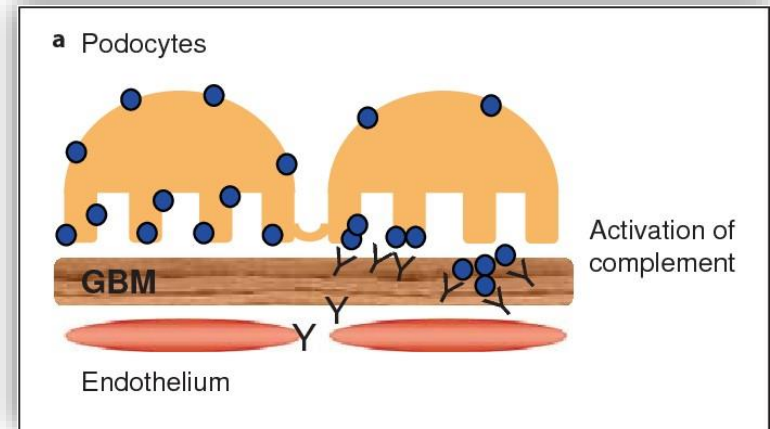


# Mechanisms of Glomerular Injury

Two types of immune mechanisms have been implicated in the development of glomerular disease:

1-Injury resulting from **antibodies reacting with fixed glomerular antigens**, and

2-Injury resulting from **circulating antigen-antibody complexes that become trapped** in the glomerular membrane.



## 1-Acute Glomerulonephritis

A sudden inflammation of the glomerulus occurs as a result of deposition of antibody-antigen complexes in the glomerular capillaries.

Complexes usually develop 7 to 10 days after a pharyngeal or skin streptococcal infection (poststreptococcal glomerulonephritis) but may follow any infection.



Inflammatory reactions in the glomeruli cause complement activation and mast-cell degranulation, leading to

- 1-increased blood flow,
- 2-increased glomerular capillary permeability, and
- 3-increased glomerular filtration.
- 4- Plasma proteins and red blood cells leak through the damaged glomeruli.

Acute glomerulonephritis usually resolves with specific antibiotic therapy, especially in children.

## 2-Chronic Glomerulonephritis

Chronic glomerulonephritis is the long-term inflammation of the glomerular cells. It may occur as a result of unresolved acute glomerulonephritis, or it might develop spontaneously.

Common causes include **diabetes mellitus** and **long-standing hypertension**.

### Clinical Manifestations

All types of glomerulonephritis are associated with

1- Decreased urine volume.

2- Blood in the urine (brownish-colored urine

)3-Fluid retention



## Diagnostic Tools

- 1-Hematuria.
- 2-Red blood cell casts in the urine.
- 3-Proteinuria greater than **3 to 5 g/day**. (Normal < 150 mg/day)
- 4-Decreased GFR as measured by creatinine clearance.
- 5- Antistreptococcal enzymes may be present.

## Complications

Renal failure may develop.

## Treatment

antibiotic therapy, corticosteroids for immunosuppression, anticoagulants to decrease fibrin deposits, ACE inhibitors .

# Renal Failure

Renal failure is the loss of function in both kidneys.

## Stages of chronic kidney disease

Stage 1: Kidney damage including abnormalities in blood or urine tests or in imaging studies) with normal or near-normal glomerular filtration rate, at or above **90 mL/min**

Stage 2: Glomerular filtration rate between 60 and 89 mL/min (approximately 50% of normal), with evidence of kidney damage.

Stage 3: Glomerular filtration rate between 30 and 59 mL/min (25 to 50% of normal).

Stage 4: Glomerular filtration rate between 15 and 29 mL/min

Stage 5: End-stage renal failure; glomerular filtration rate of less than 15 mL/min



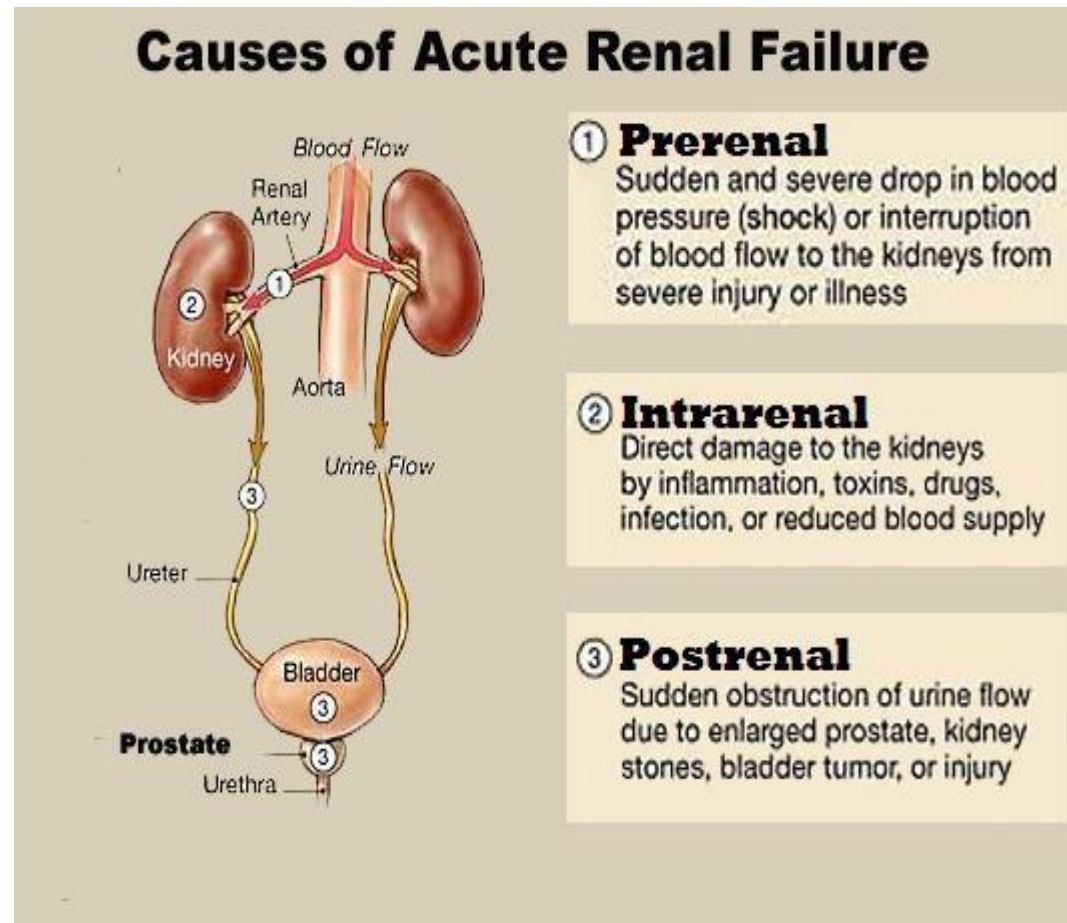


### 3-Acute Renal Failure

Causes of acute renal failure have been separated into three general categories:

- 1-prerenal,
- 2-intrarenal,
- 3- postrenal.

Identifying the cause of acute renal failure is accomplished by a study of the patient's history and the quantity and quality of his or her urine.



## Clinical Manifestations

- Oliguria. oliguria results from decreased GFR.
- Elevated BUN and creatinine.
- Hyperkalemia (increased potassium in the blood)
- Acidosis.
- Toxic tubular necrosis may be non-oliguric (high output).

## Complications

- 1-Edeme,
- 2- Congestive heart failure-
- 3-Water intoxication.
- 4-Uremic encephalopathy.
- 5-Dysrhythmia and muscle weakness may occur.



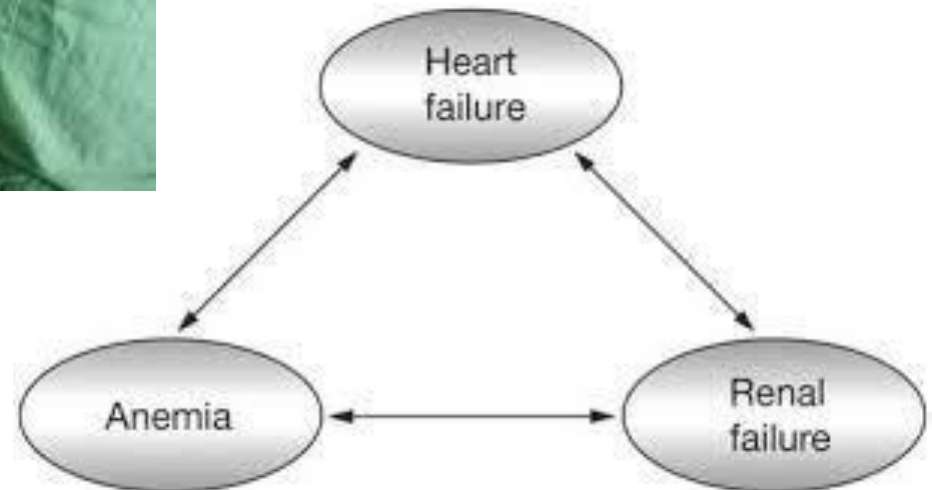
**4-Chronic renal failure** is the progressive, relentless destruction of renal structure.

Chronic renal failure can result from any of the diseases described in this lecture. In addition, the daily use of analgesic medications for many years, may lead to chronic renal failure in susceptible individuals.

25% of normal renal nephrons can do the daily kidney work

Failure of adequate production of erythropoietin by the kidneys frequently leads to anemia and a resultant fatigue that negatively impacts quality of life.

In addition, chronic anemia leads to decreased tissue oxygenation which leads to activation of the sympathetic nervous system and an increase in cardiac output and consequently congestive heart failure.



## Clinical Manifestations

- In stage 1 renal failure, no symptoms may be apparent.
- Fatigue.
- Polyuria.
- Serum BUN, creatinine, and GFR will be abnormal.
- Anemia.
- Metabolic acidosis.
- An elevated respiratory rate.
- Oliguria during the final stages.
- Cardiovascular compromise may develop.

## Complications

With progression of renal failure,  
Hypertension,  
Anemia,  
Osteodystrophy,  
Hyperkalemia,  
Uremic encephalopathy, and  
Pruritus (itching) are common complications.  
Congestive heart failure may develop.  
Without treatment, coma and death result.

## 5-Nephrotic Syndrome

Nephrotic syndrome is the loss of 3.5 g or more of protein in the urine per day. Under normal circumstances, virtually no protein is lost in the urine due to severe glomerular damage. Diabetic nephropathy is the most common cause of nephrotic syndrome.

**Clinical manifestations include** Four main symptoms of nephrotic syndrom:

- 1 Proteinuria.
  - 2 Hypoalbuminemia
  - 3 Edema.
  - 4 Hyperlipidemia(elevated plasma lipids).
- Increased susceptibility to infections (caused by hypoimmunoglobulins) and generalized edema.

## 6-Pyelonephritis

Pyelonephritis is inflammation of the parenchyma and lining of renal pelvis of kidney.



### Pathogenesis:

In the majority of UTIs bacteria **E.coli** (common) establish infection by ascending from the urethra to the bladder.

Continuing ascent up the ureter to the kidney is the pathway for most renal parenchymal infections.



## Clinical Feature

### **Mild pyelonephritis:**

- low-grade fever with or without lower-back or costovertebral-angle pain

### **Severe pyelonephritis:**

- High fever
- Nausea
- vomiting
- flank and/or loin pain



## Hypertensive Glomerular disease

**Renal failure** may occur with progressive high-pressure damage to the renal capillaries, the glomeruli.

With glomerular injury, blood flow to the functional units of the kidney, the nephrons, is impaired, and these can become hypoxic and die.

With damage to the glomerular membranes, proteins will be lost in the urine, decreasing the plasma colloid osmotic pressure and contributing to edema, which is often seen with long-standing hypertension.

# Drugs Induced Kidney Disease

- The heart pumps approximately 25% of cardiac output into the kidneys
- Any drug in the blood will eventually reach the highly vascularized kidneys May potentially cause drug-induced renal failure

**ACEIs and ARBs cause ARF**

Stopping the medication should resolve the renal failure.

Restarting the drug at a lower dose may be possible.

❖ **NSAIDs**, selective cyclooxygenase (constitutive enzyme) inhibitors cause similar renal dysfunction.

❖ **Cisplatin**, Nephrotoxicity is the major dose-limiting toxicity for **cisplatin**, through their interaction with DNA

### **Drugs of Abuse**

- Cocaine and heroin.
- Cocaine use can cause renal artery thrombosis (clotting), severe hypertension and interstitial nephritis.
- long-term cocaine use can lead to chronic renal failure.
- Long-term tobacco use also increases the risk of kidney cancer.

***Thank You..!!***

