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Introduction to kidney function & pathophysiology

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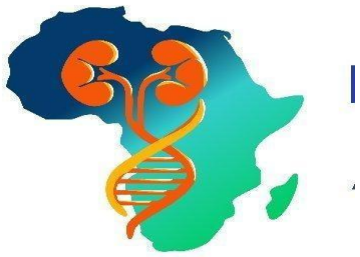

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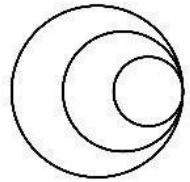

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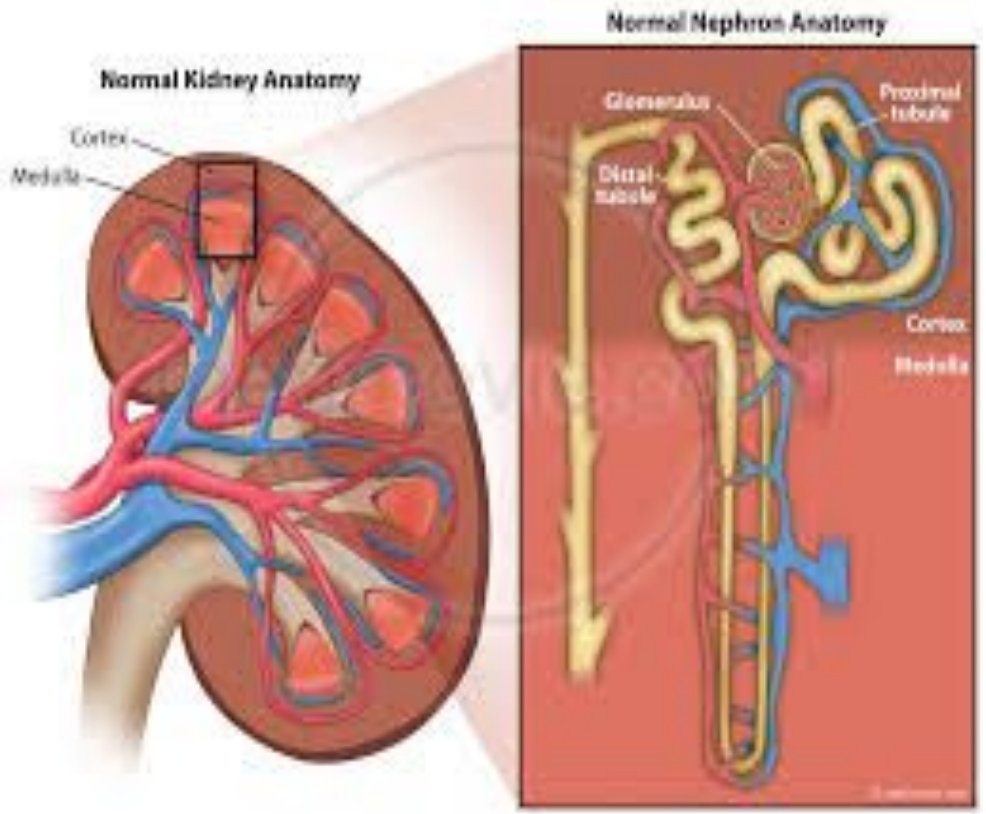
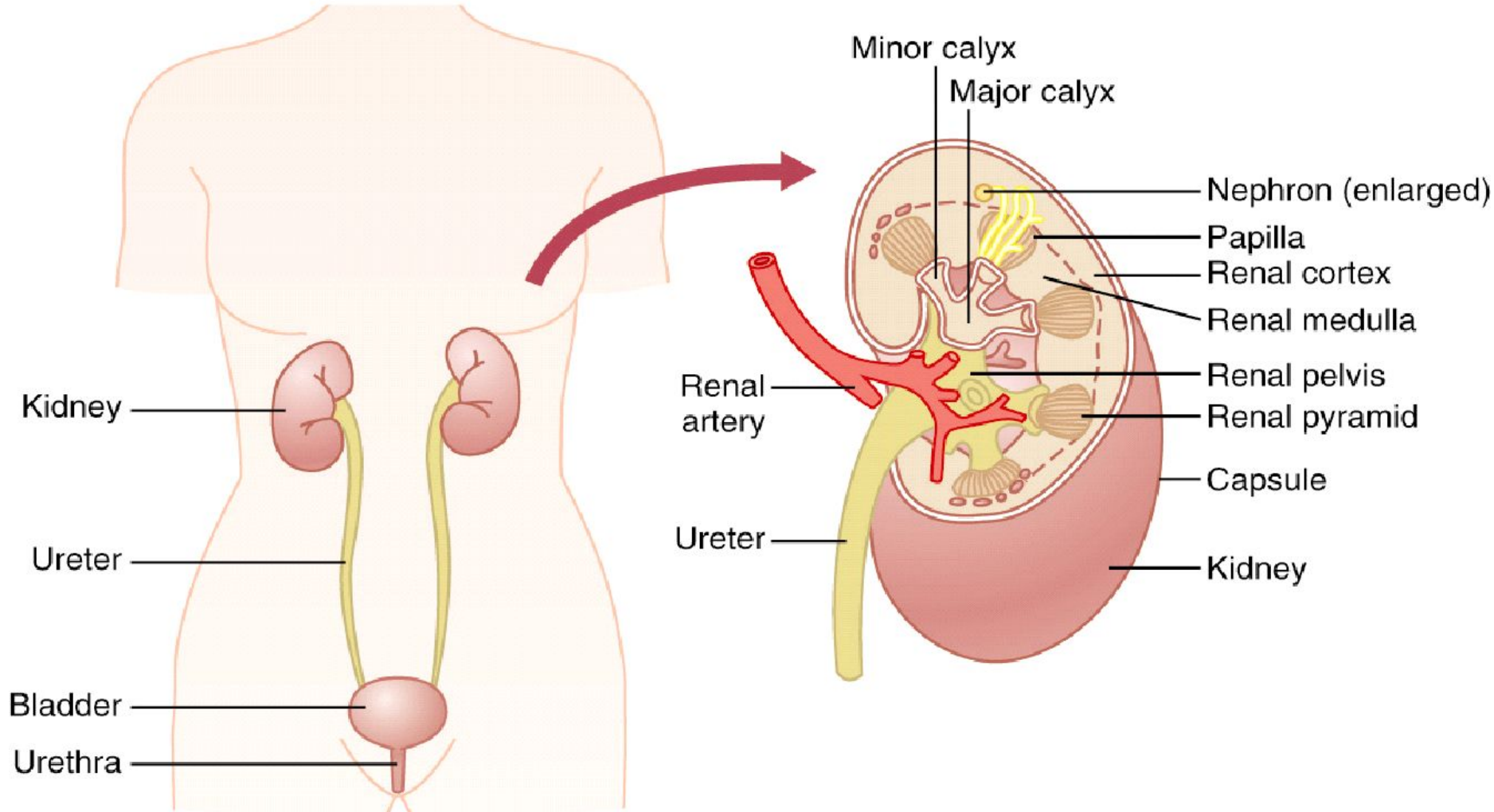
By the end of this session participants should:

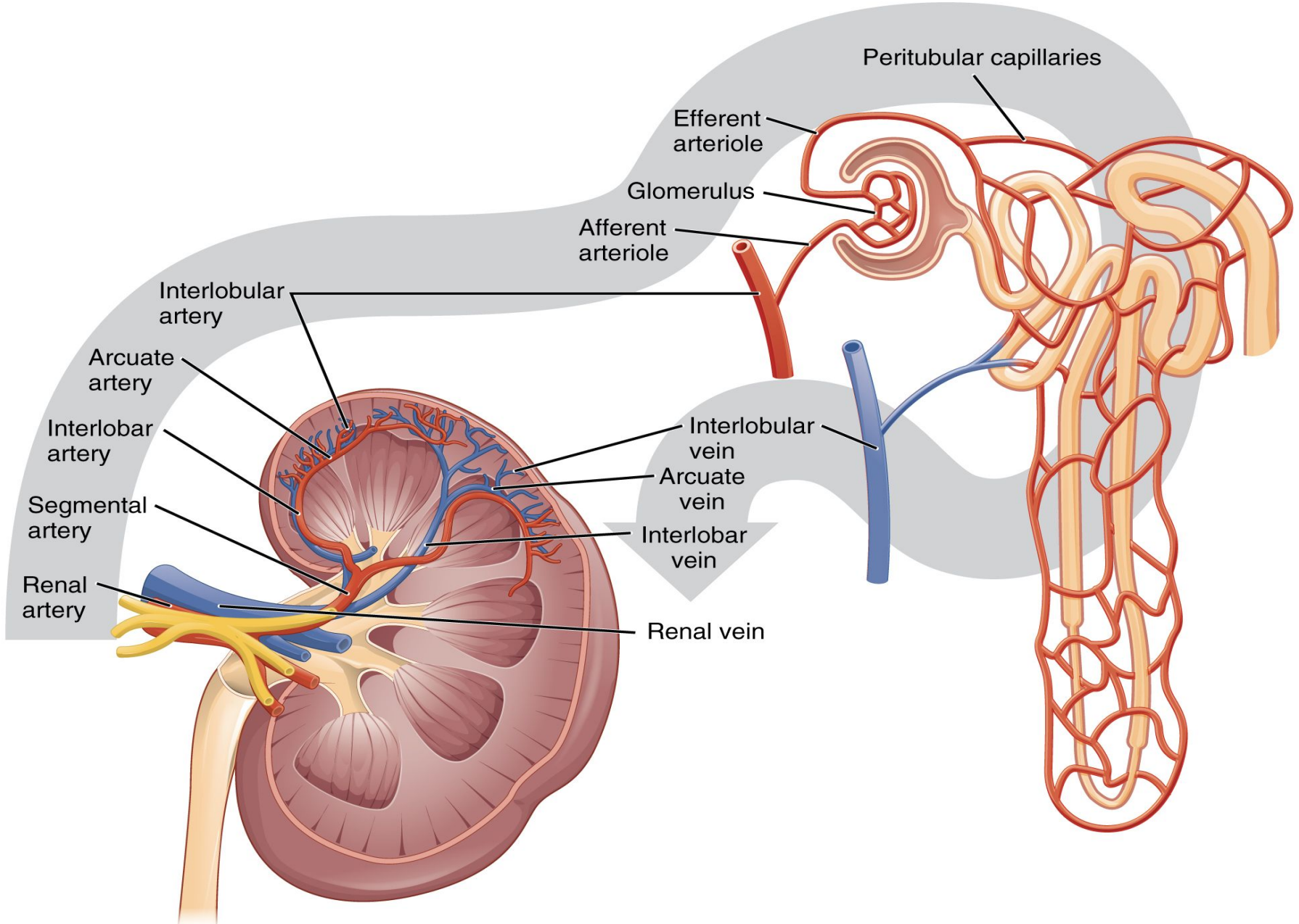
- Understand gross and microanatomy relevant to function.
- Explain core physiological processes that produce urine.
- Map major pathophysiologic mechanisms to clinical syndromes.
- Apply simple bedside tests to localize renal injury.



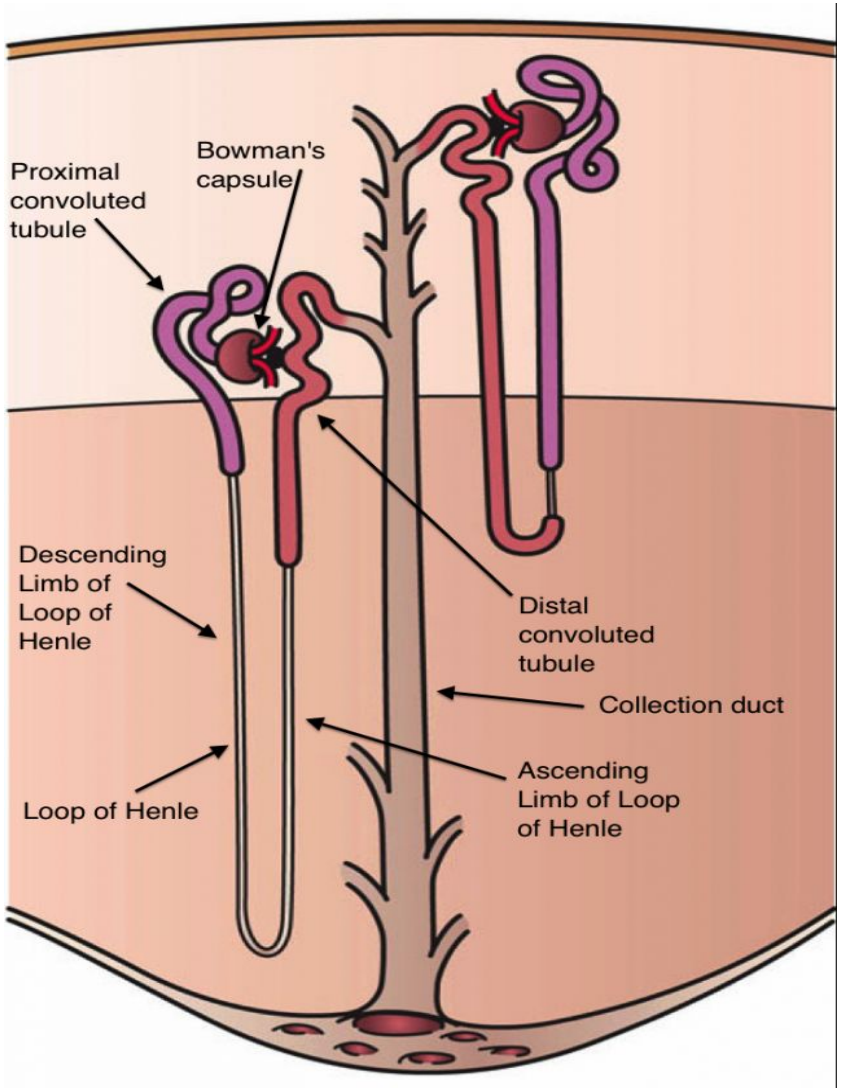
Gross Anatomy

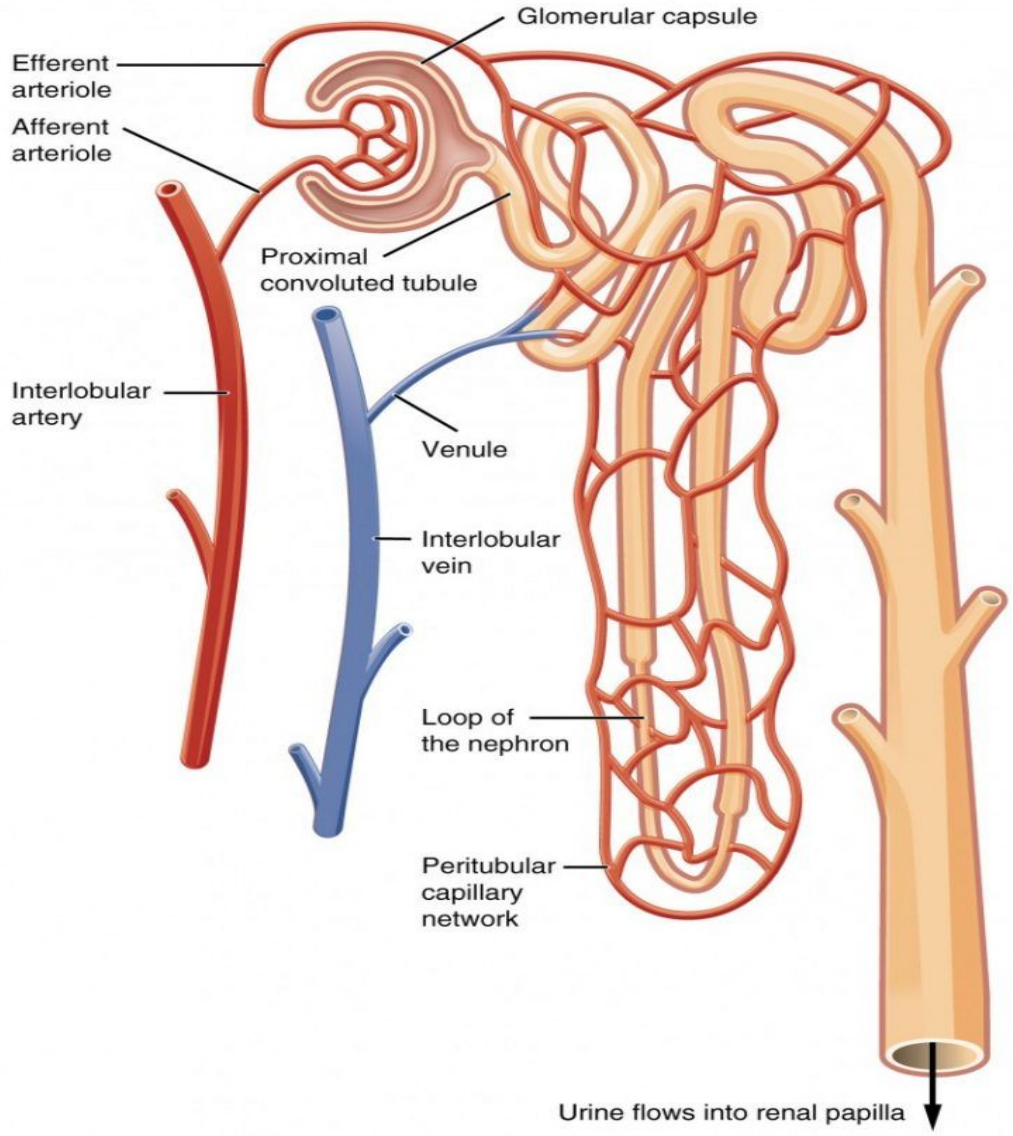


Blood Flow to the kidneys



Functional Anatomy





Functions of the kidney

Functions	Disorders in renal failure
Excretion of toxic substances(endogenous wastes, exogenous toxins and drugs	Uremia
Nacl balance (regulation of ECF volume,plamsa volume & blood pressure)	Hypertension and edema
Water balance(regulation of ECF Na concentration & osmolarity	Hyponatremia
Potassium balance	Hyperkalemia
Acid base balance	Acidosis
PO4 and Ca balance(Vitamin D activation)	Bone disease
Erythropoietin production	Anemia

Process of Urine Formation

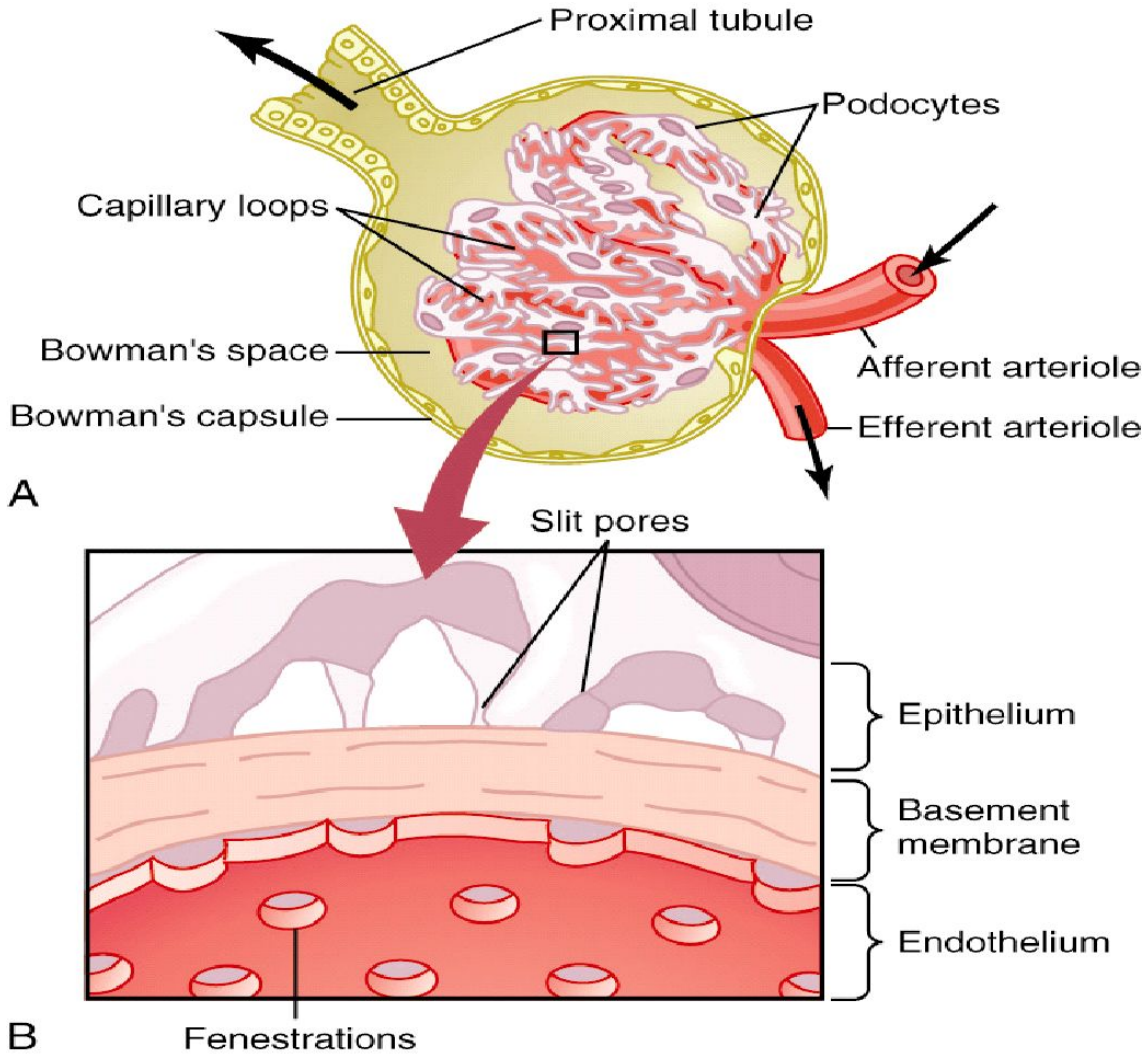
- Filtration
- Reabsorption
- Secretion
- Excretion

Filtration

- Heart output- 5litres per minute
- 20% to kidney= 1litre
- 60% plasma = 600mls
- Filtration rate= 1/5 x 600= 125
- 125mls/min/1.73m2
- 7500mls/hr
- 180L/day

Glomerular Filtration Physiology

- **Filtration barrier**: endothelium, basement membrane, podocytes.
- **Selectivity**: size and charge determine protein filtration.
- Single nephron GFR versus total GFR.

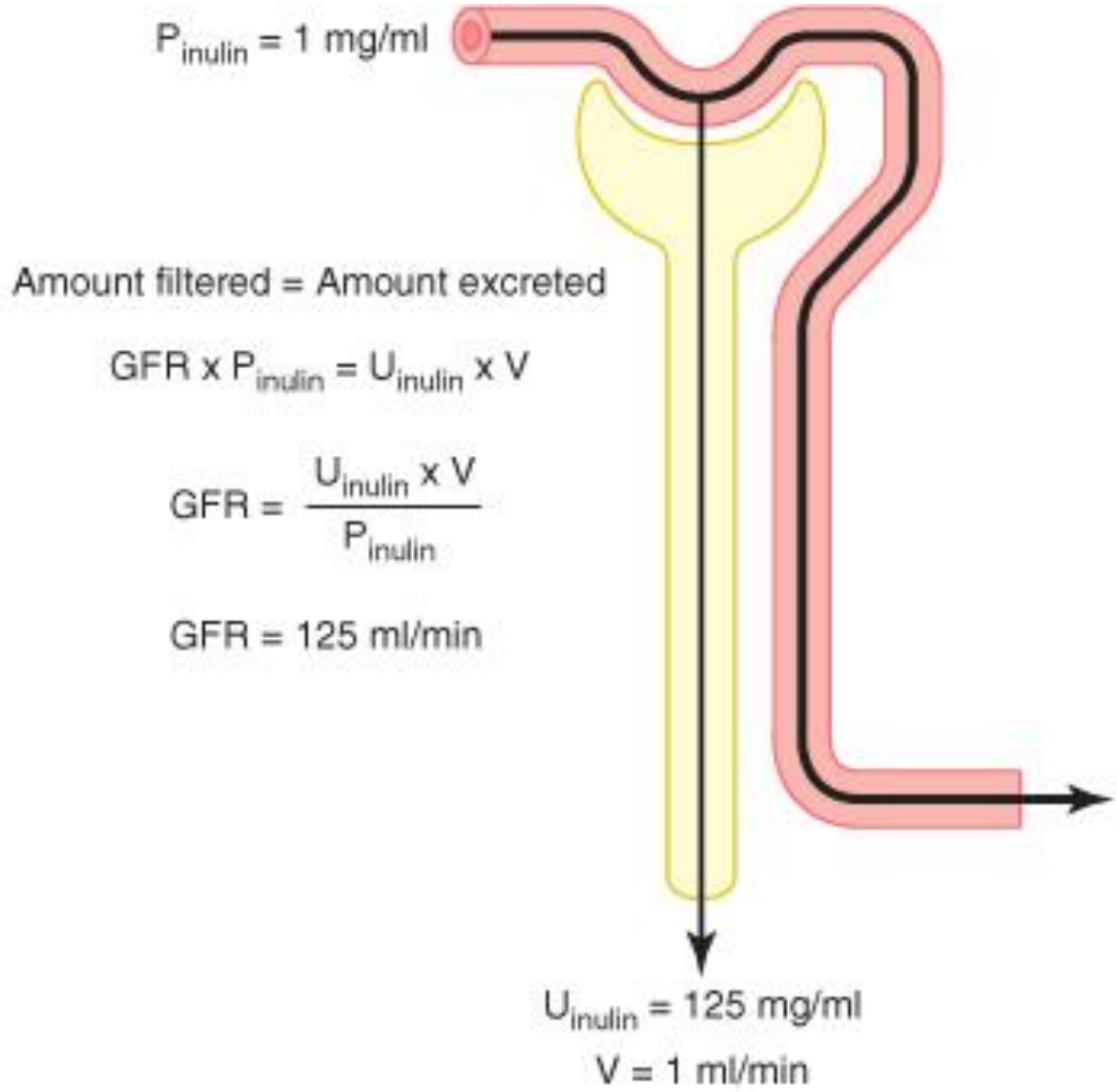


Concept of clearance

- Volume of plasma that would have to be filtered by the glomeruli in one minute to account for the amount of that substance appearing in the urine each minute under steady state conditions
- Volume of plasma that contains the amount of the substance excreted in the urine in one minute under steady state conditions

Clearance = $U_x V / P_x$

- Where,
  - U_x = urine concentration of x (mg/dL)
  - P_x = plasma concentration of x (mg/dL)
  - V = urine output (mL/min)



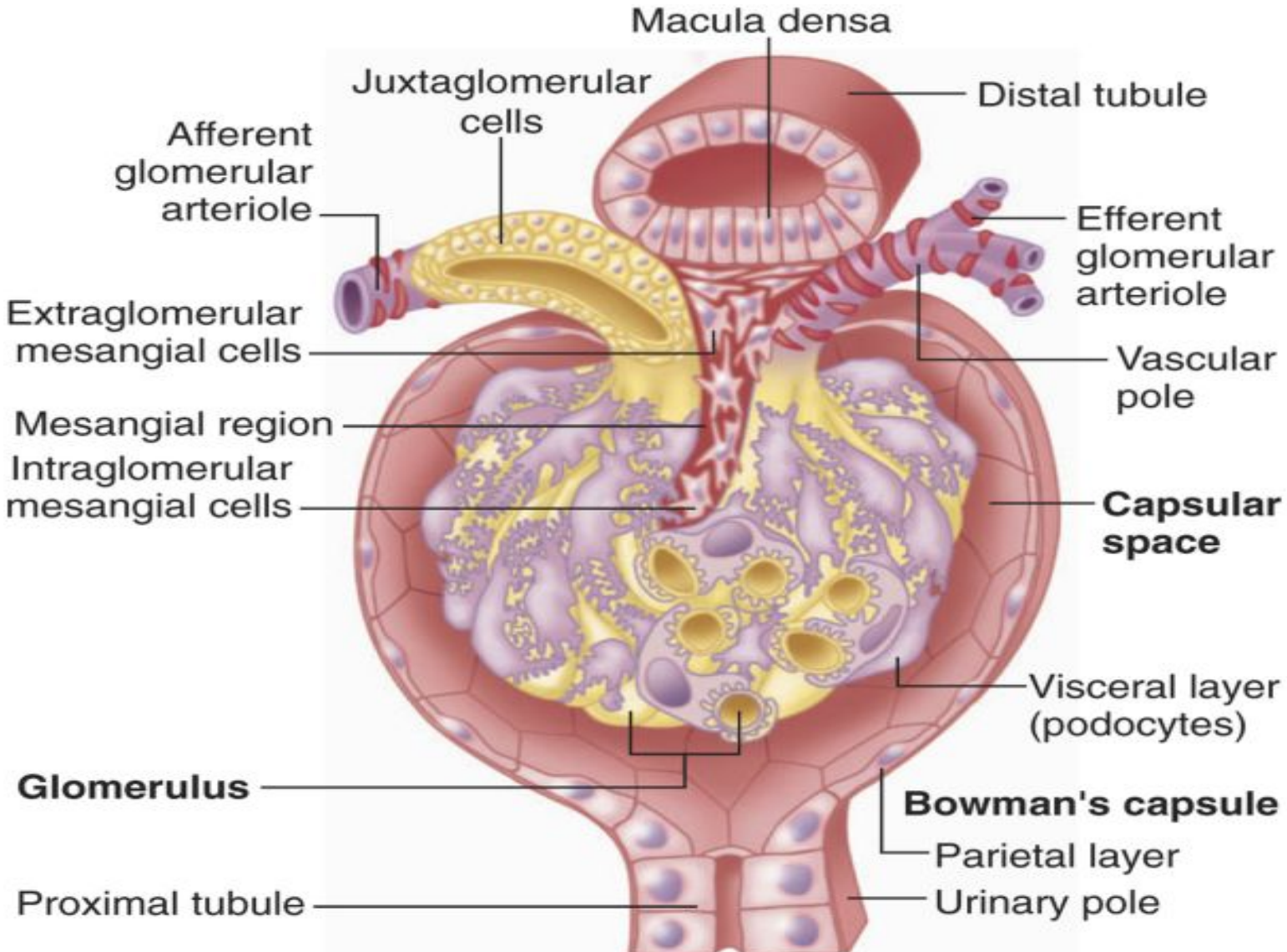
Inulin clearance

- Inulin is a polymer of fructose that meets all of the criteria for the ideal substance to measure GFR
- Inulin clearance is the “gold standard” for GFR determination
- Inulin must be continuously infused into the animal to achieve a steady state concentration in plasma

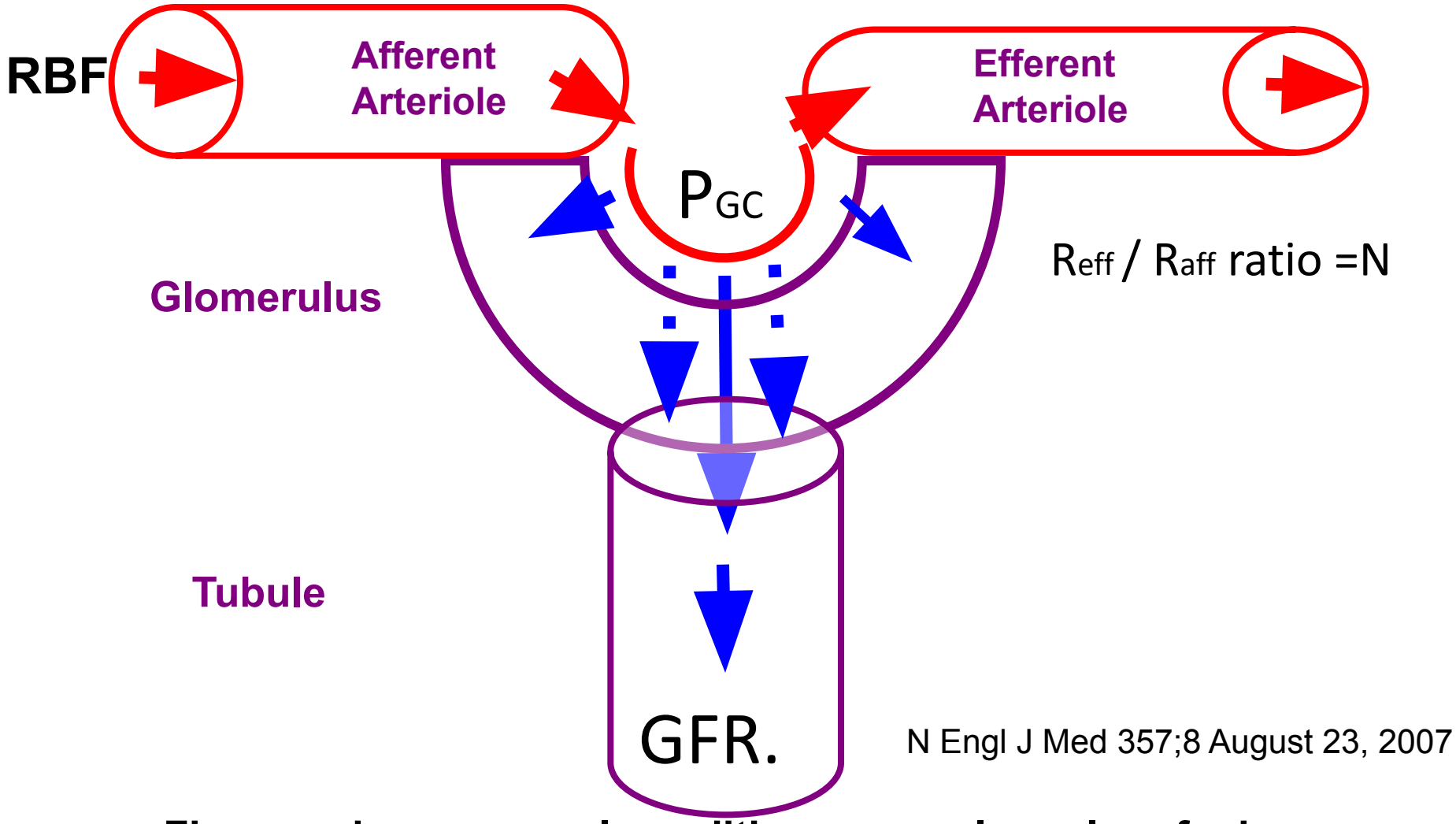
Creatinine clearance

- Measure serum and urine creatinine levels and urine volume and calculate serum volume cleared of creatinine
- Same issues as with serum creatinine, except muscle mass
- Requirements for 24 hour urine collection adds variability and inconvenience

Three dimensional depiction of the glomerulus



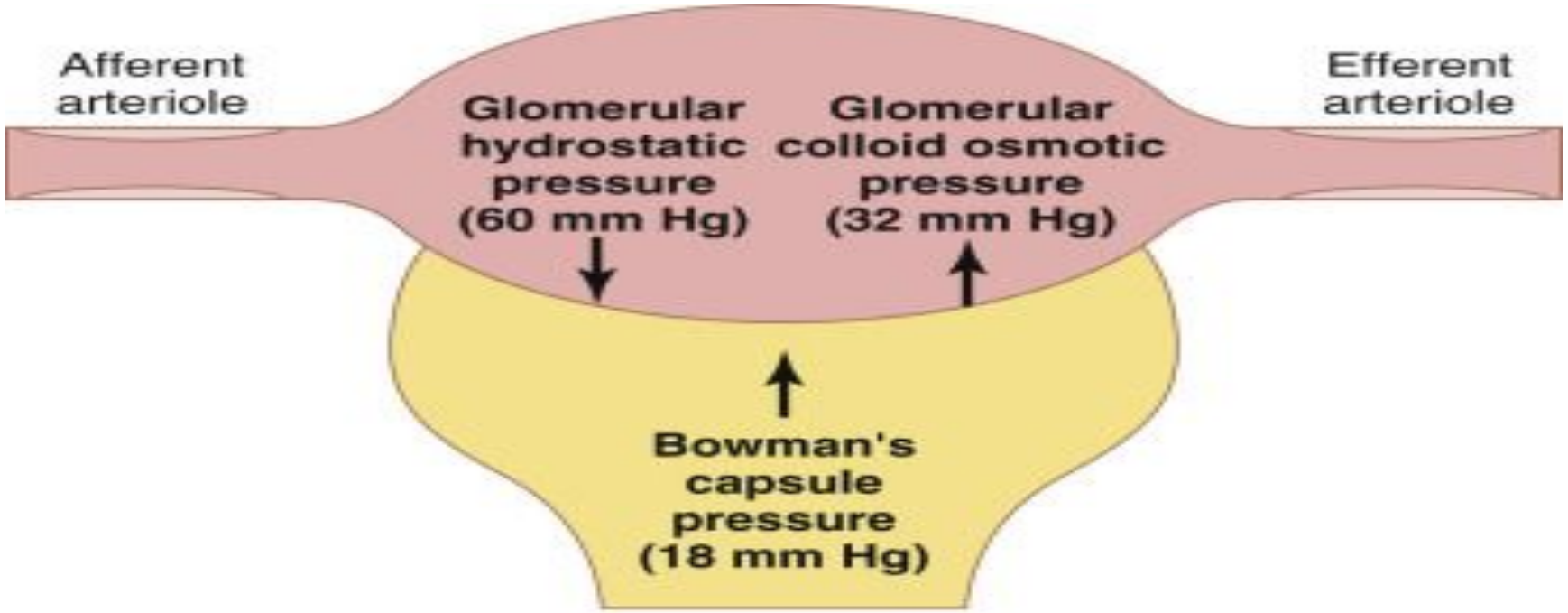
Intrarenal Mechanisms for Autoregulation



N Engl J Med 357;8 August 23, 2007

Figure - shows normal conditions normal renal perfusion pressure and a normal GFR.

Filtration dynamics



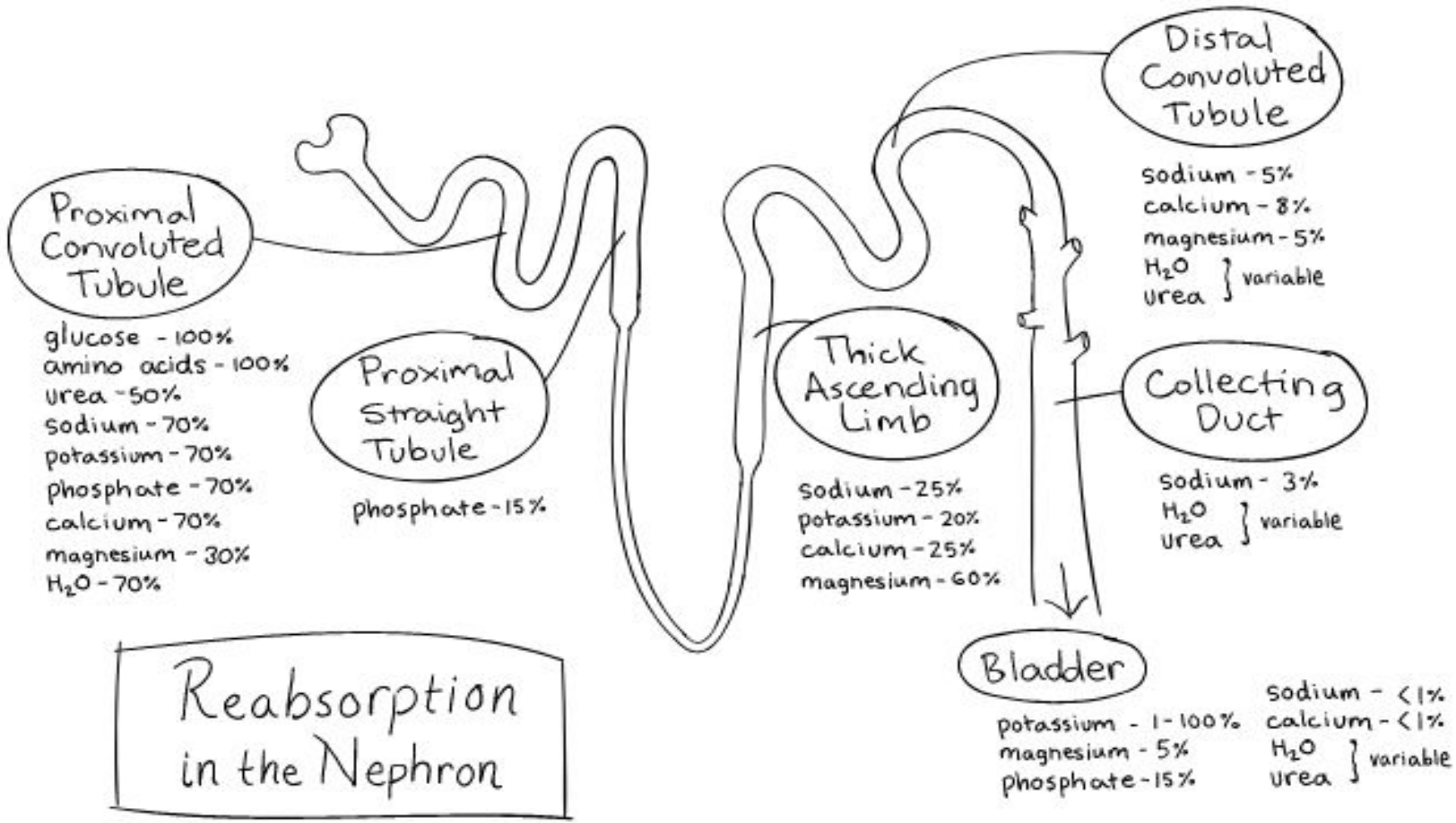
Net filtration pressure (10 mm Hg)	=	Glomerular hydrostatic pressure (60 mm Hg)	–	Bowman's capsule pressure (18 mm Hg)	–	Glomerular oncotic pressure (32 mm Hg)

Why don’t we excrete all 180 liters/day?

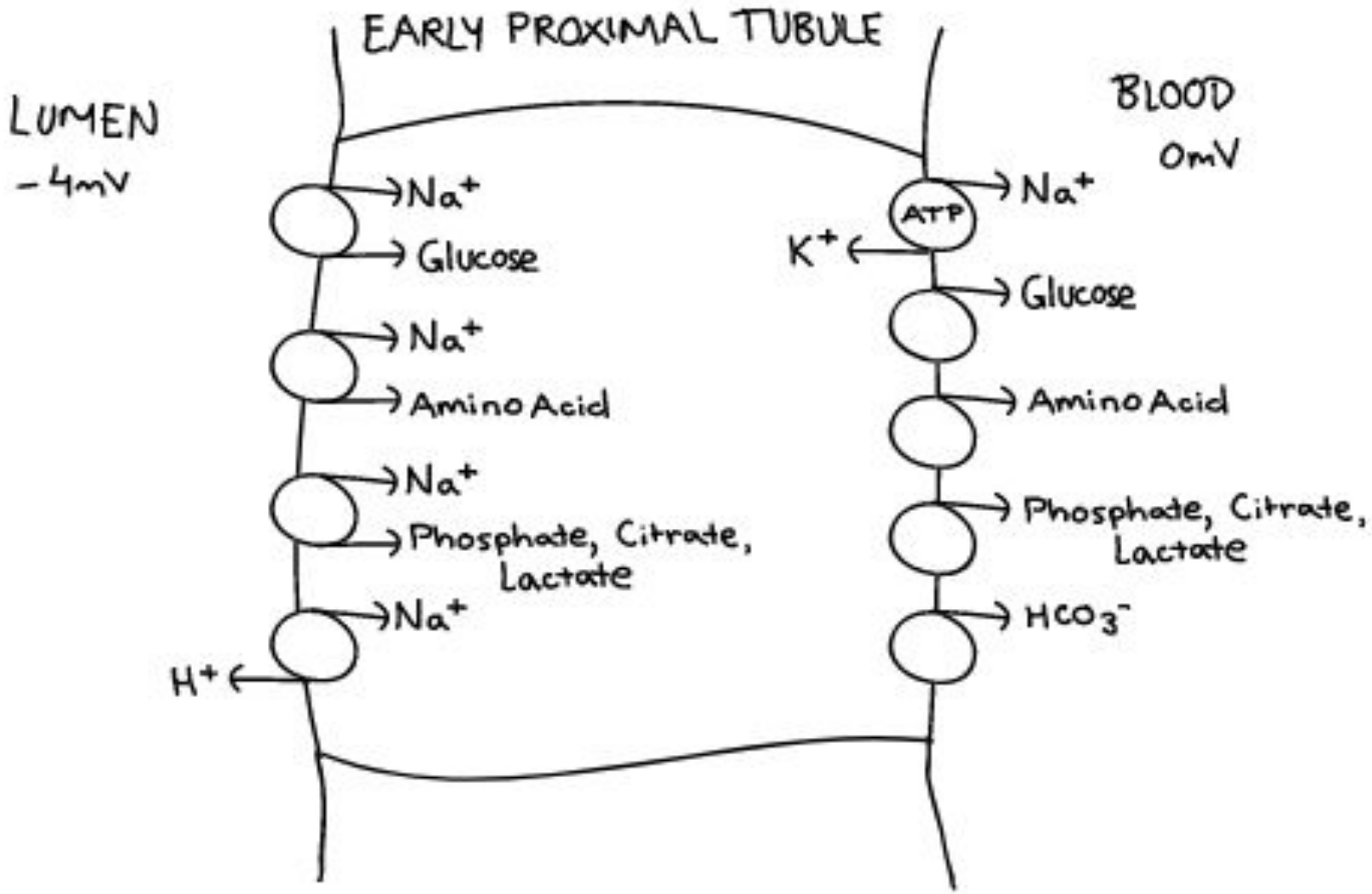
Reabsorption

- Movement of substance from the renal tubules back into the renal capillaries.
- Water, glucose, electrolytes (Na+ other ions) and other nutrients are reabsorbed
- 99% of fluids (180L) reabsorbed in the proximal tubule using passive absorption
- Glucose completely reabsorbed in proximal tubule- and actively from peri capillaries.

Nephron Segments and Primary Functions



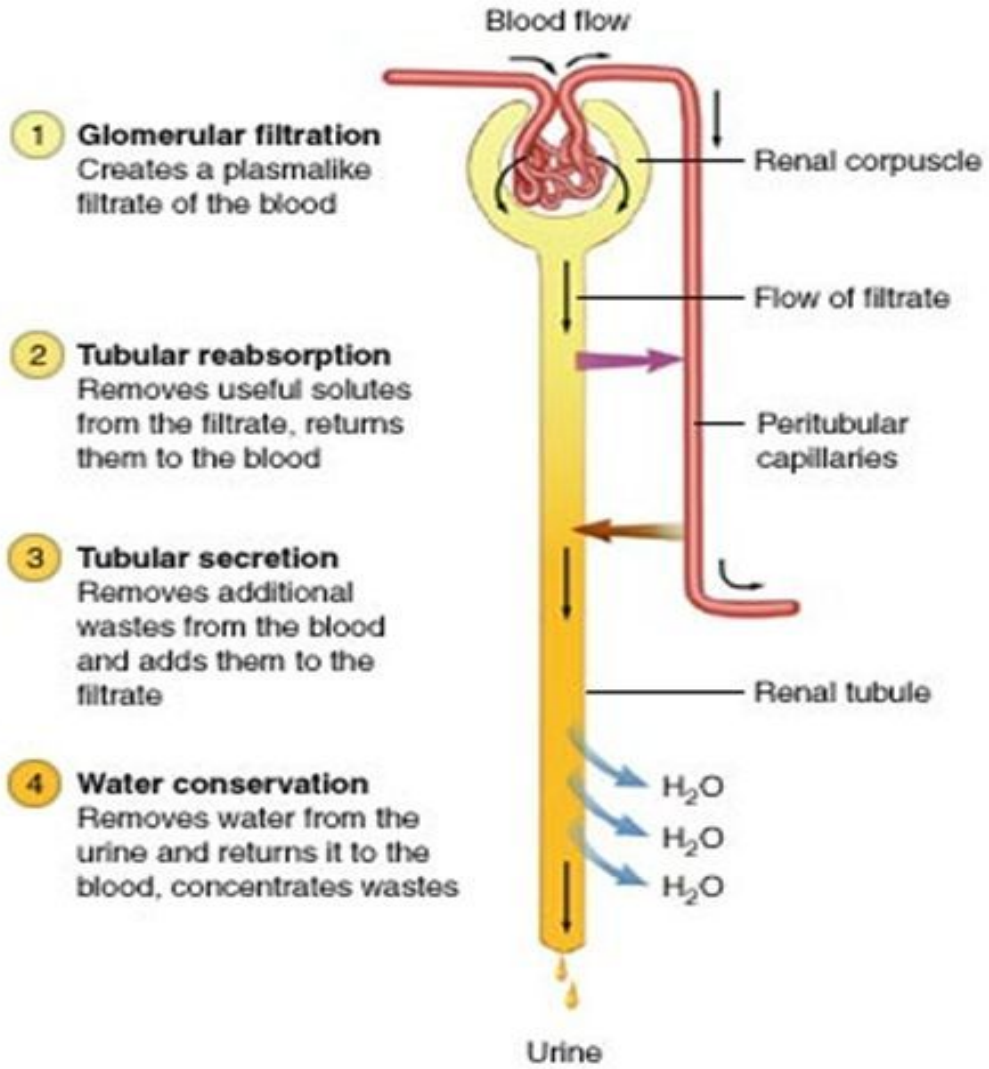
Transporters- proximal tubule



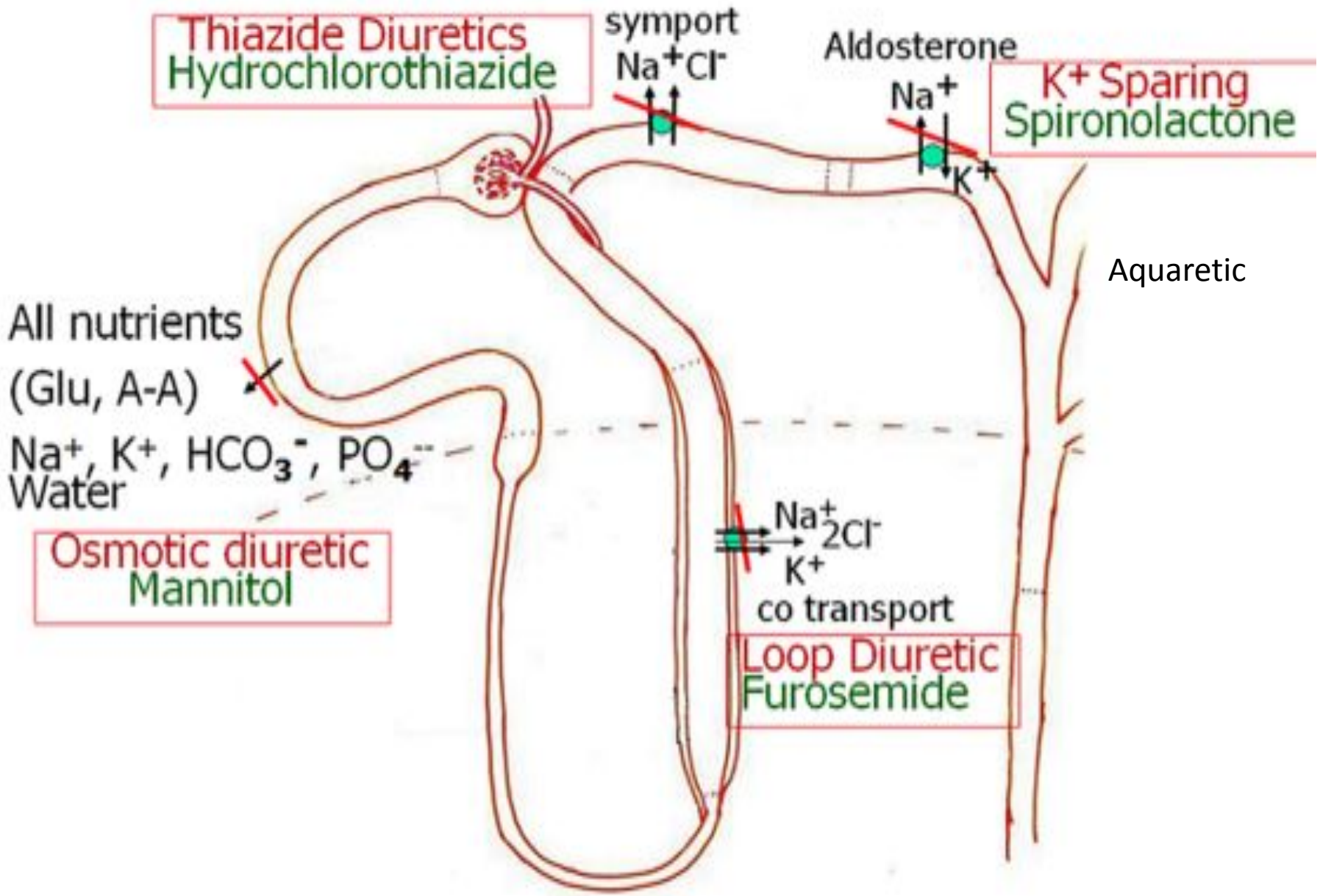
Secretion

- Substances move into the distal tubules and collecting tubules from blood into the capillaries around the tubules.
- It is the reverse of reabsorption
- Secretion is active transport or by diffusion into the lumen
- Acid base balance is largely due to this.

5. Excretion of Urine



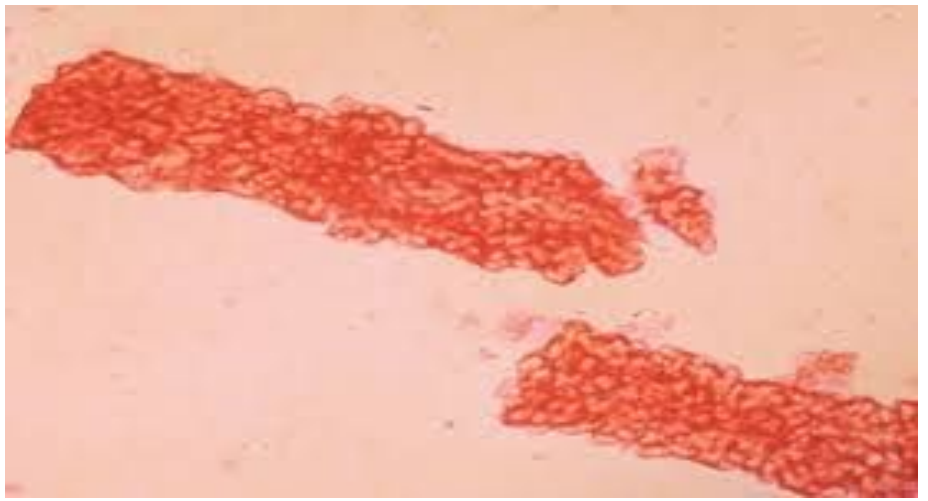
Sites of Action of Diuretics



Urine Formation and Clinical Tests

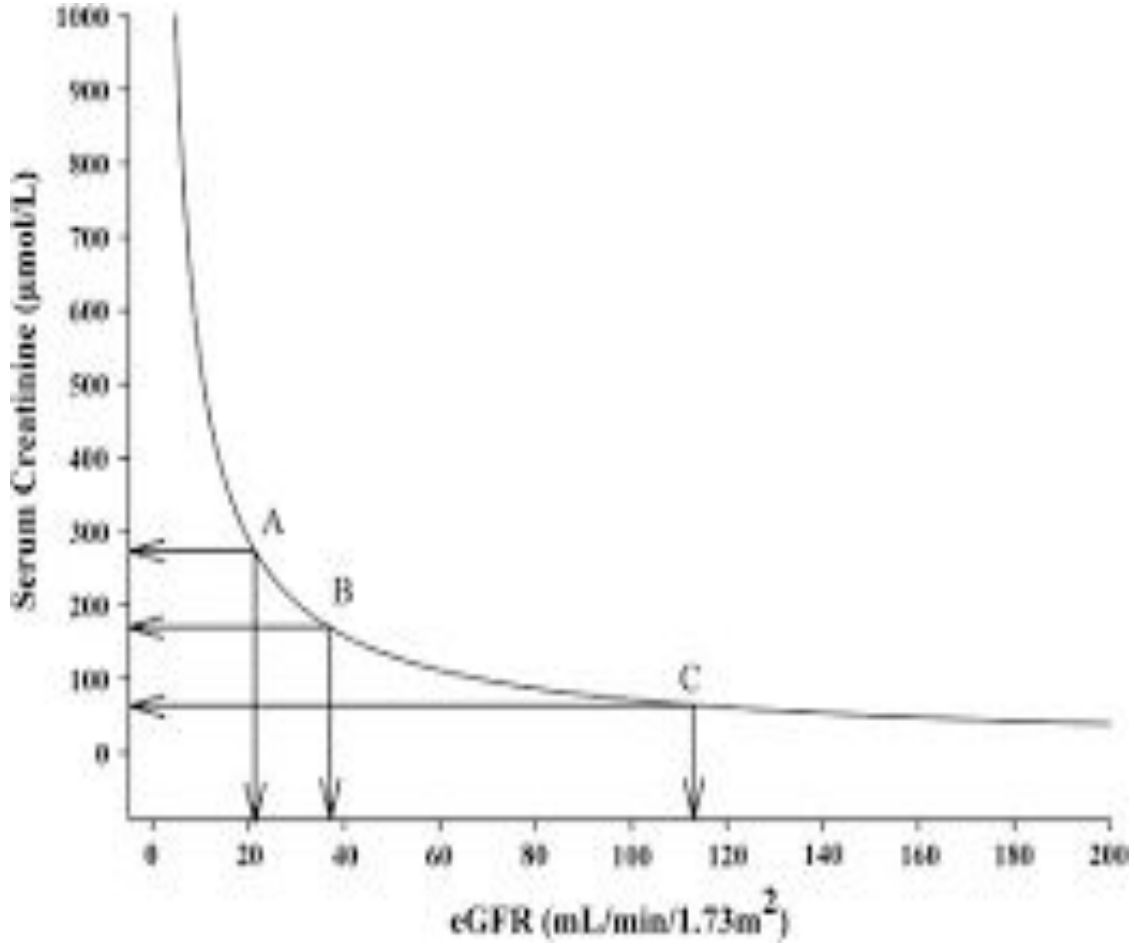
- Urinalysis components: dipstick, microscopy, specific gravity, osmolality.

- What each test tells you: proteinuria, hematuria, casts, concentrating ability.



Clinical Markers and Their Interpretation

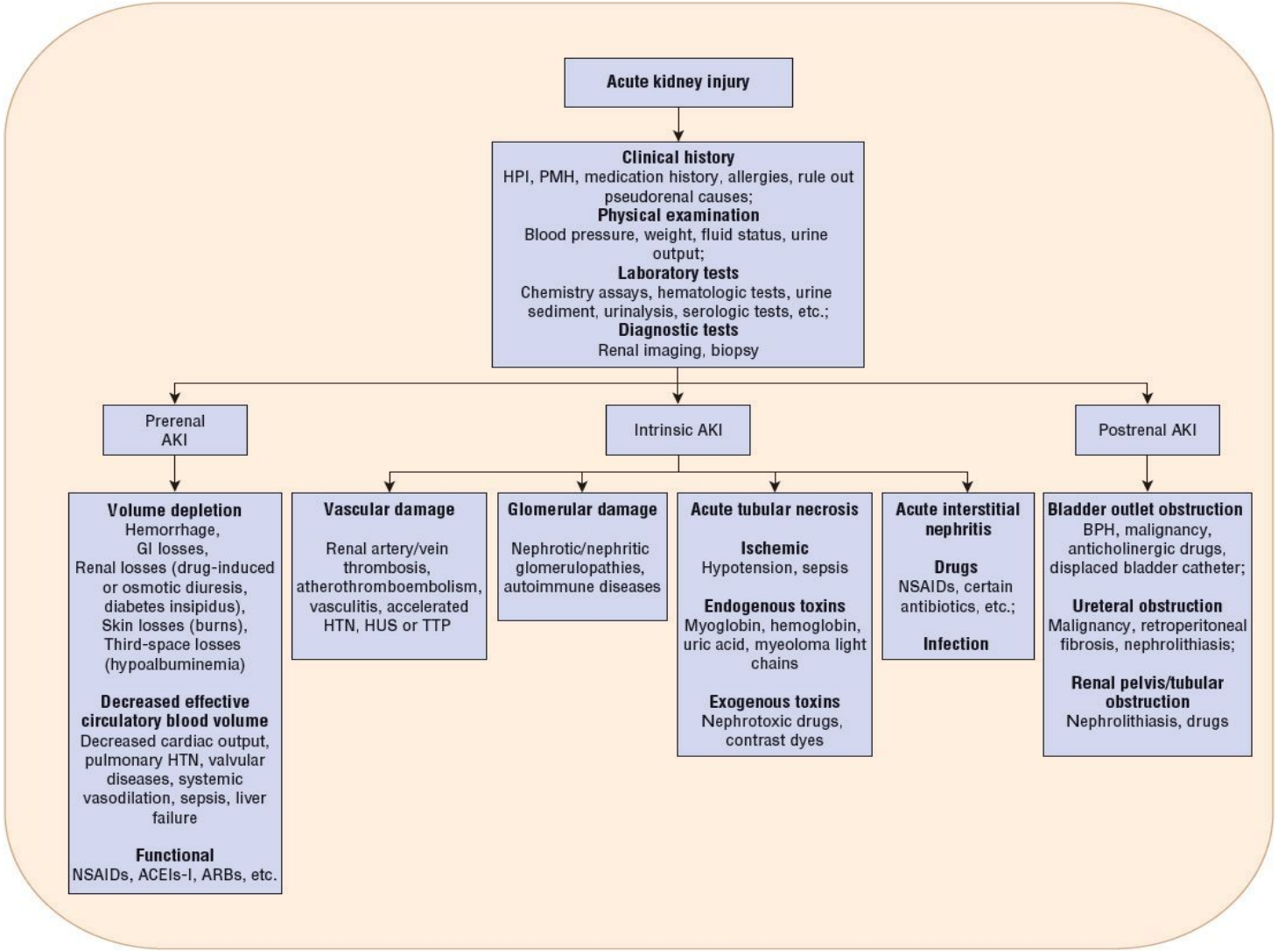
- **Serum creatinine and eGFR**: trends more important than single values.
- **Albuminuria categories**: A1, A2, A3 and prognostic implications.
- **Cystatin C** as alternative GFR marker.



Kevin Damman et al, 2011

Acute Kidney Injury Mechanisms and Classification

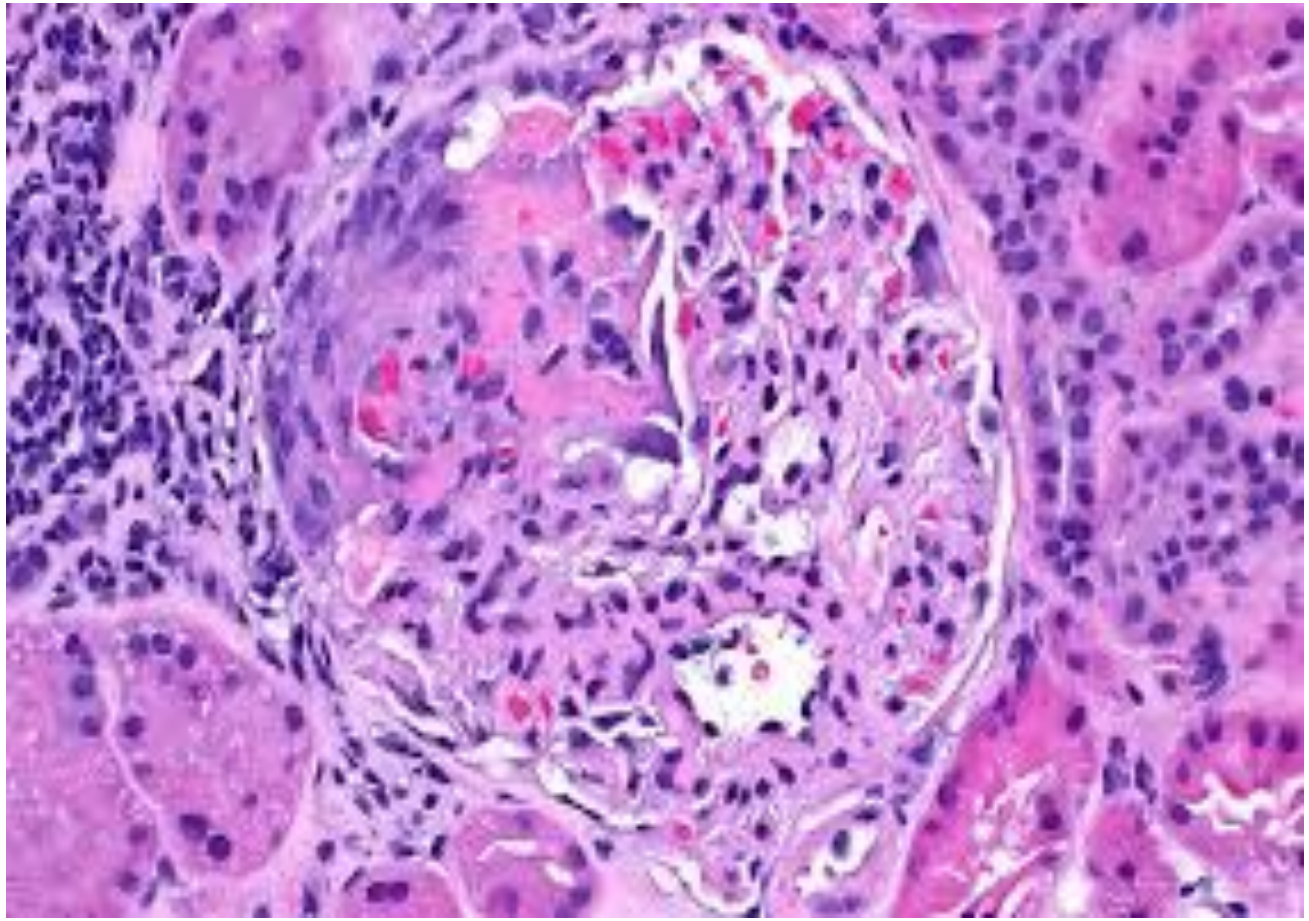
- **Categories**: pre-renal, intrinsic (glomerular, tubular, interstitial, vascular), post-renal.
- **Pathways**: ischemia, toxins, immune injury, obstruction.
- **Clinical approach**: rapid localization using history, urine, imaging.



William Dager

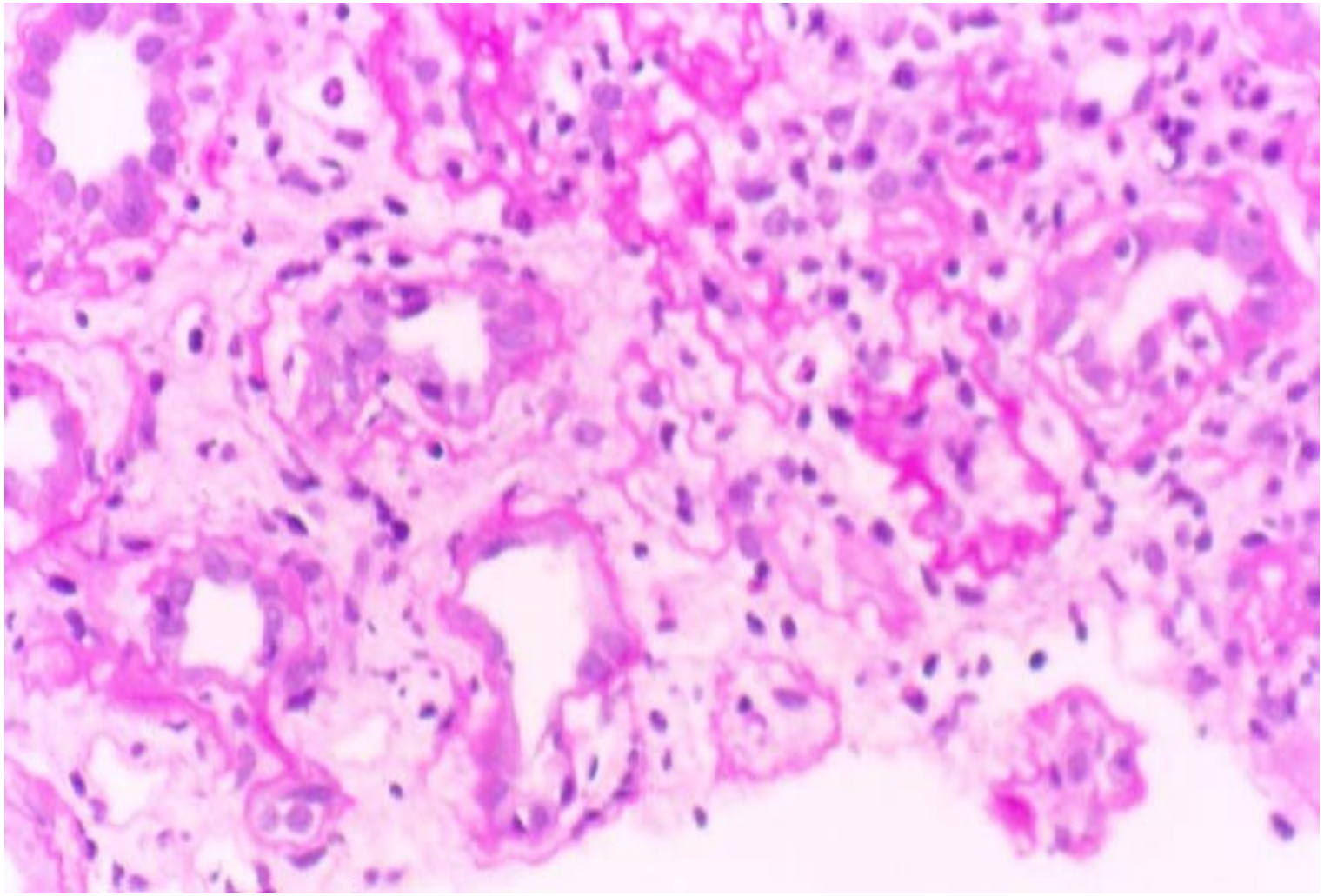
Glomerular Pathophysiology Patterns

- **Podocyte injury** → heavy proteinuria and nephrotic syndrome.
- **Immune complex deposition** → hematuria, nephritic presentations.
- **Hyperfiltration injury** → progressive glomerulosclerosis.



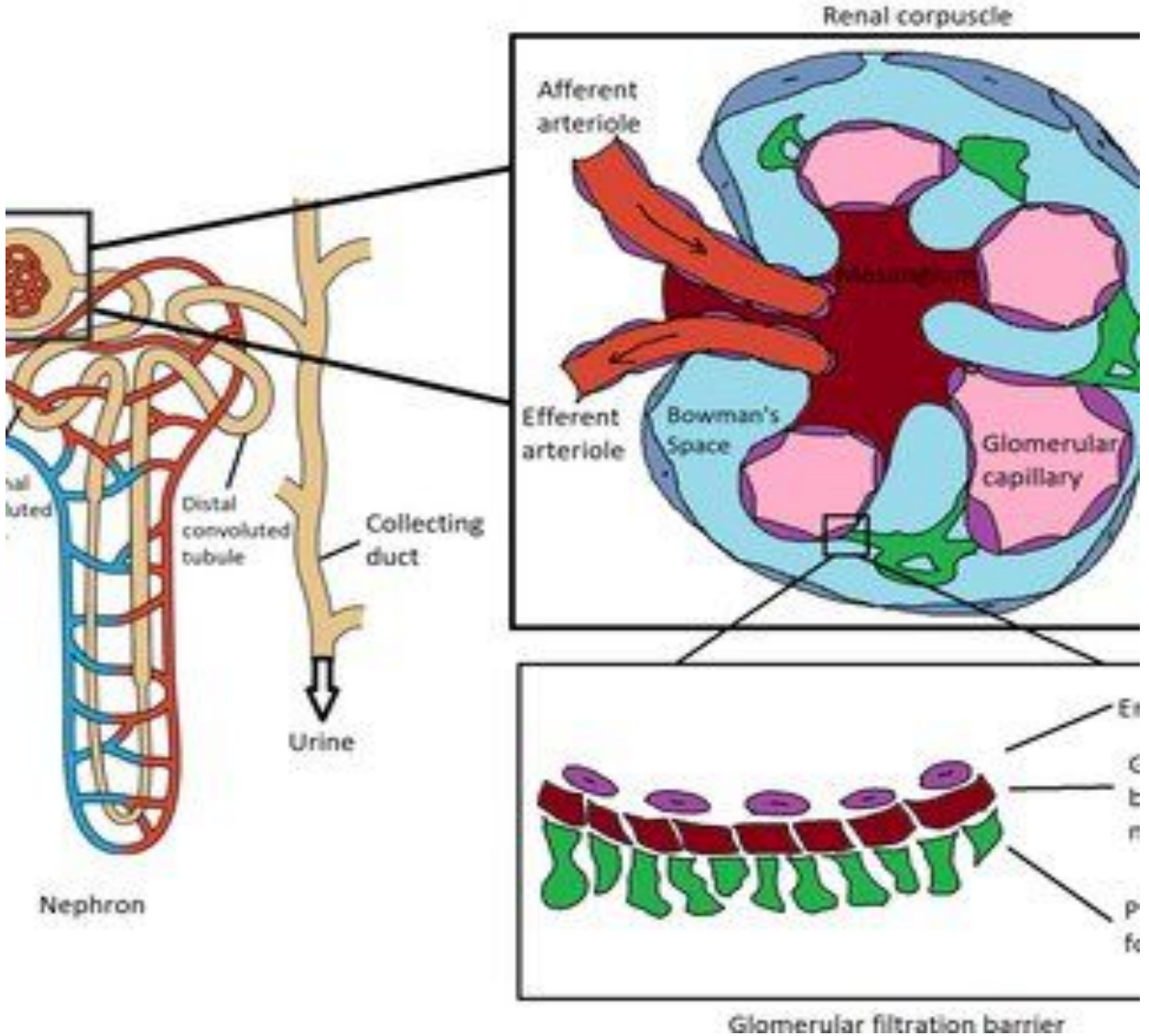
Tubular and Interstitial Pathophysiology

- **Acute tubular necrosis**: ischemic or toxic injury to tubular epithelial cells.
- **Interstitial nephritis**: immune mediated, drug or infection related.
- **Chronic interstitial** fibrosis as final common pathway to CKD.



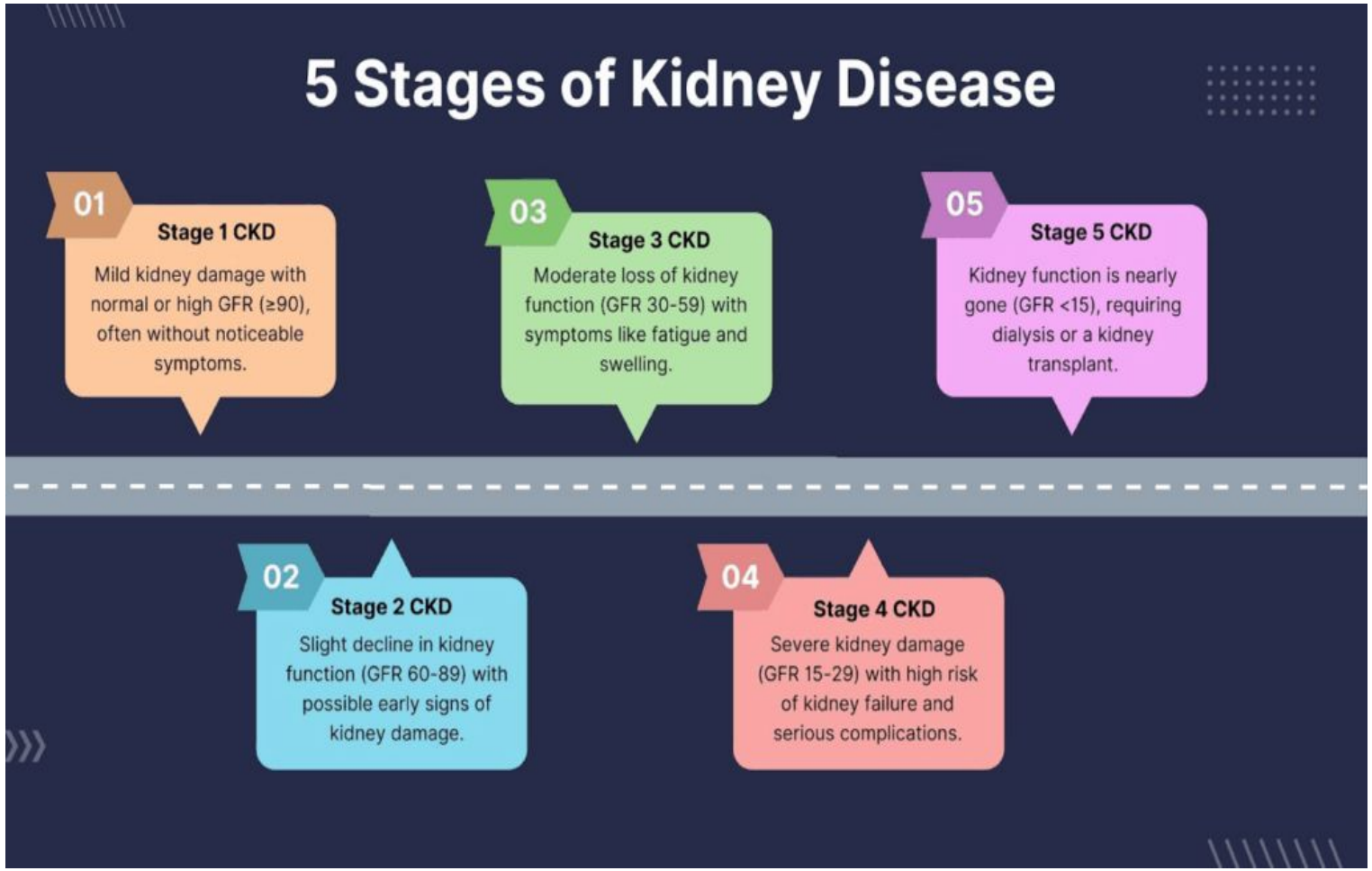
Renal Vascular Pathophysiology

- **Large vessel disease**: renal artery stenosis causing ischemic nephropathy.
- **Small vessel disease:** hyaline arteriolosclerosis from hypertension and diabetes.
- **Microangiopathy**: TMA causing acute injury.



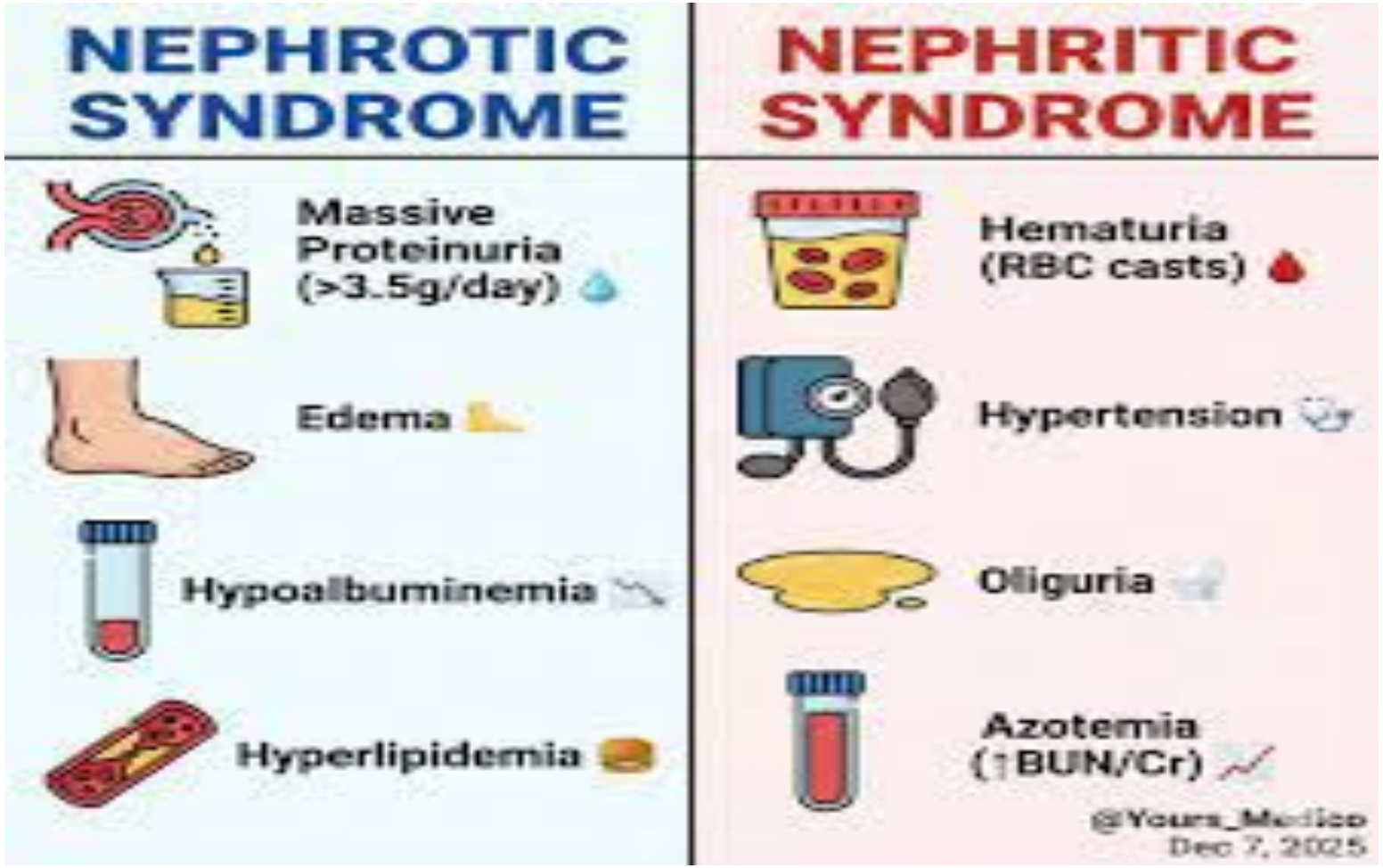
Systemic Diseases Leading to CKD and Progression Mechanisms

- **Diabetes:** metabolic and hemodynamic drivers of glomerular injury.
- **Hypertension:** pressure-mediated arteriolar damage and nephron loss.
- **Infections and toxins:** direct tubular injury and chronic scarring.

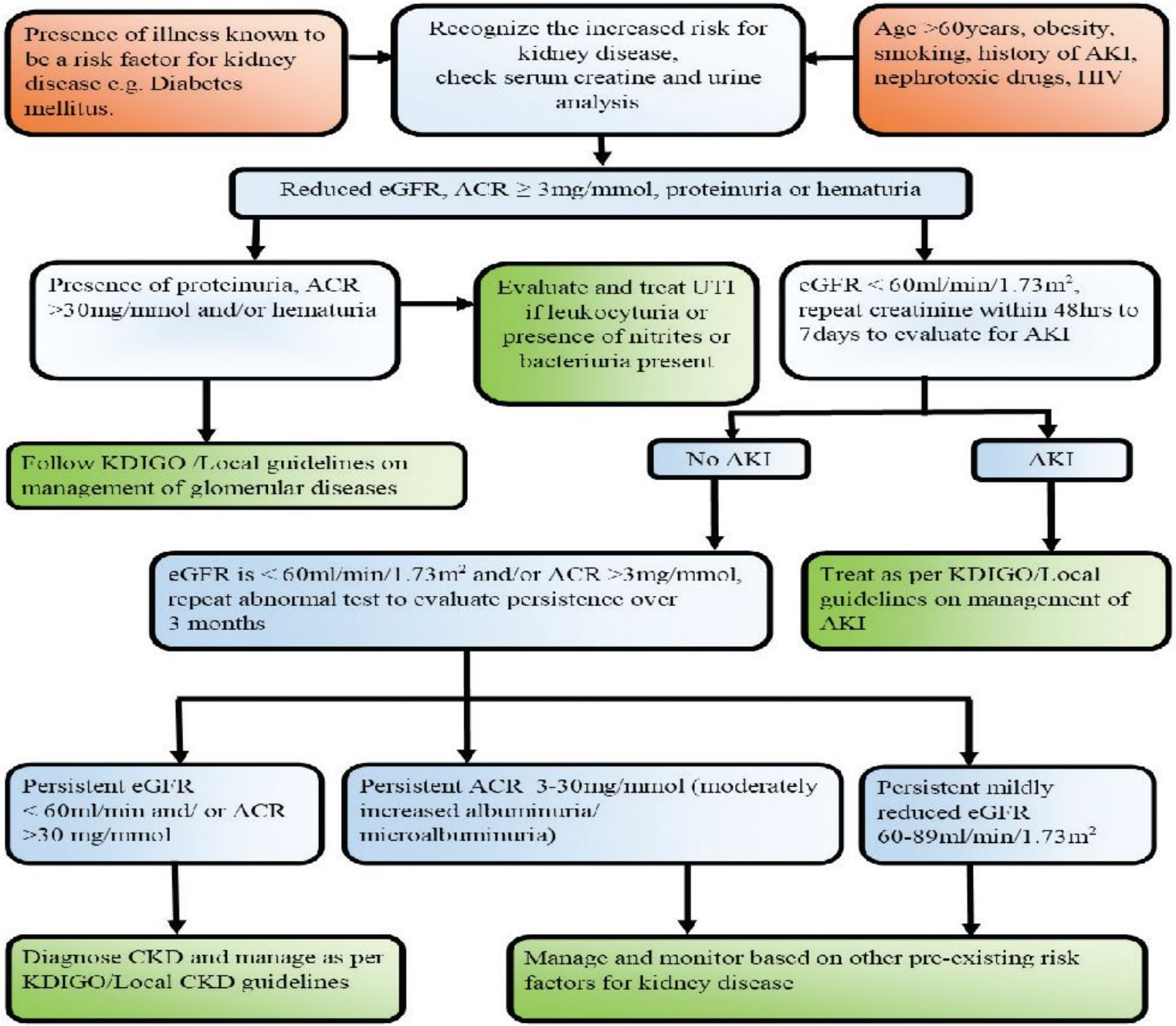


Linking Pathophysiology to Clinical Syndromes

- **Nephrotic syndrome:** heavy proteinuria, hypoalbuminemia, edema, hyperlipidemia.
- **Nephritic syndrome**: hematuria, hypertension, reduced GFR, RBC casts.
- **Tubular disorders**: polyuria, electrolyte wasting, acid-base disturbances.



Diagnostic Approach



Summary

- Anatomy informs function
- Physiology explains clinical signs
- Compartmental mapping simplifies diagnosis

THANK YOU