The Kidney

Urine Formation by the Kidneys: Glomerular Filtration, Renal Blood Flow, and Their Control

Kidney Functions

Excretion of Metabolic Waste Products

- Urea (from protein metabolism)
- Uric acid (from nucleic acid metabolism)
- Creatinine (from muscle metabolism)
- Bilirubin (from hemoglobin metabolism)

Excretion of Foreign Chemicals

- Pesticides
- Food additives
- Toxins
- Drugs

Secretion, Metabolism, and Excretion of Hormones

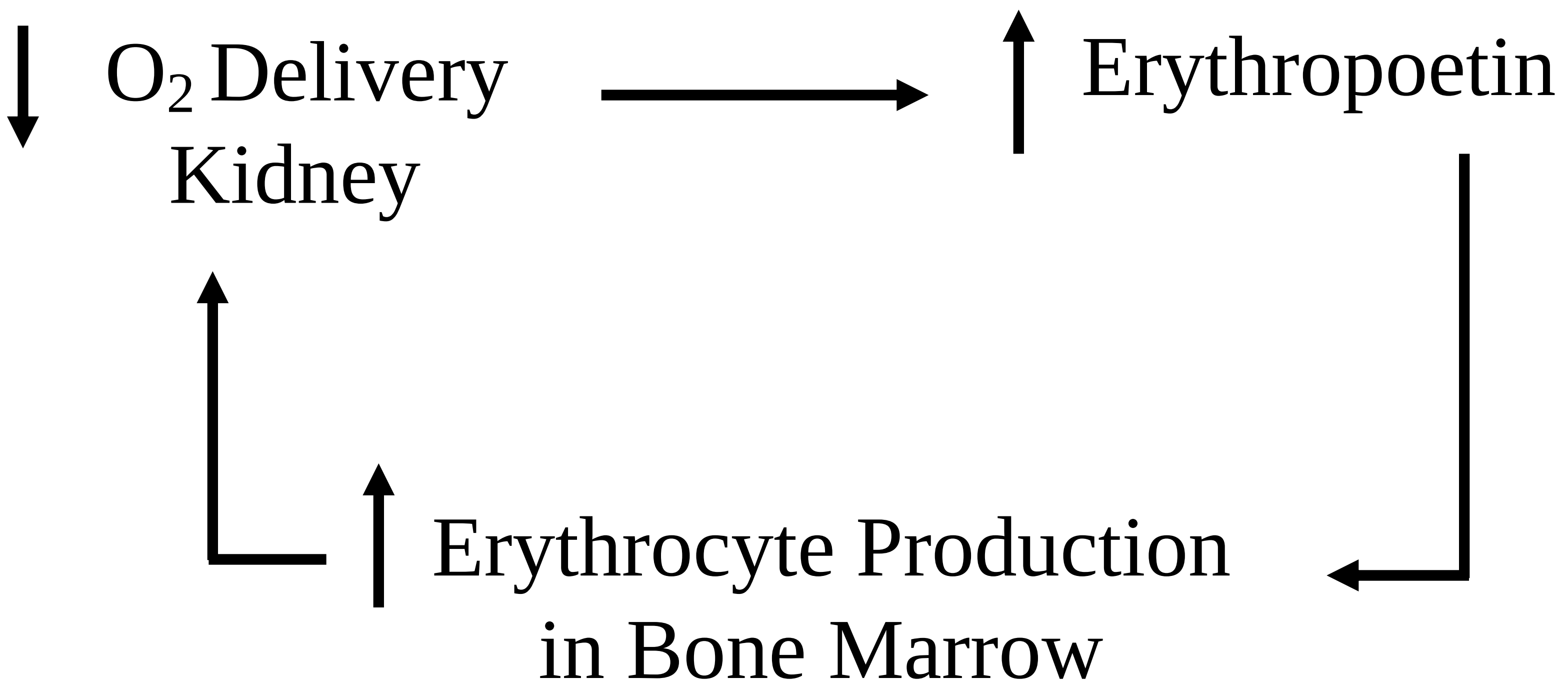
Hormones produced in the kidney

- Renal erythropoetic factor
- 1,25 dihydroxycholecalciferol (Vitamin D)
- Renin

Hormones metabolized and excreted by the kidney

- Most peptide hormones (e.g., insulin, angiotensin II, etc.)

Regulation of Erythrocyte Production



Regulation of Vitamin D Activity

- Kidney produces active form of vitamin D (1,25 dihydroxy vitamin D_3)
- Vitamin D_3 is important in calcium and phosphate metabolism

Regulation of Acid-Base Balance

- Excrete acids (kidneys are the only means of excreting non-volatile acids)

- Regulate body fluid buffers (e.g. Bicarbonate)

Glucose Synthesis

Gluconeogenesis: kidneys synthesize glucose from precursors (e.g., amino acids) during prolonged fasting

Regulation of Arterial Pressure

Endocrine Organ

- renin-angiotensin system
- prostaglandins
- kallikrein-kinin system

Control of Extracellular Fluid Volume

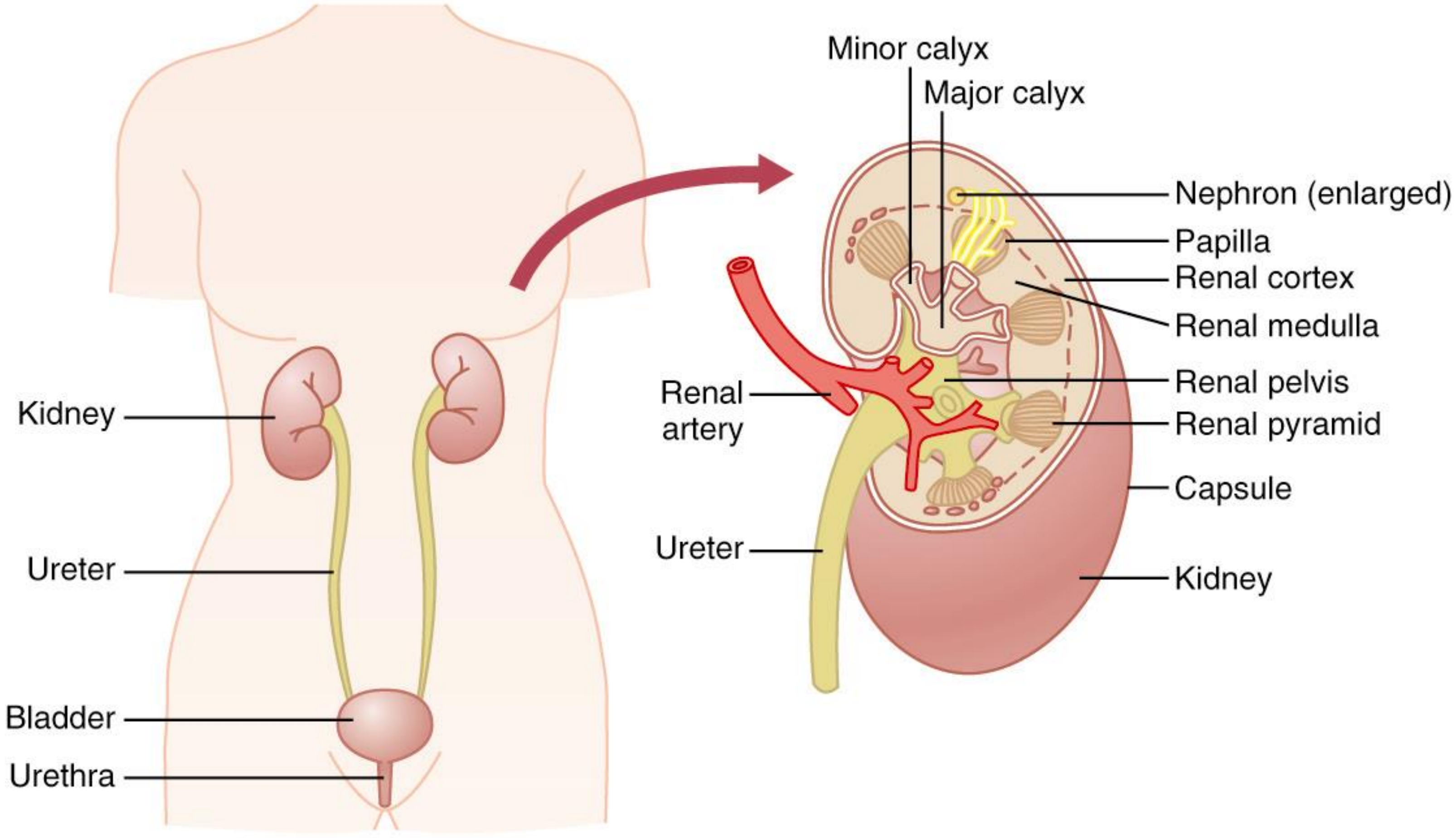
Regulation of Water and Electrolyte Balances

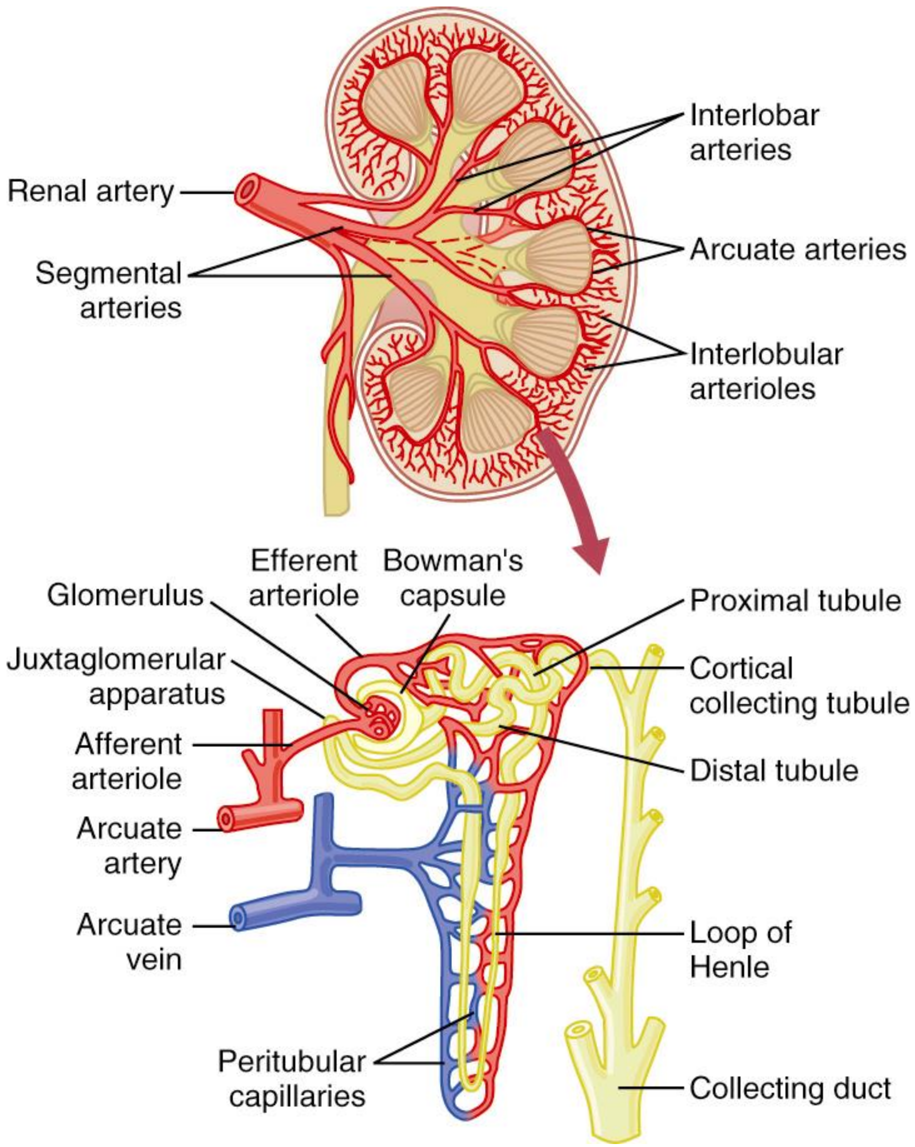
- Sodium and Water
- Potassium
- Hydrogen Ions
- Calcium, Phosphate, Magnesium

Summary of Kidney Functions

- Excretion of metabolic waste products: urea, creatinine, bilirubin, hydrogen
- Excretion of foreign chemicals: drugs, toxins, pesticides, food additives
- Secretion, metabolism, and excretion of hormones
  - renal erythropoetic factor
  - 1,25 dihydroxycholecalciferol (Vitamin D)
  - Renin
- Regulation of acid-base balance
- Gluconeogenesis: glucose synthesis from amino acids
- Control of arterial pressure
- Regulation of water & electrolyte excretion

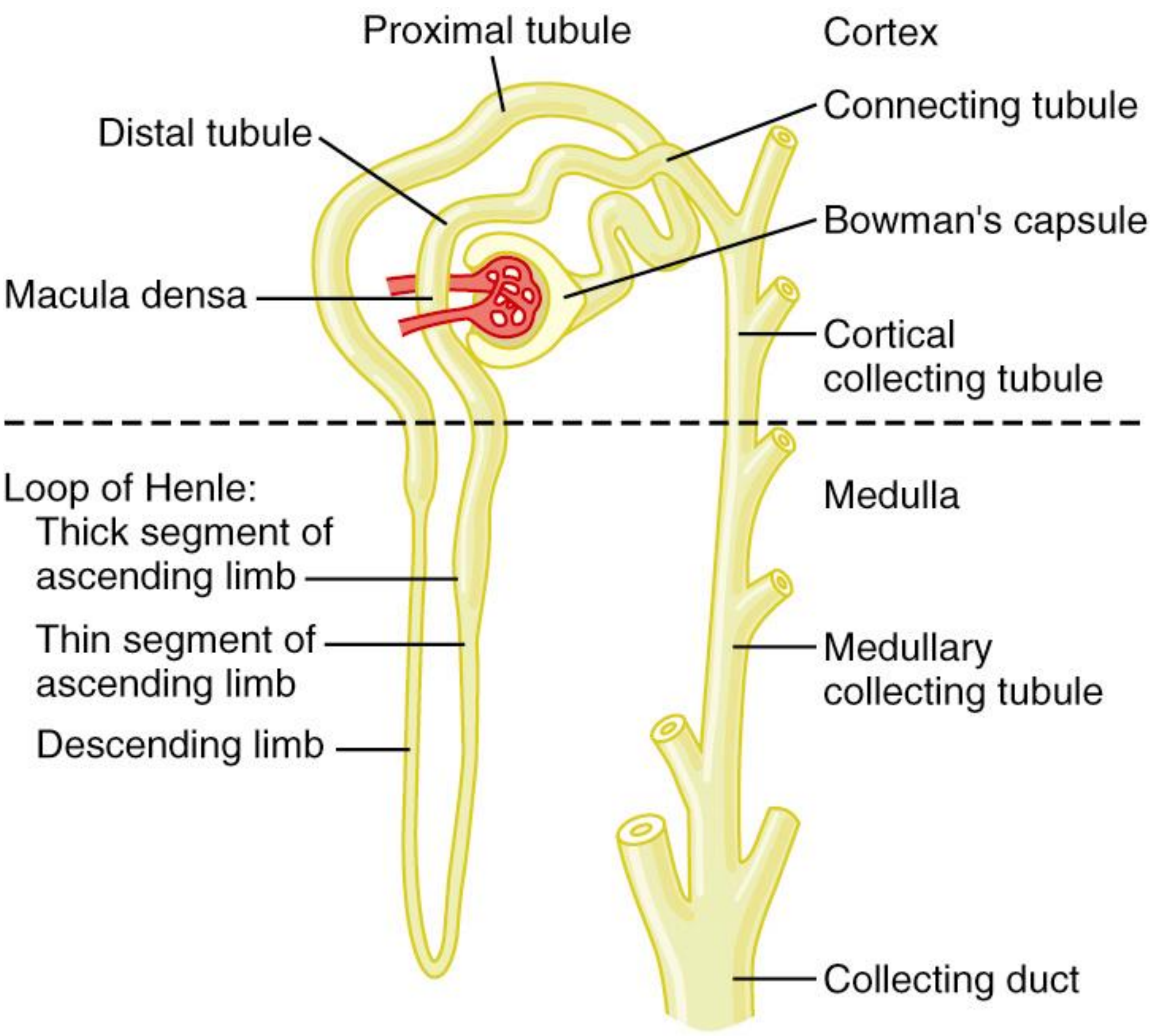
Kidneys and Urinary Tract System



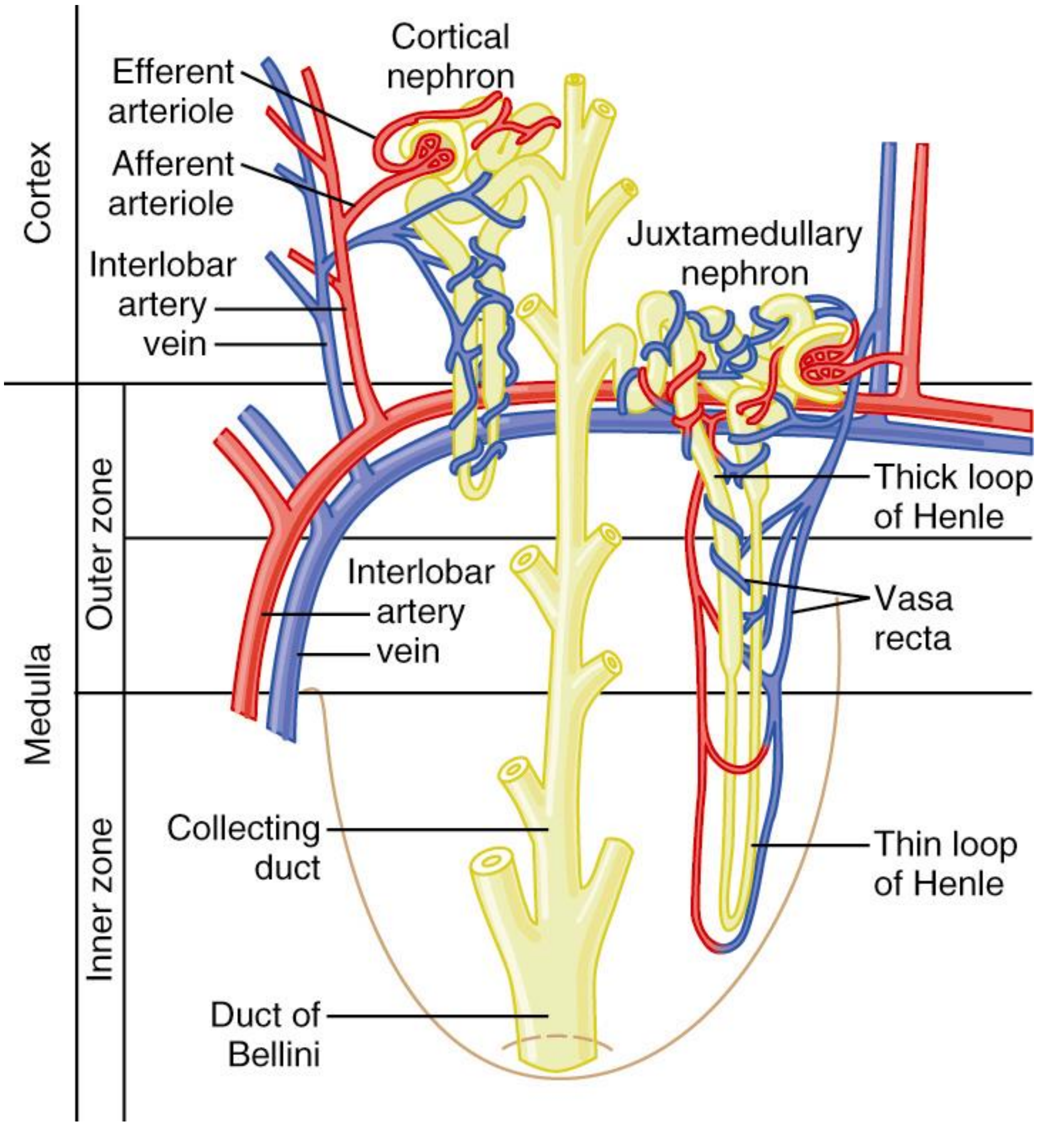


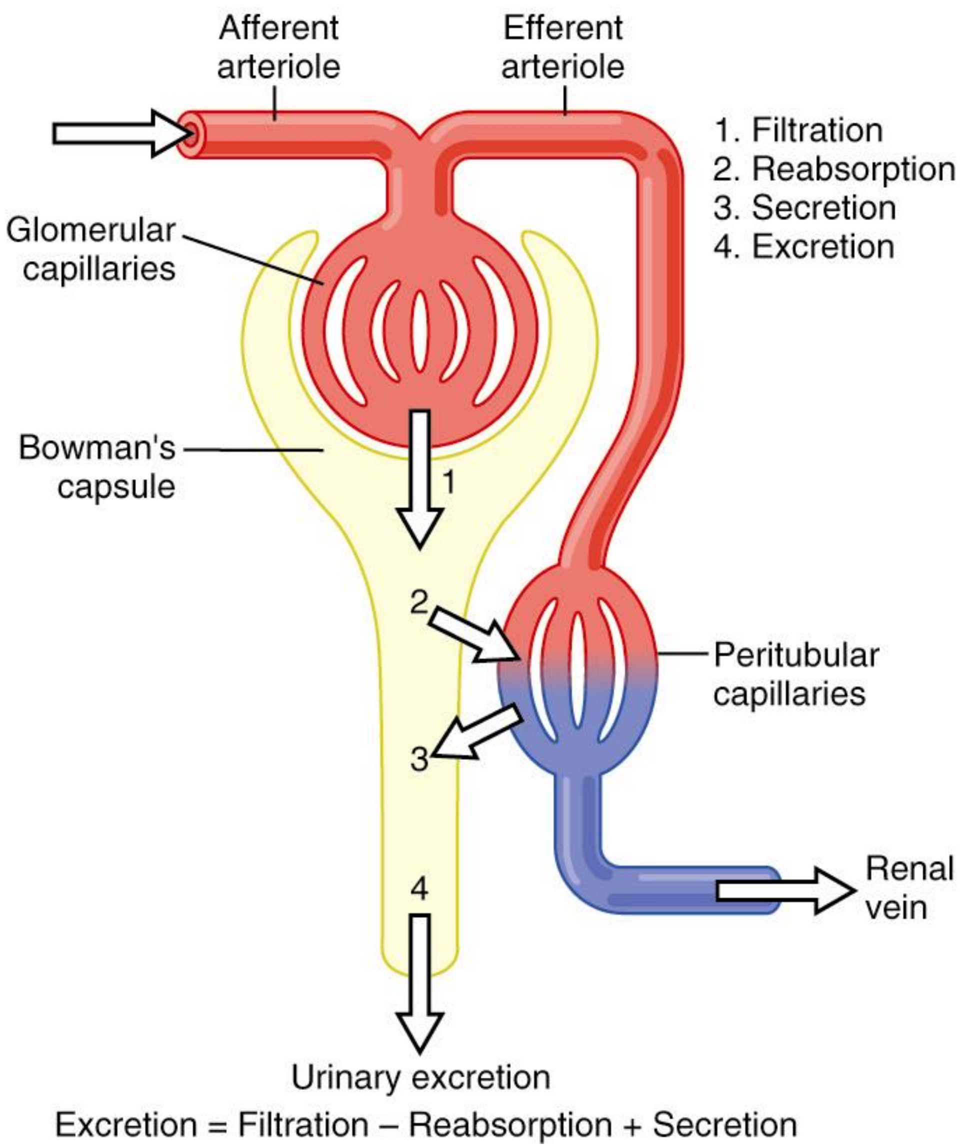
Nephron: functional unit of the kidney

Nephron Tubular Segments



Cortical and Juxtamedullary Nephron Segments





Basic Mechanisms of Urine Formation

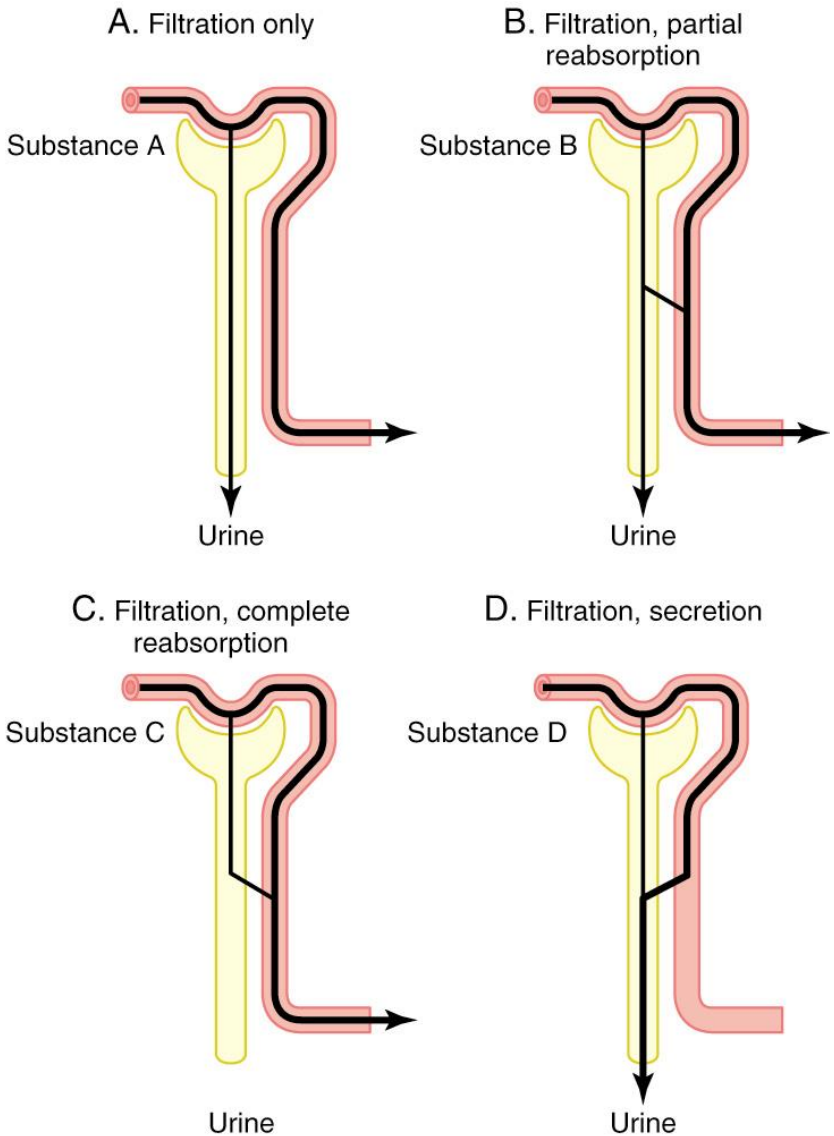
Excretion = Filtration – Reabsorption + Secretion

- Filtration: somewhat variable, not selective (except for proteins), averages 20% of renal plasma flow

- Reabsorption: highly variable and selective, most electrolytes (e.g. Na^+, K^+, Cl^-) and nutritional substances (e.g. glucose) are almost completely reabsorbed; most waste products (e.g. urea) poorly reabsorbed

- Secretion: variable; important for rapidly excreting some waste products (e.g. H^+), foreign substances (including drugs), and toxins

Renal Handling of Different Substances

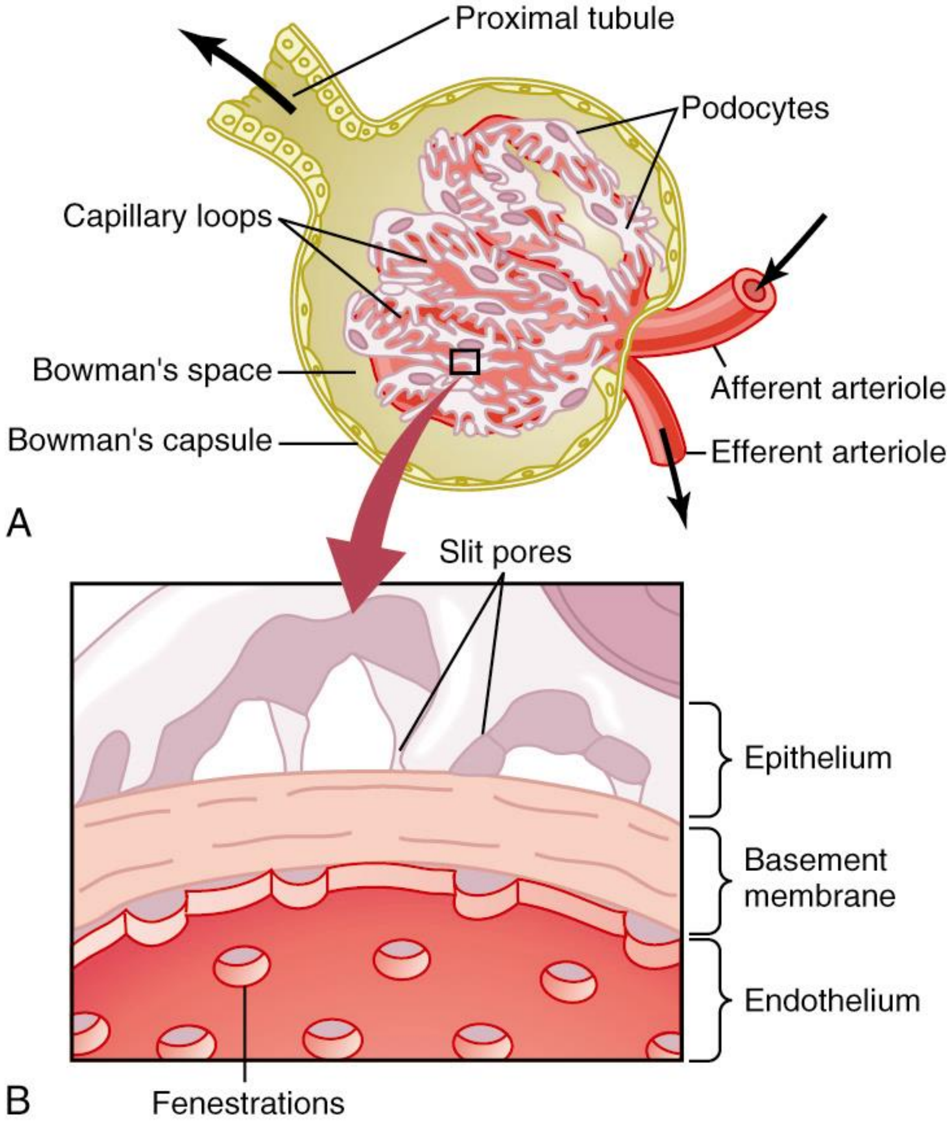


Renal Handling of Water and Solutes

	Filtration	Reabsorption	Excretion
Water (liters/day)	180	179	1
Sodium (mmol/day)	25,560	25,410	150
Glucose (gm/day)	180	180	0
Creatinine (gm/day)	1.8	0	1.8

Glomerular Filtration

- GFR = 125 ml/min = 180 liters/day
- Plasma volume is filtered 60 times per day
- Glomerular filtrate composition is about the same as plasma, except for large proteins
- Filtration fraction (GFR/Renal Plasma Flow) = 0.2 (i.e., 20% of plasma is filtered)



Glomerular Capillary Filtration Barrier

Glomerular Capillary Membrane Filtration Barrier

- Endothelium (fenestrated, 160-180 A pores)
- Basement Membrane (70-80 A pores), negative charged proteoglycans, restriction site for proteins
- Epithelial Cells (podocytes, 80-80 A pores) restriction site for proteins

The Ability of a Solute to Penetrate the Glomerular Membrane Depends on:

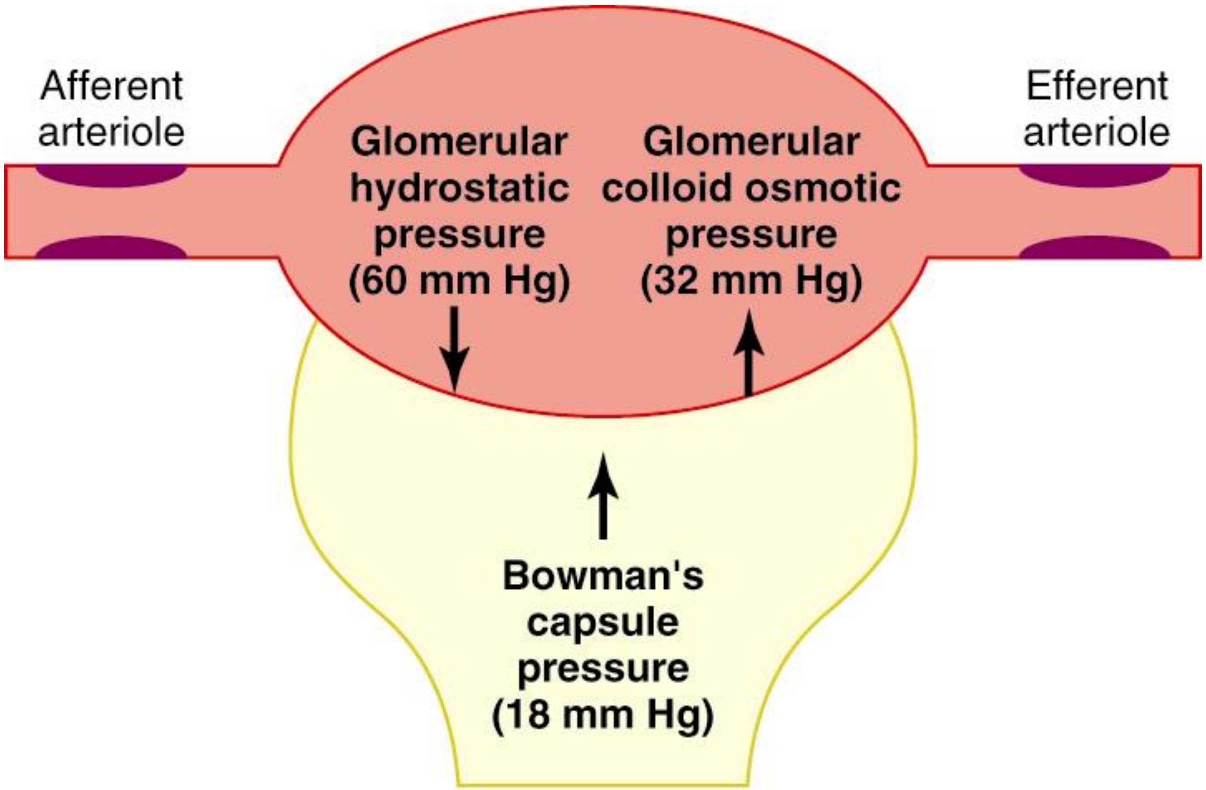
- Molecular size (small molecules > filterability)
- Ionic charge (cations > filterability)

Clinical Significance of Proteinuria

- Early detection of renal disease in at-risk patients
  - hypertension: hypertensive renal disease
  - diabetes: diabetic nephropathy
  - pregnancy: gestational proteinuric hypertension (pre-eclampsia)
  - annual “check-up”: renal disease can be silent
- Assessment and monitoring of known renal disease
- “Is the dipstick OK?”: dipstick protein tests are not very sensitive and not accurate: “trace” results can be normal & positives must be confirmed by quantitative laboratory test.

Microalbuminuria

- Definition: urine excretion of > 25-30 but < 150 mg albumin per day
- Causes: early diabetes, hypertension, glomerular hyperfiltration
- Prognostic Value: diabetic patients with microalbuminuria are 10-20 fold more likely to develop persistent proteinuria



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)

Determinants of Glomerular Filtration Rate

Normal Values:

GFR = 125 ml/min

Net Filt. Press = 10 mmHg

K_f = 12.5 ml/min per mmHg,

GFR = 12.5 x 10 = 125 ml/min

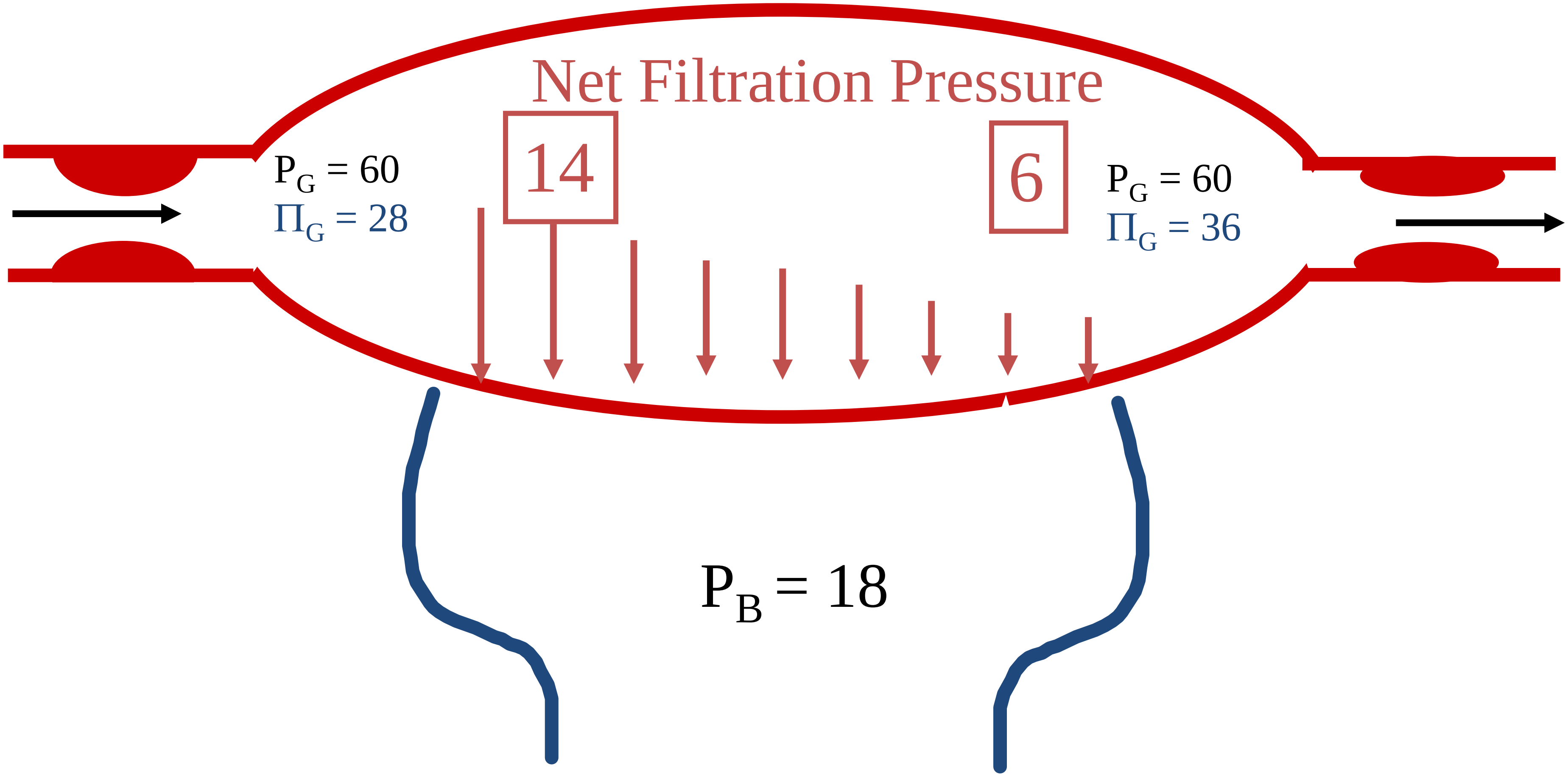
Glomerular Capillary Filtration Coefficient (K_f)

- K_f = hydraulic conductivity x surface area
- Normally not highly variable
- Disease that can reduce K_f and GFR
  - chronic hypertension
  - obesity / diabetes mellitus
  - glomerulonephritis

Bowman's Capsule Hydrostatic Pressure (P_B)

- Normally changes as a function of GFR, not a physiological regulator of GFR
- Tubular Obstruction
  - kidney stones
  - tubular necrosis
- Urinary tract obstruction
  - Prostate hypertrophy/cancer

Net Filtration Pressure Decreases Along the Glomerulus because of Increasing Glomerular Colloid Osmotic Pressure

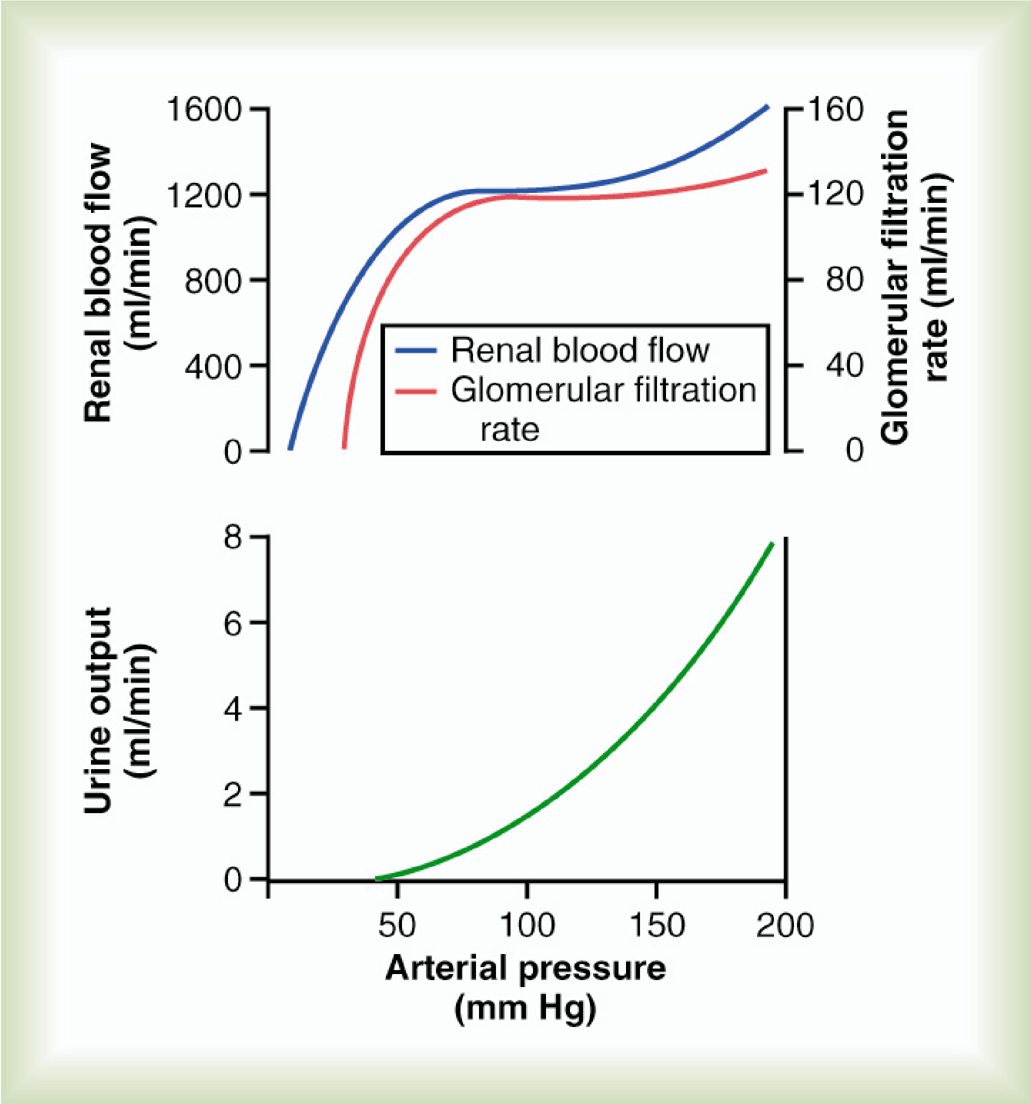


Glomerular Hydrostatic Pressure (P_G)

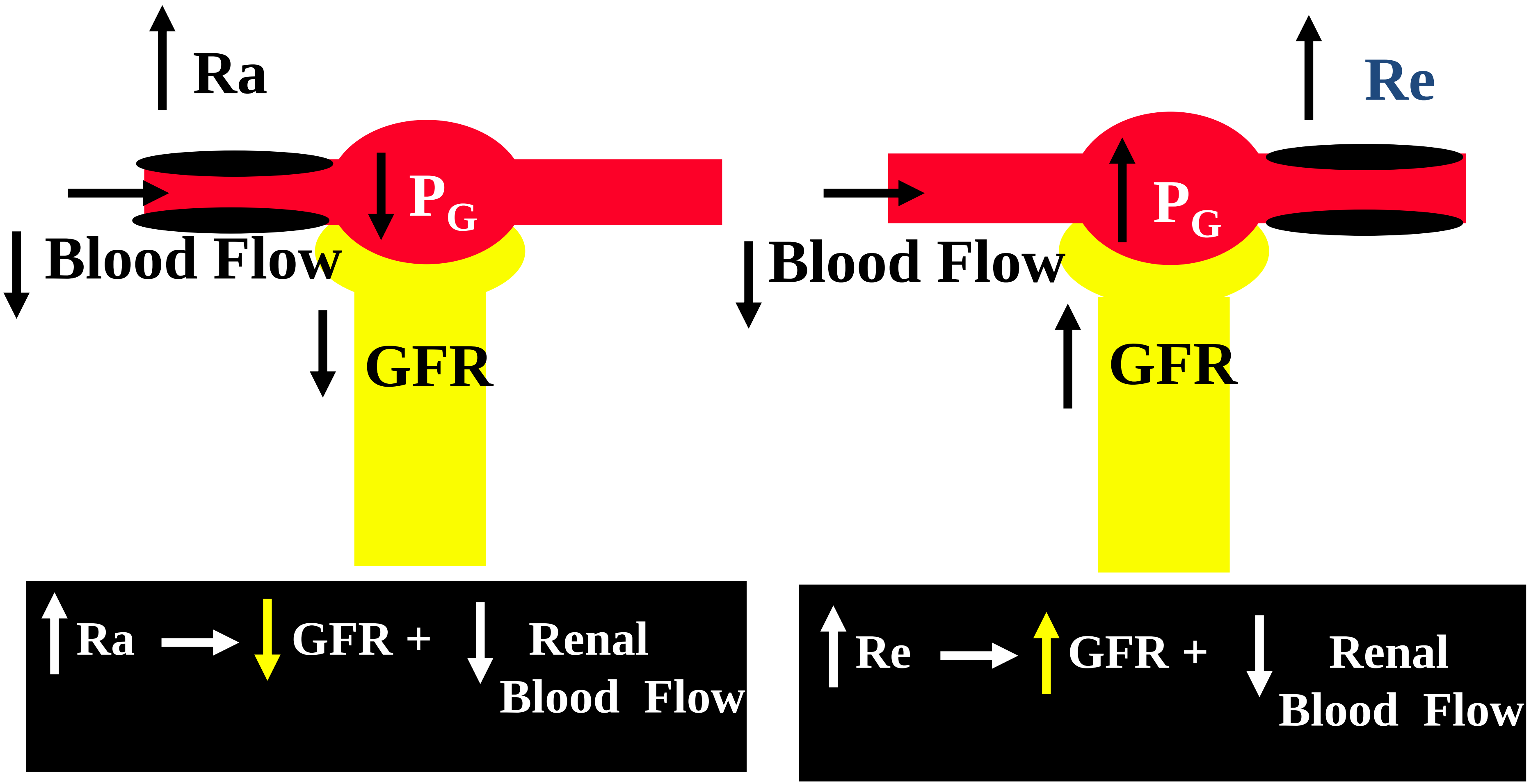
- Is the determinant of GFR most subject to physiological control

- Factors that influence P_G
  - arterial pressure (effect is buffered by autoregulation)
  - afferent arteriolar resistance
  - efferent arteriolar resistance

Renal Blood Flow and GFR Autoregulation



Effect of Afferent and Efferent Arteriolar Constriction on Glomerular Pressure



Control of Glomerular Filtration

- Neurohumoral
- Local (Intrinsic)

Control of Glomerular Filtration

1. Sympathetic Nervous System

$\uparrow\uparrow R_A + \uparrow R_E \longrightarrow \downarrow GFR + \downarrow\downarrow RBF$

2. Catecholamines (norepinephrine)

$\uparrow\uparrow R_A + \uparrow R_E \longrightarrow \downarrow GFR + \downarrow\downarrow RBF$

3. Angiotensin II

$\uparrow R_E \longrightarrow \leftrightarrow GFR + \downarrow RBF$

(prevents a decrease in GFR)

Control of Glomerular Filtration

4. Prostaglandins

$\downarrow\downarrow R_A + \downarrow R_E \longrightarrow \uparrow GFR + \uparrow\uparrow RBF$

5. Endothelial-Derived Nitric Oxide (EDRF)

$\downarrow\downarrow R_A + \downarrow R_E \longrightarrow \uparrow GFR + \uparrow\uparrow RBF$

6. Endothelin

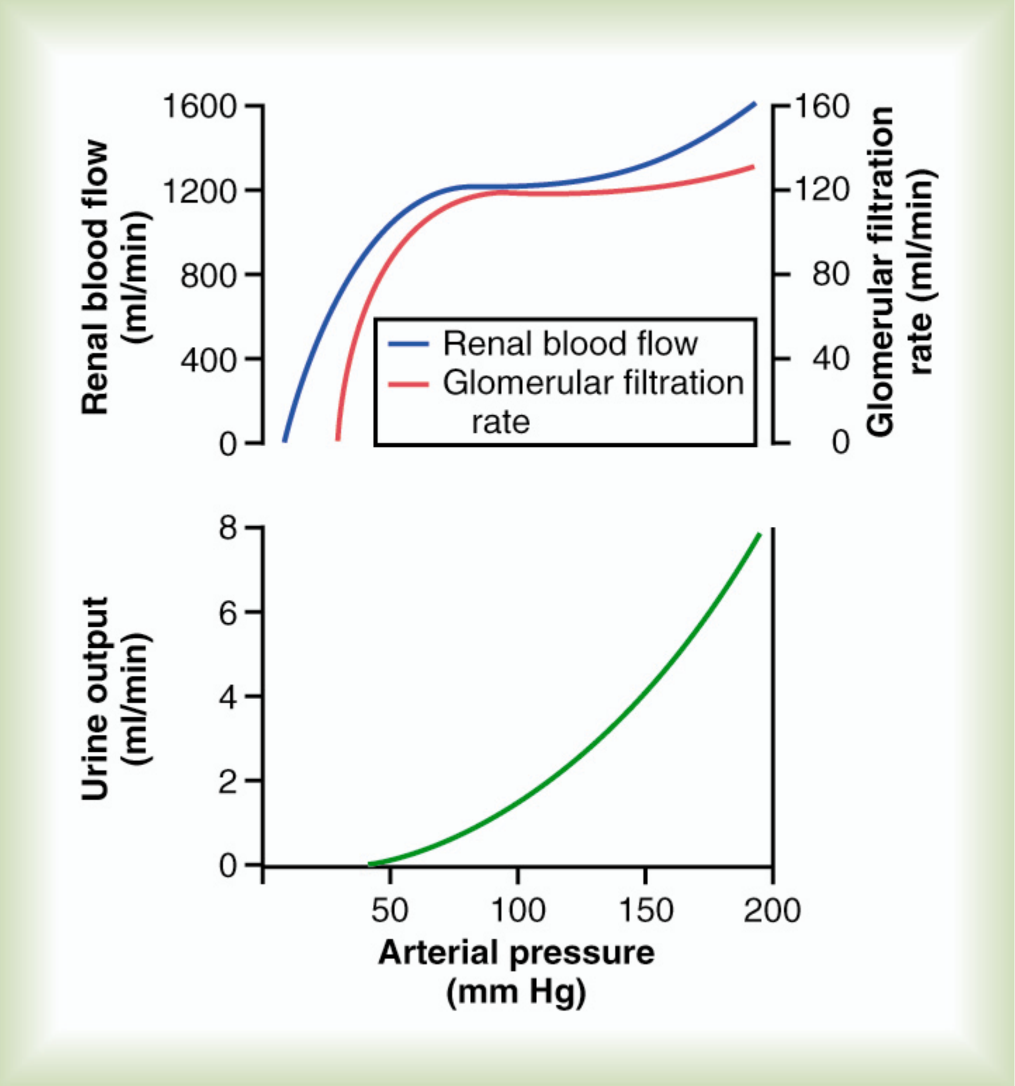
$\uparrow\uparrow R_A + \uparrow R_E \longrightarrow \downarrow GFR + \downarrow\downarrow RBF$

Control of Glomerular Filtration

7. Autoregulation of GFR and Renal Blood Flow

- Myogenic Mechanism
- Macula Densa Feedback (tubuloglomerular feedback)
- Angiotensin II (contributes to GFR but not RBF autoregulation)

Renal Blood Flow and GFR Autoregulation



Other Factors That Influence GFR

- Prostaglandins: increase GFR; non-steroidal anti-inflammatory agents can decrease GFR, especially in volume depleted states
- Fever, pyrogens: increase GFR
- Glucorticoids: increase GFR
- Aging: decreases GFR ~10%/decade after 40 yrs
- Dietary protein: high protein increases GFR
  low protein decreases GFR
- Hyperglycemia: increases GFR (diabetes mellitus)