The Urinary System: Functional Anatomy and Urine Formation by the Kidneys

U N I T V

Chapter 26

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Excretion of Metabolic Waste Products

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

Excretion of Foreign Chemicals and Drugs

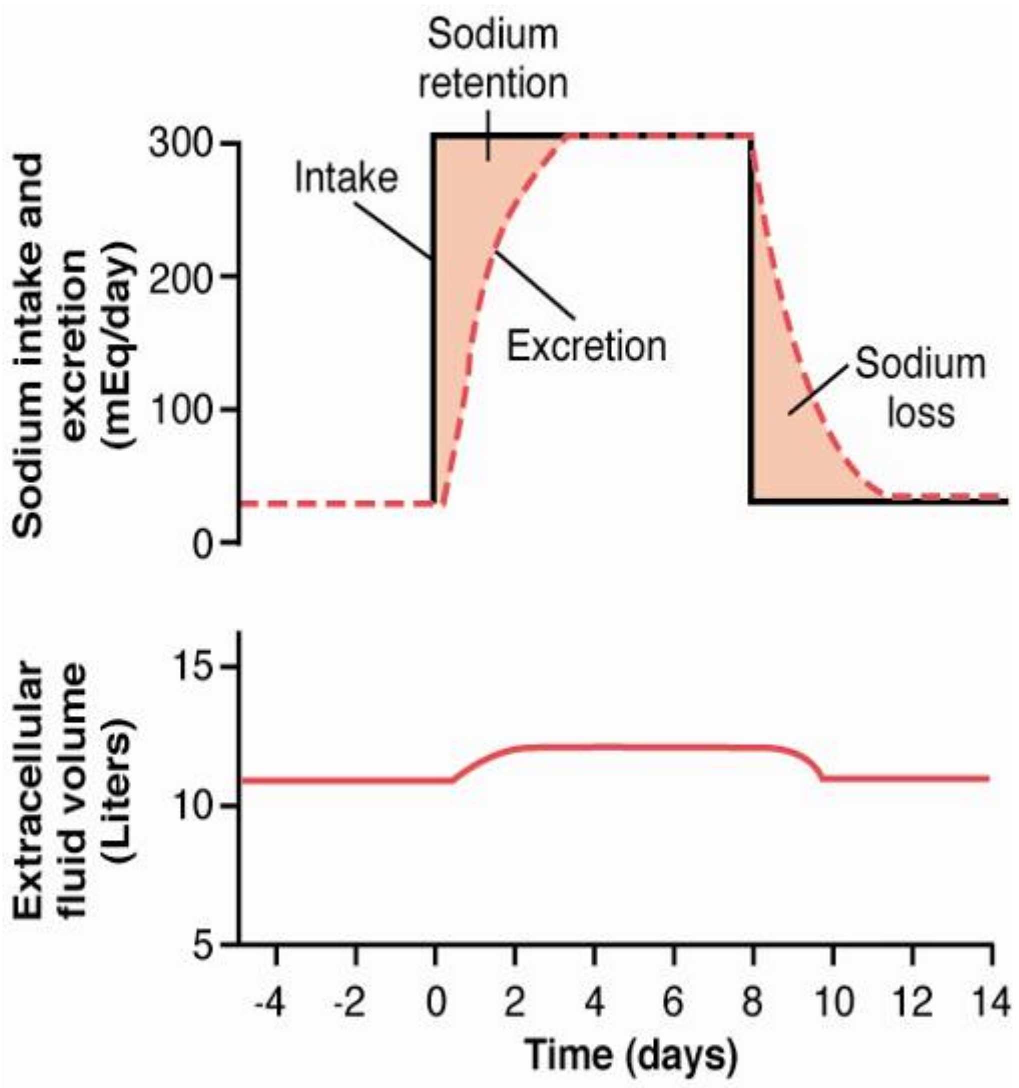
- Pesticides
- Food additives
- Toxins
- Drugs

Regulation of Water and Electrolyte Balances

- Input = output

Effect of ↑ Na (10X) intake on urinary Na excretion and ECFV

- Within 2-3 days →renal Na excretion ↑
- Modest accumulation of Na →↑ ECFV slightly → triggers hormonal changes & compensatory responses →↑ renal Na excretion
- Same for H2O, K, H^+, Ca, P, Mg



Regulation of Arterial Pressure

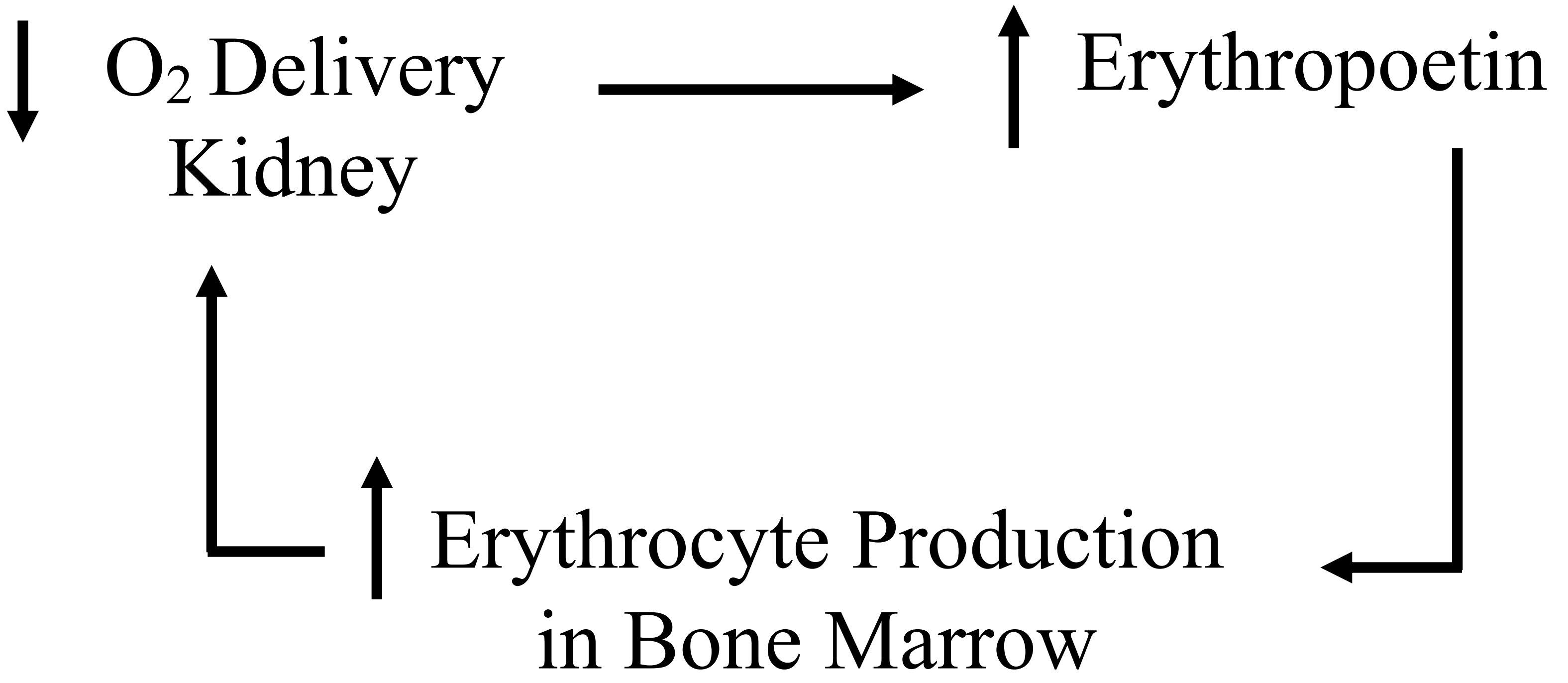
- Excretion of Na & H2O
- Secretion of hormones and vasoactive factors
  - Renin-angiotensin system
  - Prostaglandins

Regulation of Acid-Base Balance

- Excrete acids (kidneys are the only means of excreting sulfuric acid and phosphoric acid)

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

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 Ca & P metabolism

Secretion, Metabolism, and Excretion of Hormones

Hormones produced in the kidney

- Erythropoietin
- Thrombopoietin
- 1,25 dihydroxycholecalciferol (Vitamin D)
- Renin
- Prostaglandins

Hormones metabolized and excreted by the kidney

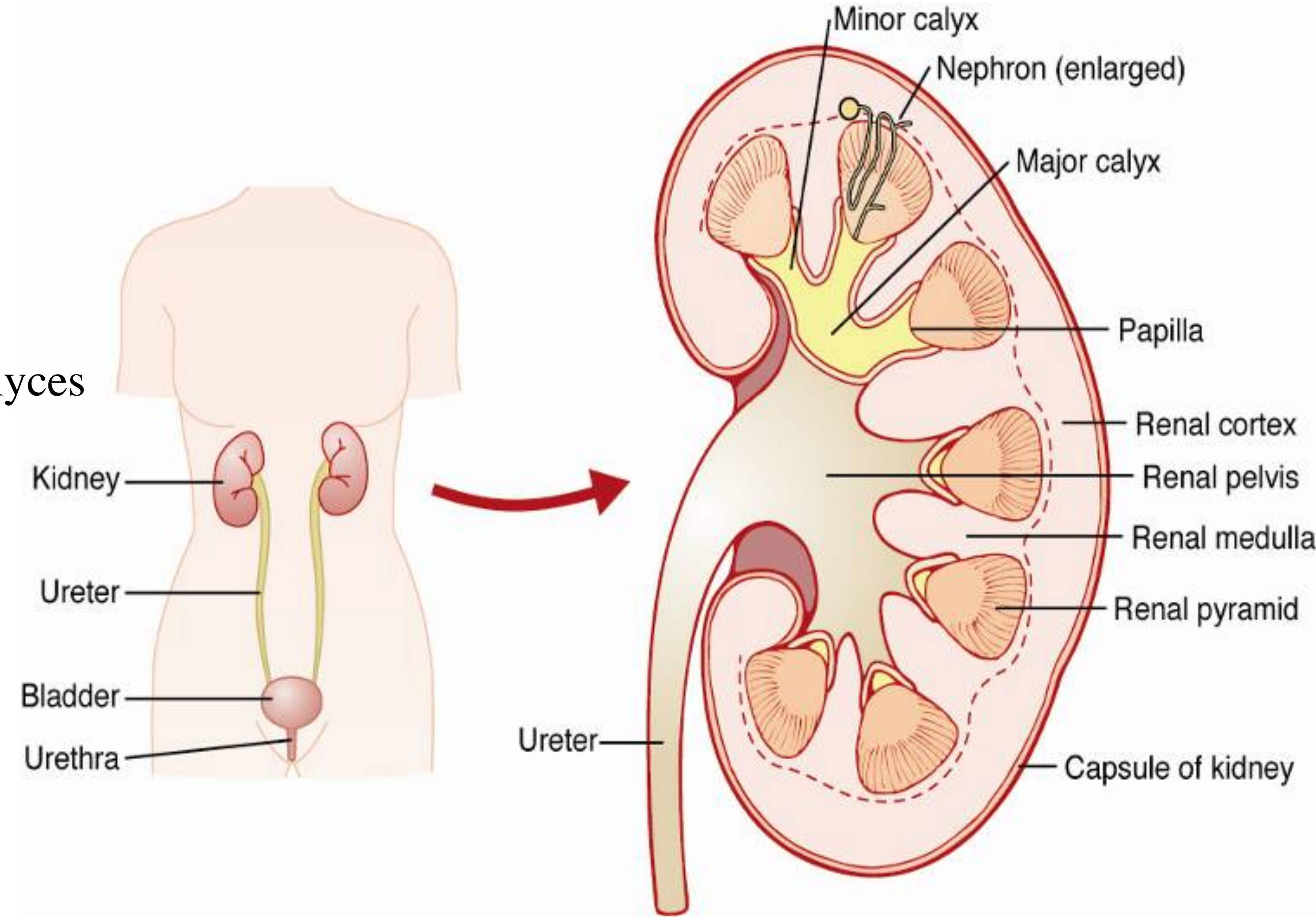
- Most peptide hormones (e.g. insulin, angiotensin II, etc.)

Glucose Synthesis

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

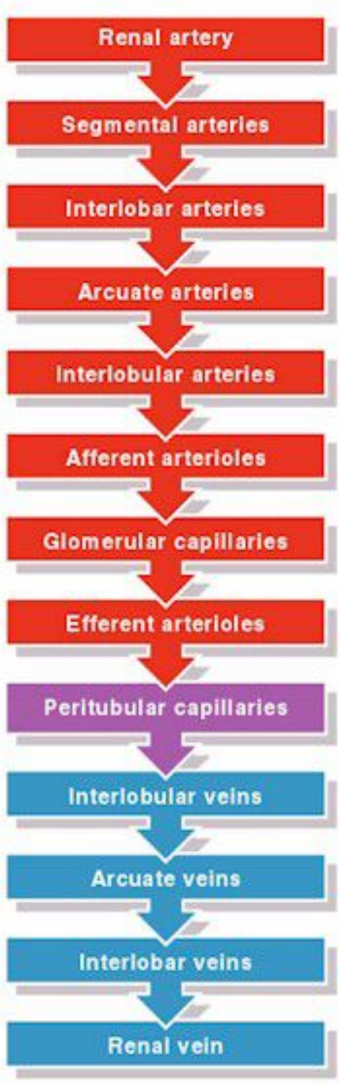
Urinary system

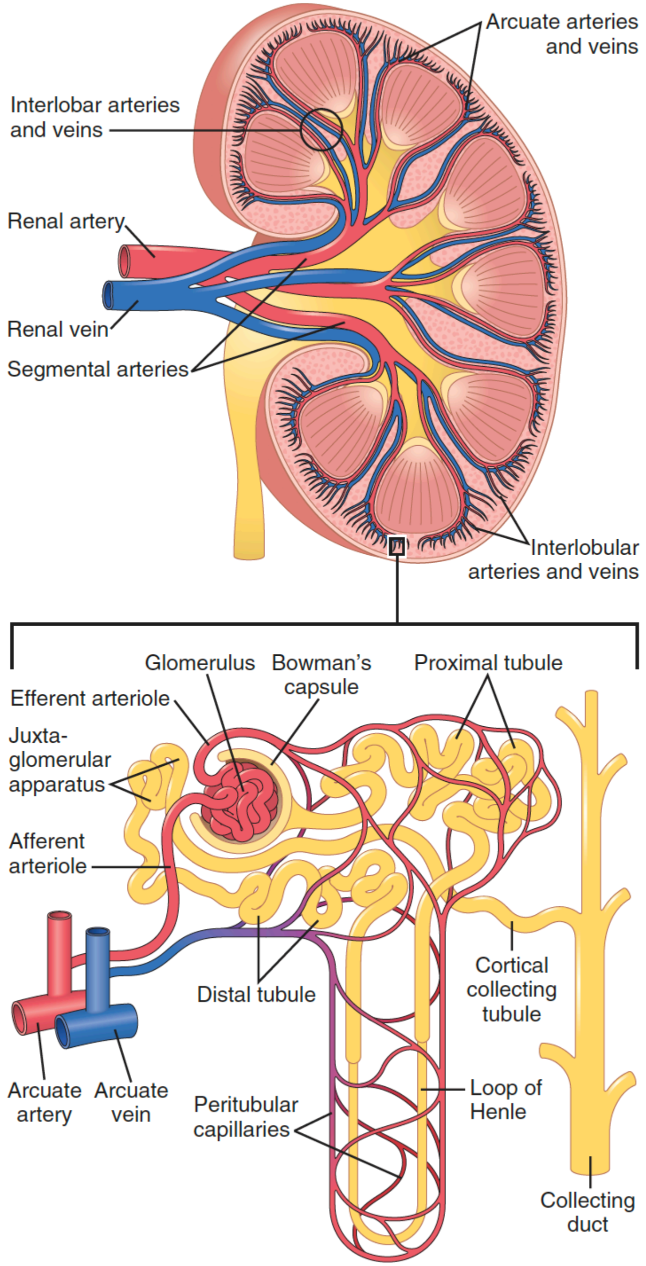
- Cortex & medulla
- Renal pyramids→ papilla→renal pelvis
- Renal pelvis→major calyces → minor calyces



Renal Blood Supply

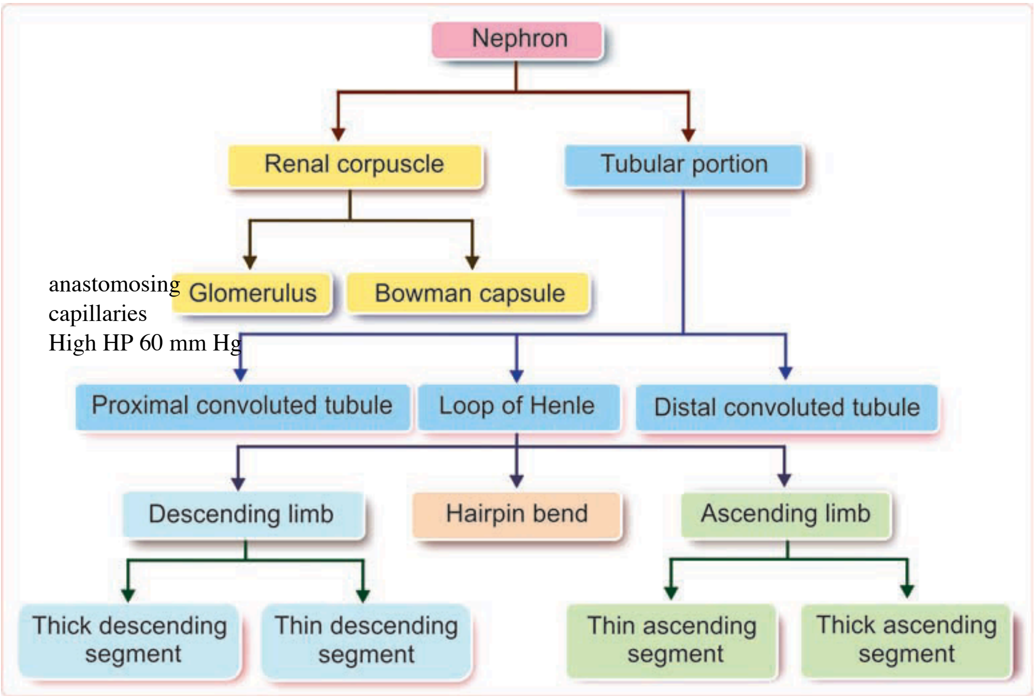
- Blood flow to What does ~22% CO = 1100 ml/min.
- 2 capillary beds (glomerular (60 mm Hg) & peritubular (13 mm Hg)→reabsorption.

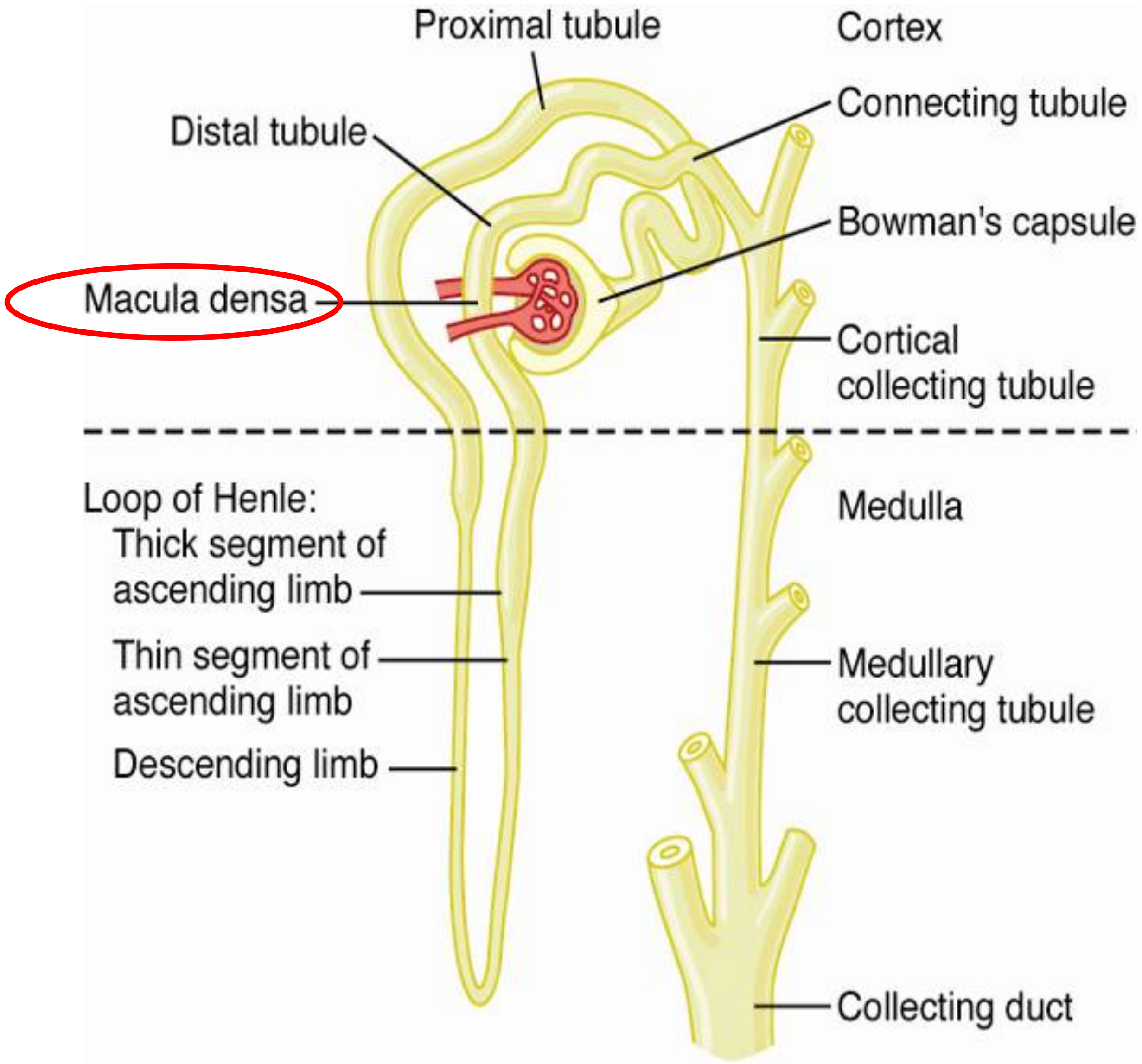




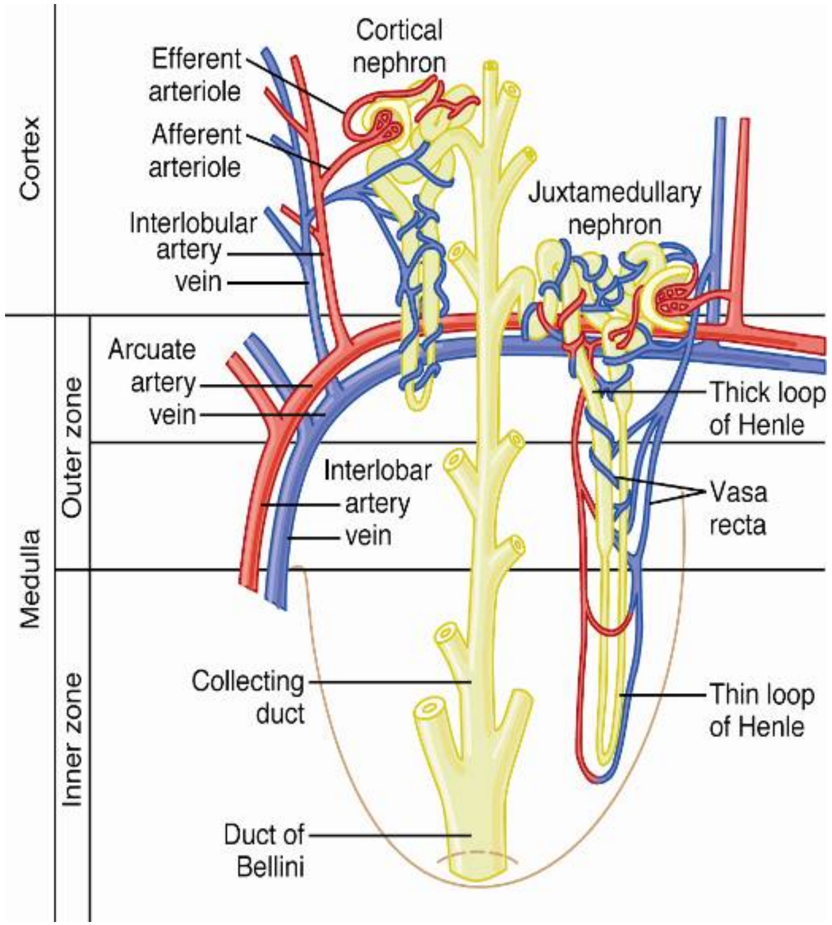
Nephron Tubular Segments

800K-1M nephrons, ↓ with ageing (adaptive response)



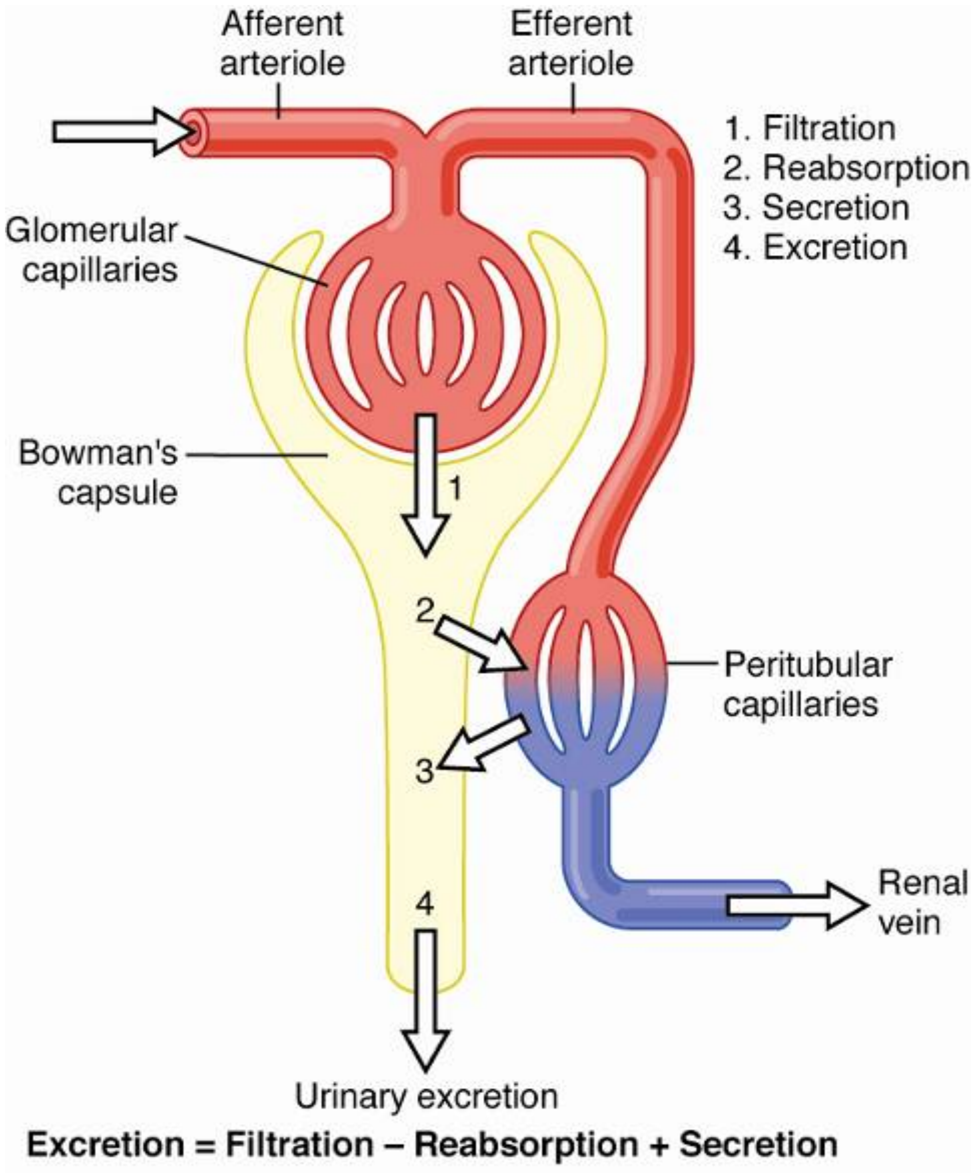


Regional Differences in Nephron Structure: Cortical & Juxtamedullary Nephrons

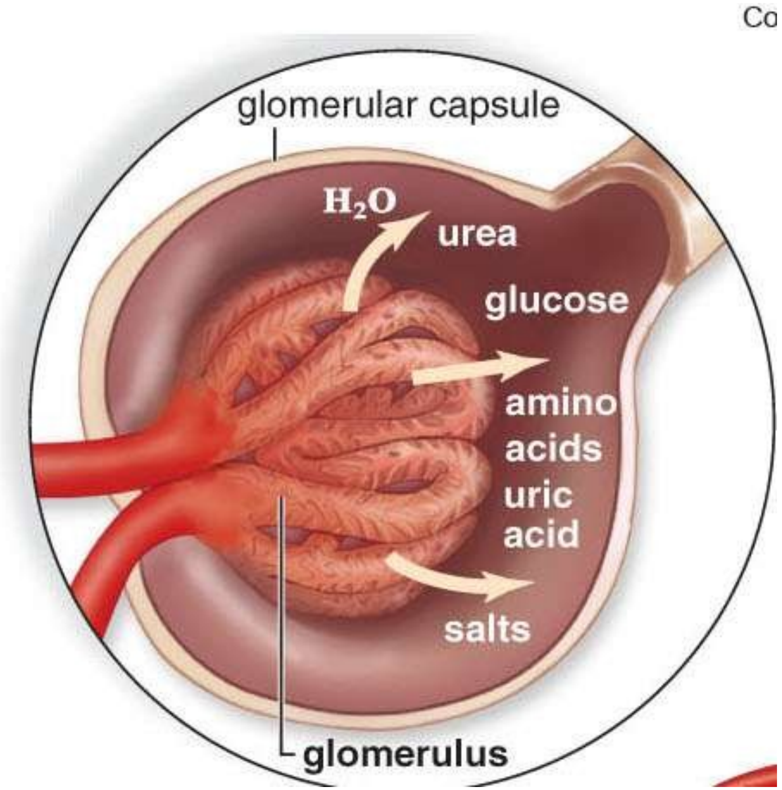


Features	Cortical nephron	Juxtamedullary nephron
Percentage	85%	15%
Situation of renal corpuscle	Outer cortex near the periphery	Inner cortex near medulla
Loop of Henle	Short	Long
	Hairpin bend penetrates only up to outer zone of medulla	Hairpin bend penetrates up to the tip of papilla
Blood supply to tubule	Peritubular capillaries	Vasa recta
Function	Formation of urine	Mainly the concentration of urine and also formation of urine

Basic Mechanisms of Urine Formation



1. filtration

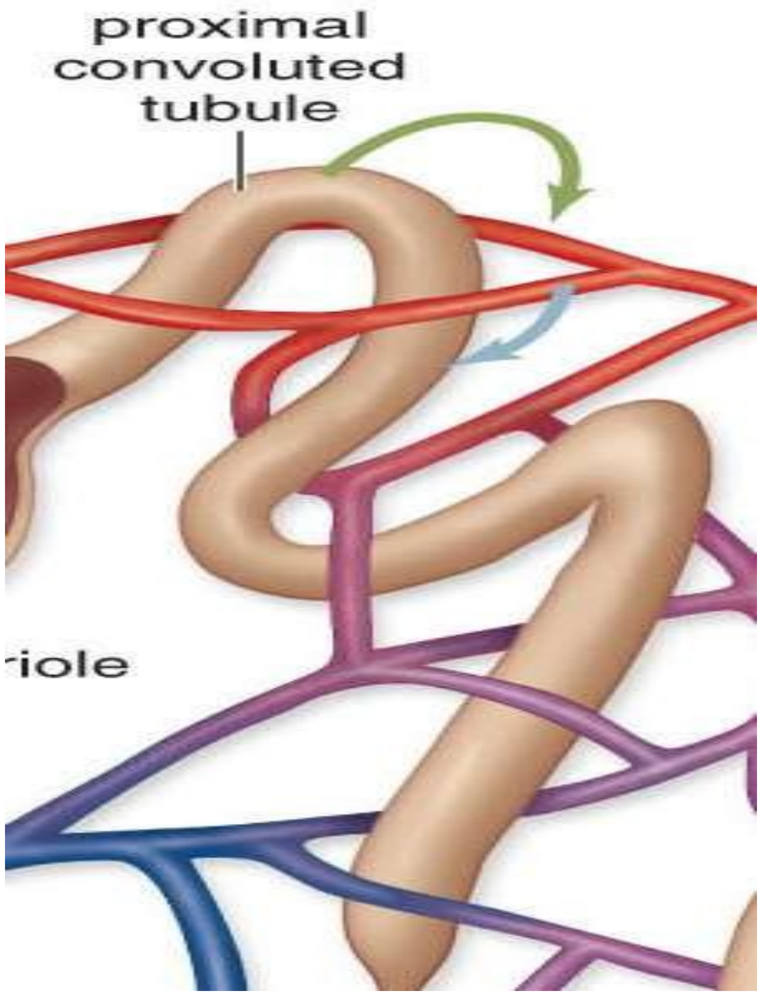


-blood pressure forces small molecules from the glomerulus to the capsule

Filtrates:
glucose, amino acids
uric acid, urea

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

2. Tubular Reabsorption

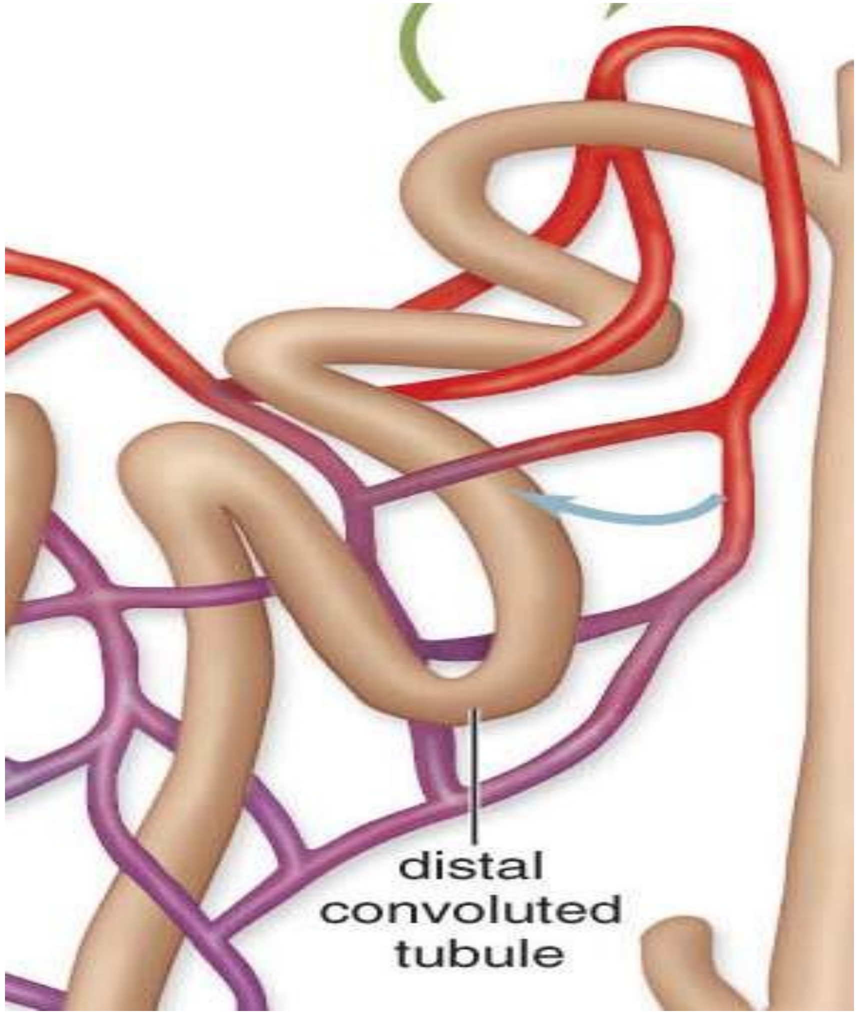


-return of filtrates tubules through diffusion and active transport

- highly variable and selective
- most electrolytes (e.g. Na^+, K^+, HCO_3^-, Cl^-), nutritional substances (e.g. glucose) are almost completely reabsorbed
- most waste products (e.g. urea, creatinine, uric acid, urates) poorly reabsorbed

3. Tubular Secretion

highly variable; important for rapidly excreting some waste products (e.g. H^+).



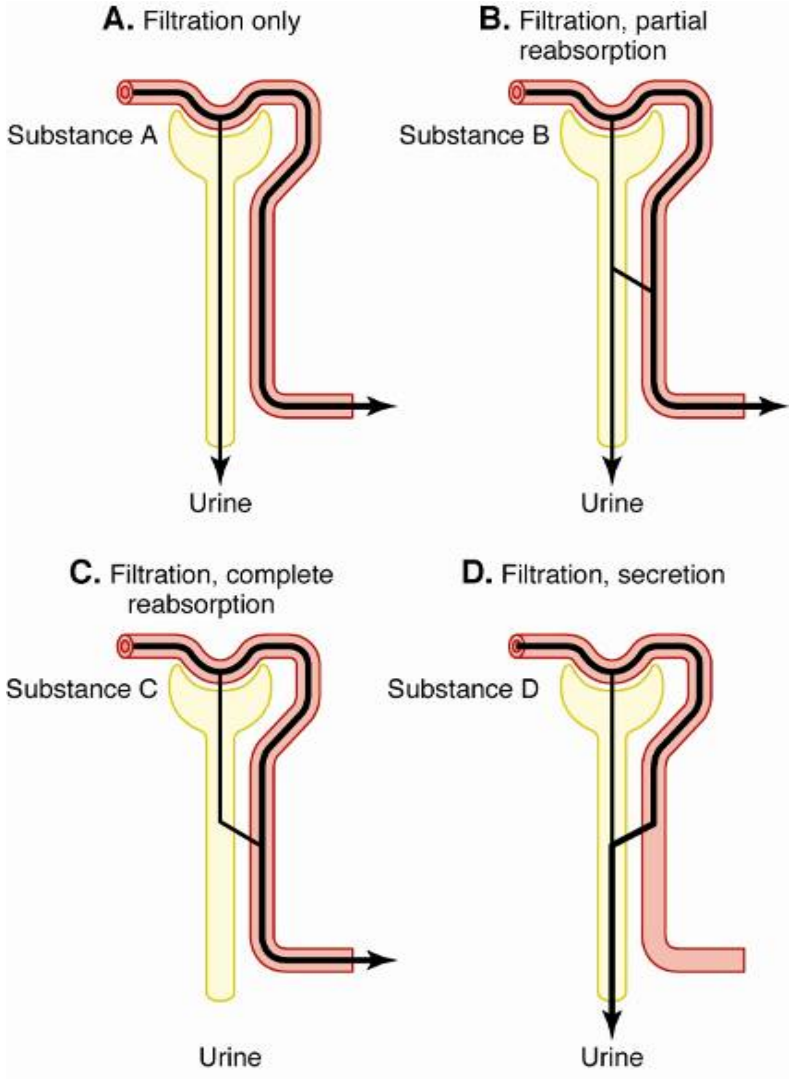
-movement of molecules from blood into the tubule

Molecules: drugs and toxins

Renal Handling of Different Substances

creatinine

electrolytes (e.g. Na^{+}& Cl^{-})



nutritional substances

amino acids & glucose

organic acids and bases

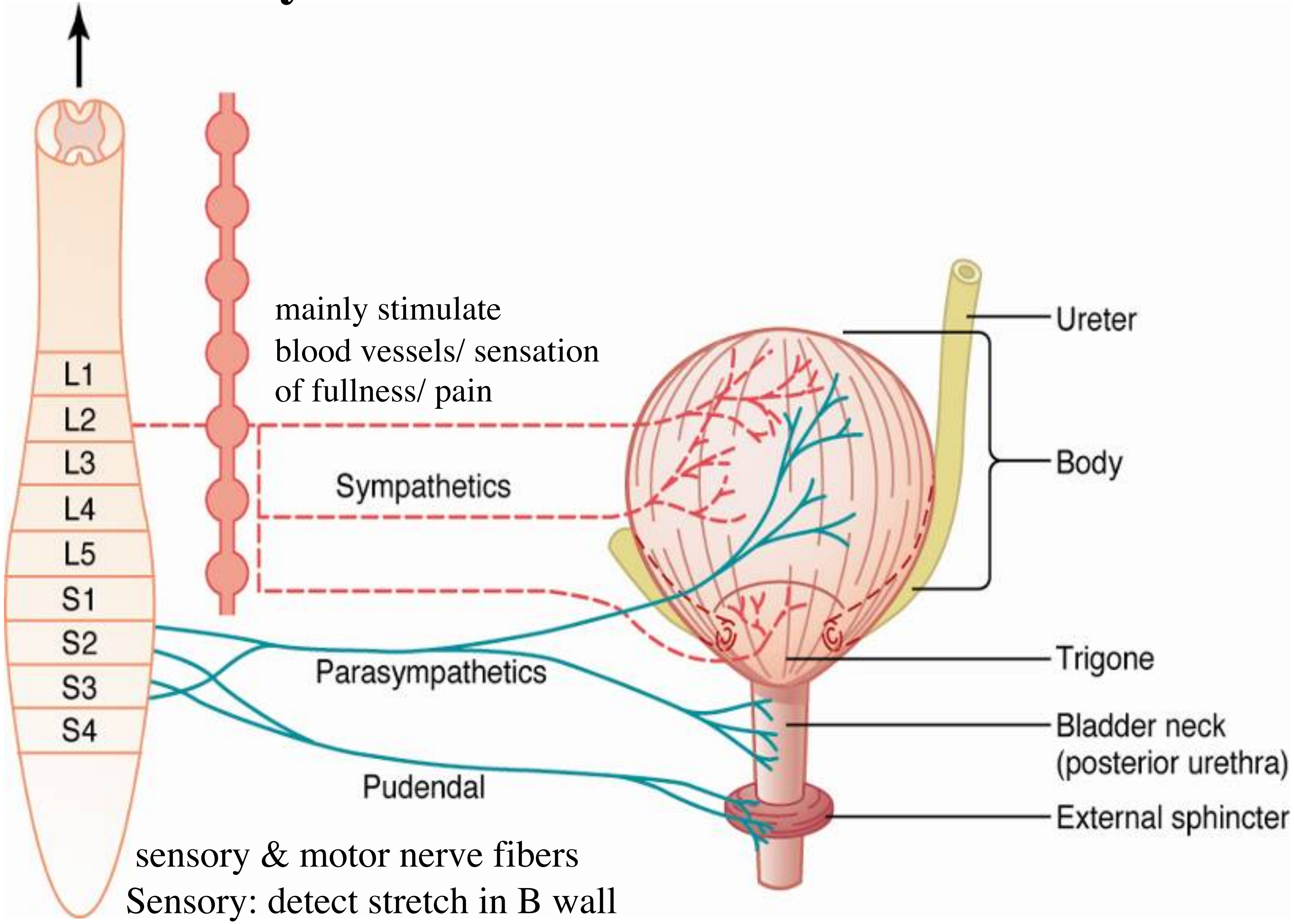
Glomerular filtration, tubular reabsorption, & tubular secretion are regulated according to needs of body

Changes in glomerular filtration and tubular reabsorption usually act in a coordinated manner to produce the necessary changes in renal excretion.

Micturition

- Process by which Urinary Bladder empties, when it becomes filled →tension in its walls > threshold level→ micturition reflex
- Contraction of detrusor muscle→↑pressure in bladder to 40-60 mm Hg →is a major step in emptying the bladder
- Internal sphincter→prevents emptying of bladder until pressure in bladder > threshold level
- External sphincter→ voluntary skeletal muscle, used to consciously prevent urination

Innervation of urinary bladder



mainly stimulate
blood vessels/ sensation
of fullness/ pain

sensory & motor nerve fibers
Sensory: detect stretch in B wall
Motor: PS (detrusor), skeletal motor fibers (external sphincter)

Transport of urine to urinary bladder

- No change in composition
- Urine from Collecting Duct→ Calyces (↑Pacemaker activity → peristalsis) →Pelvis→ Ureter →Urinary Bladder

Sympathetic stimulation:

↓Peristalsis

Parasympathetic stimulation:

↑Peristalsis

Flow of urine from ureter into urinary bladder

- Peristalsis in ureters forces urine into urinary bladder
- Oblique course+ compressed by detrusor muscle tone→Prevents Vesicoureteral Reflux
- Reflux →enlargement of ureters+ ↑pressure in renal calyces & medulla, →damage

Pain sensation in Ureters

- Well supplied with pain nerve fibers
- Irritation/ block (e.g. stone) → intense stimulation of pain nerve fibers → Intense contraction of ureters (severe pain)

↓

Sympathetic reflex back to kidney To↓the urine output **Ureterorenal reflex→ preventing excessive flow of fluid into pelvis**

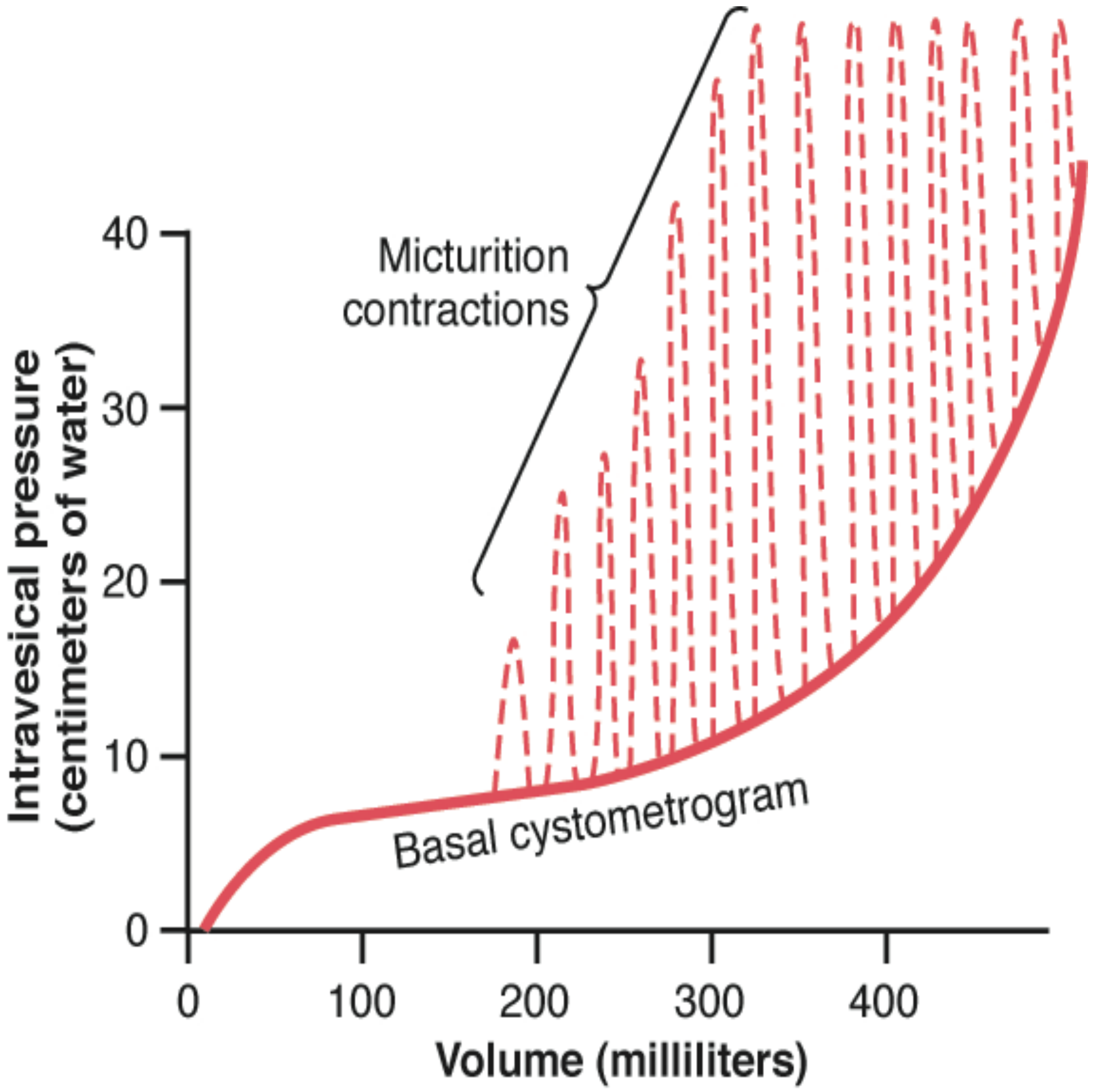
Filling of Bladder and Bladder Wall Tone; Cystometrogram

Tonic pressure changes

- No urine in bladder→intravesicular pressure is about 0
- 30-50 ml of urine →pressure rises to 5 -10 cm H_2O
- 200-300 ml—only small additional rise in pressure; caused by intrinsic tone of the bladder wall.
- Beyond 300-400 ml→pressure rise rapidly

Micturition waves

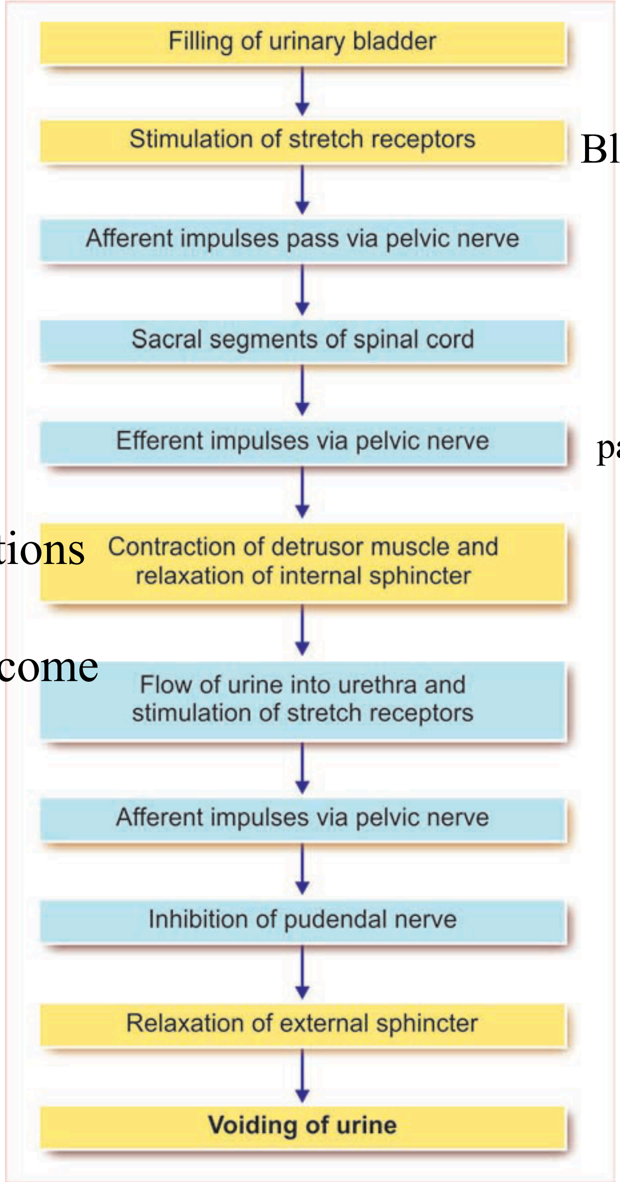
- Superimposed on the tonic pressure changes during filling
- Periodic acute increases in pressure (few->100 cm H_2O)
- Caused by the micturition reflex.



Micturition Reflex

- Autonomic cord reflex
- Contraction of Detrusor muscle
- Inhibited / facilitated by brain

- When bladder is partially filled →micturition contractions usually relax.
- As bladder continues to fill → Micturition reflexes become more **Frequent** and **Powerful**



Bladder wall/posterior urethra

parasympathetic nerve fibers

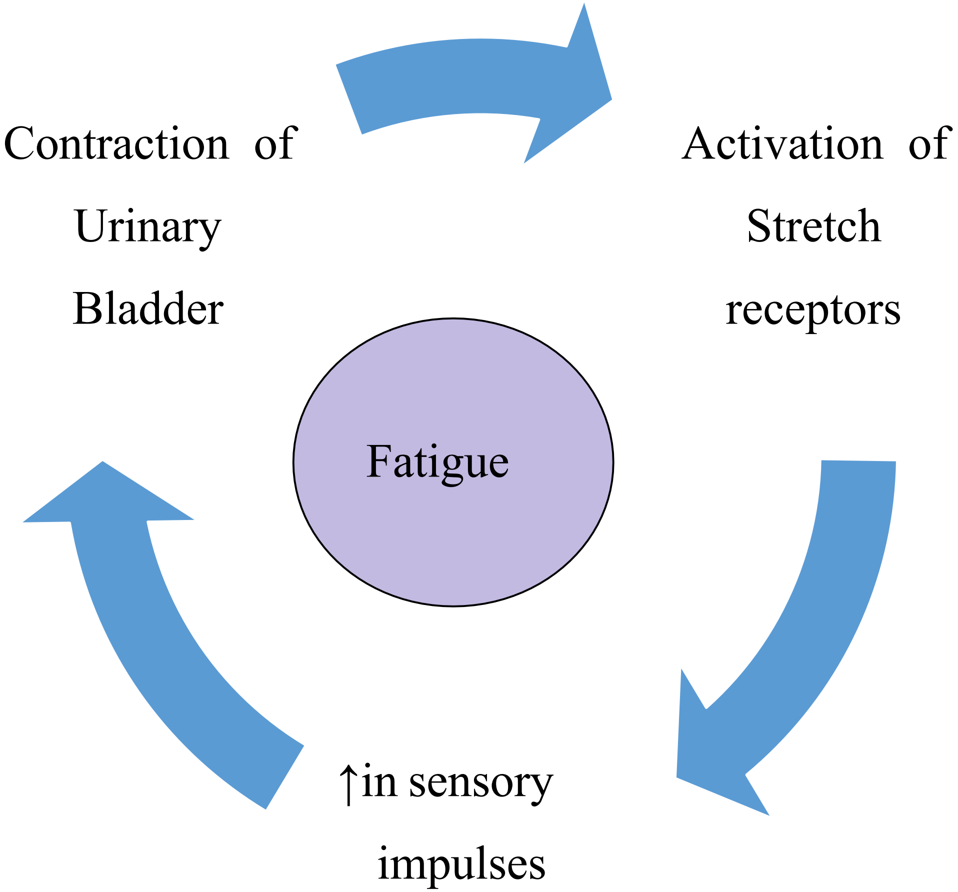
Self-Regenerative Reflex:

a single complete cycle of:

i.Progressive and Rapid increase of Pressure

ii.Sustained Pressure

ii. Relaxation



Control by Higher Centers

- Pons

  Facilitatory & inhibitory

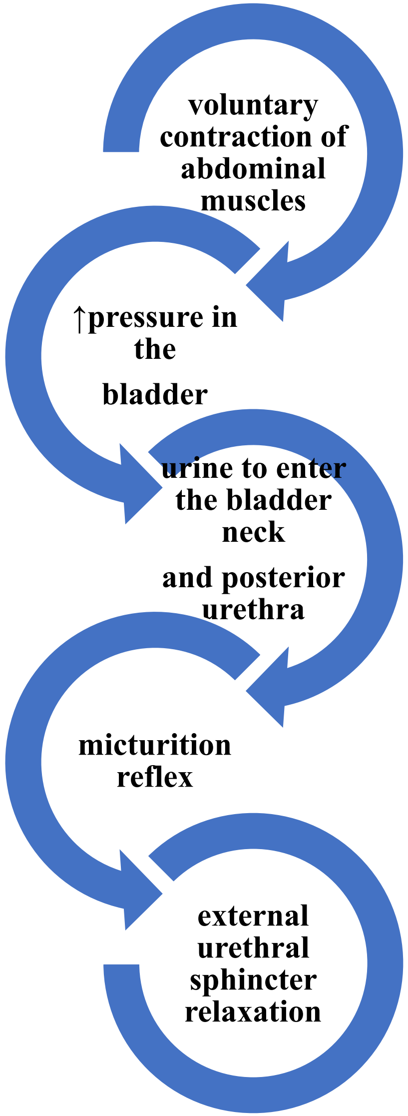
- Cerebral corte

  Normally inhibits the External sphincter

Higher centers normally exert final control of micturition

- Partial inhibition of micturition reflex, except when micturition is desired.
- Prevent micturition, even if micturition reflex occurs, by **tonic contraction of external urinary sphincter** until a convenient time presents itself.
- Cortical centers can facilitate sacral micturition centers to initiate micturition reflex & inhibit external sphincter

Voluntary urination



The end

Glomerular Filtration, Renal Blood Flow, and Their Control

U N I T V
Chapter 27

Importance of Glomerular Filtration

- Remove waste products
- Waste products are poorly reabsorbed by the tubules

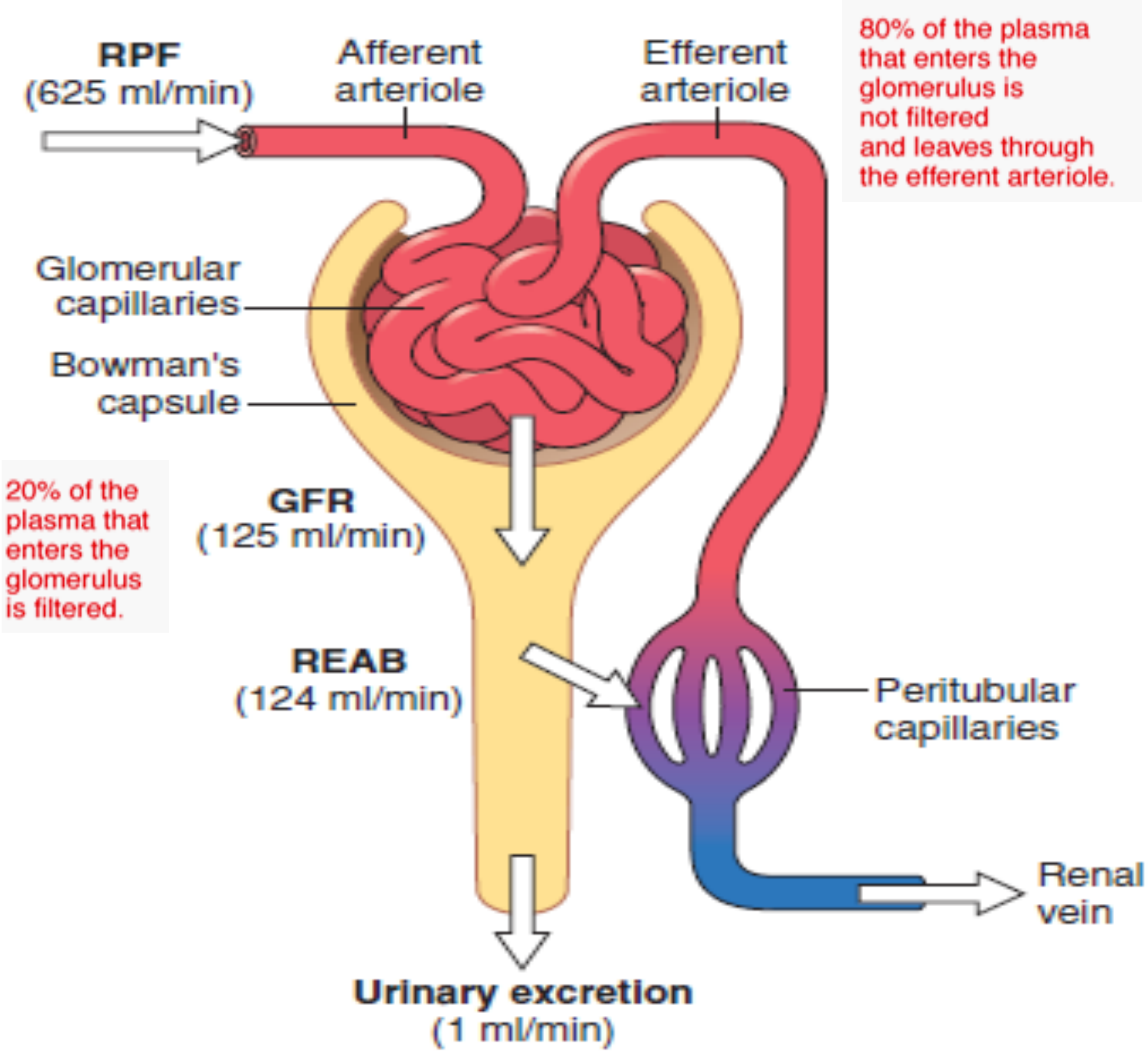
plasma volume= 3 L, GFR is about 180 L/day → entire plasma can be filtered and processed about 60 times/day. This high GFR allows the kidneys to precisely and rapidly control the volume and composition of the body fluids.

Average values for total renal plasma flow (RPF), glomerular filtration rate (GFR), tubular reabsorption (REAB), and urine flow rate

- Glomerular filtrate composition is about the same as plasma, except for large proteins

No blood cells

Ca & FA bound to protein→↓[] in filtrate



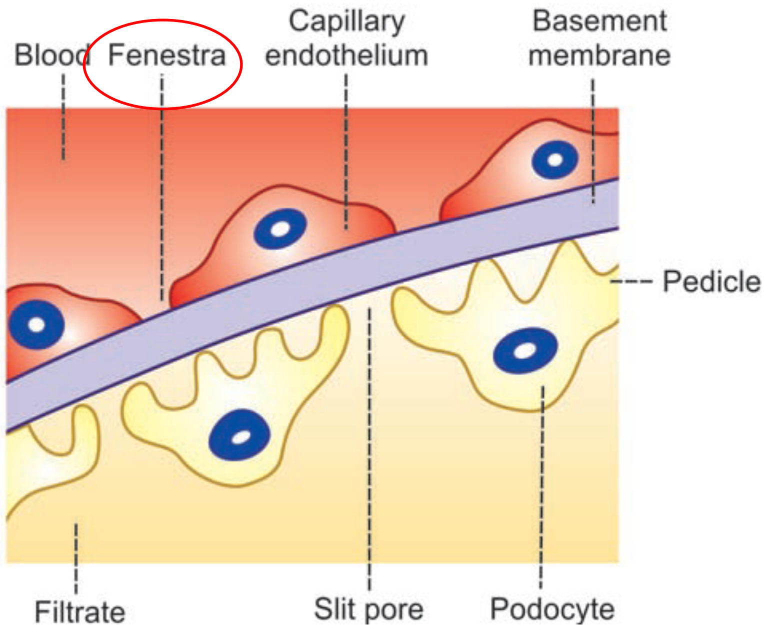
Glomerular capillary filtration barrier

Fenestrated endothelium

- pores exclude blood cells and large plasma proteins (-ve charges)

Basement membrane
Proteoglycan gel -excludes molecules
–ve charge
Podocytes not continuous footlike processes (-ve charges)

Slit diaphragm pores
Excludes particles



Epithelium

Filterability of Solutes Across Glomerular Barrier

- Molecular size (inverse relationship)
- Electrical charge (-ve charged large molecules are filtered **less** easily than +ve charged molecules of equal molecular size due to electrostatic repulsion, any defect→ proteinuria/albuminuria
- Shape (rigid or deformable)

Filterability of Solutes Across Glomerular Barrier

Filterability of 1.0 means= substance is filtered as freely as water; [plasma] =[Bowman's capsule]
Filterability of 0.75 =substance is filtered only 75% as rapidly as water.

Table 27-1 Filterability of Substances by Glomerular Capillaries Based on Molecular Weight

Substance	Molecular Weight	Filterability
Water	18	1.0
Sodium	23	1.0
Glucose	180	1.0
Inulin	5500	1.0
Myoglobin	17,000	0.75
Albumin	69,000	0.005

Determinants of Glomerular Filtration Rate

Normal Values:

GFR = 125 ml/min or 180 L/day

- Filtration fraction (GFR/Renal Plasma Flow)

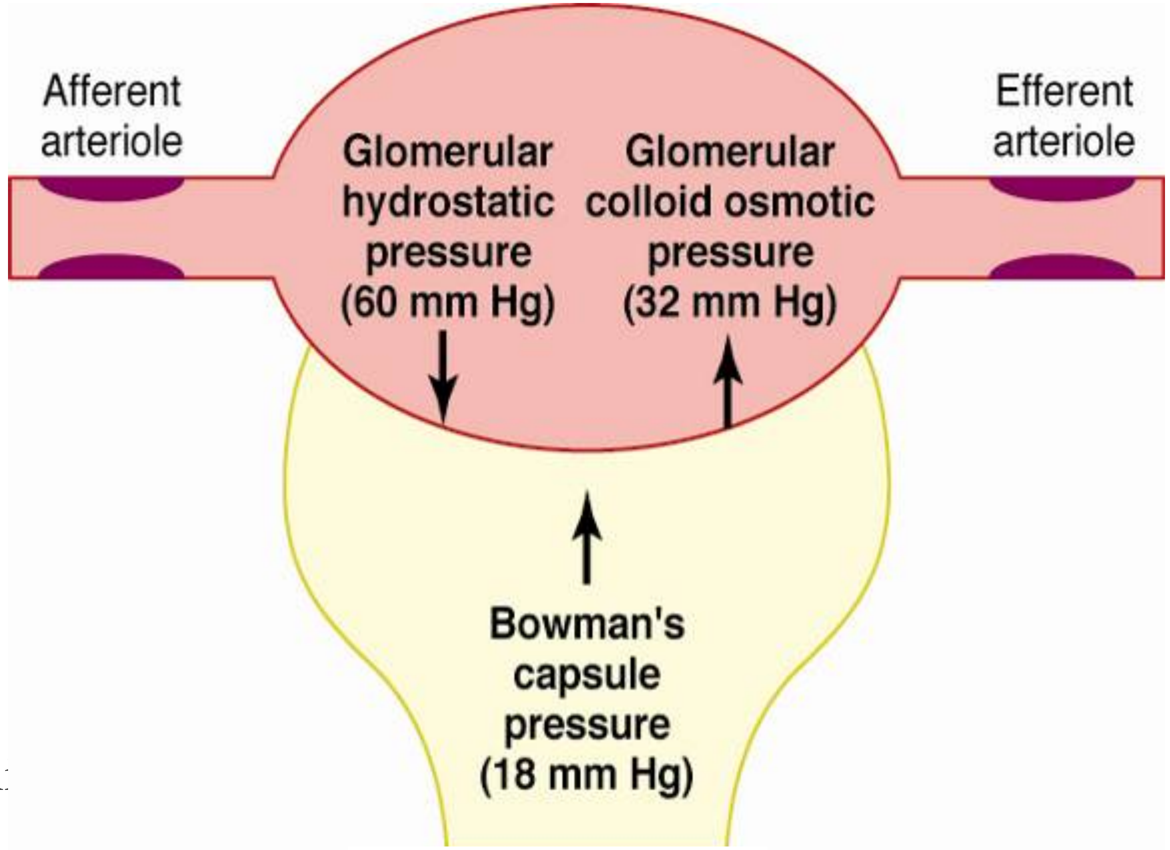
  125/625= 0.2

GFR is determined by:

(1) balance of hydrostatic & colloid osmotic forces acting across capillary membrane

(2) capillary filtration coefficient (Kf), product of permeabil

and filtering surface area of capillaries



$$(P_G - P_B - \pi_G + \pi_B)$$

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)

Filtration coefficient

Kf = GFR/Net filtration pressure

Normally, GFR=125 ml/min, Net filt. P= 10
Kf=125/10
=12.5 ml/min/ mm Hg
Very high compared to other body capillaries Kf (0.01)→rapid rate of filtration

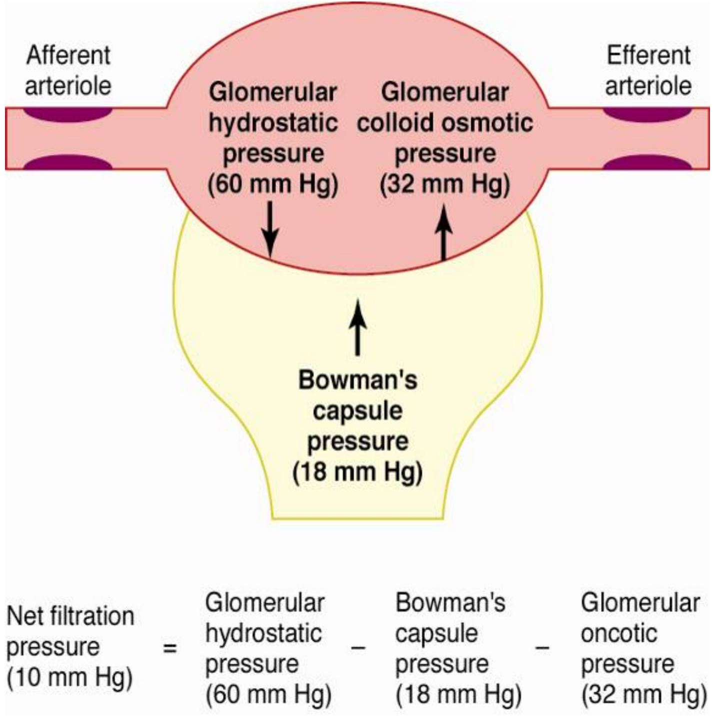
Glomerular Capillary Filtration Coefficient (K_f)

- ↑ Kf→↑GFR
- ↓ Kf →↓GFR

- Changes in Kf probably do not provide a primary mechanism for normal day-to-day regulation of GFR.

- Disease that can reduce K_f and GFR
  - chronic hypertension
  - obesity/diabetes mellitus
  - glomerulonephritis

Bowman's Capsule hydrostatic Pressure (P_B)



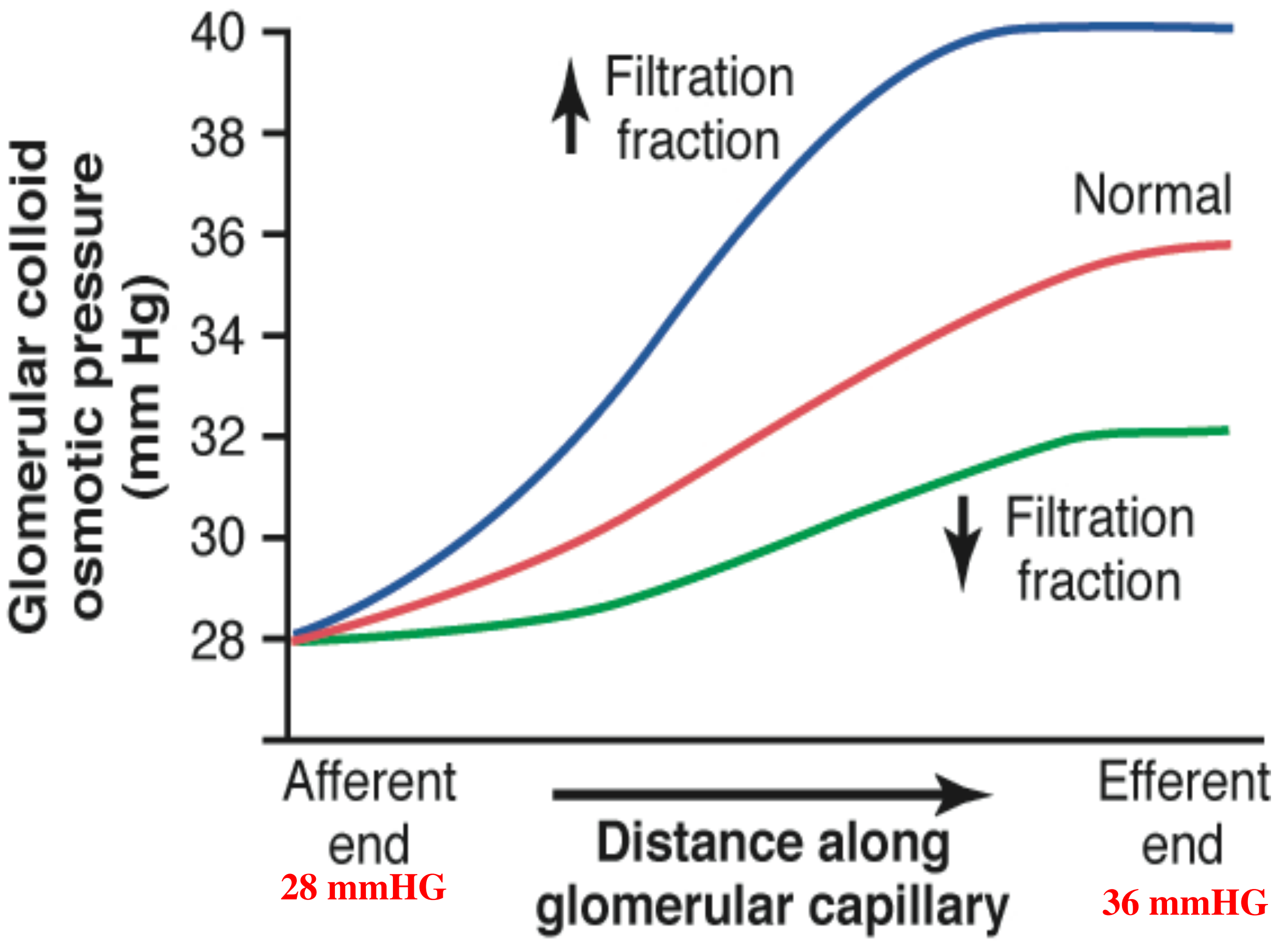
- Normally changes as a function of GFR,
  not a physiological regulator of GFR
- Tubular Obstruction
  kidney stones
  tubular necrosis

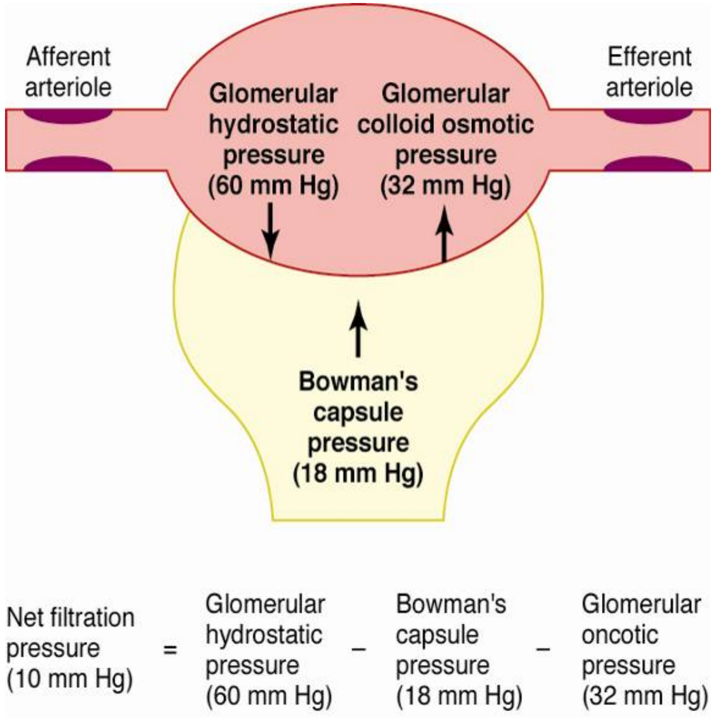
$\rightarrow \downarrow$GFR

- Urinary tract obstruction
  Prostate hypertrophy/cancer

$\rightarrow$hydronephrosis

Increase in colloid osmotic pressure in plasma reduces GFR





[plasma protein] ↑about 20%, due to filtration of plasma→concentrating glomerular proteins

Factors Influencing Glomerular Capillary Oncotic/colloid Pressure (π_G)

- Arterial Plasma Oncotic Pressure (π_A)

$$\uparrow \pi_A \longrightarrow \uparrow \pi_G \longrightarrow \downarrow GFR$$

- Filtration Fraction (FF)

$$\uparrow FF \longrightarrow \uparrow \pi_G \longrightarrow \downarrow GFR$$

FF = GFR/Renal plasma flow

GFR $\propto$ Renal plasma flow

$\uparrow P_G \rightarrow \uparrow GFR$

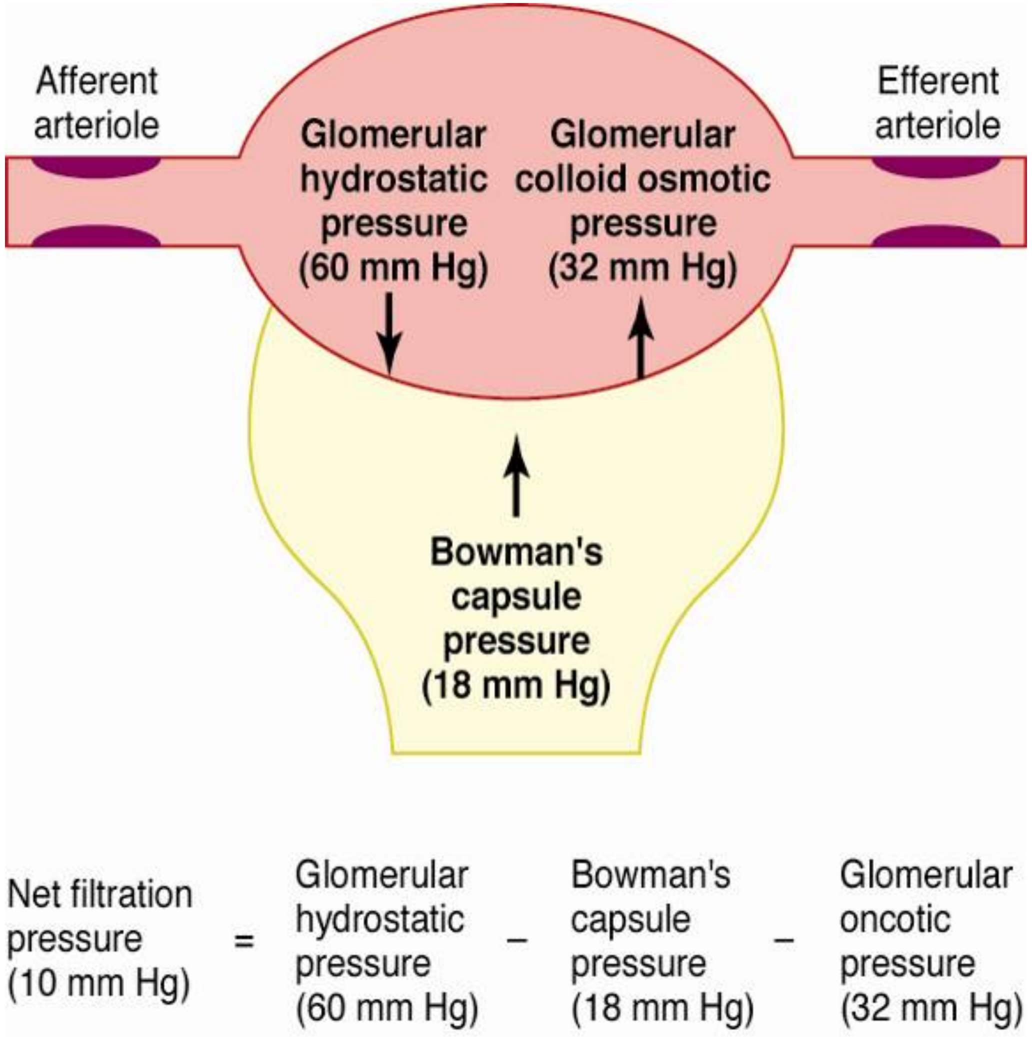
Changes in P_G serve as the means for physiological regulation of GFR.

Factors affecting Glomerular Capillary hydrostatic Pressure (P_G) :

1-Arterial pressure (Proportional, buffered by autoregulation (constant P_G)

2- Afferent arteriolar resistance

3- Efferent arteriolar resistance



$\uparrow P_G \rightarrow \uparrow$ GFR

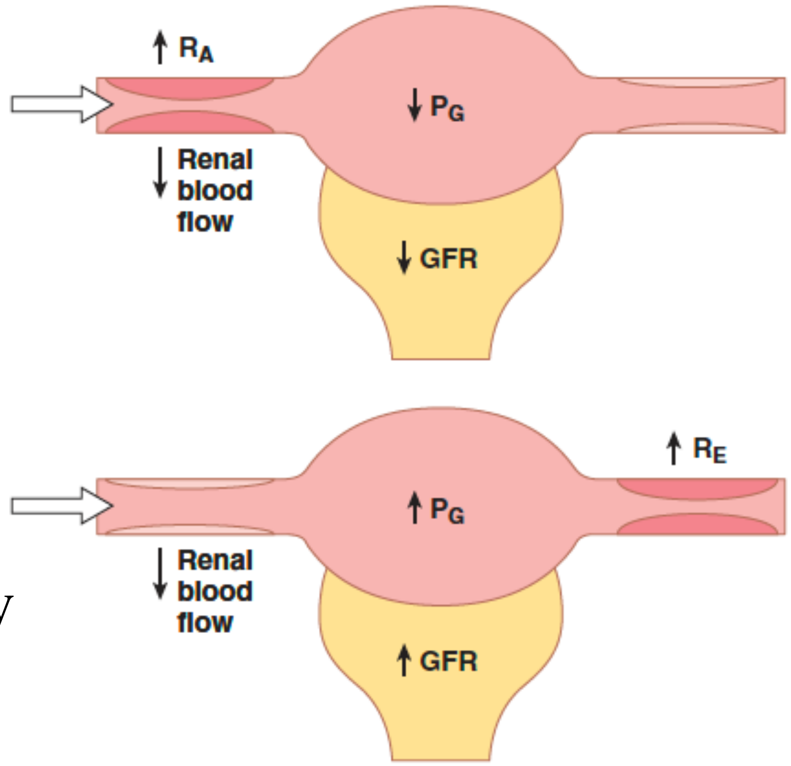
Factors affecting Glomerular Capillary hydrostatic Pressure (P_G) :

2- Afferent arteriolar resistance (Inverse)

3- Efferent arteriolar resistance (Proportional)

efferent arteriolar constriction→↓reduces renal blood flow

$\uparrow R_E \rightarrow \uparrow$ FF & $\boldsymbol{\pi_G} \rightarrow \boldsymbol{\pi_G} > \mathbf{P_G} \rightarrow$ net ↓GFR



Effect of changes in afferent arteriolar or efferent arteriolar resistance

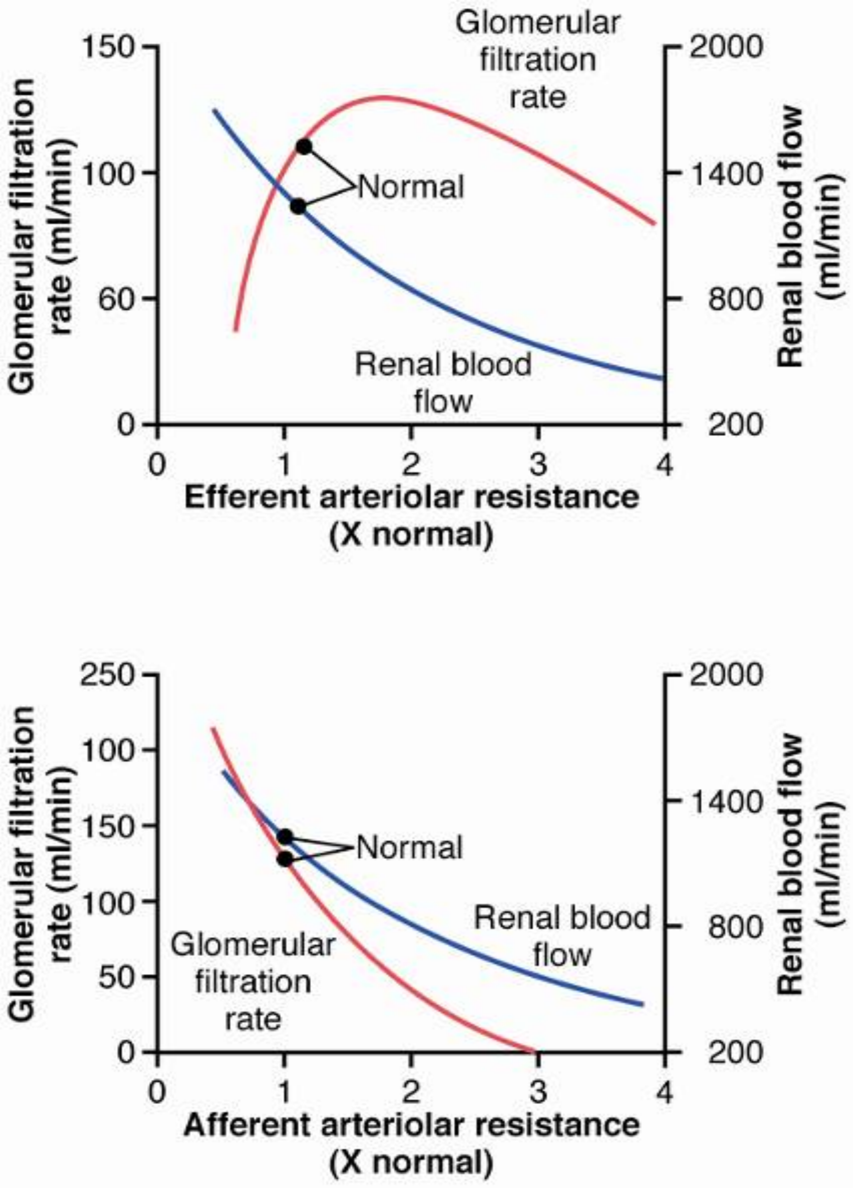


Figure 26-15

Table 27-2 Factors That Can Decrease the Glomerular Filtration Rate

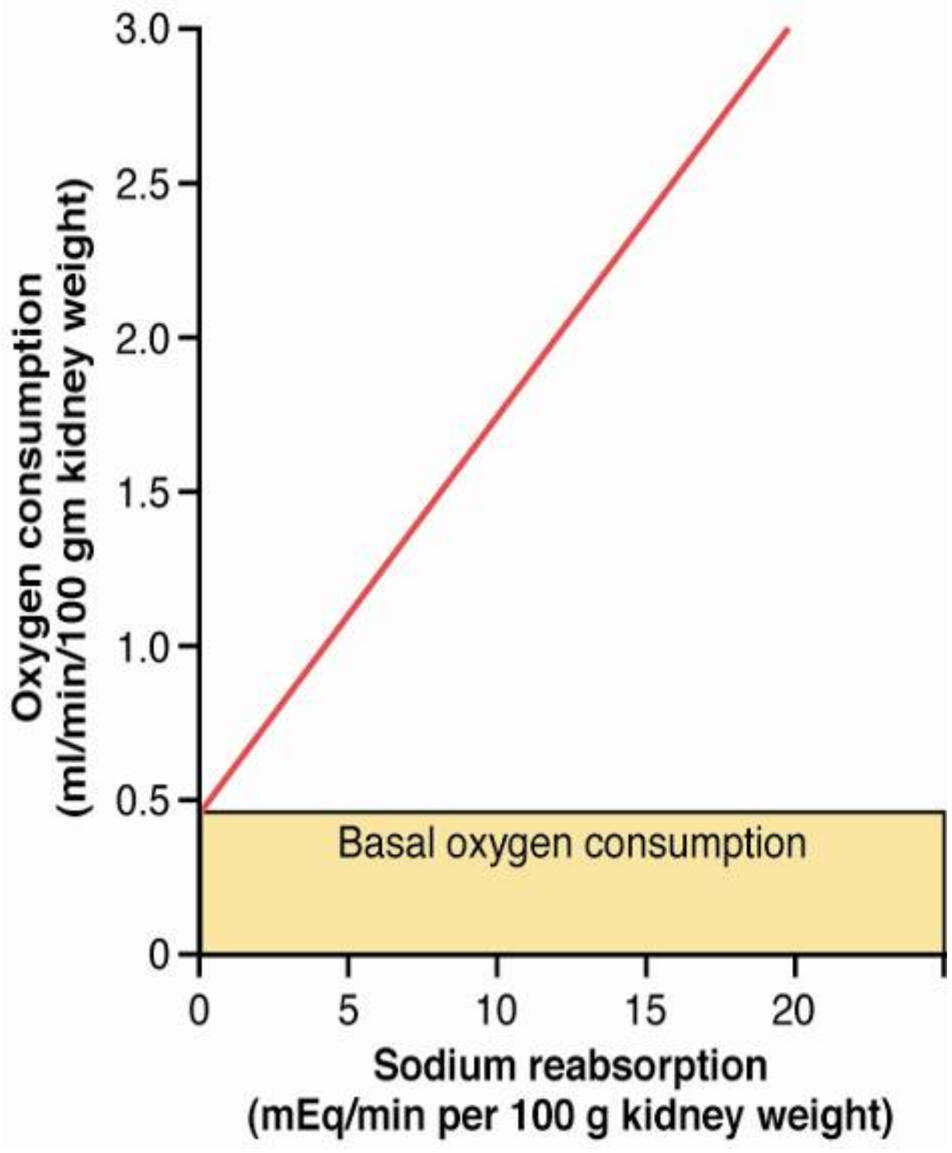
Physical Determinants*	Physiological/Pathophysiological Causes
$\downarrow K_f \rightarrow \downarrow$GFR	Renal disease, diabetes mellitus, hypertension
$\uparrow P_B \rightarrow \downarrow$GFR	Urinary tract obstruction (e.g., kidney stones)
$\uparrow \pi_G \rightarrow \downarrow$GFR	↓ Renal blood flow, increased plasma proteins
$\downarrow P_G \rightarrow \downarrow$GFR	
$\downarrow A_P \rightarrow \downarrow P_G$	↓ Arterial pressure (has only a small effect because of autoregulation)
$\downarrow R_E \rightarrow \downarrow P_G$	↓ Angiotensin II (drugs that block angiotensin II formation)
$\uparrow R_A \rightarrow \downarrow P_G$	↑ Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)

Renal blood flow

- High blood flow (1100 ml/min ~22% of cardiac output)
- High blood flow needed for high GFR
- Oxygen and nutrients delivered to kidneys normally greatly exceeds their metabolic needs
- A large fraction of renal oxygen consumption is related to renal tubular Na reabsorption

Renal O2 consumption varies in proportion to renal tubular Na reabsorption

↓renal blood flow& GFR →less Na is filtered →less Na is reabsorbed →less O2 consumed



Determinants of Renal Blood Flow (RBF)

$$RBF = \Delta P/R$$

ΔP = difference between renal artery pressure and renal vein pressure

renal artery P=systemic arterial pressure

renal vein P=3-4 mmHg

R = total renal vascular resistance
= sum of all resistances in kidney vasculature (arteries, arterioles, capillaries &veins)

Determinants of Renal Blood Flow (RBF)

Most of renal vascular resistance resides in:
1-interlobular arteries
2-afferent arterioles
3-efferent arterioles

↑ resistance of any of vascular segments of kidneys →↓RBF and vice versa if renal artery & renal vein pressures remain constant.

Autoregulation

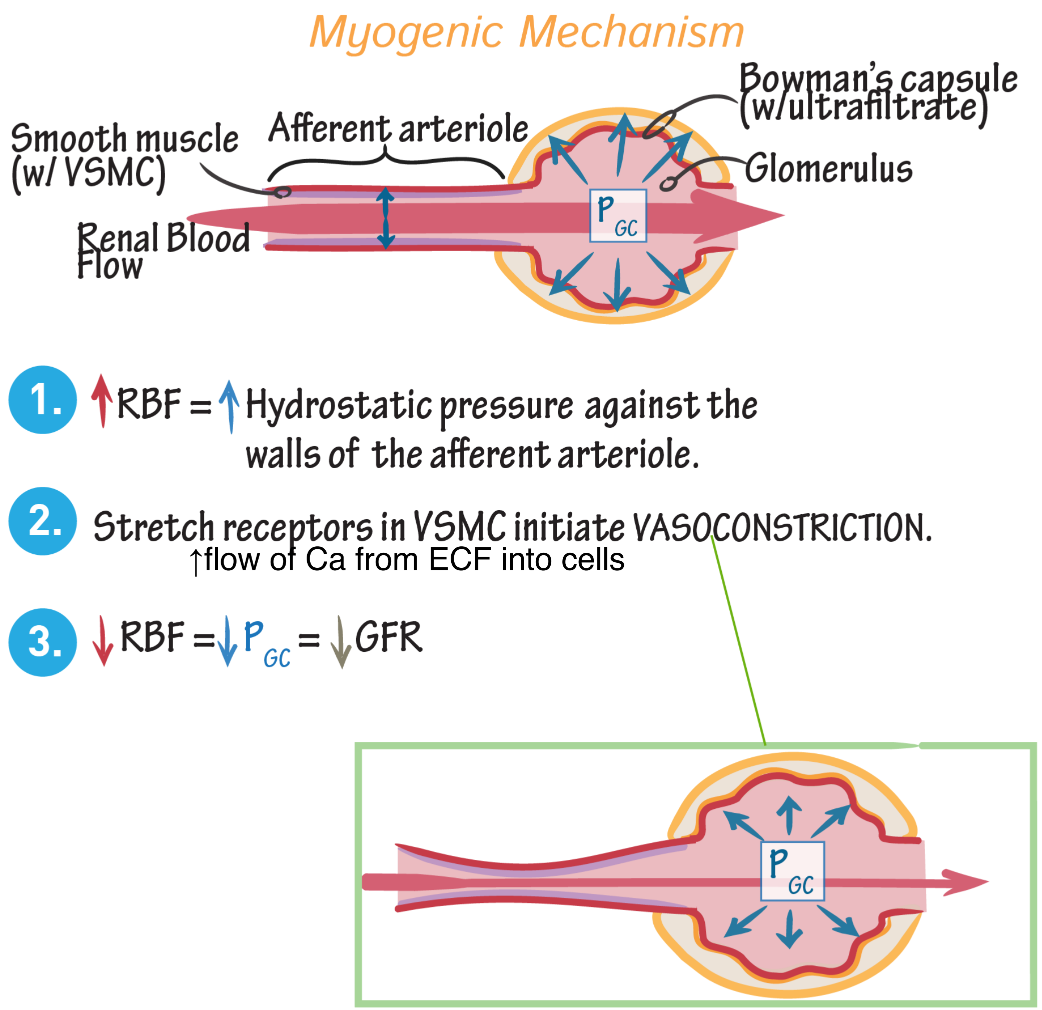
Intrinsic ability of kidneys to regulate its own **blood flow** to maintain GFR

Autoregulation → constant RBF & GFR over P changes 80-170 mmHg

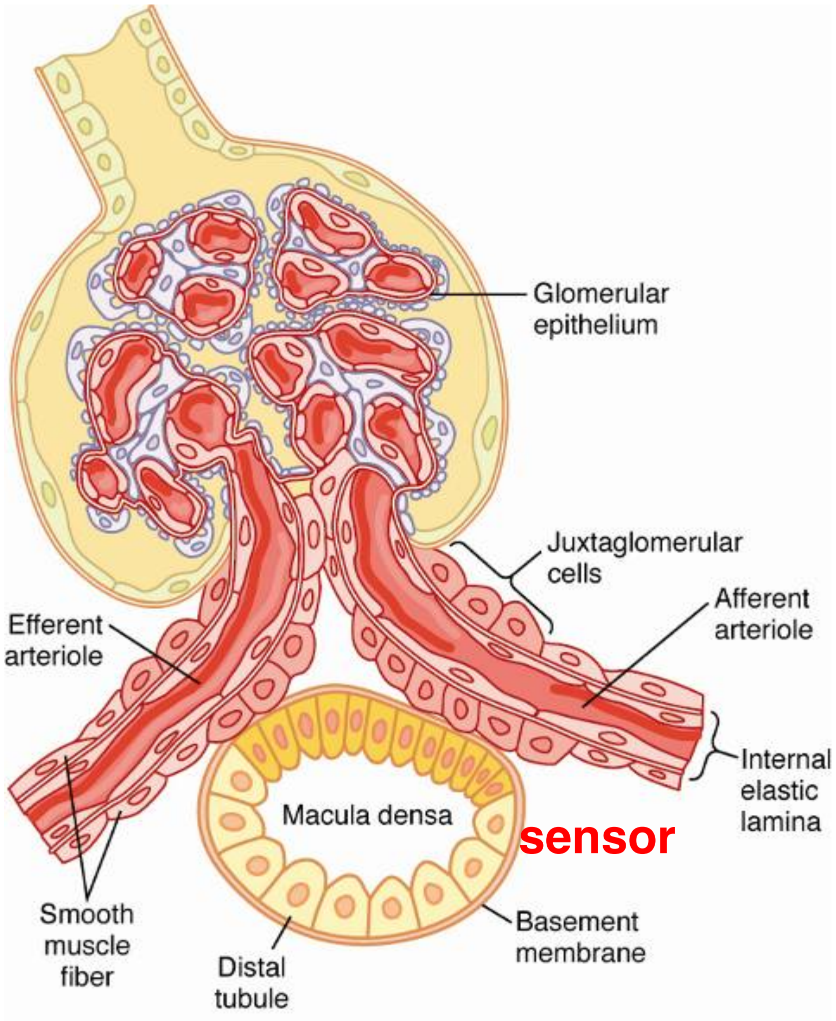
Two mechanisms involved in renal autoregulation:
1. Myogenic response
2. Tubuloglomerular feedback

Myogenic response

Myogenic Mechanism Pressure dependent mec

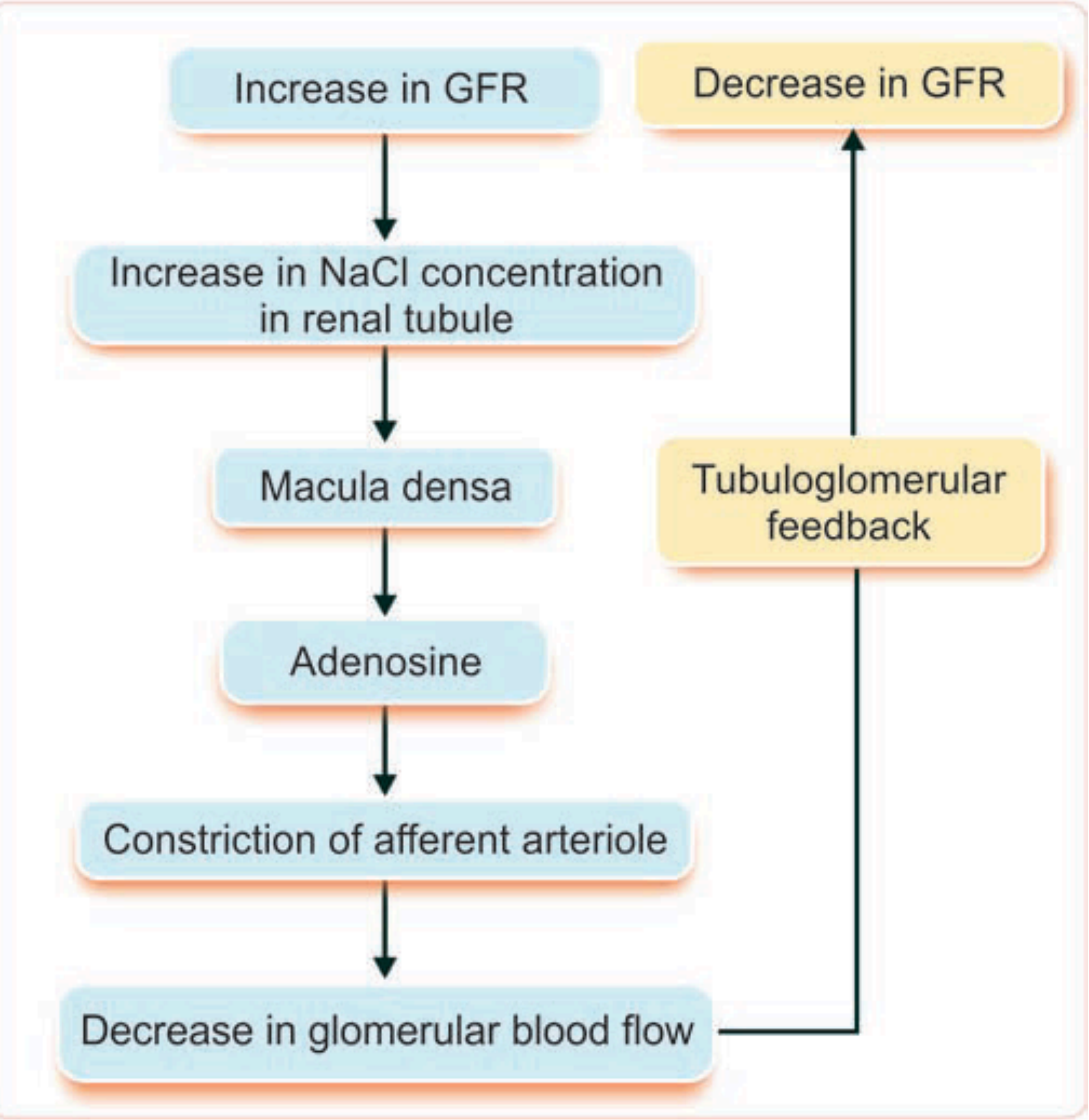


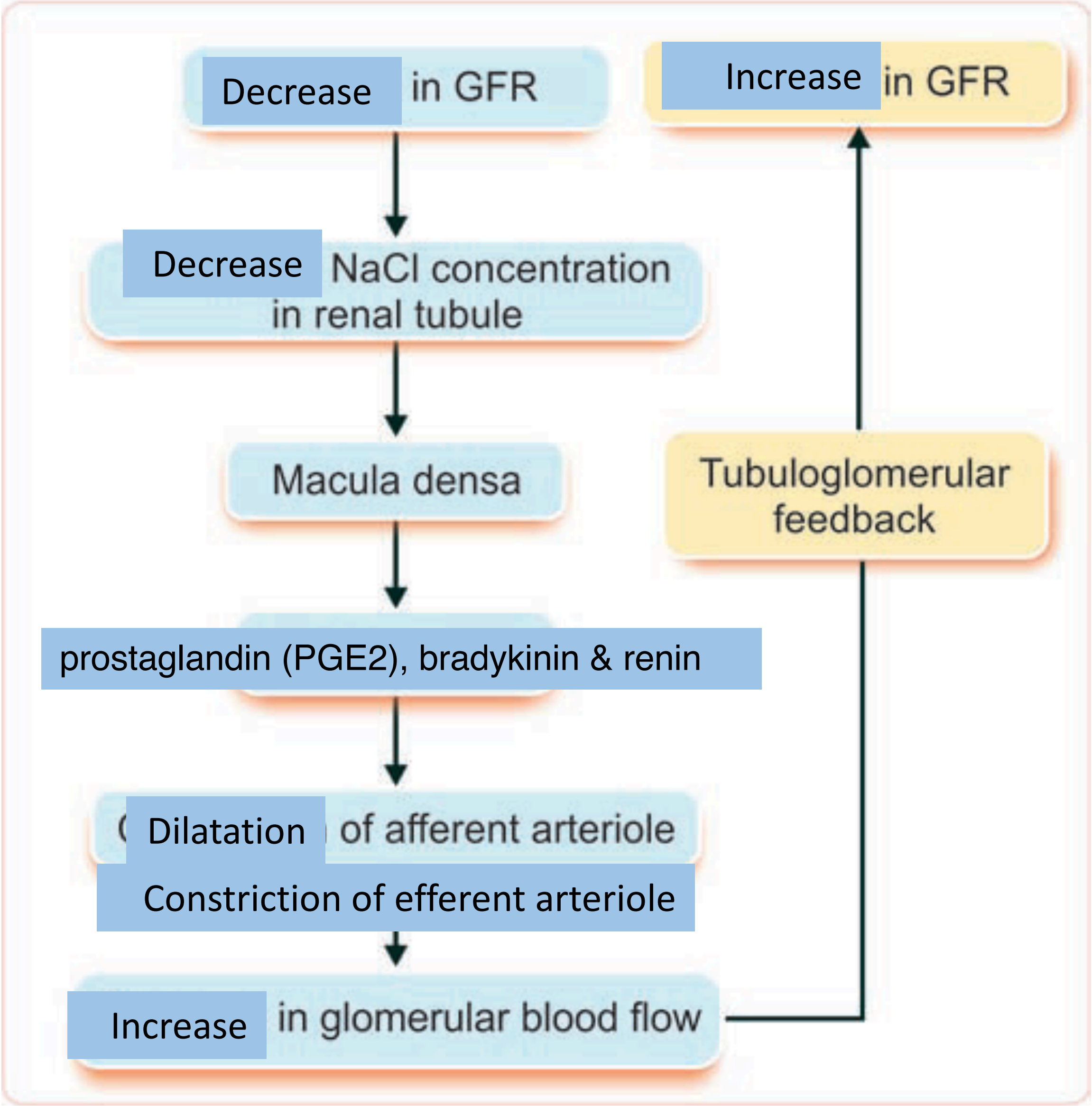
Tubuloglomerular feedback



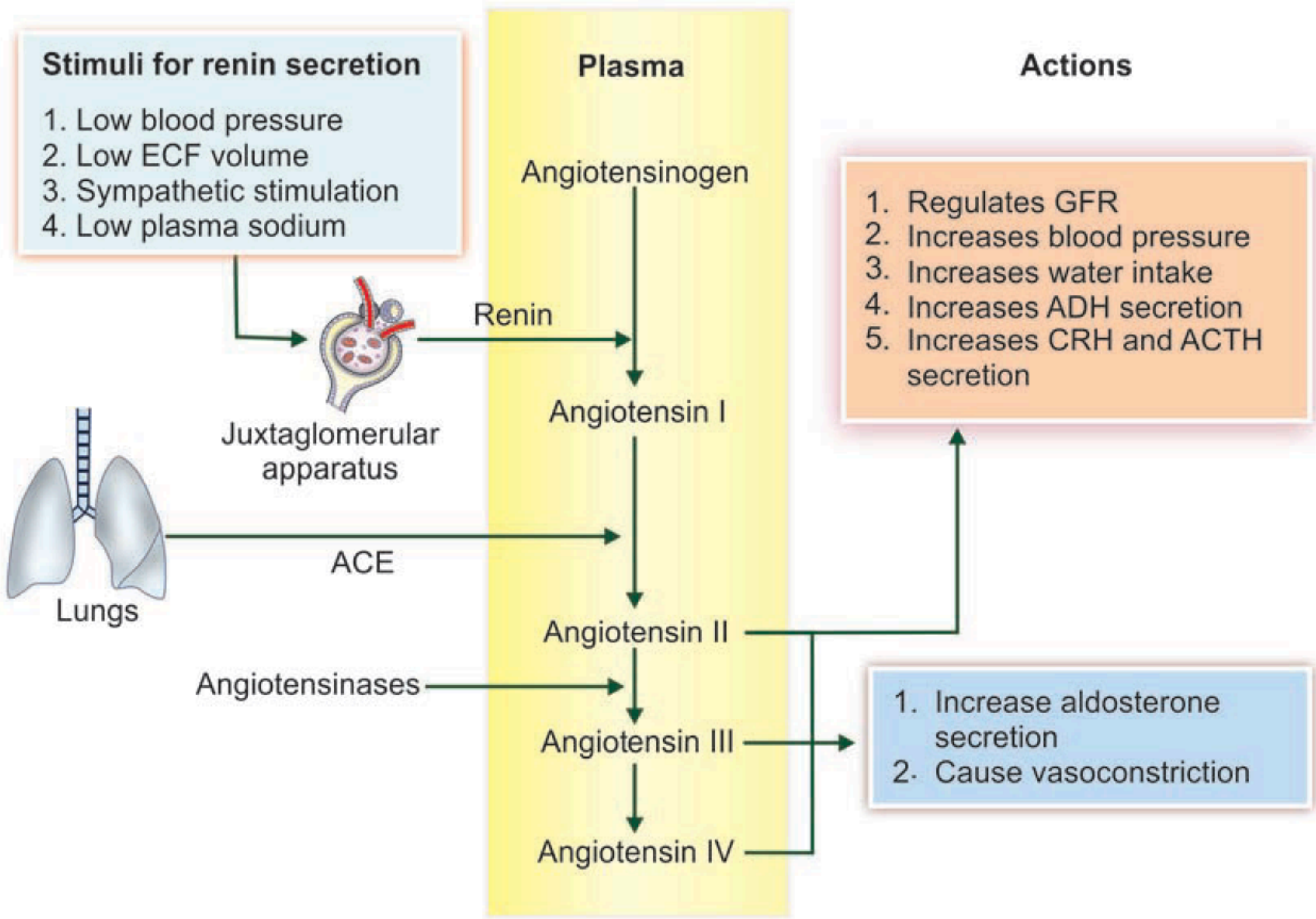
Macula densa of juxtaglomerular apparatus in the terminal portion of thick ascending limb is sensitive to the NaCl in the tubular fluid

Tubuloglomerular feedback





Renin-Angiotensin system



Tubuloglomerular feedback

Factors increasing the sensitivity of tubuloglomerular feedback:

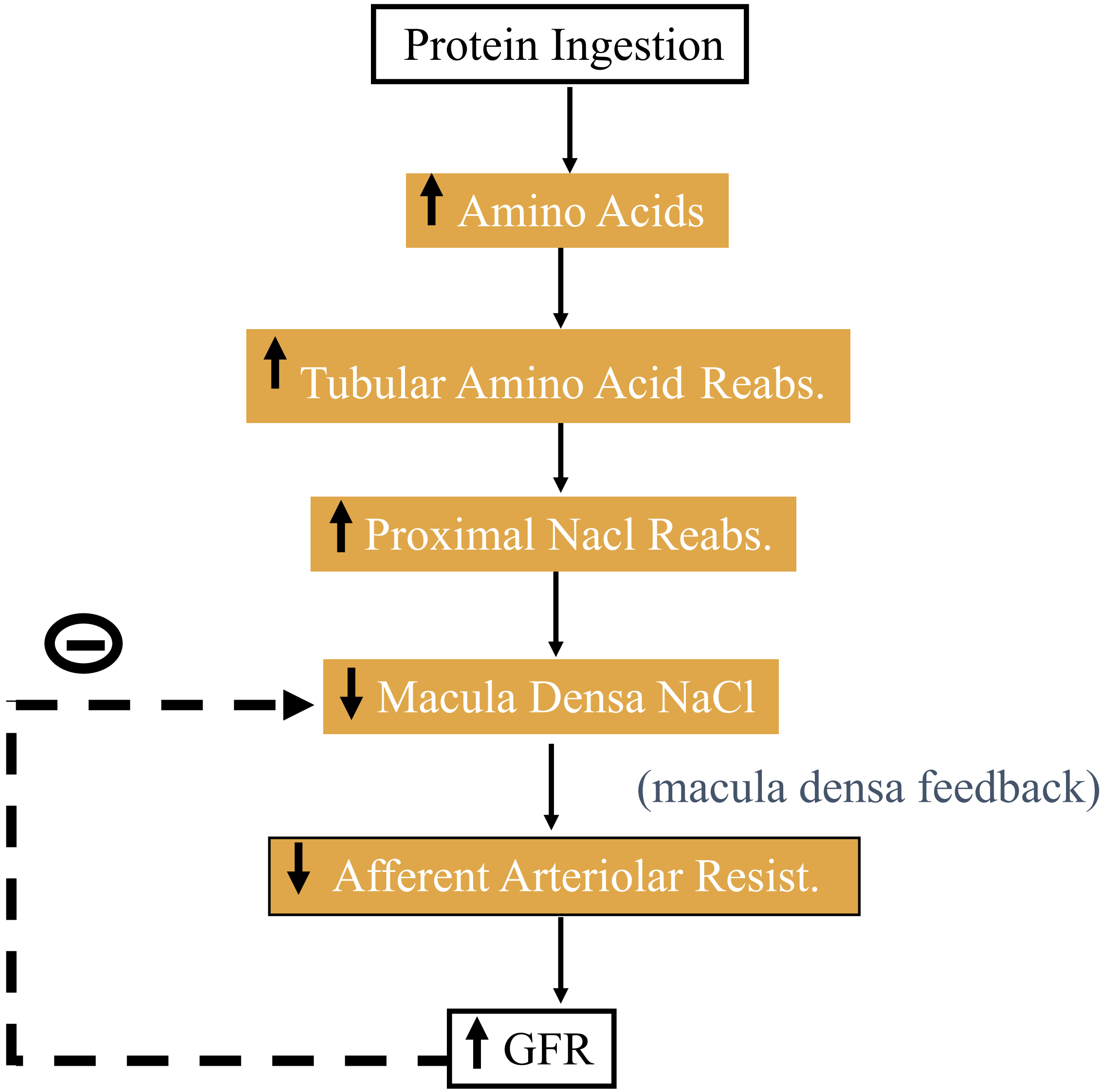
i. Adenosine
ii. Thromboxane
iii. Prostaglandin E2

Factors decreasing the sensitivity of tubuloglomerular feedback:

i. Atrial natriuretic peptide
ii. Prostaglandin I2
iii. Cyclic AMP (cAMP)
iv. Nitrous oxide.

Other Factors That Influence GFR

- Fever, pyrogens: increase GFR
- Glucorticoids: increase GFR
- Aging: decreases GFR 10%/decade after 40 yrs
- Hyperglycemia: increases GFR (diabetes mellitus)
- Dietary protein: high protein increases GFR
  low protein decreases GFR



Protein Ingestion
↑ Amino Acids
↑ Tubular Amino Acid Reabs.
↑ Proximal Nacl Reabs.
↓ Macula Densa NaCl
(macula densa feedback)
↓ Afferent Arteriolar Resist.
↑ GFR

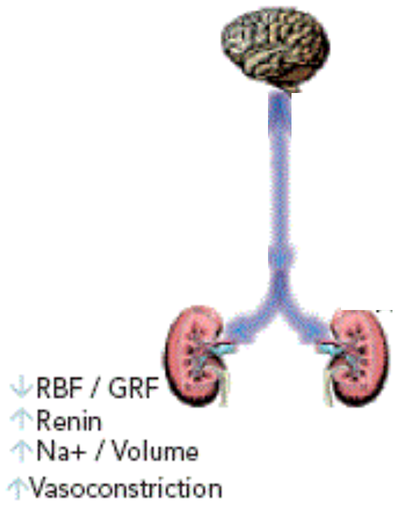
Control of GFR and RBF

Control over P_G & π_G

- Neurohormonal
- Local (autacoids, Intrinsic)

Neurohormonal regulation of GFR and RBF

Strong Sympathetic stimulation



- In healthy person, sympathetic have little influence on RBF.
- Sympathetic is important in acute disturbances (e.g. defense reaction, brain ischemia, or severe haemorrhage)

Hormonal regulation of GFR and RBF

- Constrict **Efferent** arterioles
- Powerful
- Physiological conditions
- low Na diet, volume depletion & ↓ arterial P
- prevents ↓ P_G & GFR
- ↓ flow in peritubular capillaries ↑ Na reabsorption
- NO & PG Counteract the angiotensin II mediated vasoconstriction in afferent A.

Table 27-4 Hormones and Autacoids That Influence GFR

Hormone or Autacoid	Effect on GFR
Norepinephrine	↓
Epinephrine	↓
Endothelin	↓
Angiotensin II	↔ (prevents ↓)
Endothelial-derived nitric oxide	↑
Prostaglandins	↑

Constrict Renal Blood Vessels
Little effect normally
Hrrge
Toxemia of preg
ARF
Chronic uremia

- vasodilator
- Help in Na & H_2O excretion

- vasodilator
- important only when there are
other disturbances that are already tending to lower GFR
- Inhibited by NSAIDs