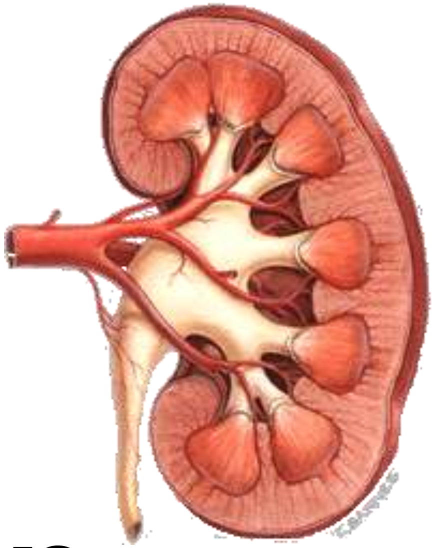
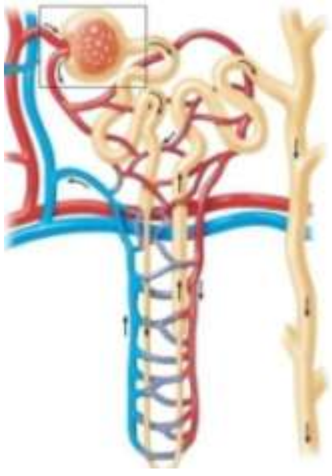


Renal Function



Jacqueline M. Powell, Ph.D.

Learning Objectives

1. List the basic functions of the kidneys

2. List and identify the structures of the nephron and associated vasculature

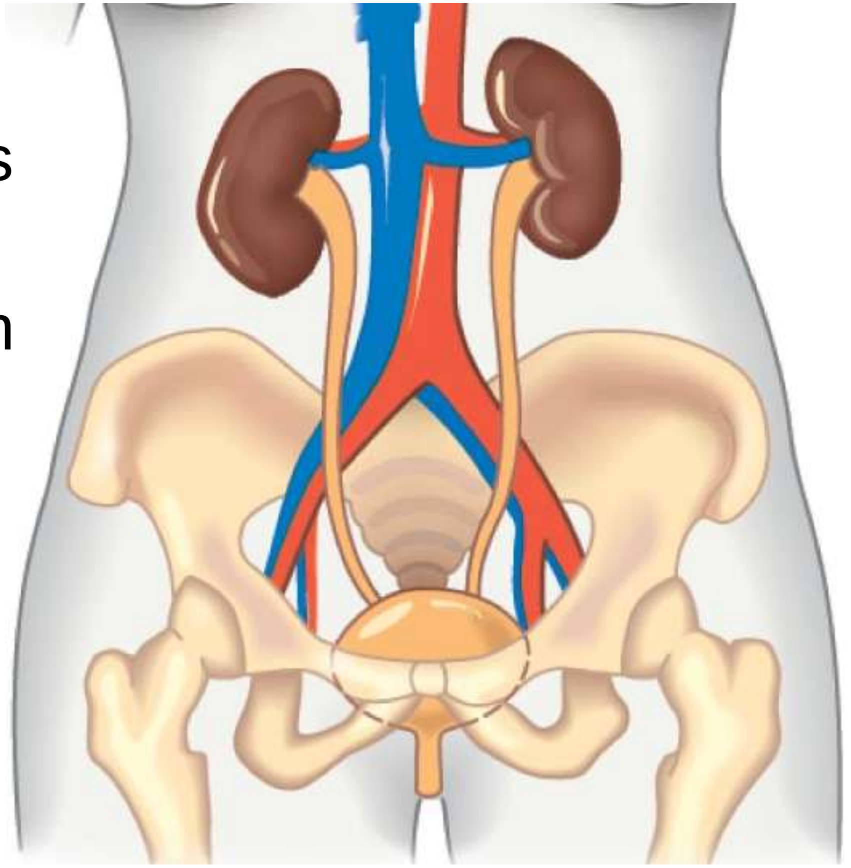
3. Discuss filtration and the factors that affect filtration

4. Discuss reabsorption, secretion and excretion

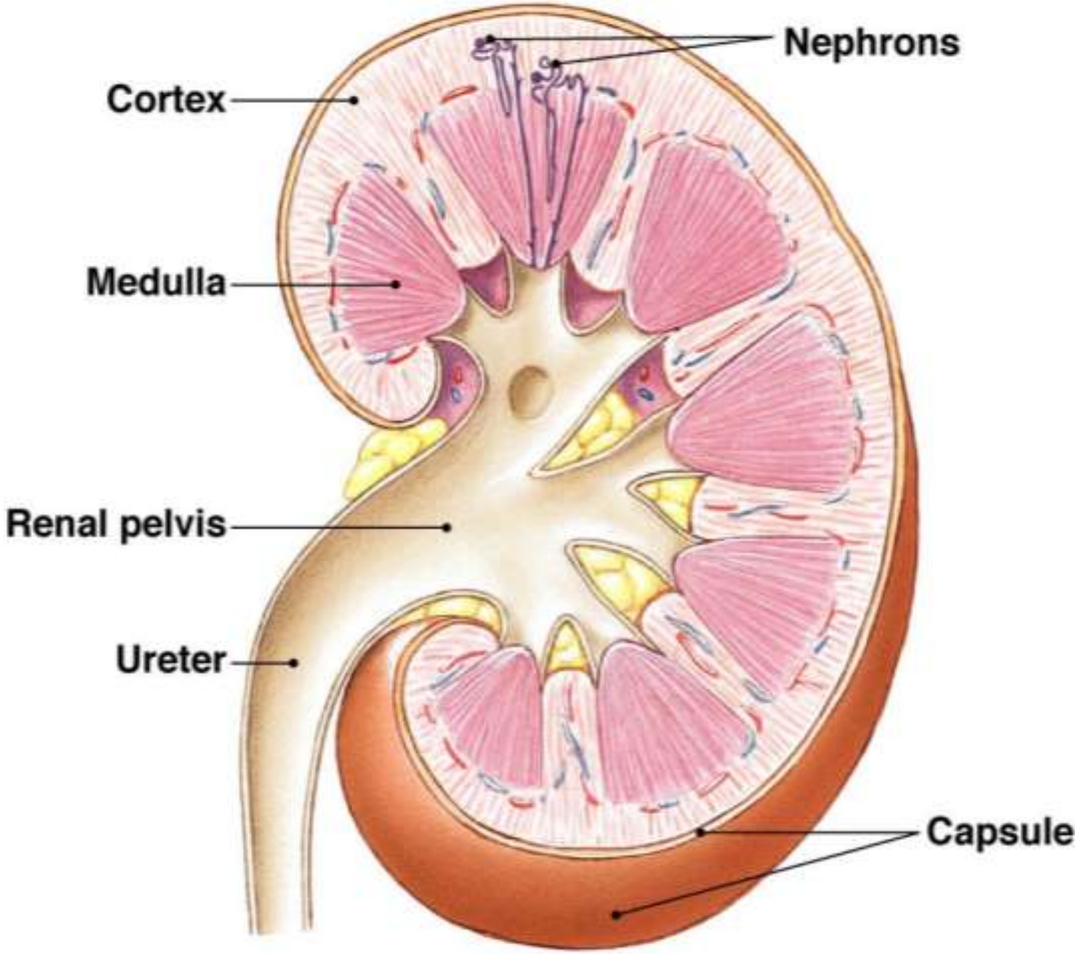
5. Discuss the tubuloglomerular feedback mechanism the myogenic response

The Kidneys

- Bean shaped
- Approximately the size of your fist
- Retroperitoneal (behind the abdominal cavity lining) position
- Located between 12th thoracic vertebra-3rd lumbar vertebra
- Partially protected by floating ribs (false ribs)
- Right kidney is slightly lower than left



(c) In cross section, the kidney is divided into an outer cortex and an inner medulla. Urine leaving the nephrons flows into the renal pelvis prior to passing through the ureter into the bladder.



Urine drains into the minor calyces → major calyces →renal pelvis→ ureter

The Kidney

- Excretory, regulatory, & endocrine organ

  Responsible for:

  a) Producing urine (1 L/day excreted): Maintains proper balance between water, salts, acids and bases

  b) Controlling blood pressure, blood volume, blood constituents

  c) Filtering and cleaning blood: Allows toxins, metabolic wastes, and excess ions to be excreted in the urine → Body's "washing machine"

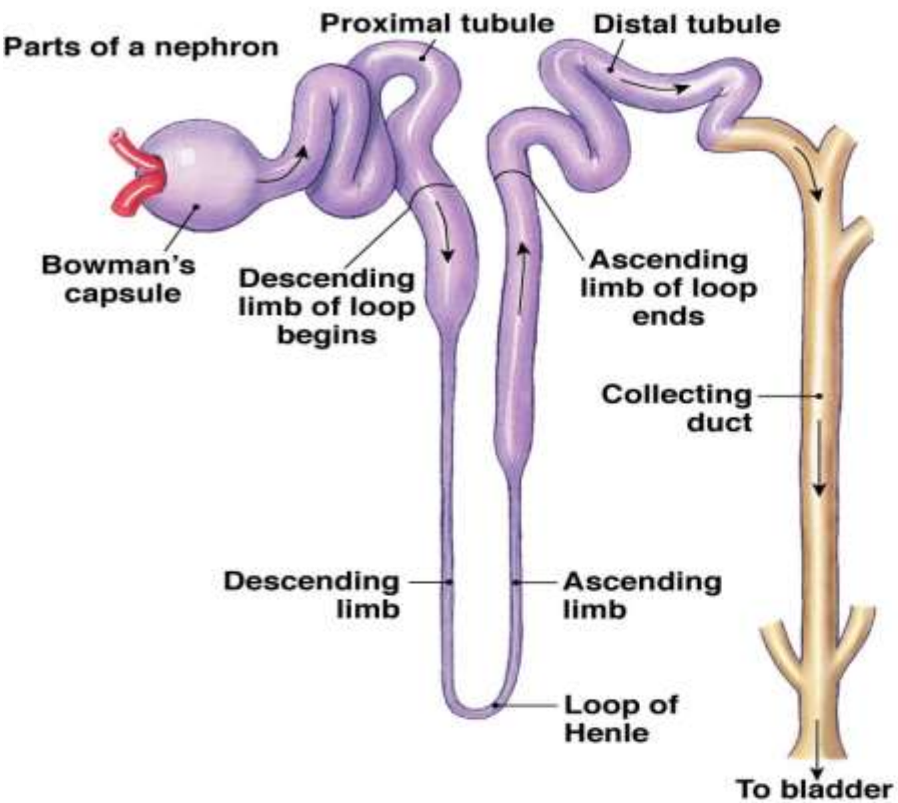
  d) Synthesizing and secreting hormones: Renin to regulate blood pressure; erythropoietin to stimulate red blood cell production, activates vitamin- D -1,25-dihydroxycholecalciferol)

- Total renal blood flow ~25% of cardiac output (1800 L/day or 1.25 L/min)

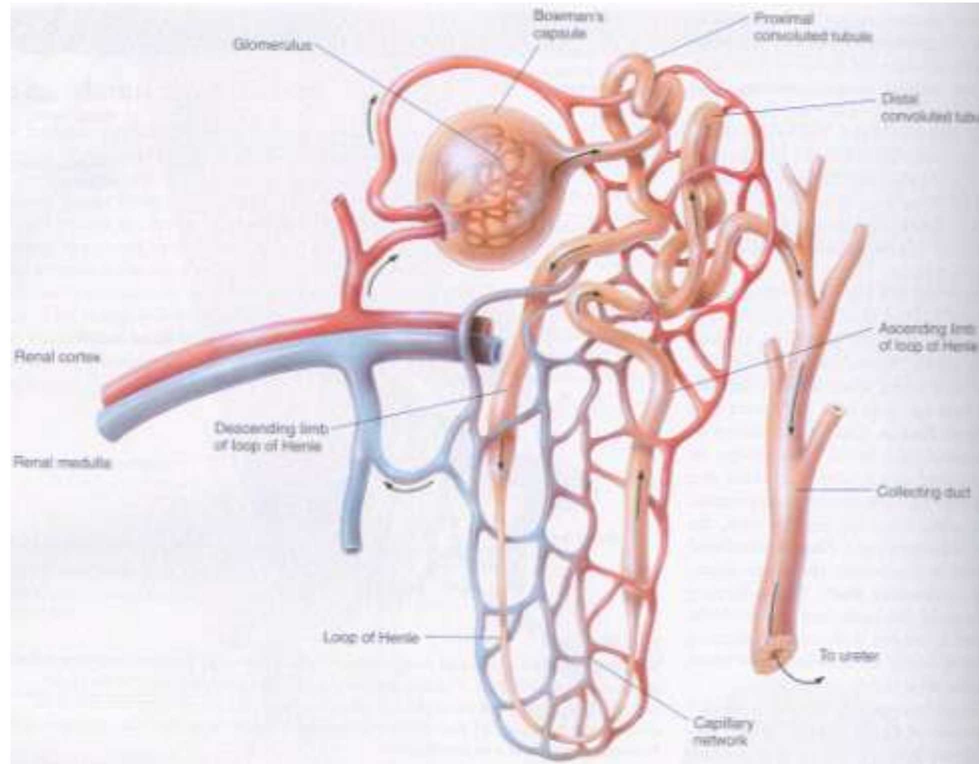
- From 1800 L/day → filters about 180 L/day; reabsorbs >99% of plasma ultra-filtrate to make urine

- Nephron: functional unit of kidney
  - millions per kidney

The Nephron

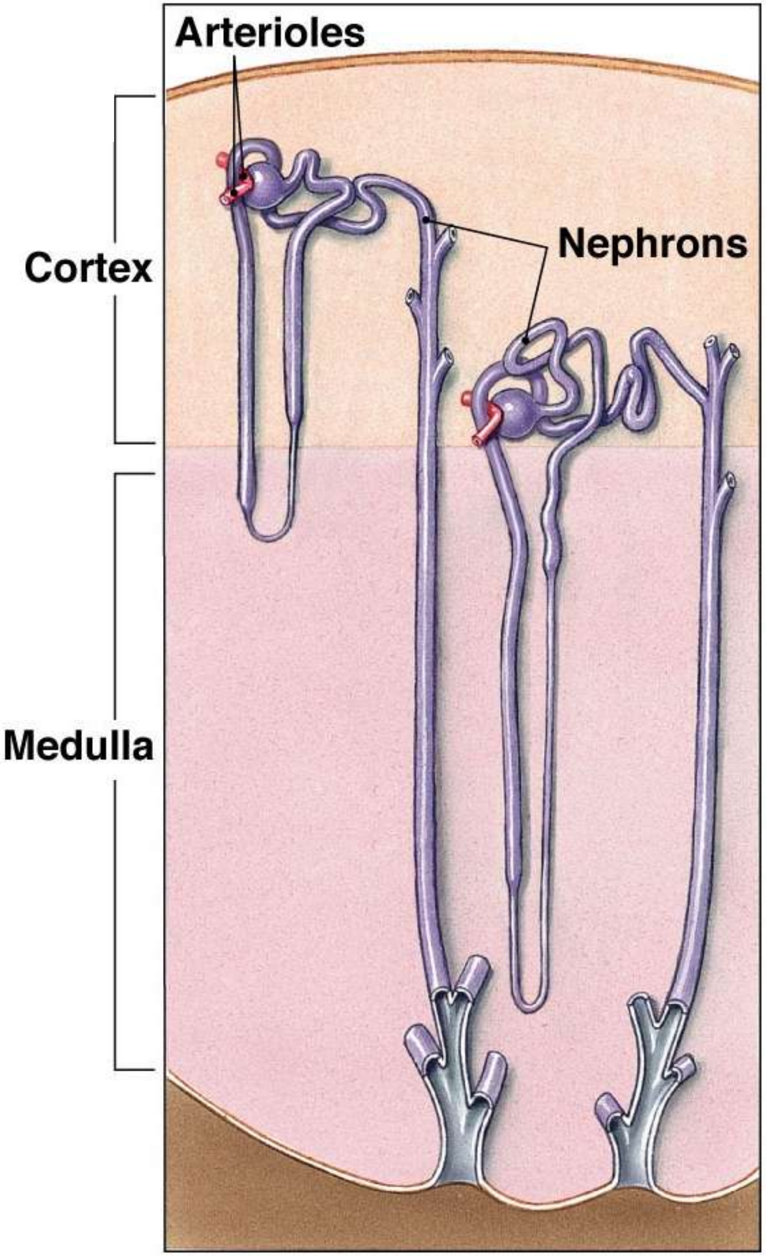


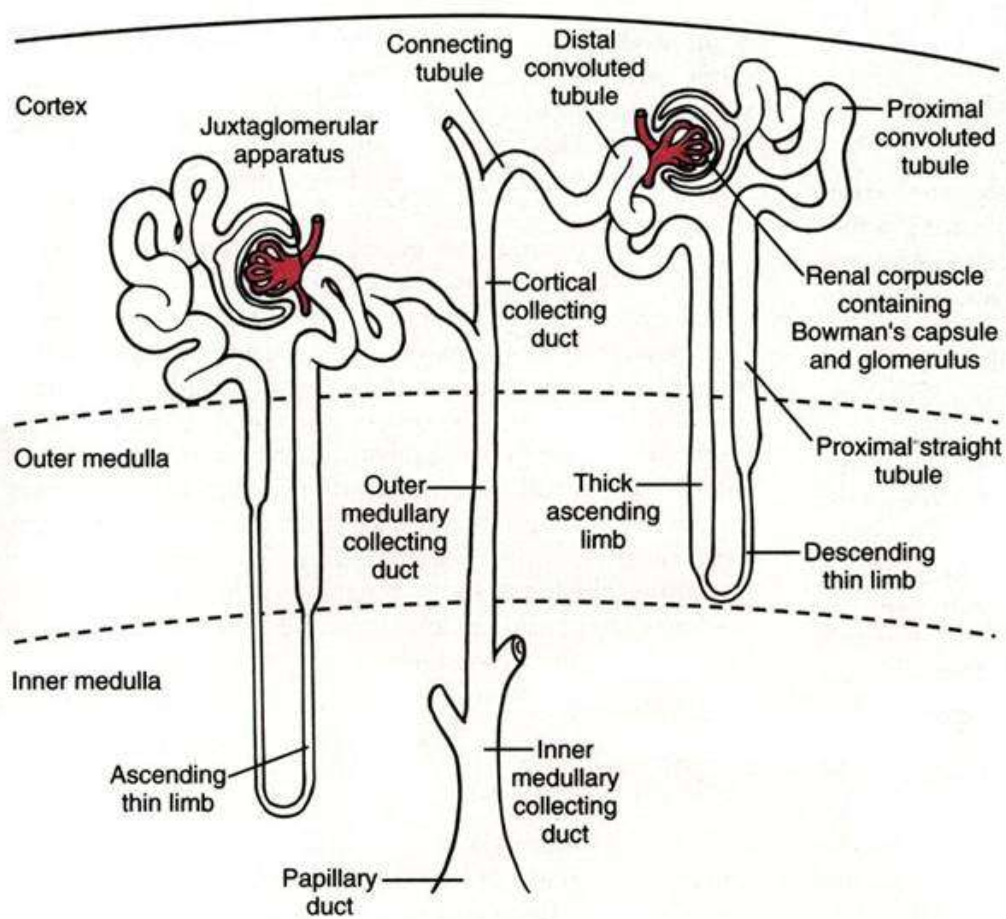
Parts of a nephron
Proximal tubule
Distal tubule
Bowman's capsule
Descending limb of loop begins
Ascending limb of loop ends
Collecting duct
Descending limb
Ascending limb
Loop of Henle
To bladder



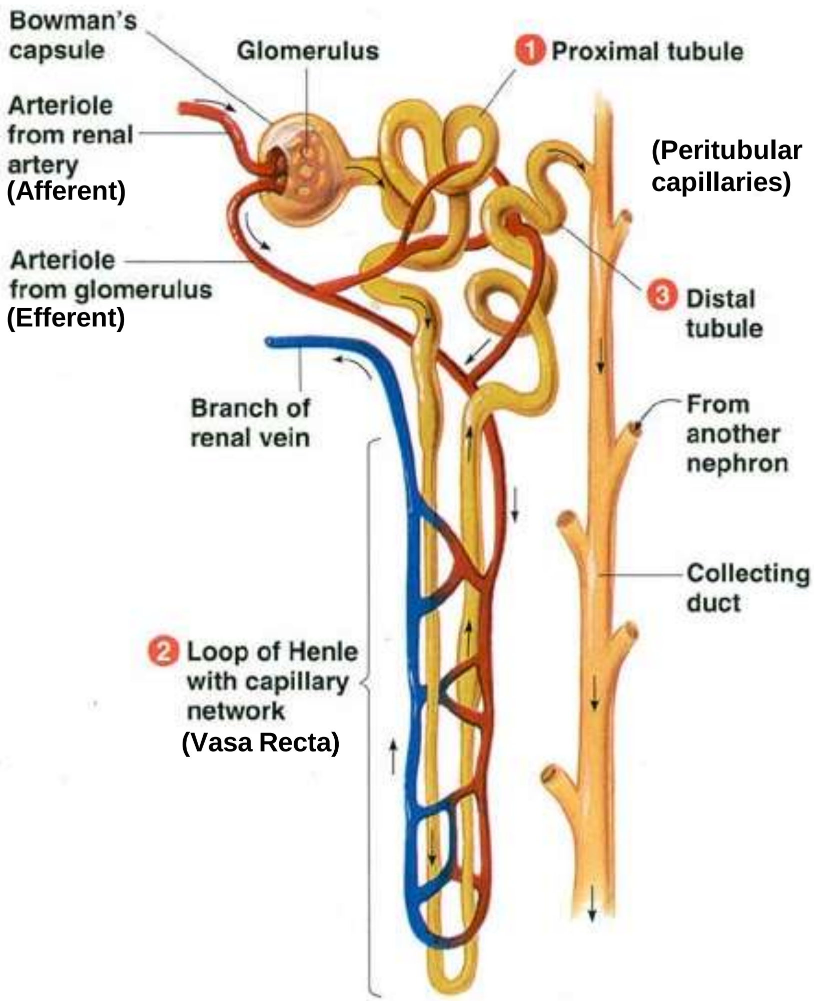
Glomerulus
Bowman's capsule
Proximal convoluted tubule
Distal convoluted tubule
Renal cortex
Ascending limb of loop of Henle
Descending limb of loop of Henle
Renal medulla
Collecting duct
Loop of Henle
To ureter
Capillary network

Juxtamedullary vs Cortical Nephron





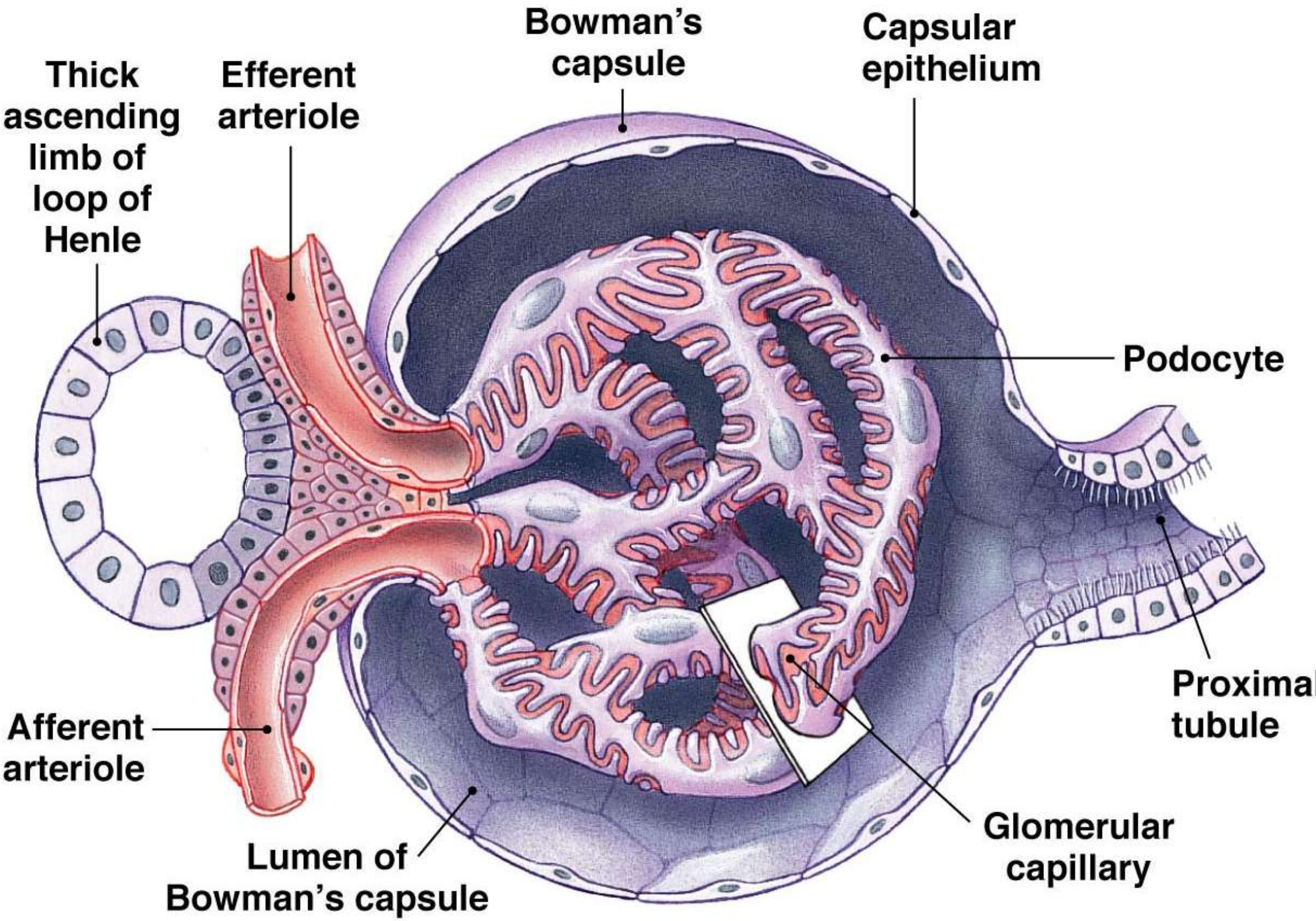
Blood Supply to Nephrons

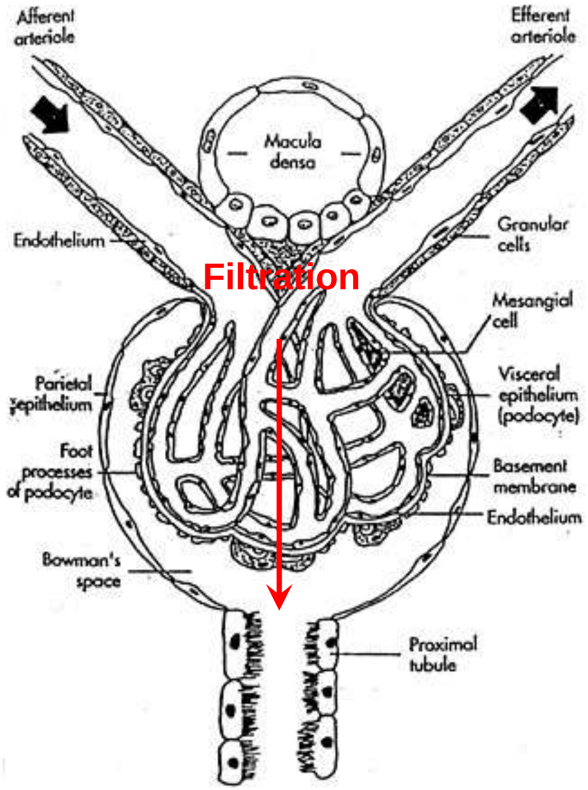


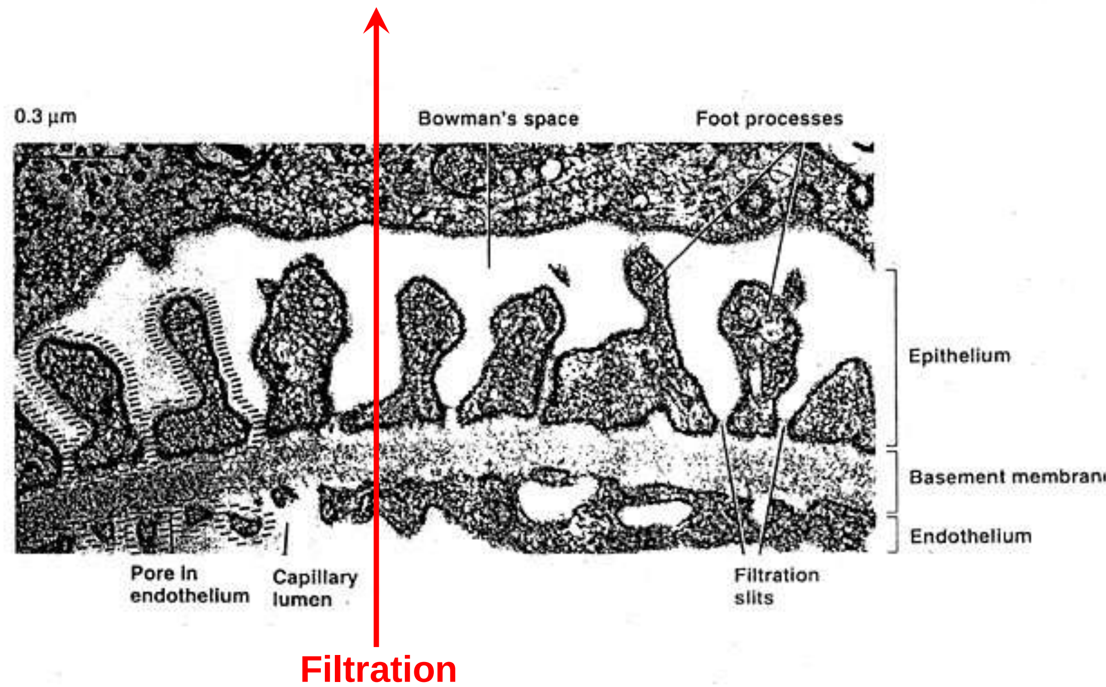
- Vasculature on top of tubules - arterioles on either side of glomerular capillaries
- Afferent artery - glomerular capillaries (filtration here) (Not all blood is filtered) - efferent artery via peritubular capillaries (wrap around epithelium portion of nephron (proximal/distal tubules))
  - 99% reabsorption - proximal tubules into peritubular capillaries into vasculature
- Vasa Recta - capillaries close to juxtamedullary nephrons only
  - Specialized peritubular caps
  - Hairpins close to thin/thick ascending and thin descending limbs of loop of Henle

Filtration

Anatomy of the Glomerulus







The basement membrane is major barrier with endothelium in intimate contact with glomerular capillaries

The epithelial layer of Bowman's capsule has specialized cells (**podocytes**) that form many extensions (**pedicels**) →Pedicels interdigitate forming **filtration slits**

The surface of the pedicels is negatively charged

Glomerular Filtration

- 2 components to determine flux across glomerulus:
  1) Permeability 2) Glomerular filtration pressure

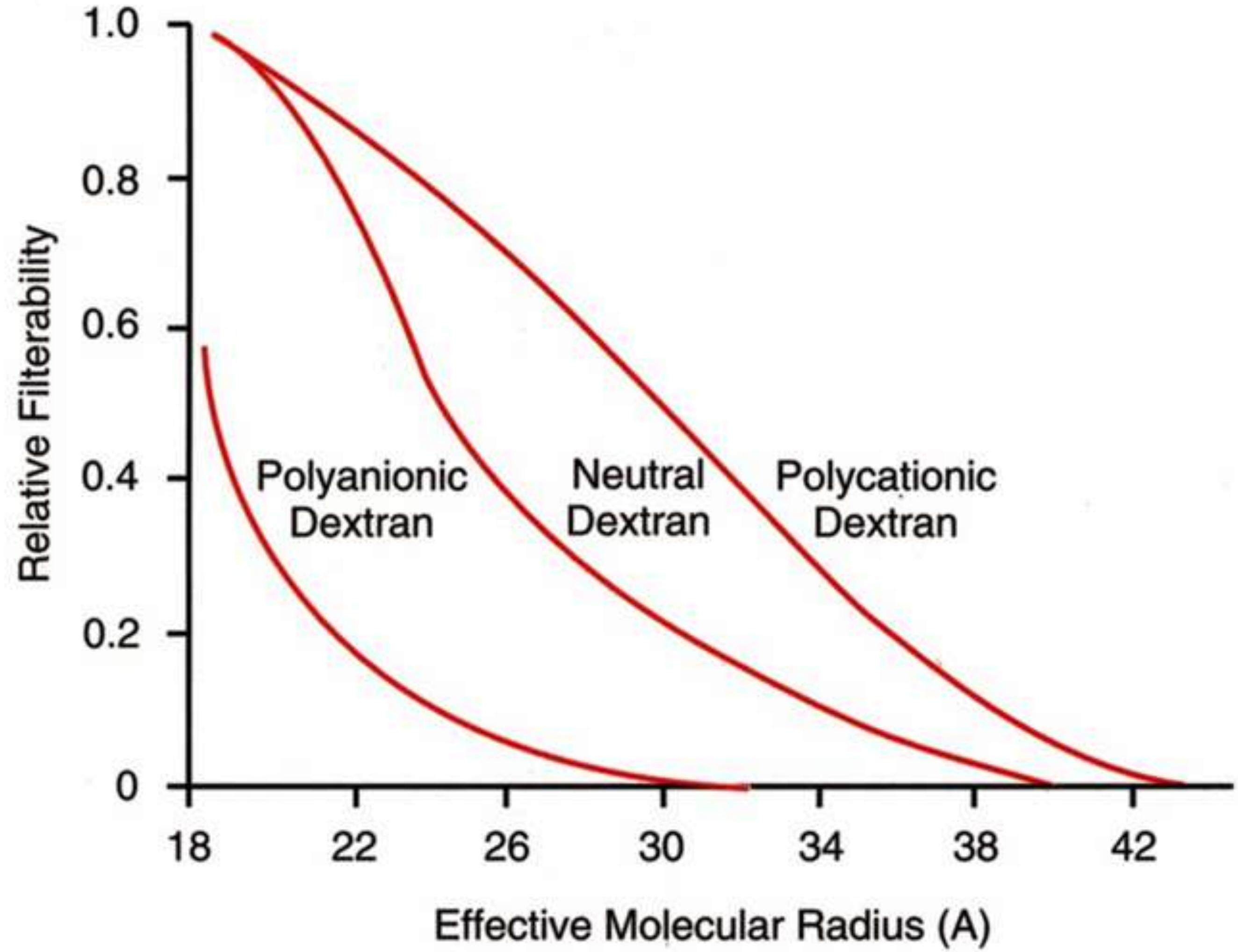
1) Permeability

a. Size:
- Small molecules radii < 15 Å : freely filterable
- 15 - 35 Å : inverse relationship with size and filterability
- Large molecules > 35 Å : no filterability at all

Freely filtered molecules: [plasma] = [Bowman's space]
Non-freely filtered molecules: [plasma] > [Bowman's space]

b. Charge :
- 15 - 35 Å : Cations > neutral > anions

Effect of Size and Charge on Filterability



Test Question

Which of the following solutes is not freely filtered?

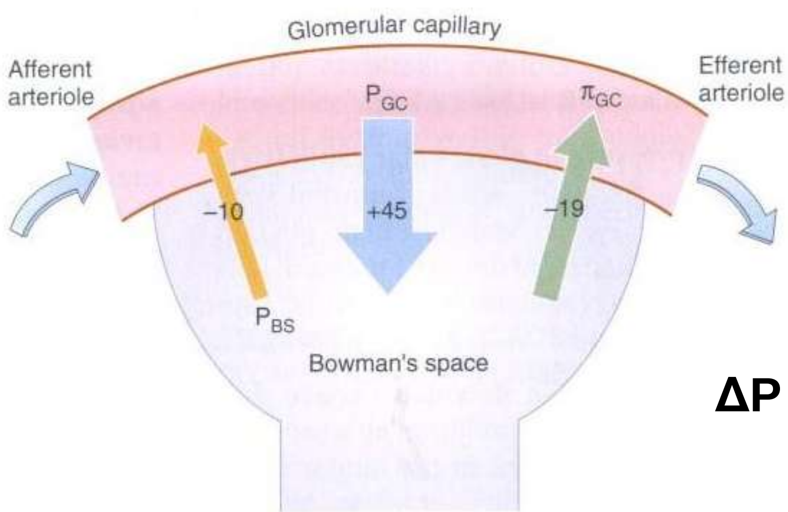
1. Urea
2. Leucine
3. PAH
4. Inulin
5. Hemoglobin

2) Glomerular Filtration Pressures

"Starling Forces": 4 pressures affecting fluid movement across capillary wall

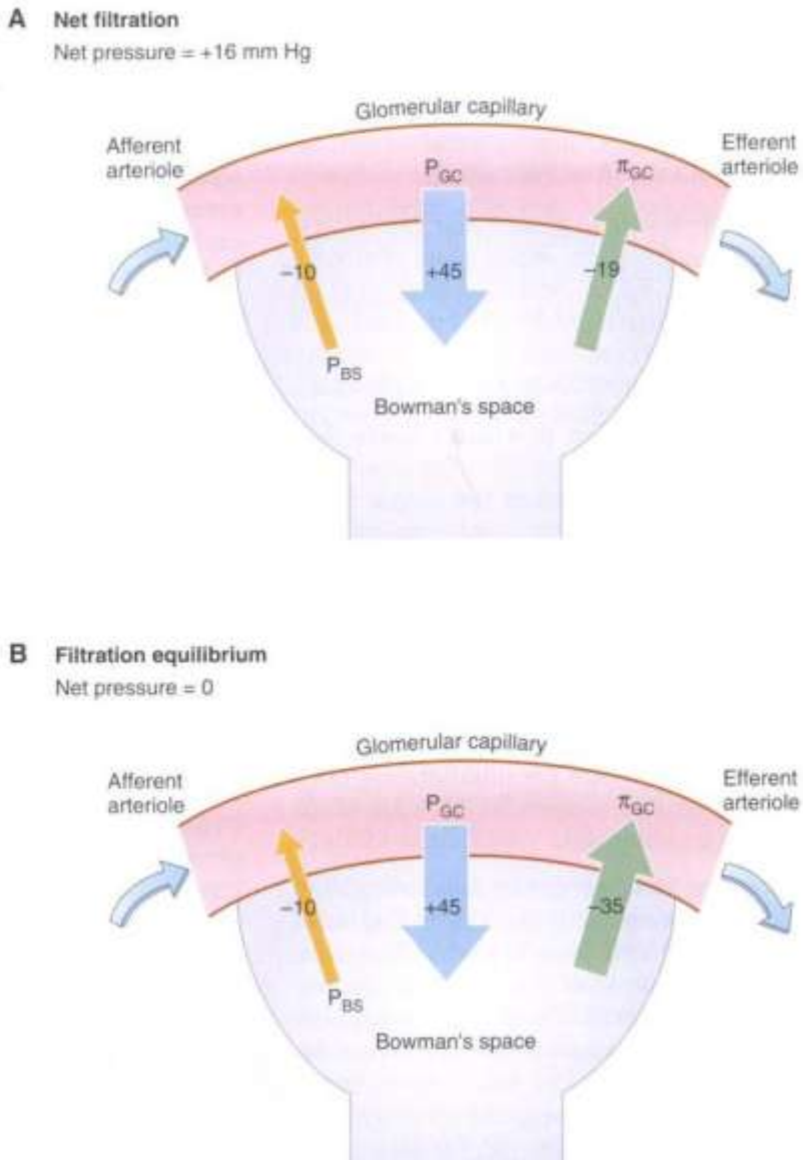
- 2 hydrostatic pressures: push H_2O away (out capillary/interstitium)
- 2 oncotic pressures: proteins drawing H_2O towards them (into the capillary/interstitium)

1. Hydrostatic pressure of capillary (P_G) – favours filtration
2. Hydrostatic pressure of interstitium (P_B) – opposes filtration/ favours reabsorption
3. Oncotic pressure of blood (plasma) (p_G) – opposes filtration/ favours reabsorption
4. Oncotic pressure of interstitial fluid/Bowman's space (p_B) – favours filtration (+) – no proteins in Bowman's space (0 mmHg)



$$\Delta P = [(P_G + \pi_B) - (P_B + \pi_G)]$$

Starling Equation



P_{GC} = 45 mmHg

P_{BS} = 10 mmHg

π_{GC} = 19 mmHg

π_{BS} = ?

0 mmHg

$\Delta P = [(P_G + \pi_B) - (P_B + \pi_G)]$

$[(P_G - P_{BS} - \pi_G)] = ?$

= +16 mmHg

Therefore net force favours ??

Filtration

Test Question

If a patient presents with protein in the urine which of the following Starling forces is most affected?

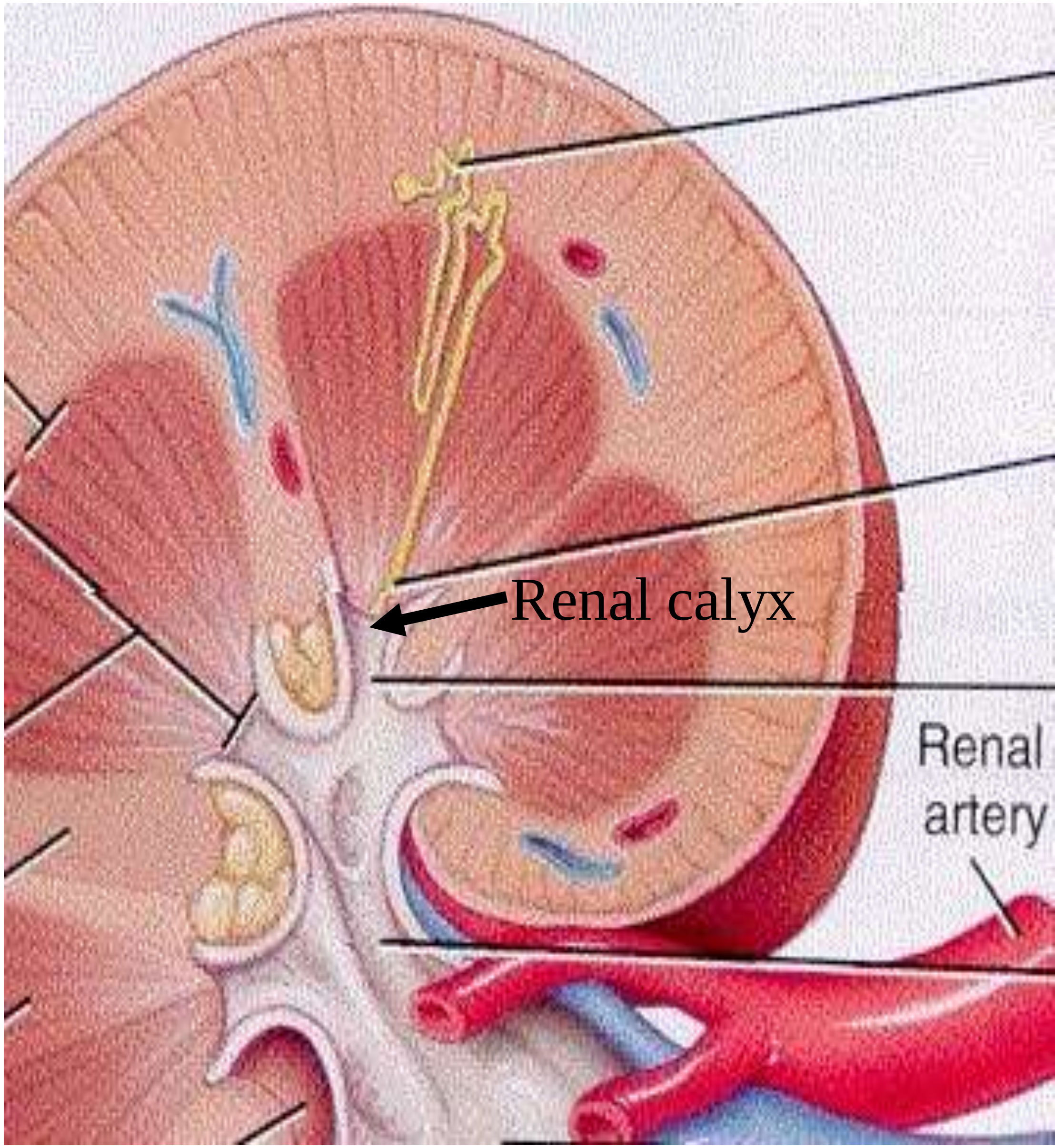
a. P_{GC}

b. π_{GC}

c. P_{BS}

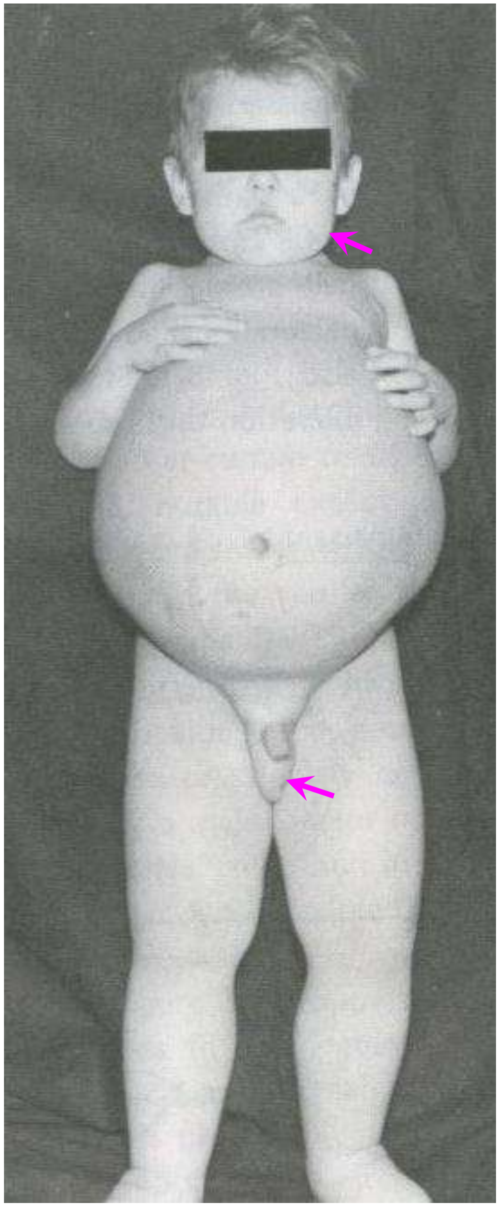
d. π_{BS}

If a kidney stone blocked a renal calyx, how would this affect filtration pressure in the nephrons emptying into it?



Diseases That Change Starling Forces

Nephrotic Syndrome



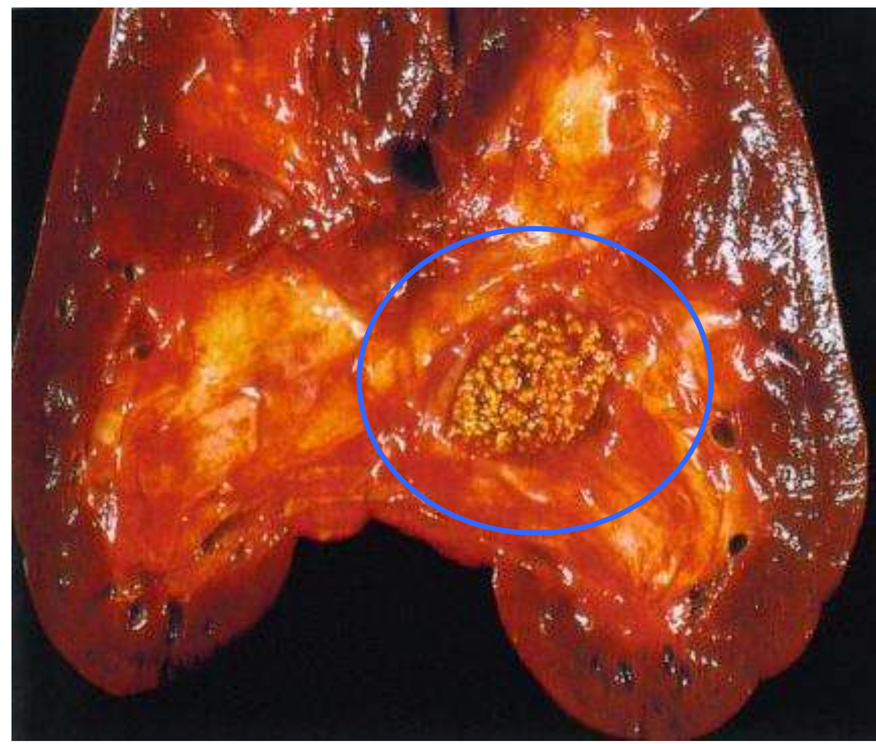
Increased permeability of glomerular capillaries to plasma proteins

Results in Increased (π_B)

Urinary Tract Obstruction (Obstructive Uropathy)

Backs up tubular flow

Results in Increased (P_B)



Glomerular Filtration Rate (GFR)

GFR = Rate at which the ultrafiltrate forms in Bowman's space

GFR = K_f x ΔP

Normal values of GFR = 90 - 140 ml/min

K_f invariant constant 10-15 ml/min/mmHg

K_f ~ 12 ml/min/mmHg

ΔP = 10 mmHg

THEREFORE:

GFR = 12 ml/min/mmHg x 10 mmHg = 120 ml/min

Test Question

If the average hydrostatic pressure in the glomerular capillaries is 50 mmHg, the hydrostatic pressure in Bowman's space is 12 mmHg, the average colloid osmotic pressure in the glomerular capillaries is 30 mmHg, and there is no protein in the glomerular ultrafiltrate, what is the net pressure driving glomerular filtration?

A. 8 mmHg
B. 32 mmHg
C. 48 mmHg
D. 60 mmHg
E. 92 mmHg

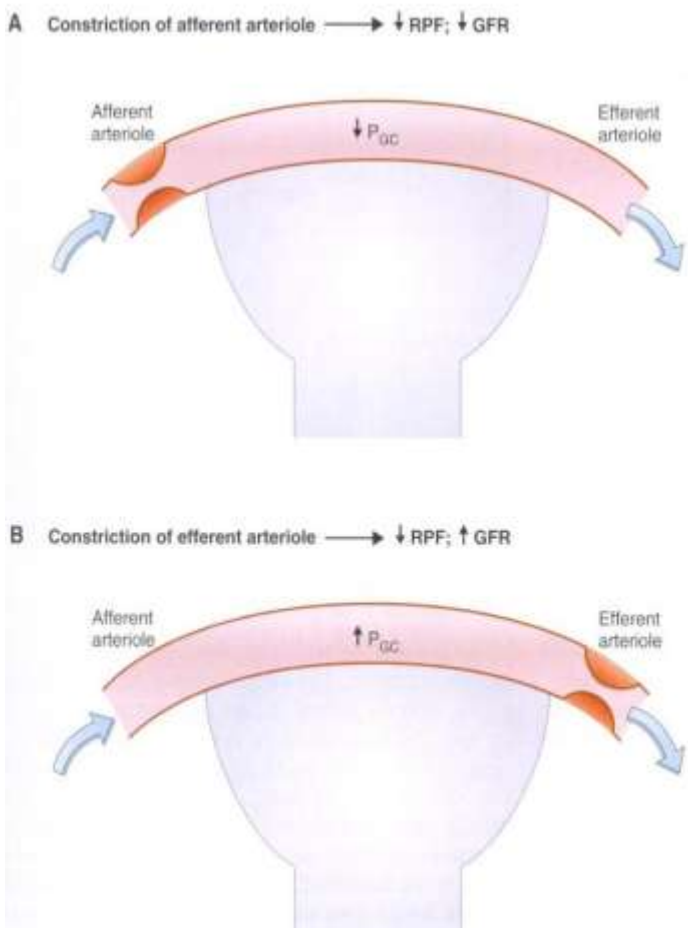
If K_f = 12 ml/min/mmHg what is this patient's GFR?

96 ml/min

Glomerular Pressure Variation

Glomerular blood hydrostatic pressure varies with constriction of afferent and efferent arterioles

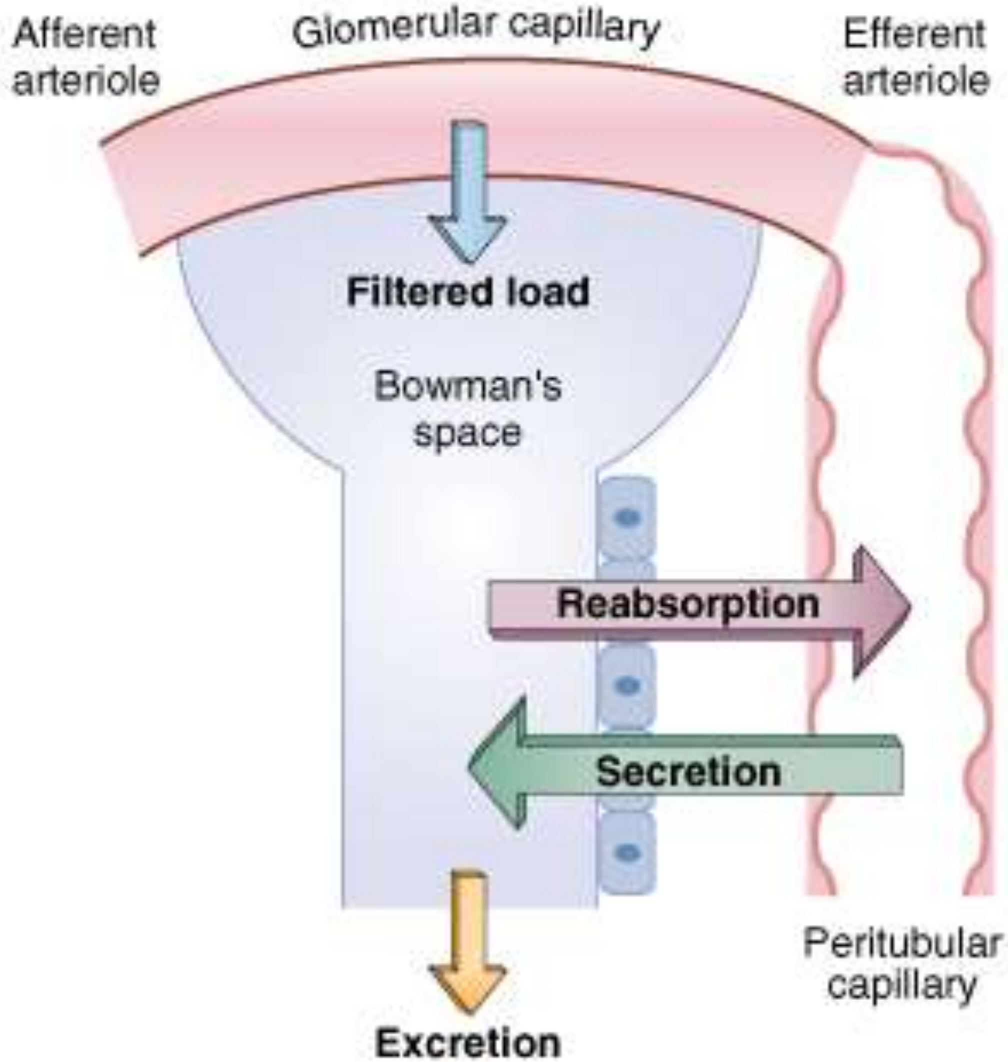
What would be the effect of afferent arteriole constriction? Efferent arteriole constriction?



- <u>Constrict afferent</u>:
  - ↓ Renal plasma flow (RPF)
  - ↓ GFR
- <u>Dilate afferent</u>:
  - ↑ RPF
  - ↑ GFR
- <u>Constrict efferent</u>:
  - ↓ RPF
  - ↑ GFR
- <u>Dilate efferent</u>:
  - ↑ RPF
  - ↓ GFR

Net Transport for Urine Formation and Autoregulation

Concepts of Net Transport for Urine Formation

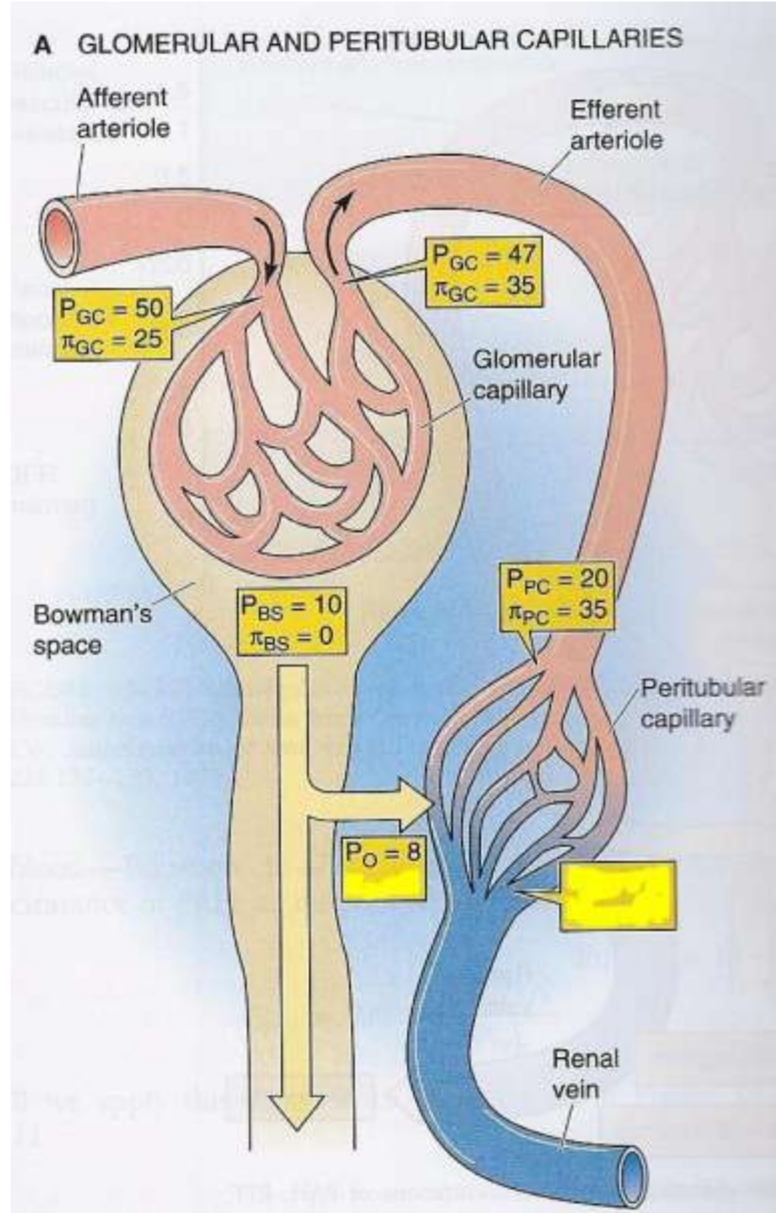


- <u>Filtration</u>: Movement of solutes from glomerular capillaries to Bowman's Space
- <u>Reabsorption</u>: Returns most filtered solutes to circulation
- <u>Secretion</u>: Transports solutes from peritubular capillaries and vasa recta into the tubular lumen
- <u>Excretion</u>: Solute in urine due to filtration, secretion, reabsorption (sum of 3 processes)

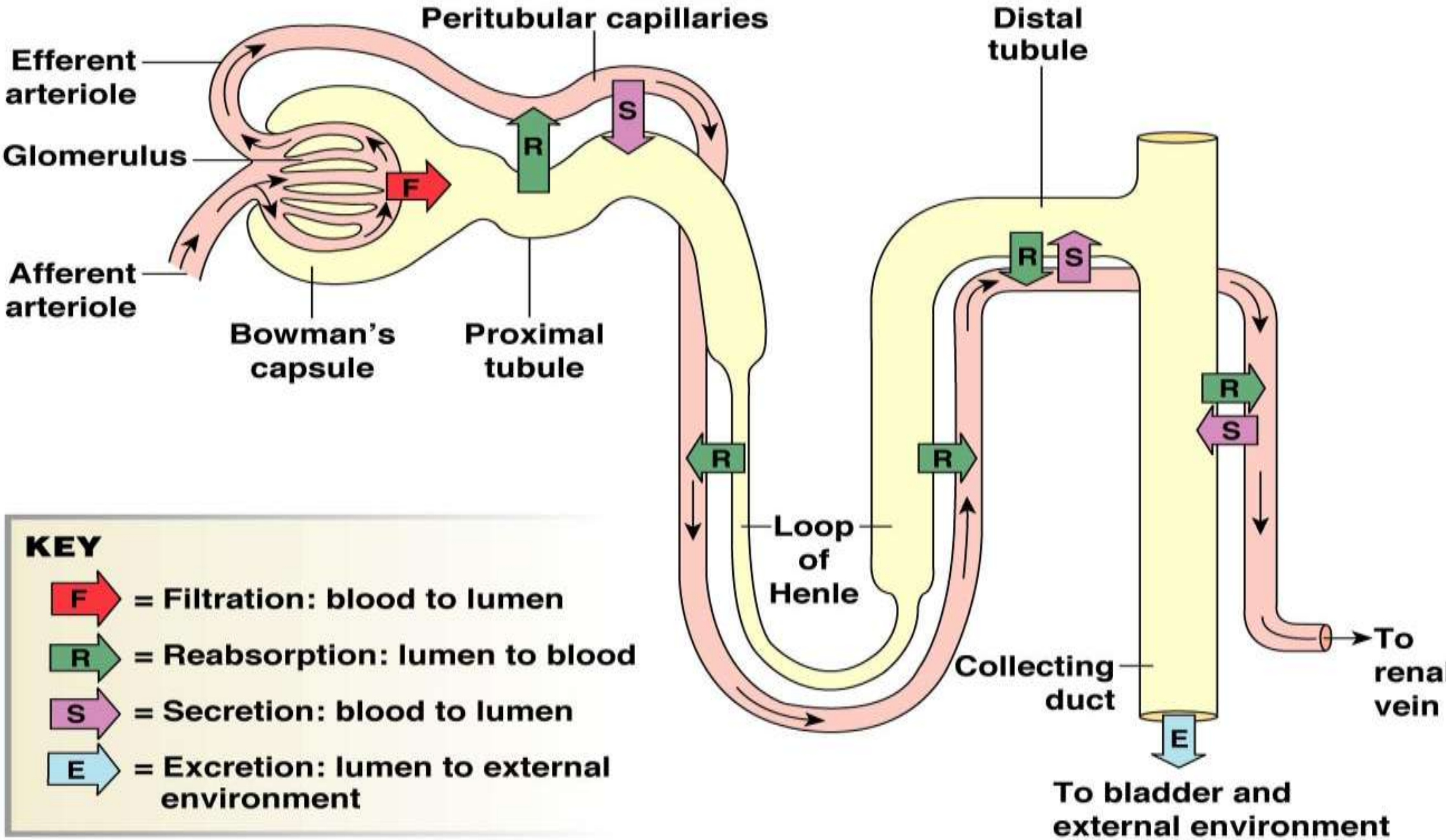
Peritubular Capillaries

- **67% $H_2$0/solutes reabsorbed by proximal tubule – returned to bloodstream by peritubular capillaries**

- **3 Starling forces that control H_2O movement (missing one force π_i …why????)**
  1. **Plasma oncotic pressure in peritubular capillary (π_{PC})**
     - driving force for reabsorption
  2. **Hydrostatic pressure in peritubular capillary (P_{PC})**
     - force that prevents water from entering capillary
  3. **Hydrostatic pressure in interstitial space (P_i / P_o)**
     - H_2O follows solutes – increase pressure – forces H_2O into capillary



Overall Solute Movement



Kidney Blood Flow and Autoregulation

Afferent arteriole constriction: Glomerular hydrostatic pressure decreases, decreasing filtration → decrease GFR

Efferent arteriole constriction: Glomerular hydrostatic pressure increases, increasing filtration → increase GFR

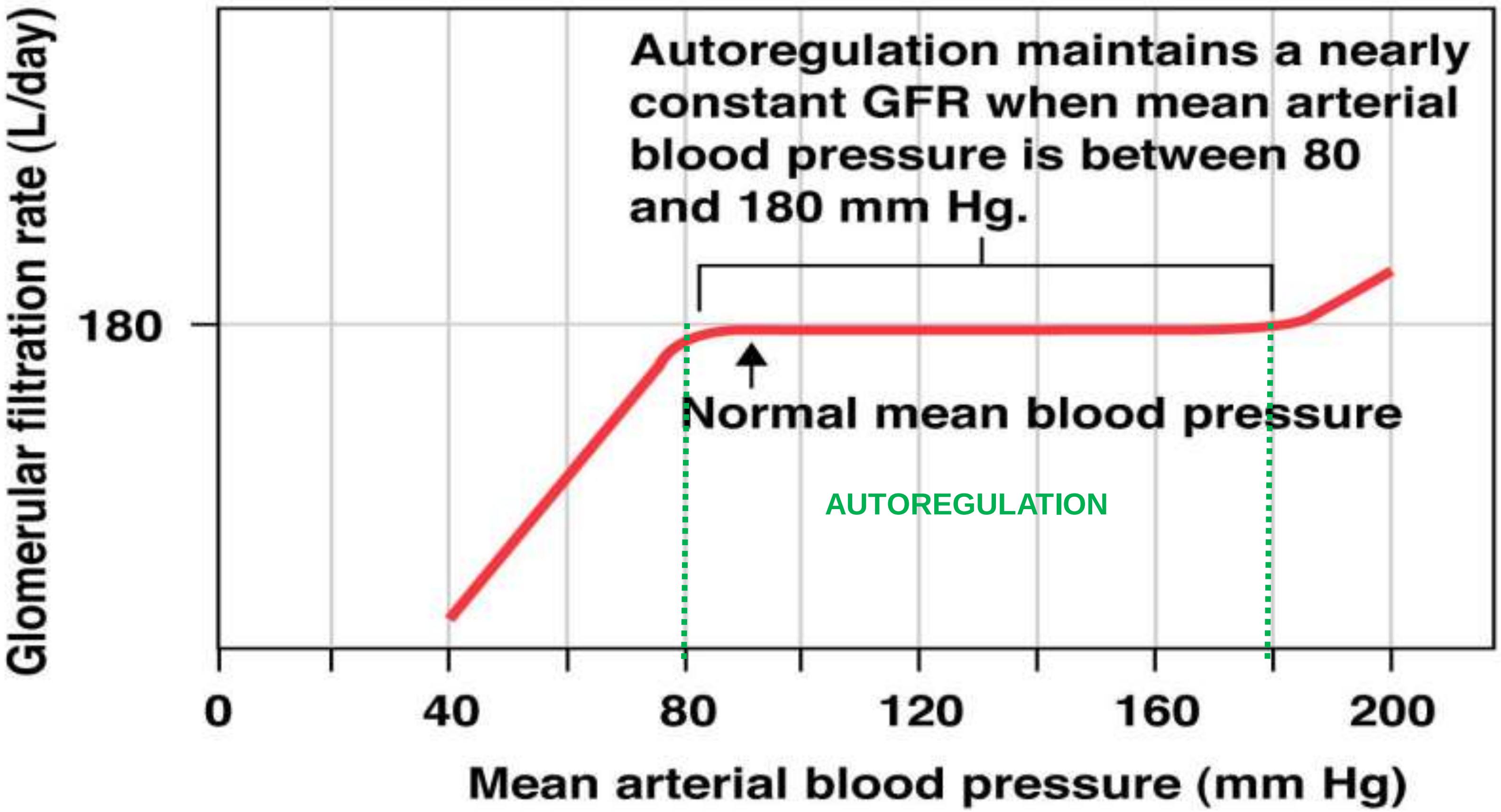
If the GFR is too high:

Needed substances cannot be reabsorbed quickly enough and are lost in the urine

If the GFR is too low:

Everything is reabsorbed, including wastes that are normally disposed

Autoregulation: GFR and RBF constant 80-180 mmHg
< 80 mmHg – reduced renal blood flow
> 180 mmHg – severe hypertension; autoregulation stops



<u>Autoregulation</u>

1. <u>Myogenic response</u>: Increased arterial pressure stretches smooth muscle in blood vessel walls - induces constriction of afferent arteriole; therefore GFR????

↑ Blood Pressure

↓

↑ Afferent Arteriole Stretch

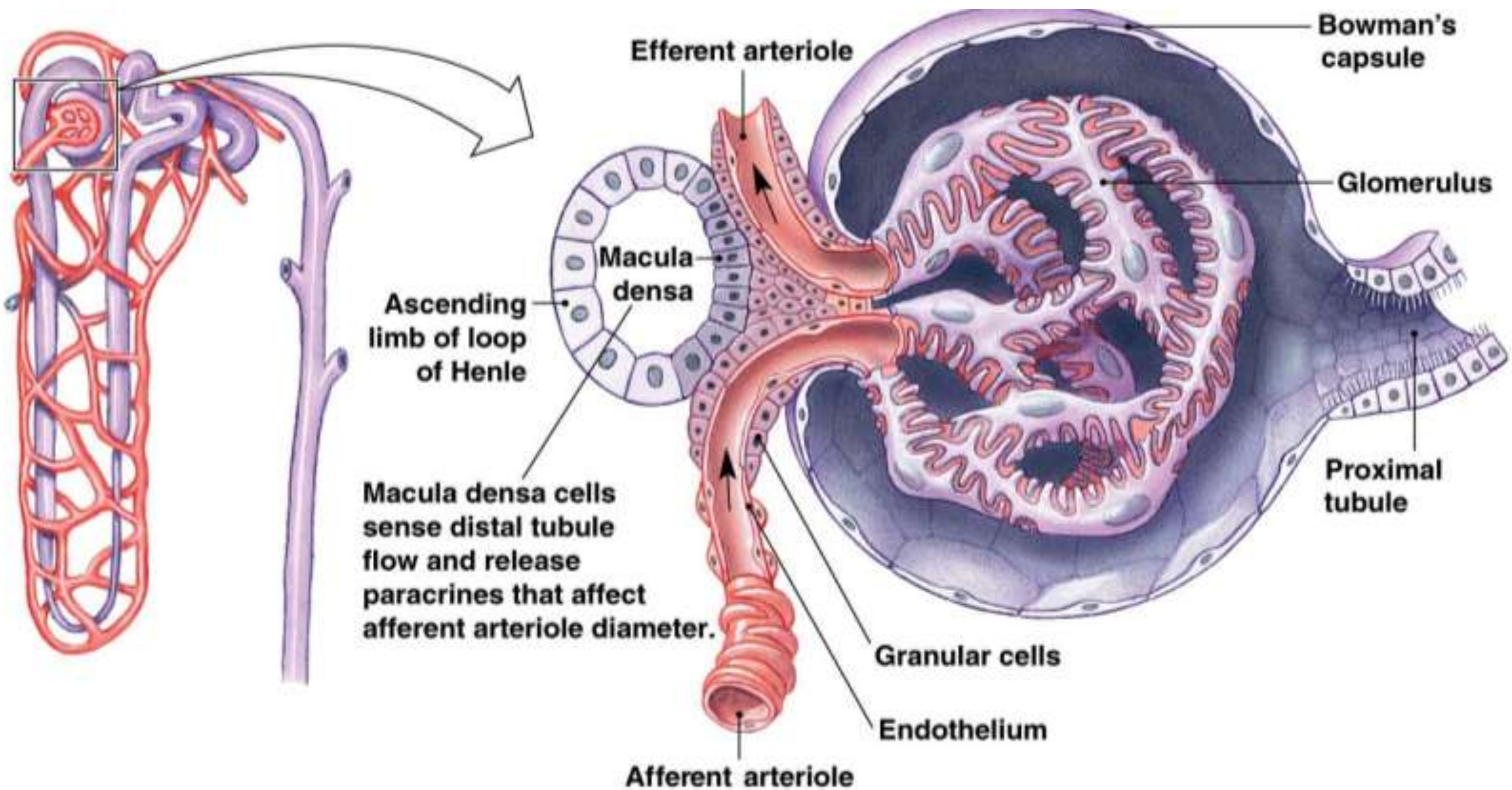
↓

Calcium Channels Open

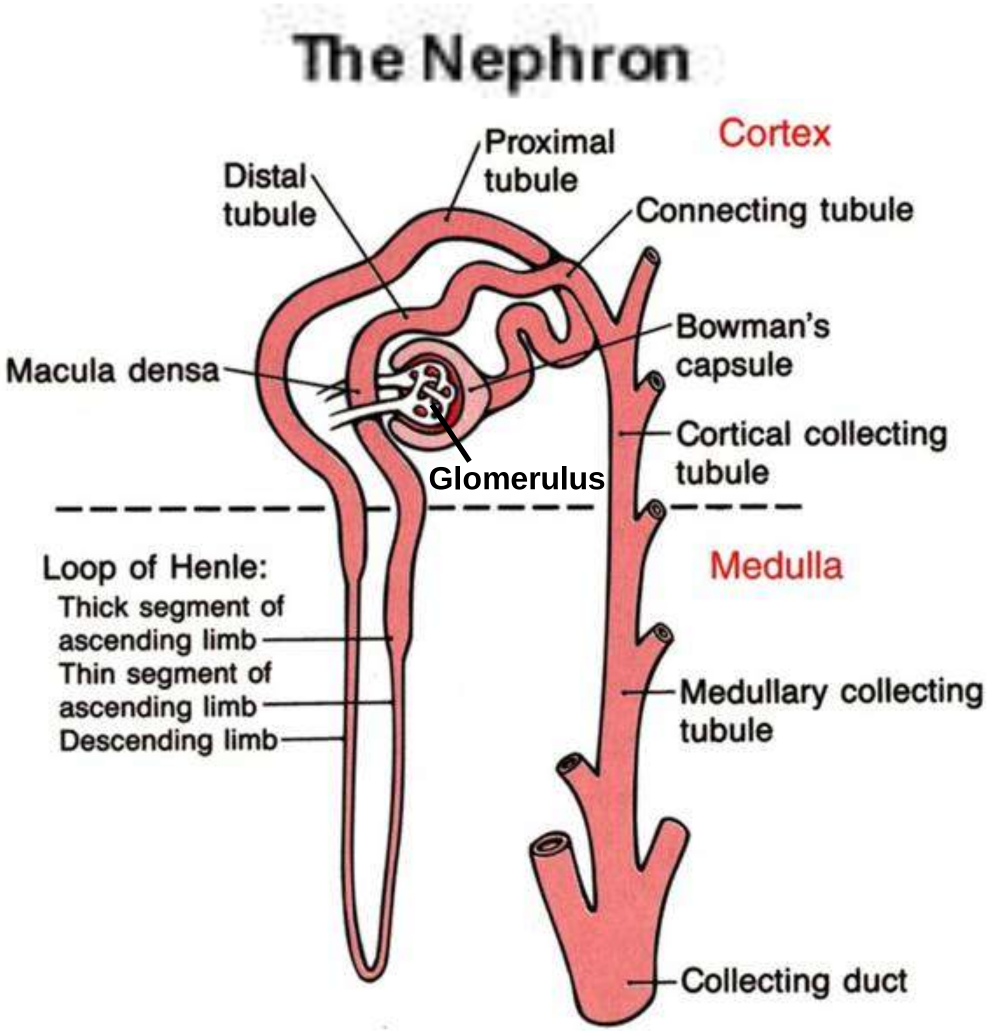
↓

↑ Afferent Arteriole Contraction

2. Tubuloglomerular Feedback: Involves macula densa and vasoactive substances (adenosine, kinins, PGs) to constrict afferent/efferent arteriole



Summary



- <u>The nephron</u> – cortical vs juxtamedullary
- <u>Glomerular filtration</u> – permeability; filtration pressures (Starling's Law); effects on GFR & RBF
- <u>Autoregulation of blood flow</u> – myogenic response; tubuloglomerular feedback