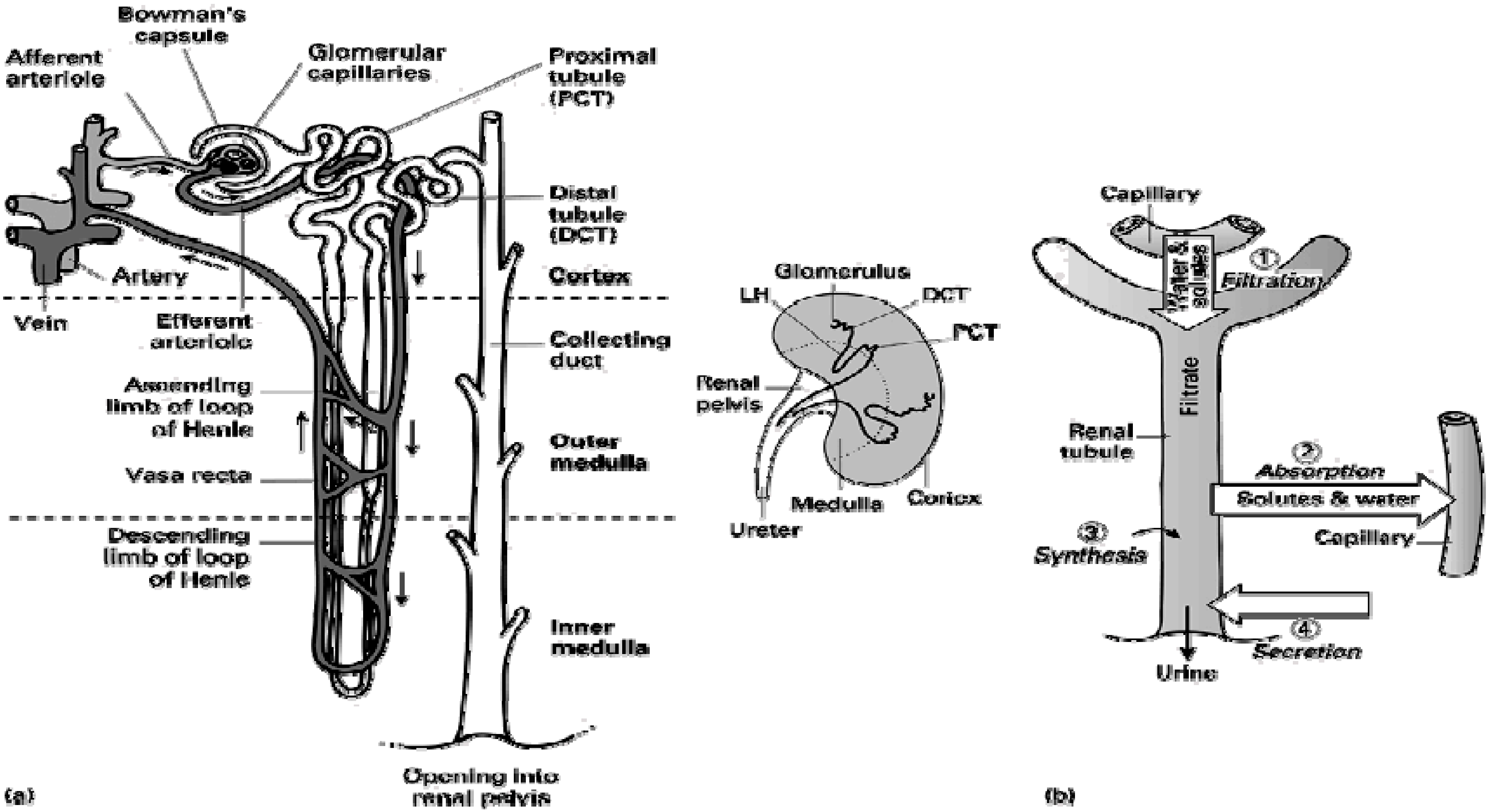
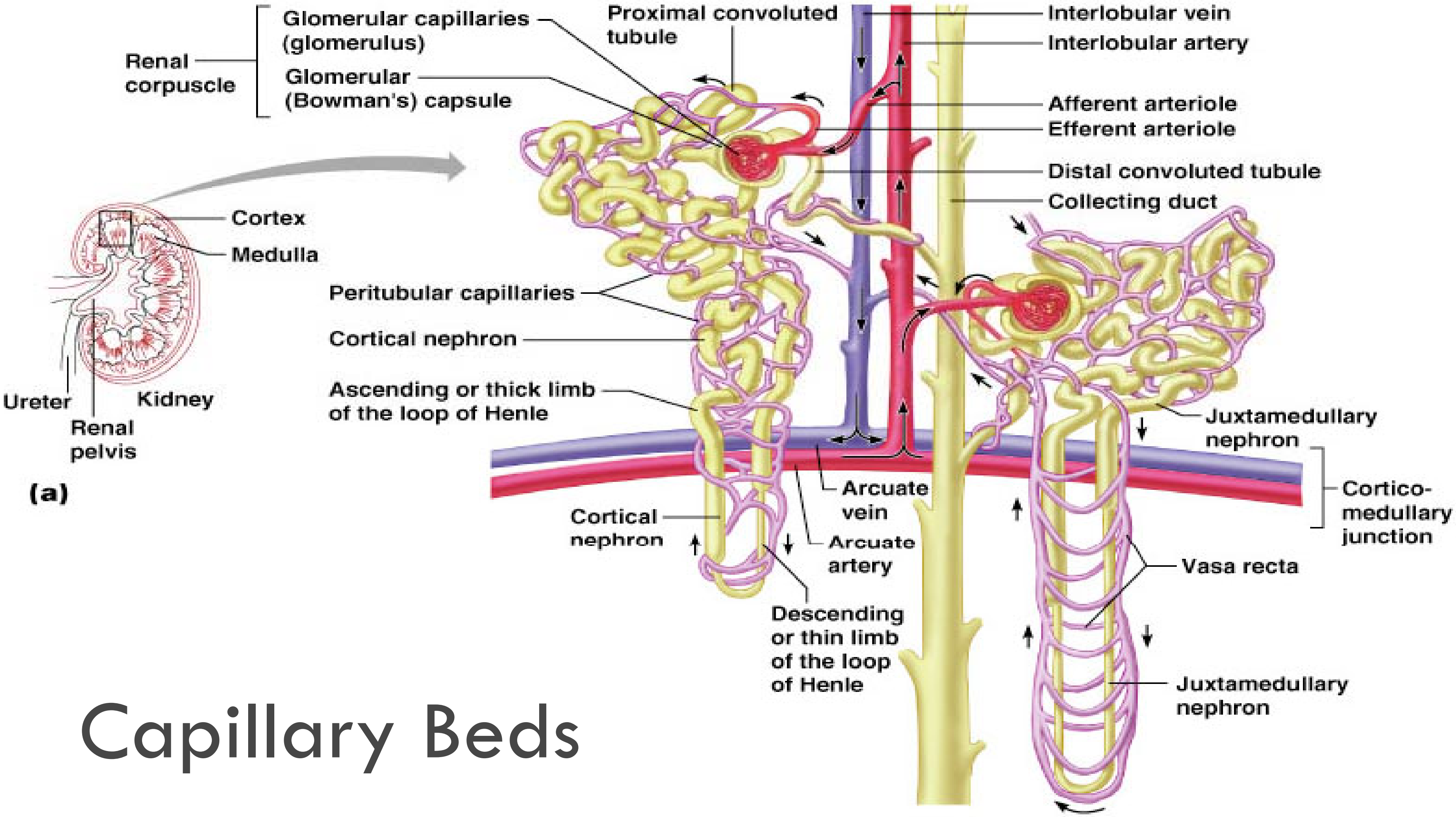
RENAL PHYSIOLOGY REVIEWED

DANIL HAMMOUDI.MD


Bowman's capsule
Afferent arteriole
Glomerular capillaries
Proximal tubule (PCT)
Distal tubule (DCT)
Artery
Cortex
Vein
Efferent arteriole
Collecting duct
Ascending limb of loop of Henle
Outer medulla
Vasa recta
Descending limb of loop of Henle
Inner medulla
Opening into renal pelvis
(a)
Glomerulus
LH
DCT
PCT
Renal pelvis
Medulla
Cortex
Ureter
Capillary
Water & solutes
① Filtration
Filtrate
Renal tubule
② Absorption
Solutes & water
Capillary
③ Synthesis
④ Secretion
Urine
(b)



Capillary Beds

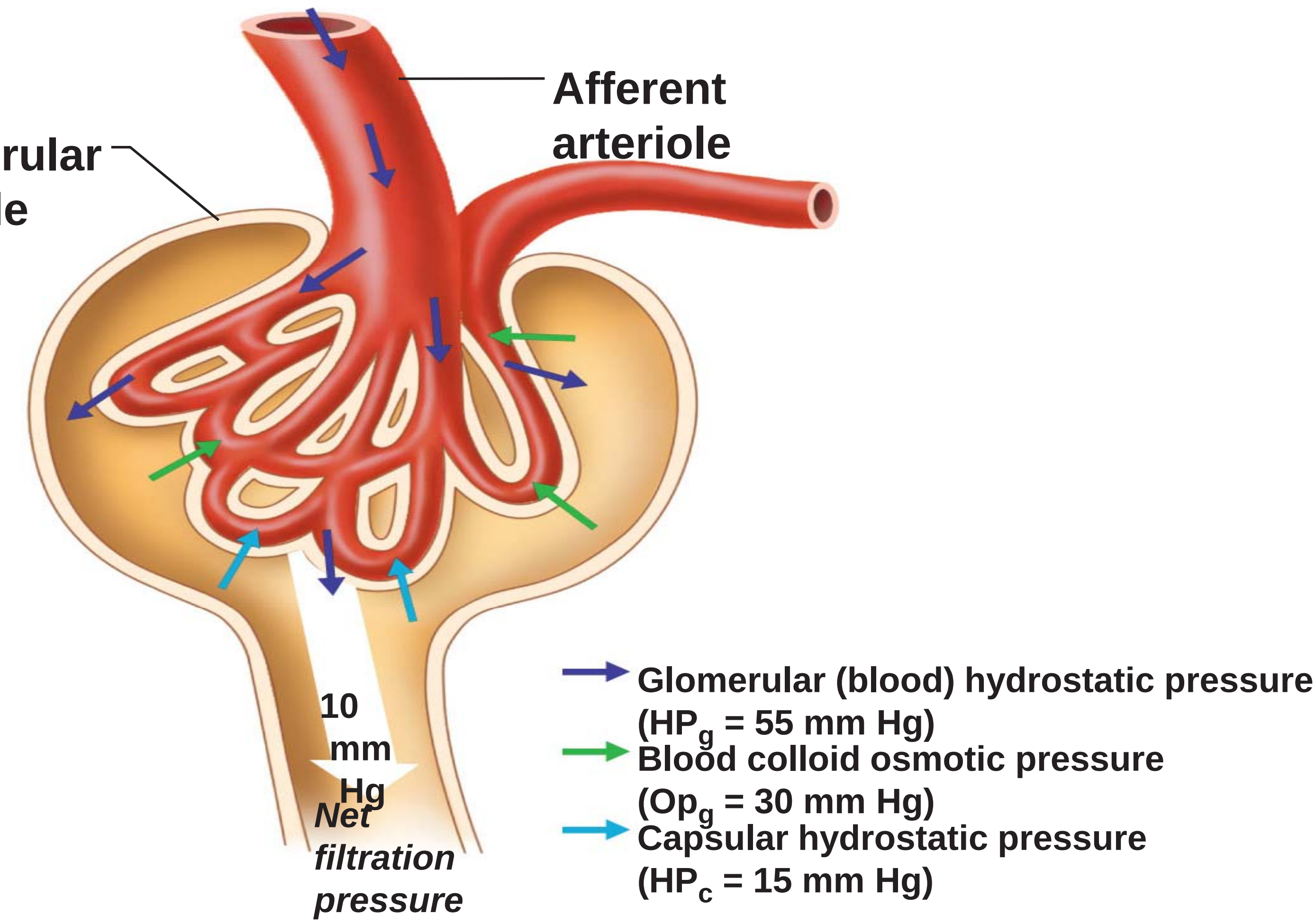
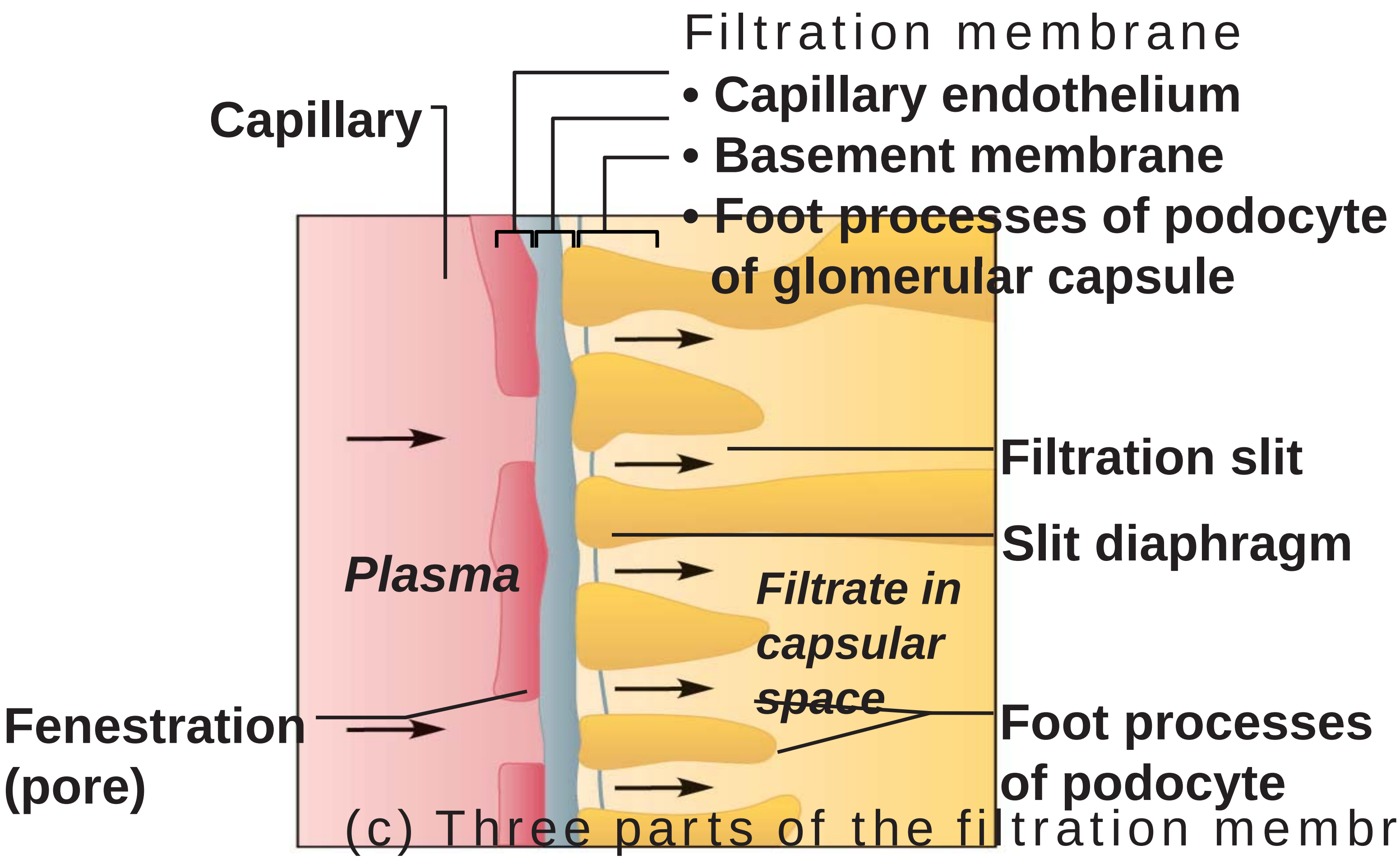
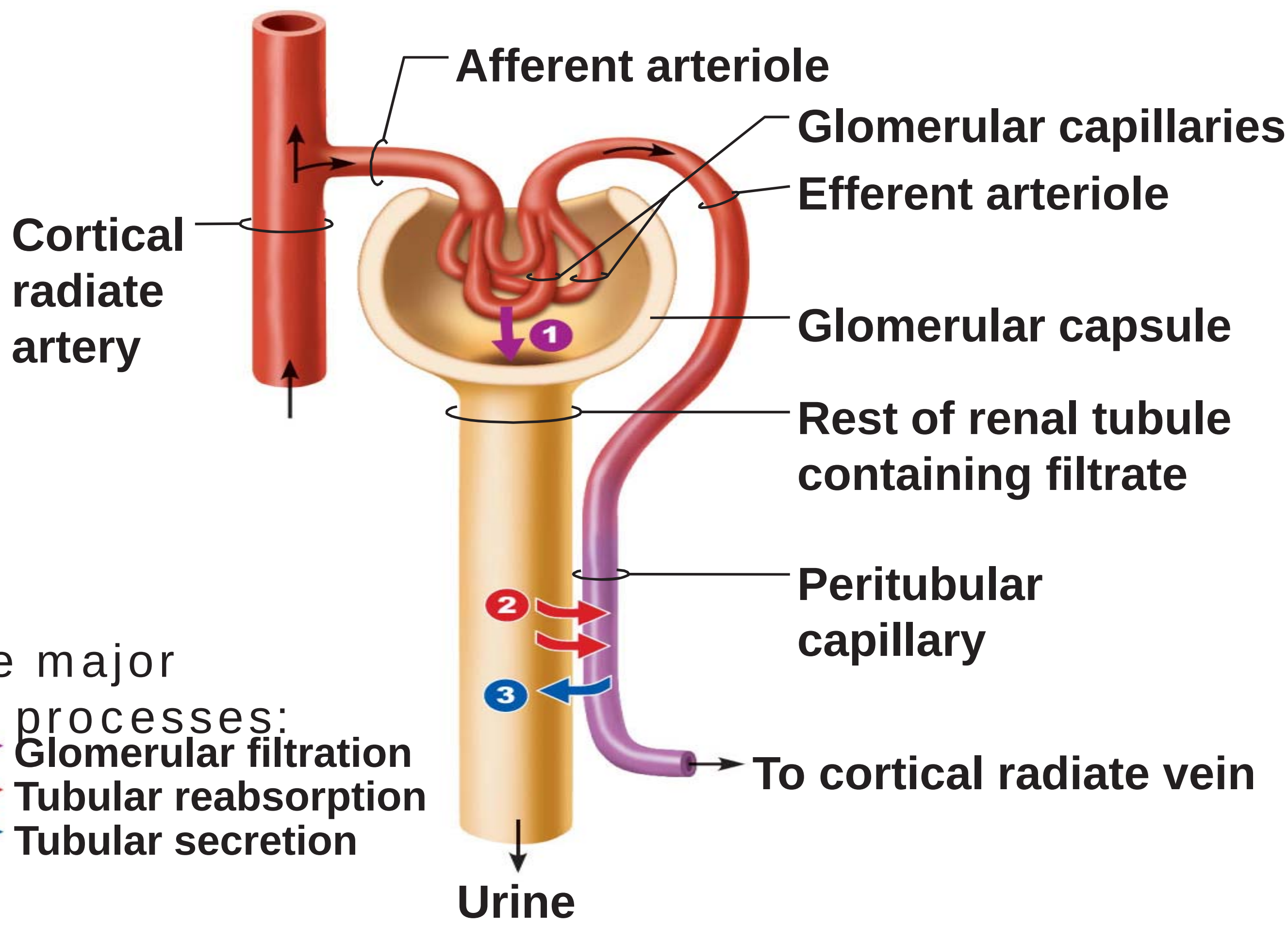

Glomerular capsule
Afferent arteriole
10 mm Hg
Net filtration pressure
Glomerular (blood) hydrostatic pressure
(HP_g = 55 mm Hg)
Blood colloid osmotic pressure
(Op_g = 30 mm Hg)
Capsular hydrostatic pressure
(HP_c = 15 mm Hg)

Figure 25.11



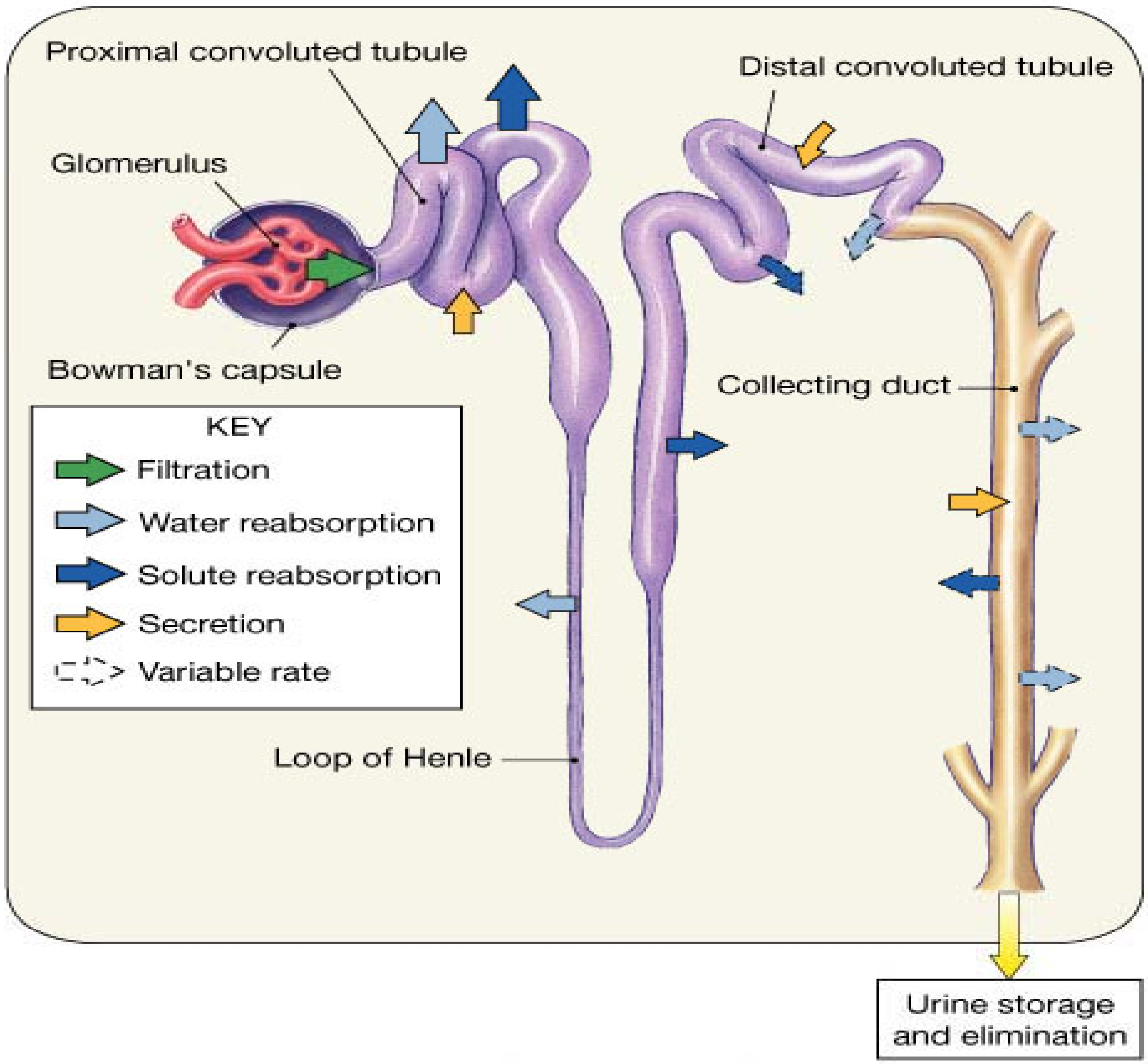
(c) Three parts of the filtration membrane



Three major renal processes:

1. Glomerular filtration
2. Tubular reabsorption
3. Tubular secretion

Figure 25.10



Proximal convoluted tubule
Distal convoluted tubule
Glomerulus
Bowman's capsule
Collecting duct
KEY
Filtration
Water reabsorption
Solute reabsorption
Secretion
Variable rate
Loop of Henle
Urine storage
and elimination

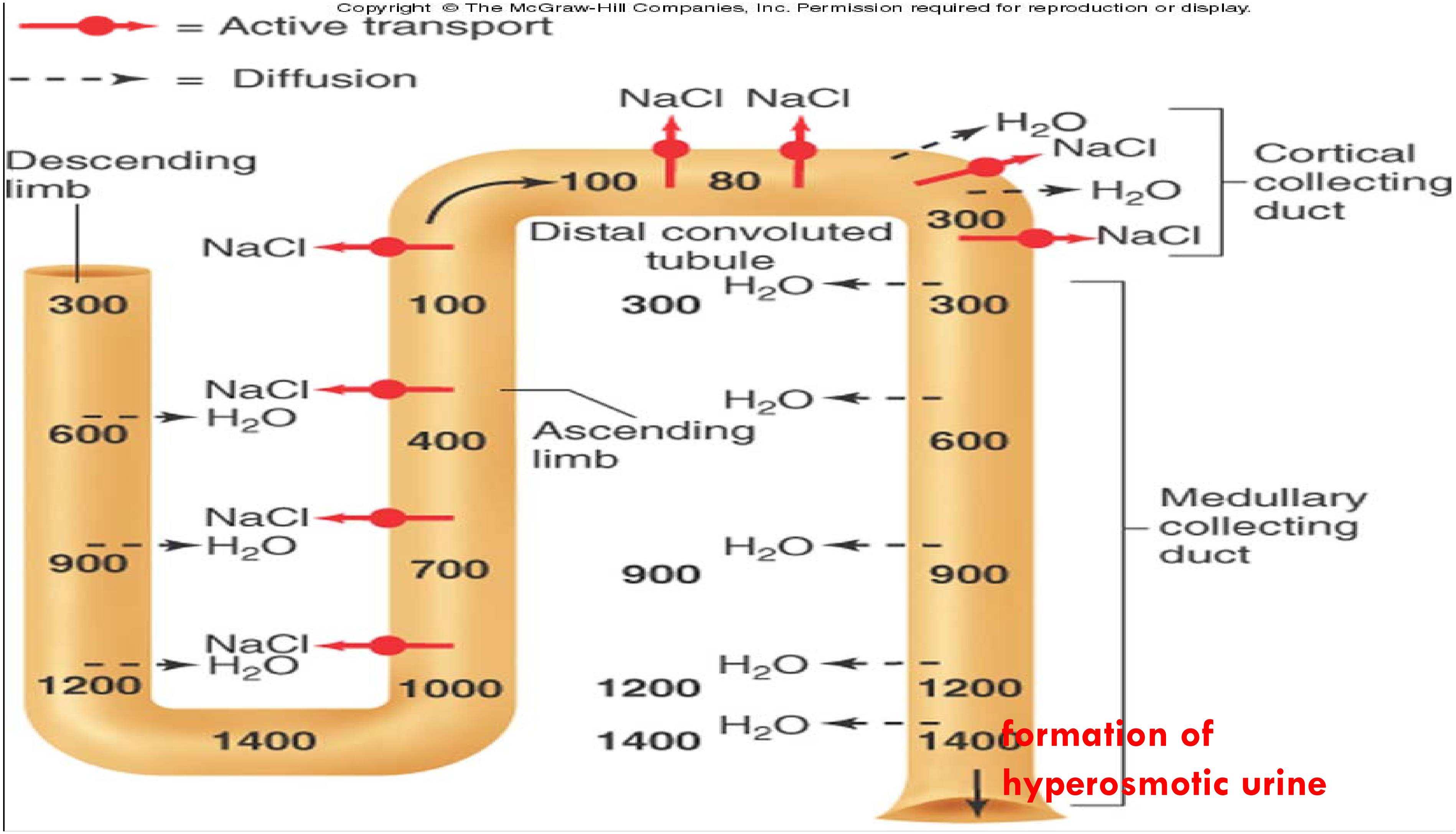
Body Fluid Compartments

Table 27.1 Approximate Volumes of Body Fluid Compartments*					
Age of Person	Total Body Water	Intracellular Fluid	Extracellular Fluid		
			Plasma	Interstitial	Total
Infants	75	45	4	26	30
Adult males	60	40	5	15	20
Adult females	50	35	5	10	15

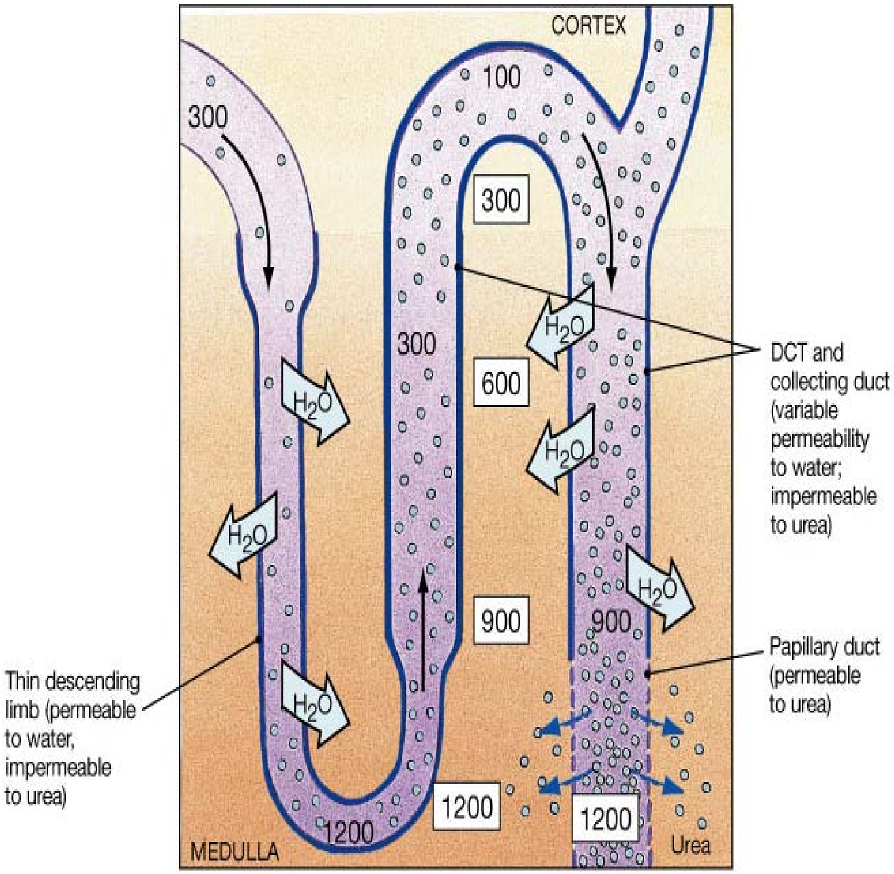
*Expressed as percentage of body weight.

Table 27.2 Approximate Concentration of Major Solutes in Body Fluid Compartments*			
Solute	Plasma	Interstitial Fluid	Intracellular Fluid†
Cations			
Sodium (Na^+)	153.2	145.1	12.0
Potassium (K^+)	4.3	4.1	150.0
Calcium (Ca^{2+})	3.8	3.4	4.0
Magnesium (Mg^{2+})	1.4	1.3	34.0
TOTAL	162.7	153.9	200.0
Anions			
Chloride (Cl^-)	111.5	118.0	4.0
Bicarbonate (HCO_3^-)	25.7	27.0	12.0
Phosphate (HPO_4^{2-} plus HPO_4^-)	2.2	2.3	40.0
Protein	17.0	0.0	54.0
Other	6.3	6.6	90.0
TOTAL	162.7	153.9	200.0

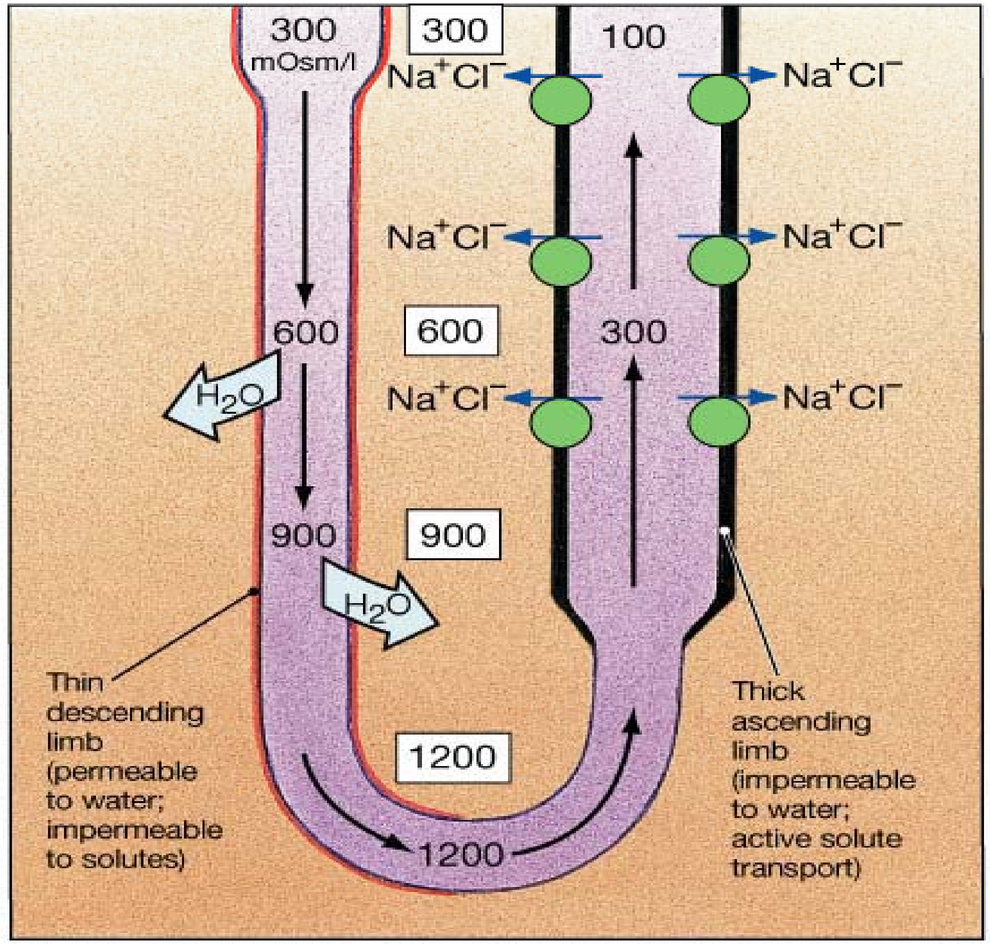
*Expressed as milliequivalents per liter (mEq/L).
†Data are from skeletal muscle.



formation of hyperosmotic urine

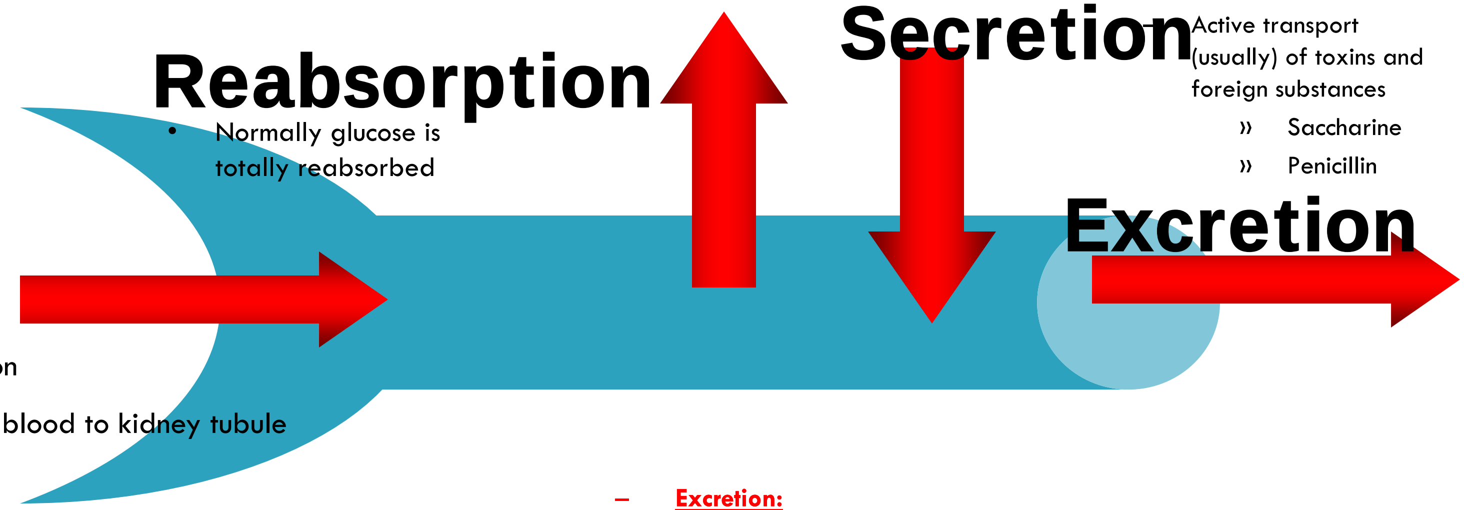


(c) The permeability characteristics of both the loop and the collecting duct tend to concentrate urea in the tubular fluid and in the medulla. The loop of Henle, DCT, and collecting duct are impermeable to urea. As water reabsorption occurs, the urea concentration rises. The papillary ducts' permeability to urea accounts for roughly one-third of the solutes in the deepest portions of the medulla.



(b) Active transport of NaCl along the ascending thick limb results in the movement of water from the descending limb.

Functions of the Nephron



Filtration

- First step in urine formation
- Bulk transport of fluid from blood to kidney tubule
- Result of hydraulic pressure
- GFR = 180 L/day

Reabsorption

- Normally glucose is totally reabsorbed

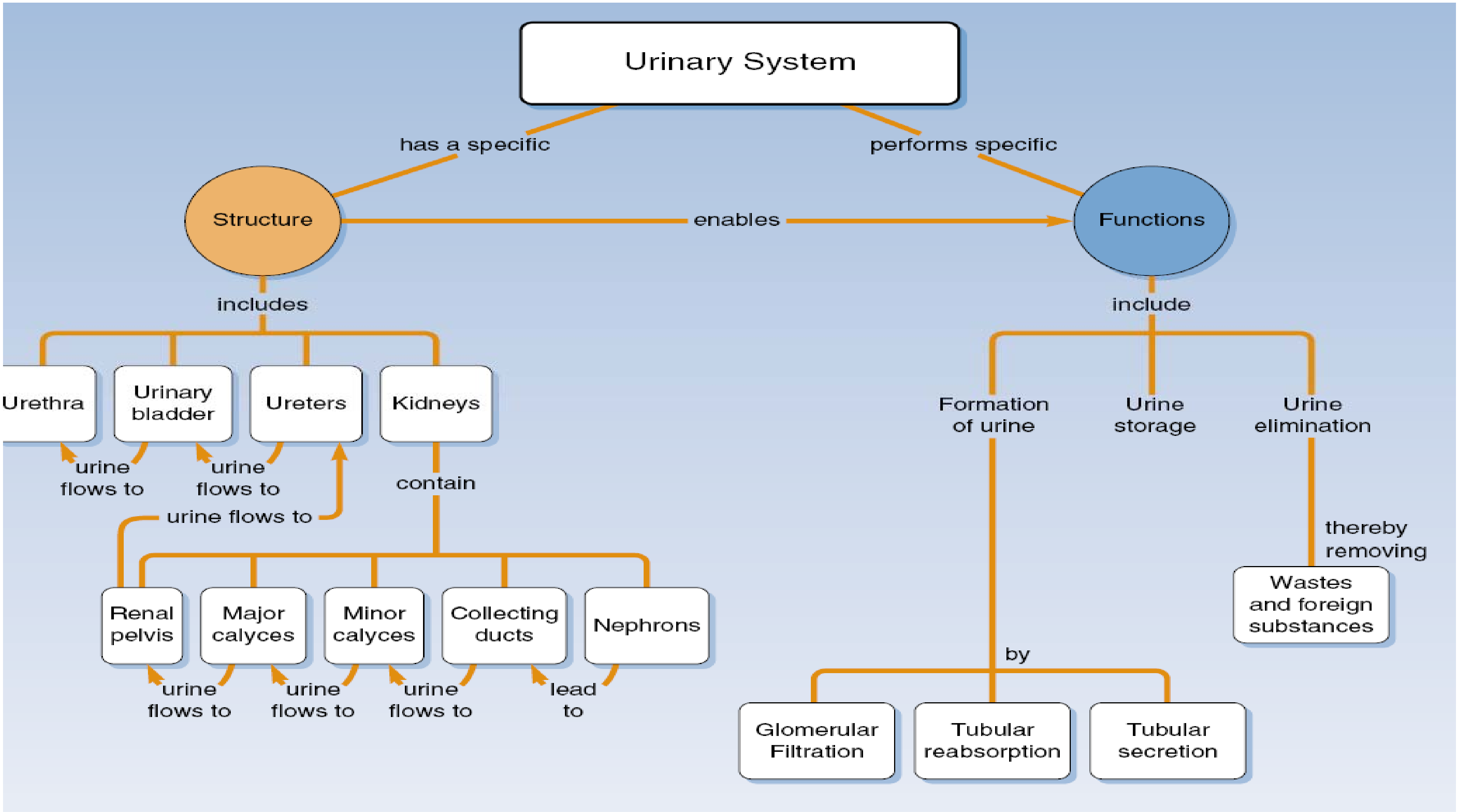
Secretion

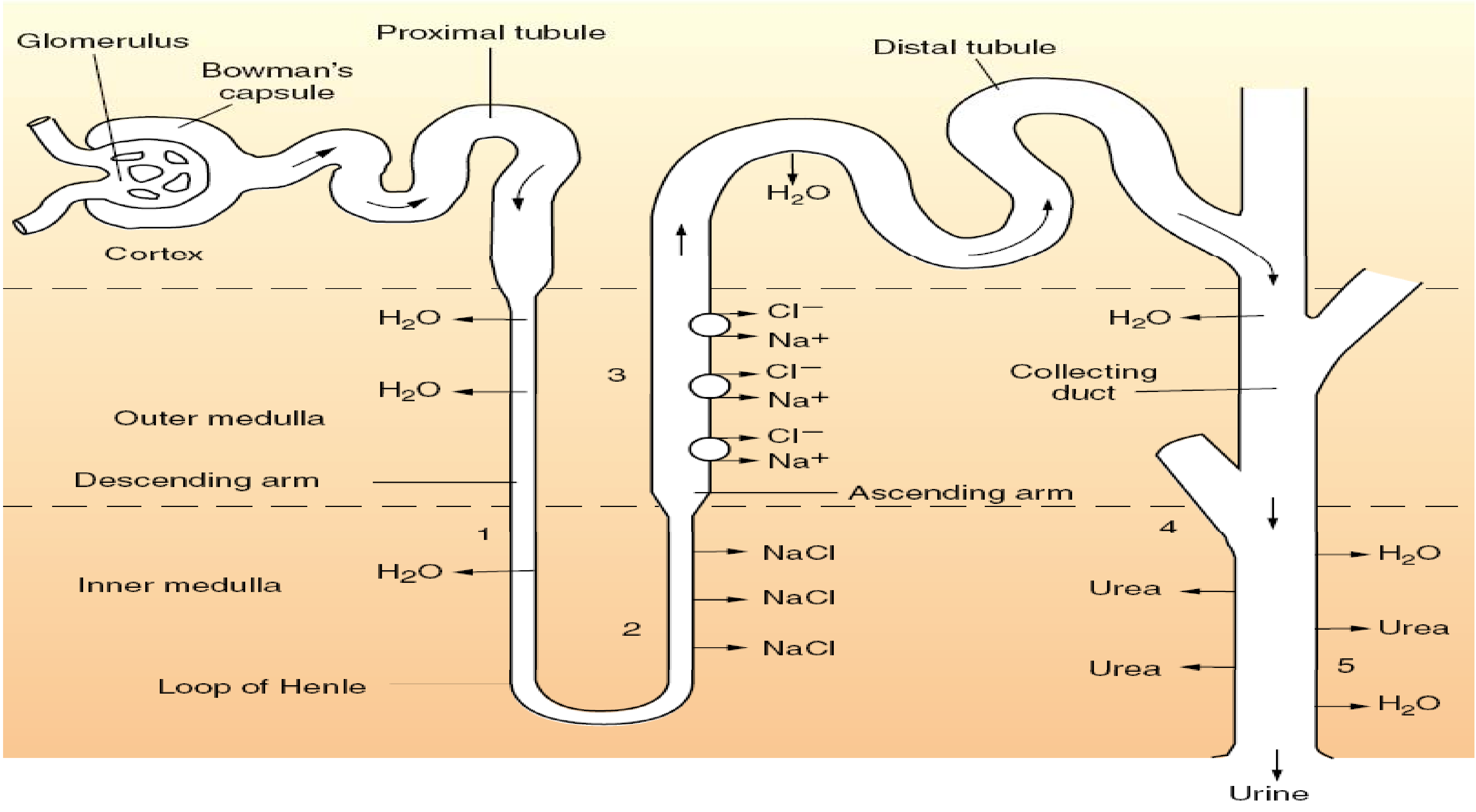
- Material added to lumen of kidney from blood
- Active transport (usually) of toxins and foreign substances
  - Saccharine
  - Penicillin

Excretion

- **Excretion:**
  - **Loss of fluid from body in form of urine**

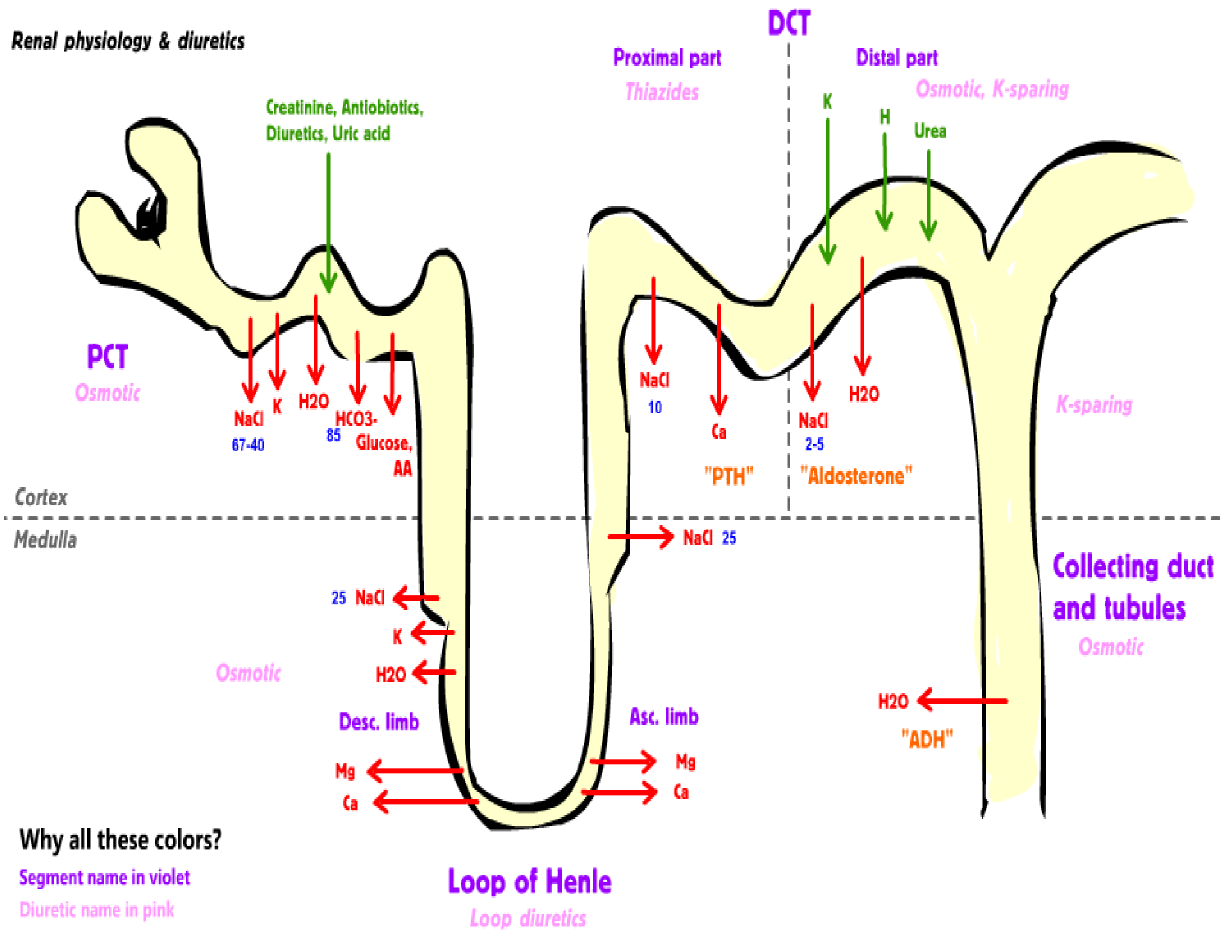
Amount of Solute Excreted = Amount Filtered + Amount Secreted – Amount Reabsorbed

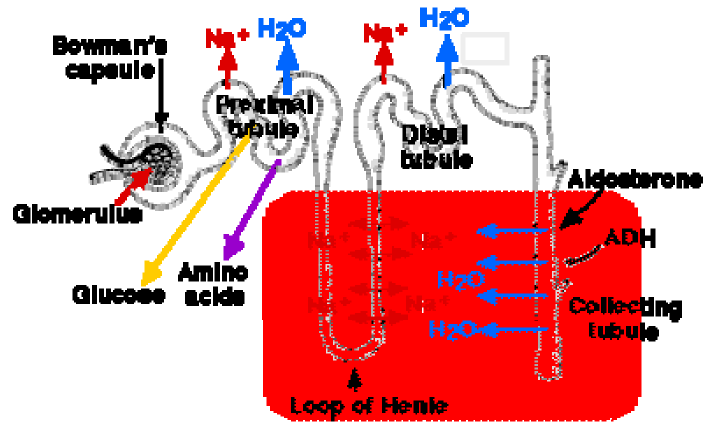

Urinary System
has a specific
performs specific
Structure
enables
Functions
includes
include
Urethra
Urinary bladder
Ureters
Kidneys
urine flows to
urine flows to
urine flows to
contain
Renal pelvis
Major calyces
Minor calyces
Collecting ducts
Nephrons
urine flows to
urine flows to
urine flows to
lead to
Formation of urine
Urine storage
Urine elimination
thereby removing
Wastes and foreign substances
by
Glomerular Filtration
Tubular reabsorption
Tubular secretion



Glomerulus
Bowman's capsule
Proximal tubule
Distal tubule
Cortex
H_2O
Outer medulla
Descending arm
Ascending arm
Inner medulla
Loop of Henle
Cl^-
Na^+
NaCl
Urea
Collecting duct
1
2
3
4
5
Urine

Renal physiology & diuretics





Why all these colors?

Segment name in violet

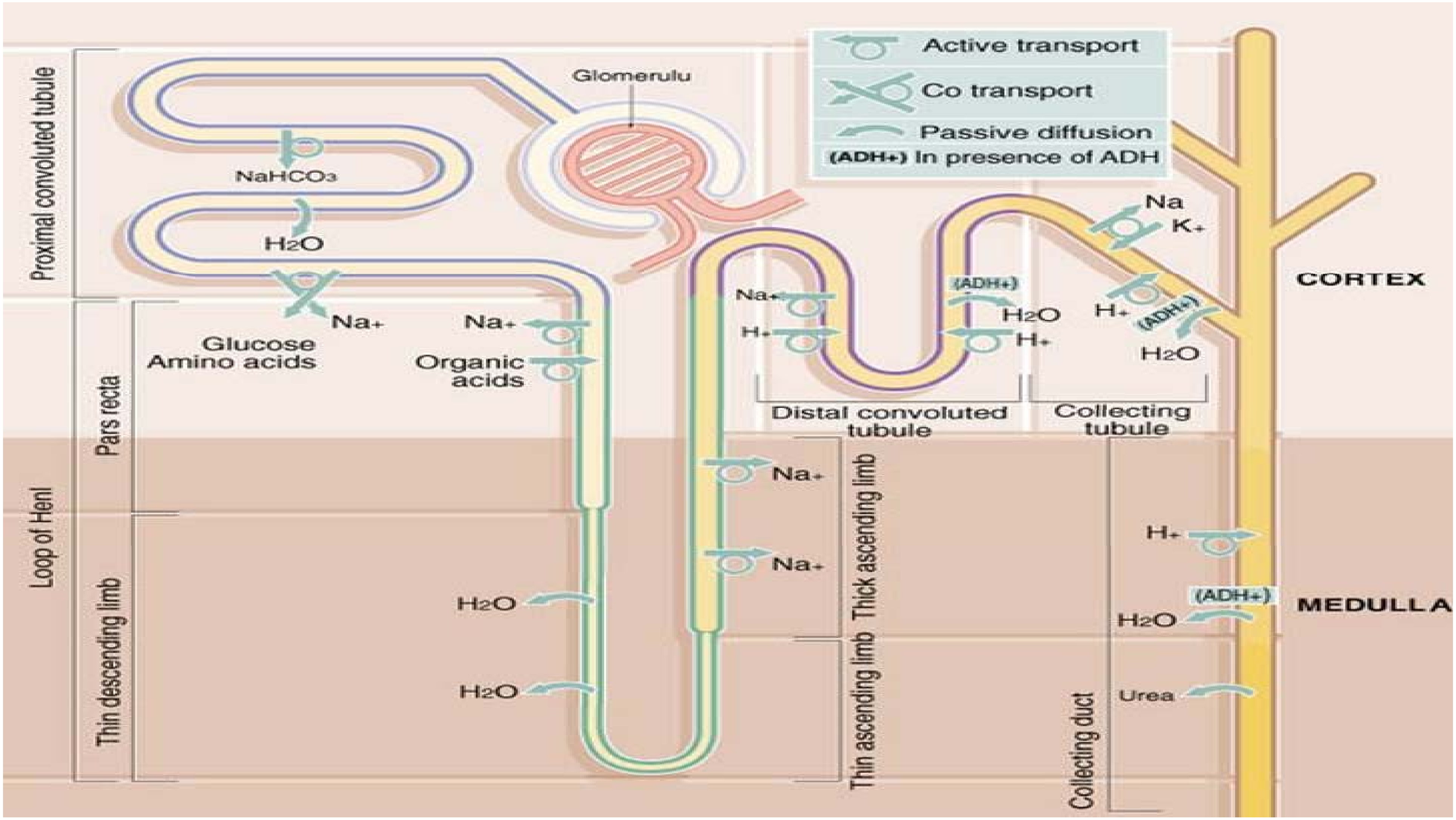
Diuretic name in pink

Reabsorption in red

Secretion in green

Percentage in blue

Hormone in orange



Active transport
Co transport
Passive diffusion
(ADH+) In presence of ADH
Proximal convoluted tubule
Glomerulu
NaHCO3
H2O
Na+
Glucose
Amino acids
Na+
Organic acids
Pars recta
Loop of Henl
Thin descending limb
H2O
H2O
Na+
Na+
Thick ascending limb
Thin ascending limb
Na+
H+
(ADH+)
H2O
H+
Distal convoluted tubule
Na
K+
H+
(ADH+)
H2O
Collecting tubule
CORTEX
H+
(ADH+)
H2O
Urea
Collecting duct
MEDULLA

Functions

- Regulating blood ionic composition
- Regulating blood pH
- Regulating blood volume
- Regulating blood pressure
- Produce calcitrol and erythropoietin
- Regulating blood glucose
- Excreting wastes

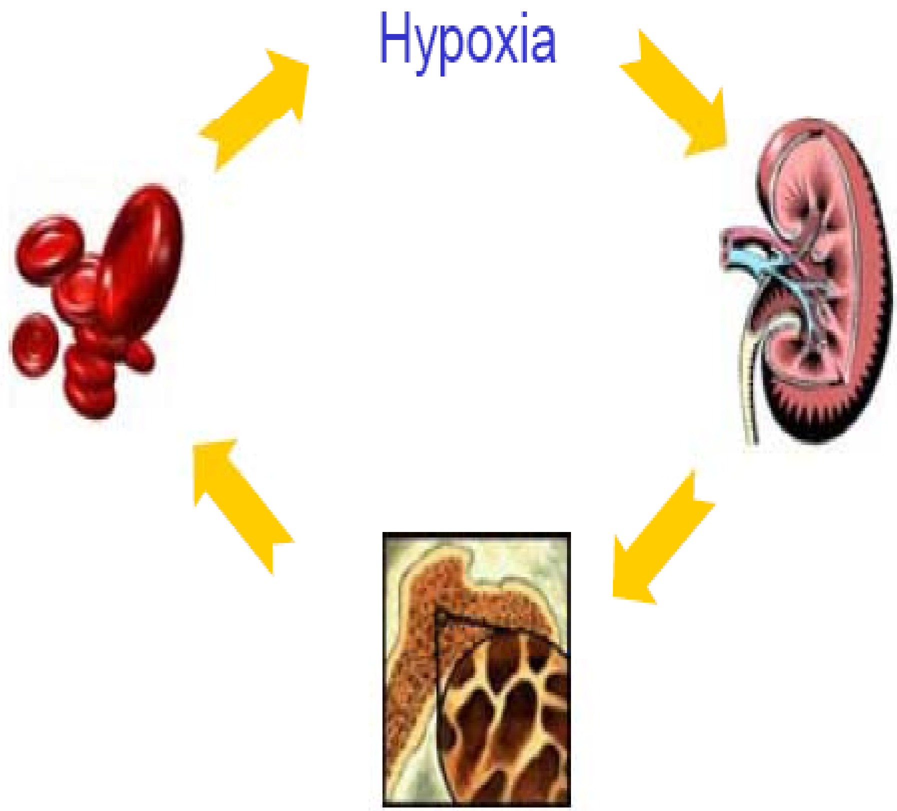
Major Functions of the Kidneys

1. **Regulation of:**
- body fluid osmolarity and volume
- electrolyte balance
- acid-base balance
- blood pressure

2. **Excretion of**
- metabolic products
- foreign substances (pesticides, chemicals etc.)
- excess substance (water, etc)

3. **Secretion of**
- erythropoitin
- 1,25-dihydroxy vitamin D_3 (vitamin D activation)
- renin
- prostaglandin

Erythropoietin

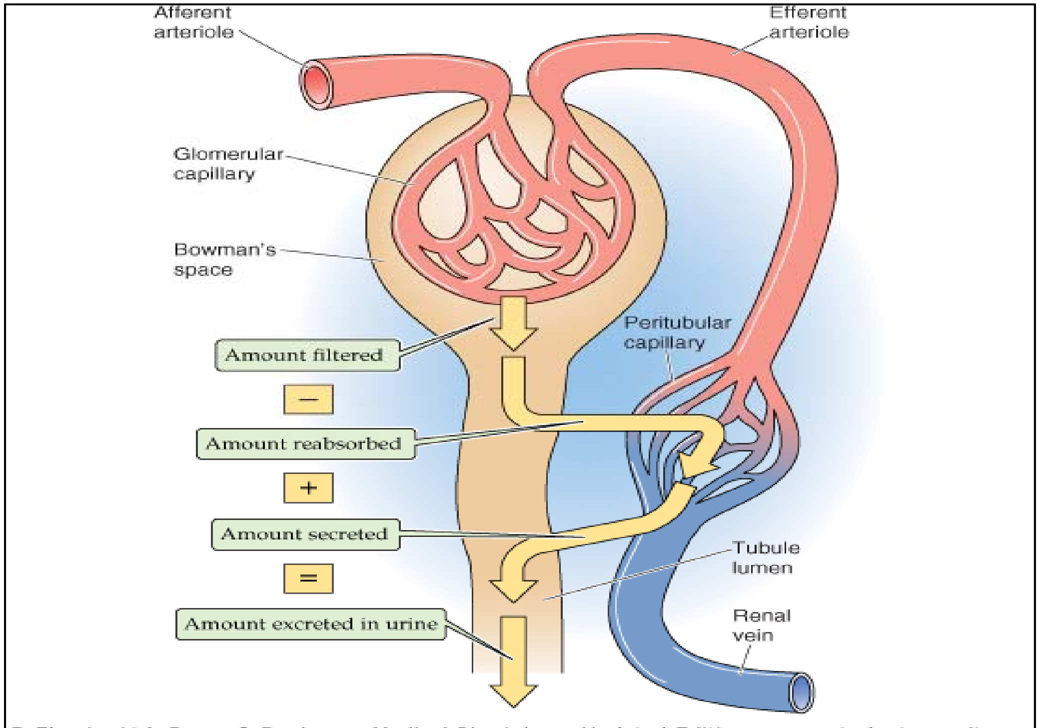


The three basic renal processes

- Glomerular filtration
- Tubular reabsorption
- Tubular secretion

- GFR is very high: ~180l/day. Lots of opportunity to precisely regulate ECF composition and get rid of unwanted substances.

- N.B. it is the ECF that is being regulated, NOT the urine.



Mechanisms of Urine Formation

- The kidneys filter the body's entire plasma volume 60 times each day
- The filtrate:
  - Contains all plasma components except protein
  - Loses water, nutrients, and essential ions to become urine
- The urine contains metabolic wastes and unneeded substances

Assessing Renal Function

- Creatinine clearance as an estimate of GFR
- BUN
- Creatinine / BUN ratio (ex. >20:1)
- Creatinine clearance <50 and <25

Mechanisms of Urine Formation

- The kidneys filter the body's entire plasma volume 60 times each day
- The filtrate:
  - Contains all plasma components except protein
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- The urine contains metabolic wastes and unneeded substances

Assessing Renal Function

- Mathematically

$$CrCl = \frac{(140 - age) \times weight \times constant}{72 \times serum\ creatinine}$$

Net Filtration Pressure (NFP)

- The pressure responsible for filtrate formation
- NFP equals the glomerular hydrostatic pressure (HP_g) minus the oncotic pressure of glomerular blood (OP_g) combined with the capsular hydrostatic pressure (HP_c)

$$NFP = HP_g - (OP_g + HP_c)$$

Glomerular Filtration Rate (GFR)

- The total amount of filtrate formed per minute by the kidneys
- Factors governing filtration rate at the capillary bed are:
  - Total surface area available for filtration
  - Filtration membrane permeability
  - Net filtration pressure

Glomerular Filtration Rate (GFR)

- GFR is directly proportional to the NFP
- Changes in GFR normally result from changes in glomerular blood pressure

Extracellular Fluid Osmolality

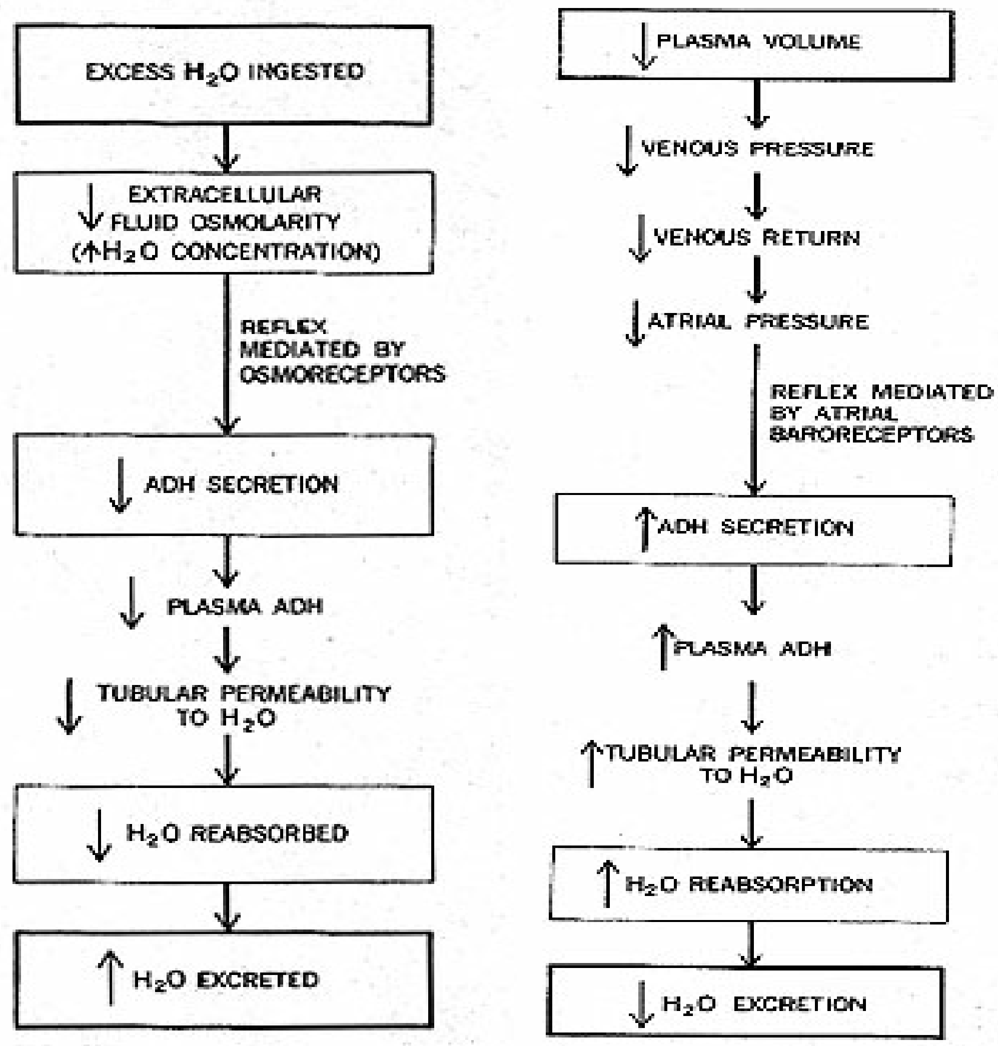
- Osmolality
  - Adding or removing water from a solution changes this
- Increased osmolality
  - Triggers thirst and ADH secretion
- Decreased osmolality
  - Inhibits thirst and ADH secretion

Antidiuretic Hormone: ADH

ADH is also known as arginine vasopressin (AVP= ADH) because of its vasopressive activity, but its major effect is on the kidney in preventing water loss.

•It is primarily regulated by osmotic and volume stimuli.

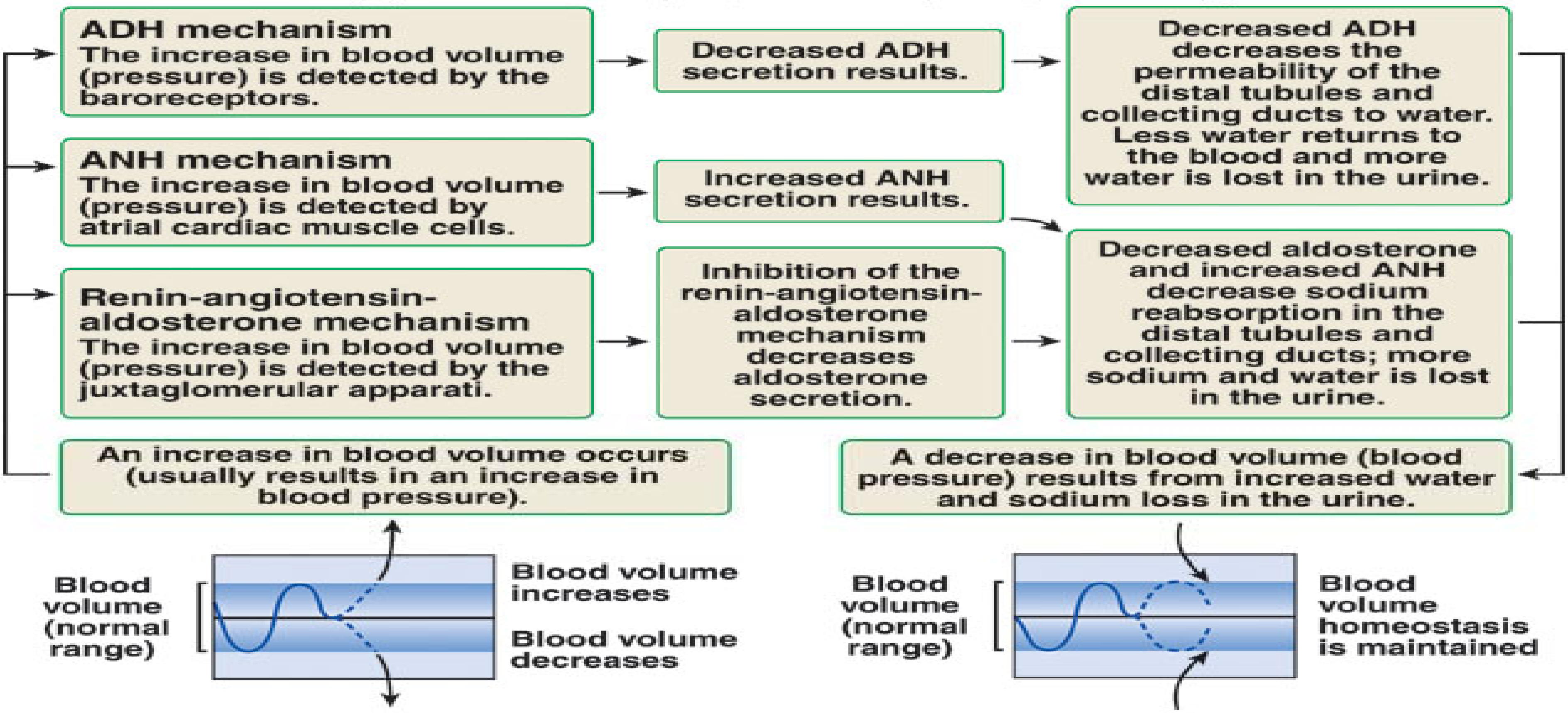
•Water deprivation increases osmolality of plasma which activates hypothalmic osmoreceptors to stimulate ADH release.



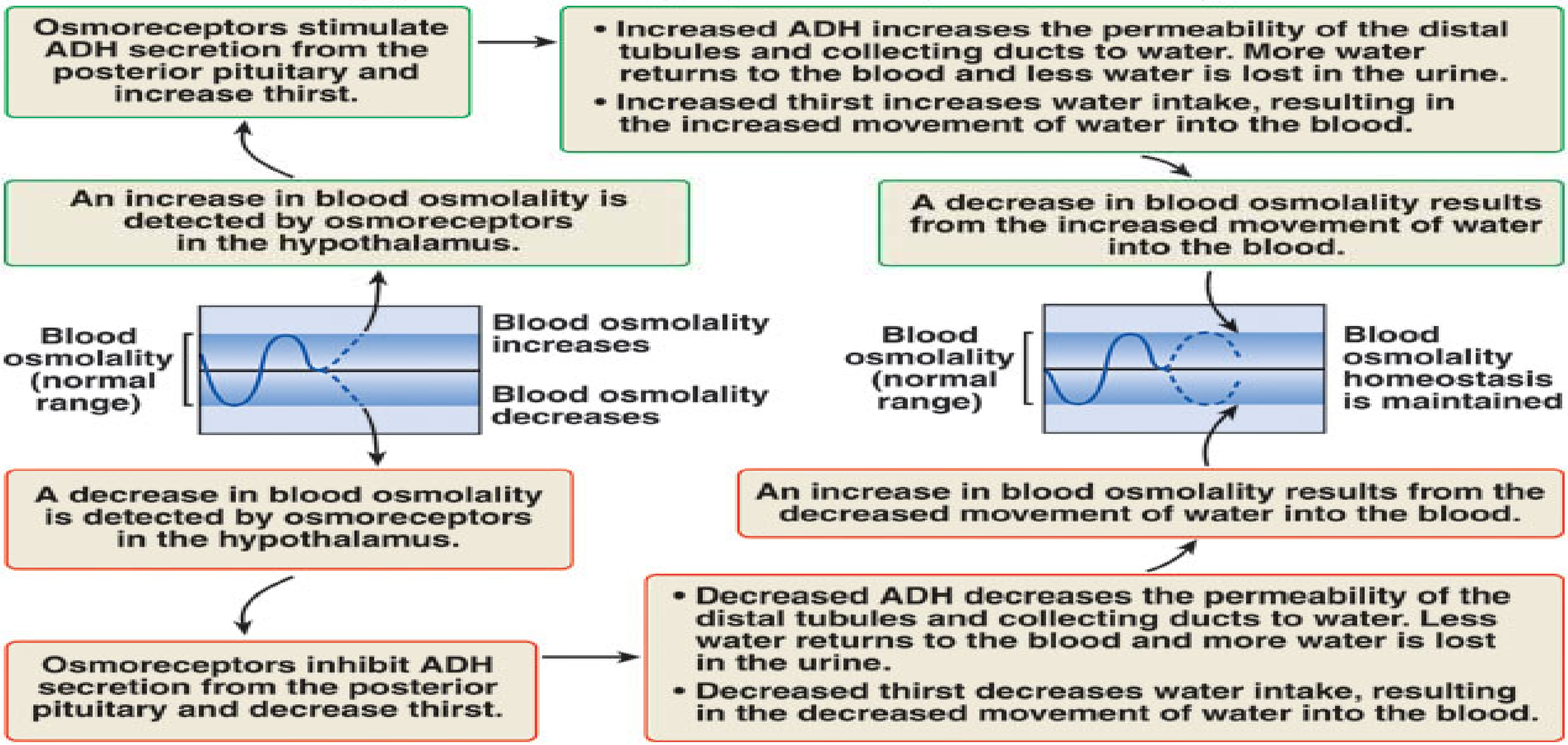
Regulation of ECF Volume

- Mechanisms
  - Neural
  - Renin-angiotensin-aldosterone
  - Atrial natriuretic hormone (ANH)
  - Antidiuretic hormone (ADH)
- Increased ECF results in
  - Decreased aldosterone secretion
  - Increased ANH secretion
  - Decreased ADH secretion
  - Decreased sympathetic stimulation
- Decreased ECF results in
  - Increased aldosterone secretion
  - Decreased ANH secretion
  - Increased ADH secretion
  - Increased sympathetic stimulation

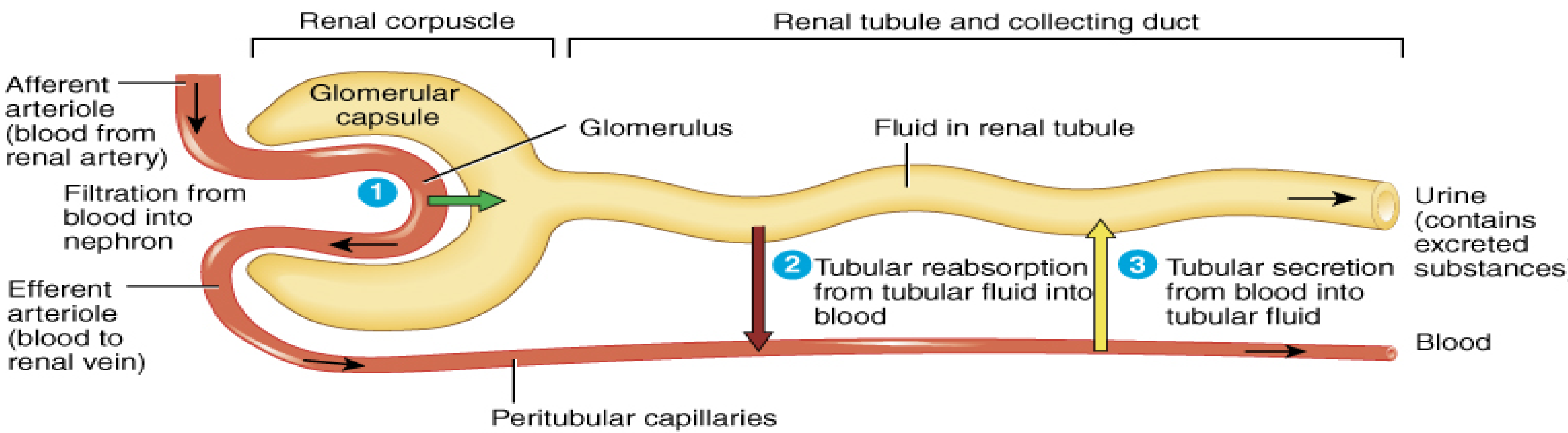
Hormonal Regulation of Blood Volume



Hormonal Regulation of Blood Osmolality



Overview: the 3 phases of urine formation

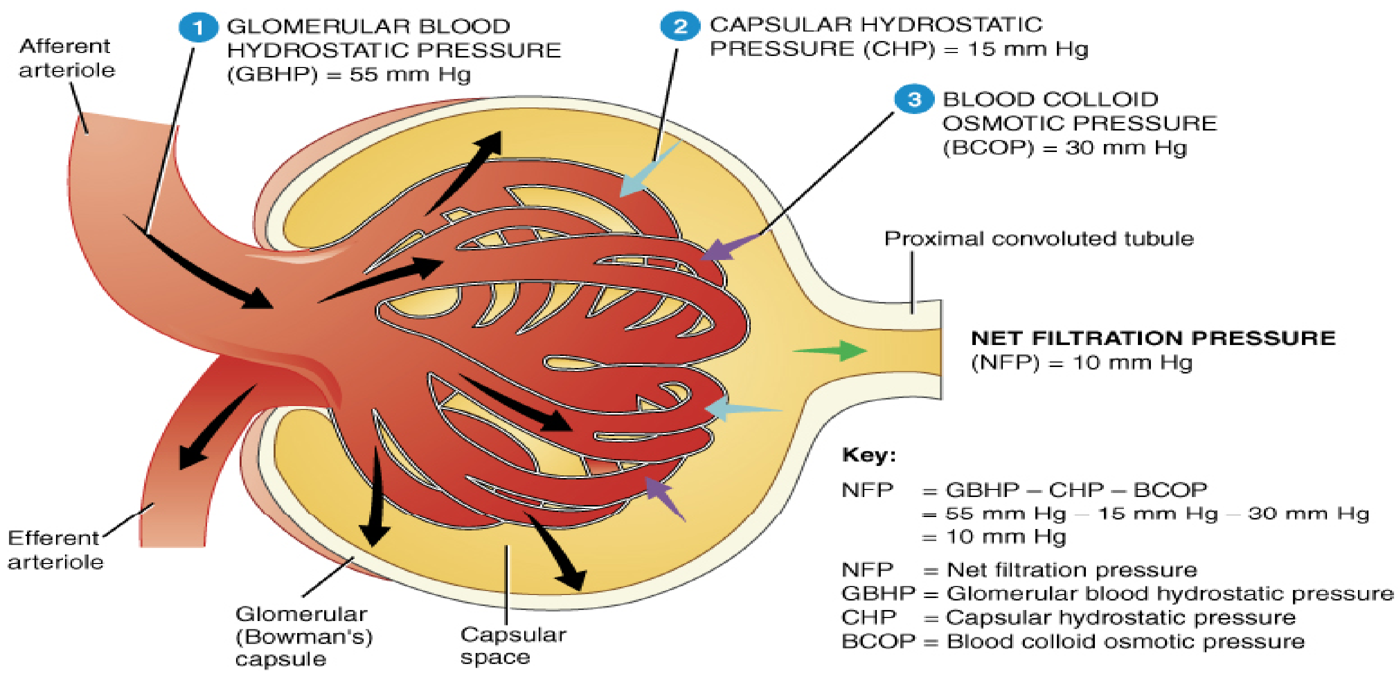


Explain why the functional unit of the kidney is best described as more than just the nephron.

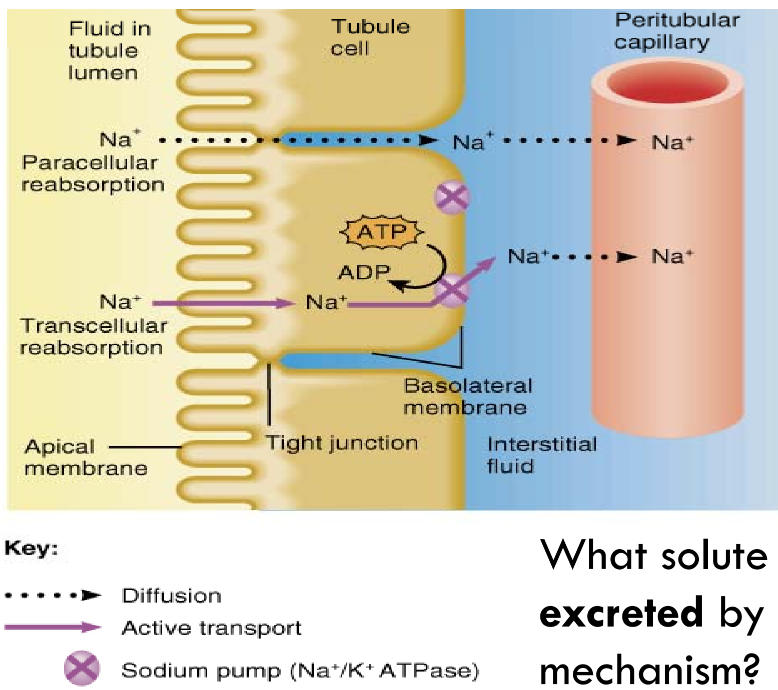
For each phase, describe the 1) location along the nephron, 2) the mechanism(s) of transport, and 3) the net direction of movement.

Filtration: the first phase in urine formation

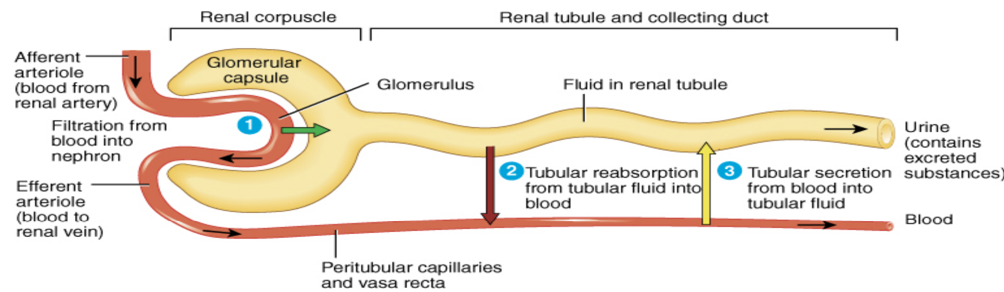
Briefly compare the composition of blood plasma and of urinary filtrate as it enters the proximal convoluted tubule.



Tubular Reabsorption: the second phase in urine formation



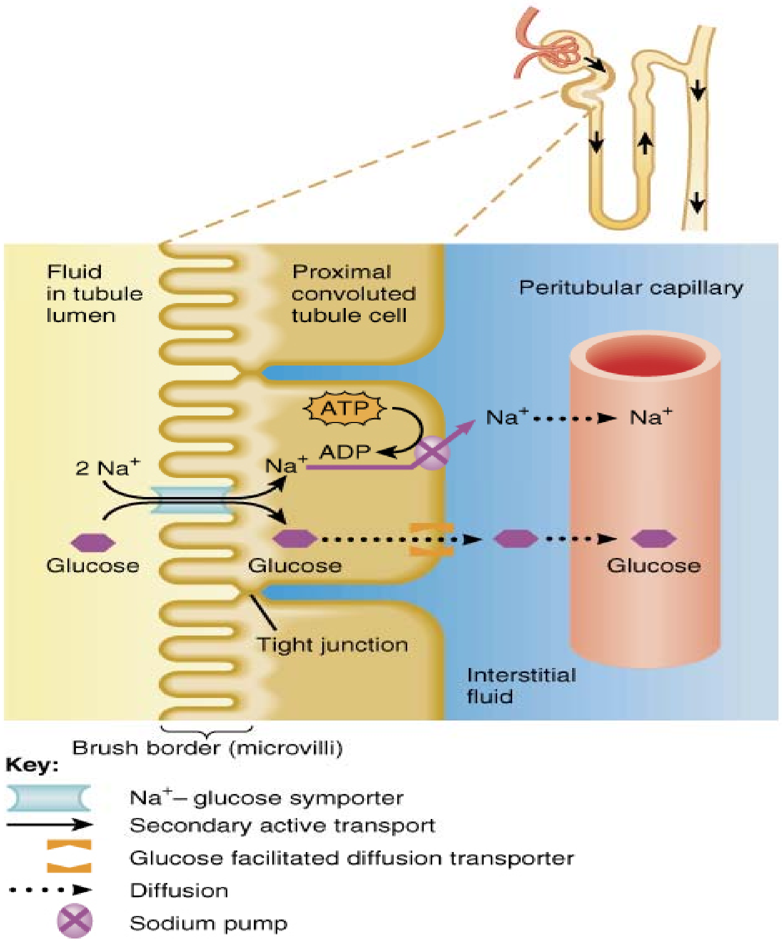
What solute is **excreted** by this mechanism?



Describe the features of cells in the proximal convoluted tubule that make them well suited for selective transport.

What is **obligatory water reabsorption**? Where and why does this occur?

Tubular Reabsorption of Glucose



In which direction does Na^+ leave the cell? Why?

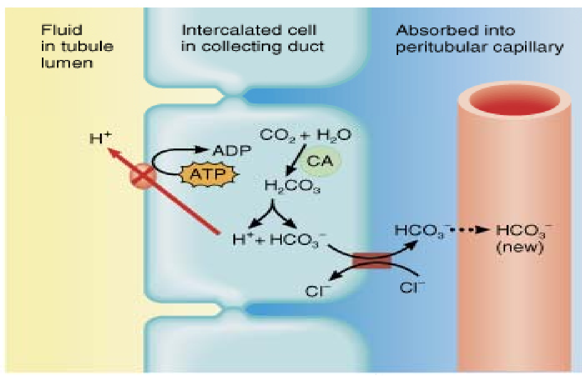
In which direction does Na^+ enter the cell? Why?

In which direction does glucose enter the cell? Why?

In which direction does glucose leave the cell? Why?

What other solutes are selectively reabsorbed by similar means?

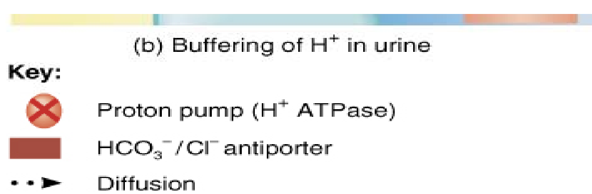
Tubular Secretion: the third (and last) phase in urine formation



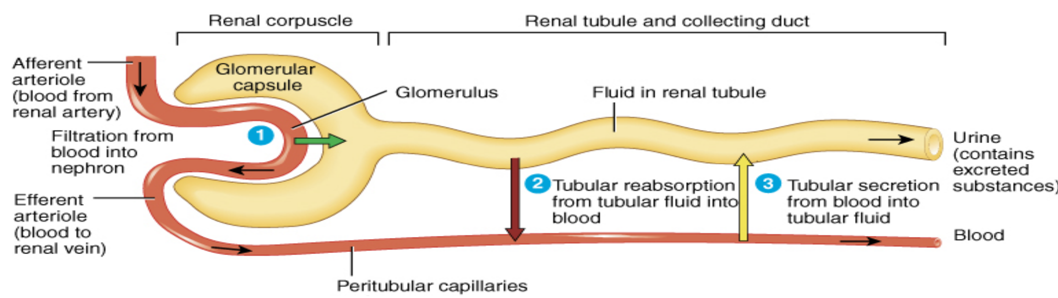
(a) Secretion of H^+

What is the normal pH range of urine?

What is the advantage of using this enzyme-catalyzed reaction to generate H^+?



(b) Buffering of H^+ in urine



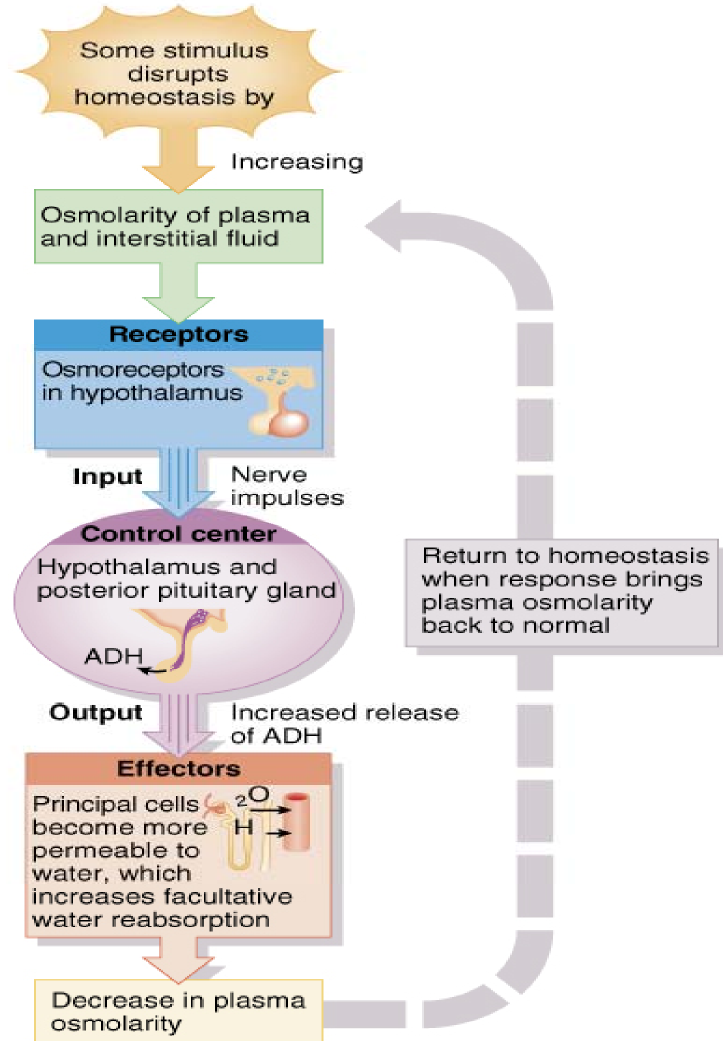
What is the net direction for the movement of materials by tubular secretion? Is this the same direction as in filtration at the renal corpuscle?

What other solutes are secreted this way? Why?

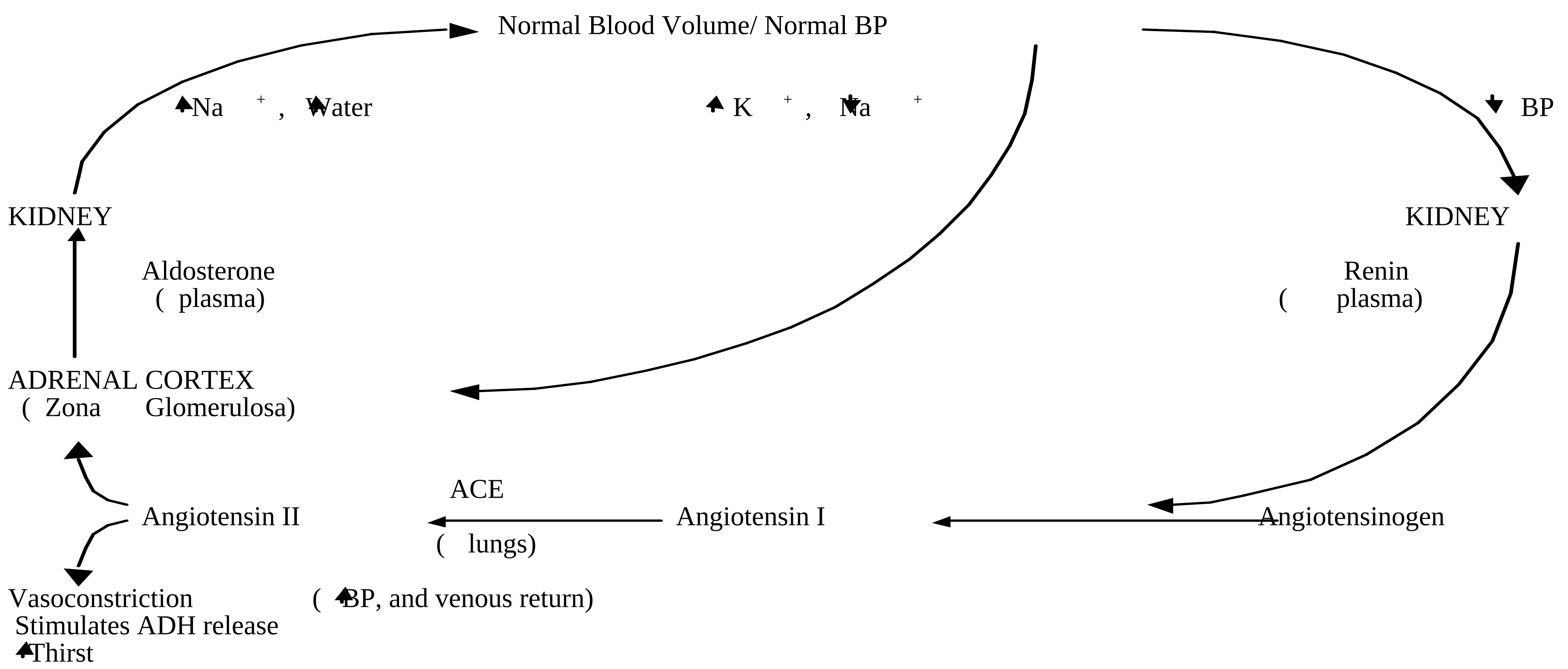
Homeostatic Mechanism involving **ADH** to Regulate Water Balance

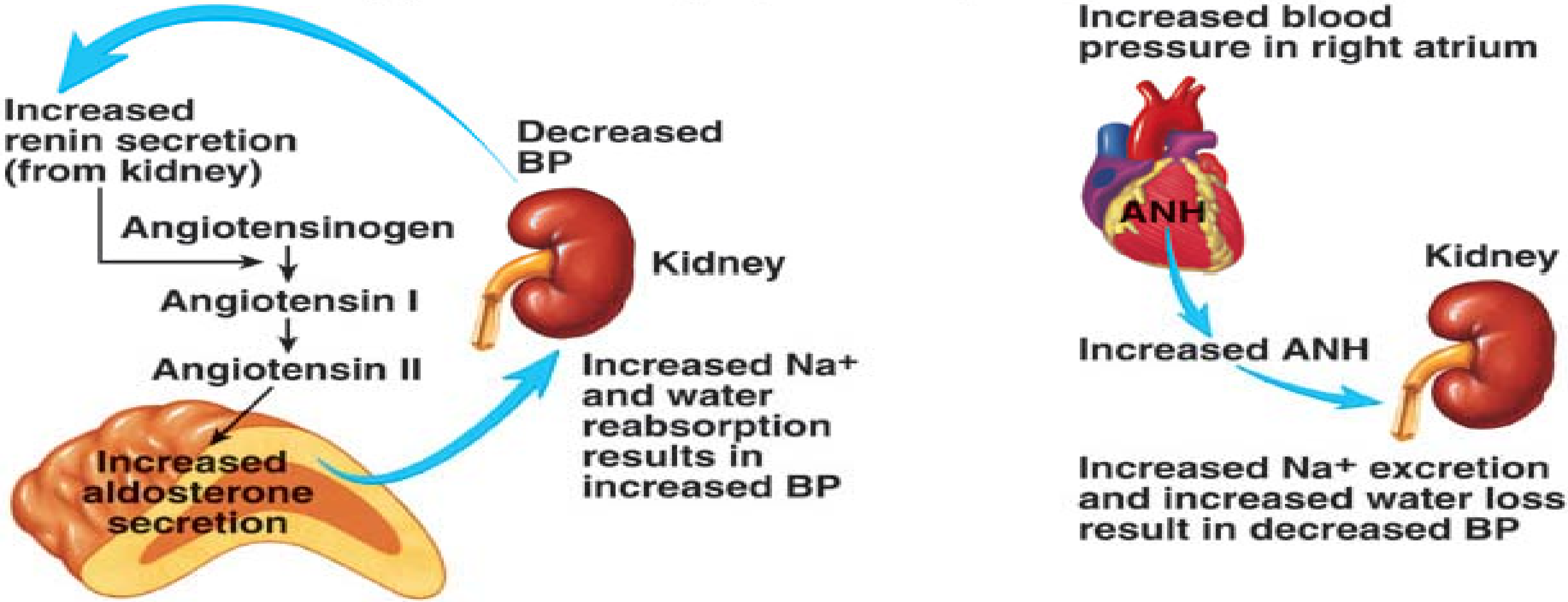
Is this obligatory or facultative water reabsorption?

What **two** types of changes result in increased osmolarity of body fluids, and so would stimulate ADH release?



Renin-Angiotensin-Aldosterone System in the Regulation of Water Balance

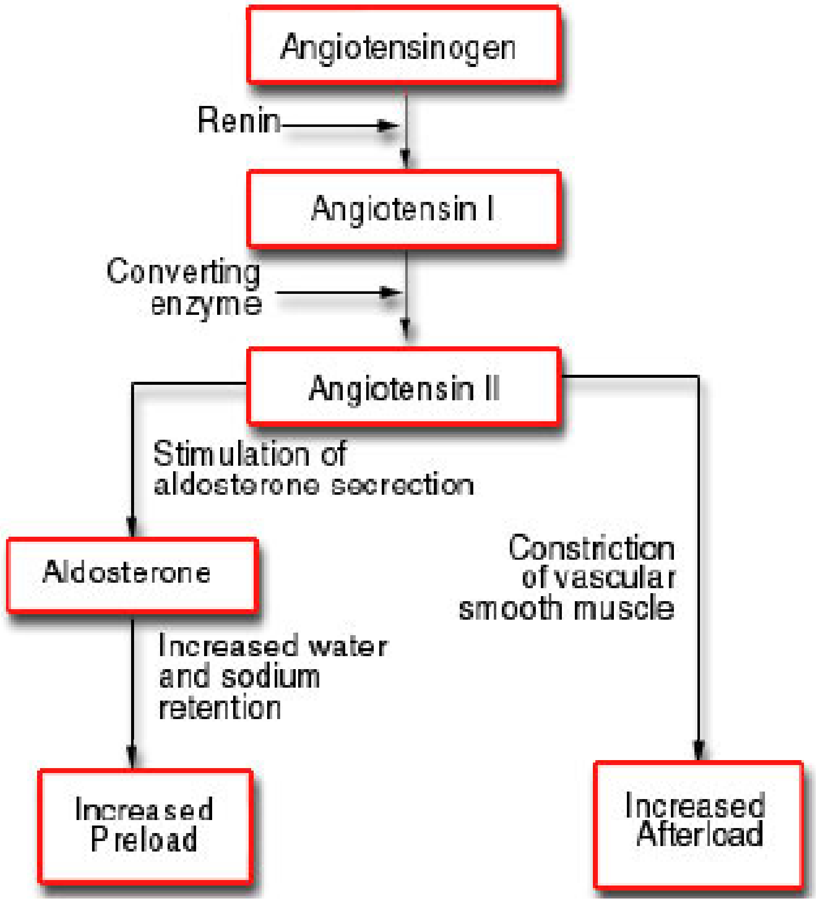




(a) Low blood pressure (BP) stimulates renin secretion from the kidney. Renin stimulates the production of angiotensin I, which is converted to angiotensin II, which in turn stimulates aldosterone secretion from the adrenal cortex. Aldosterone increases Na^+ and water reabsorption in the kidney.

(b) Increased blood pressure in the right atrium of the heart causes increased secretion of atrial natriuretic hormone (ANH), which increases Na^+ excretion and water loss in the form of urine.

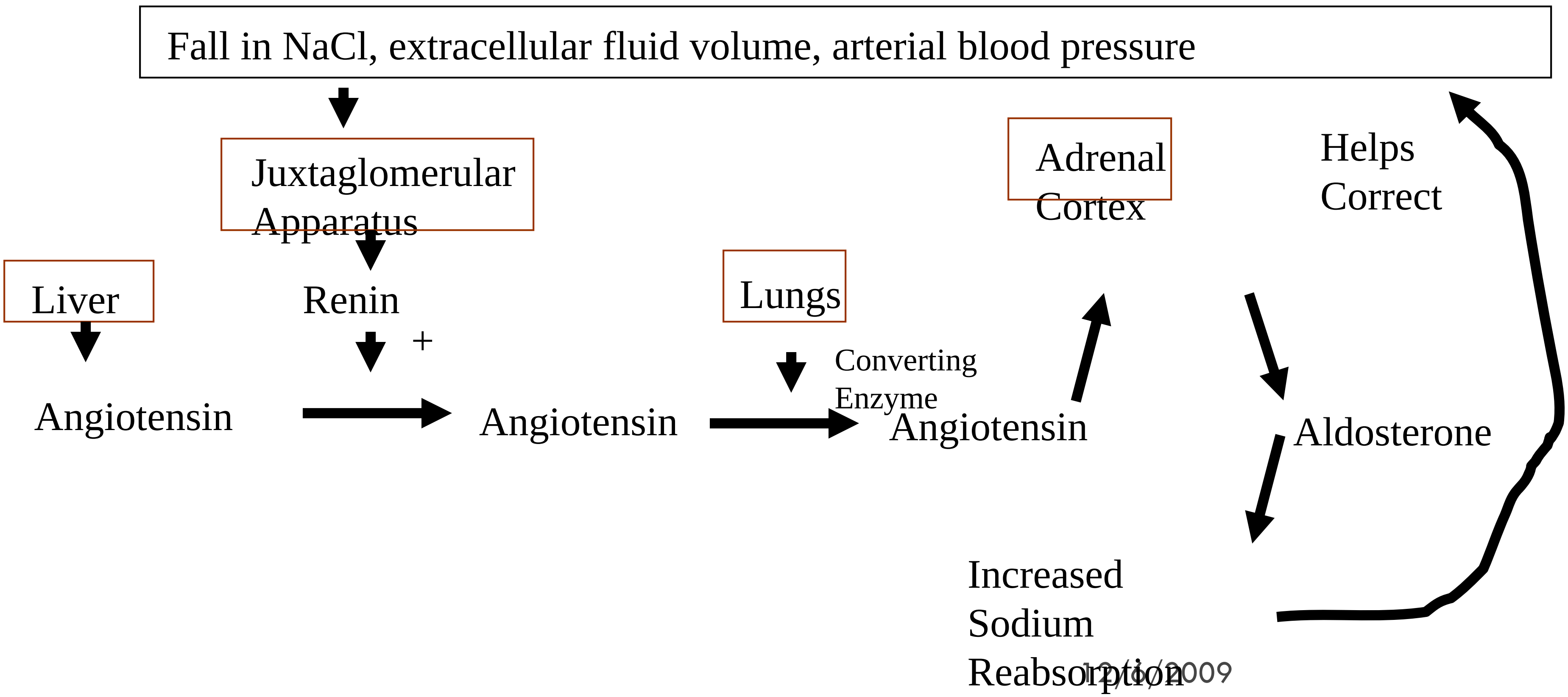
Renin – Angiotensin System



Rennin-Angiotensin-Aldosterone System

- Stimulates Sodium Reabsorption in distal and collecting tubules
- Naturetic peptide inhibits
- In absence of Aldosterone, 20mg of sodium/day may be excreted
- Aldosterone can cause 99.5% retention

Rennin-Angiotensin-Aldosterone System



Glomerular Filtration

- First step in urine formation
- 180 liters/day filtered
- Entire plasma volume filtered 65 times/day
- Proteins not filtered

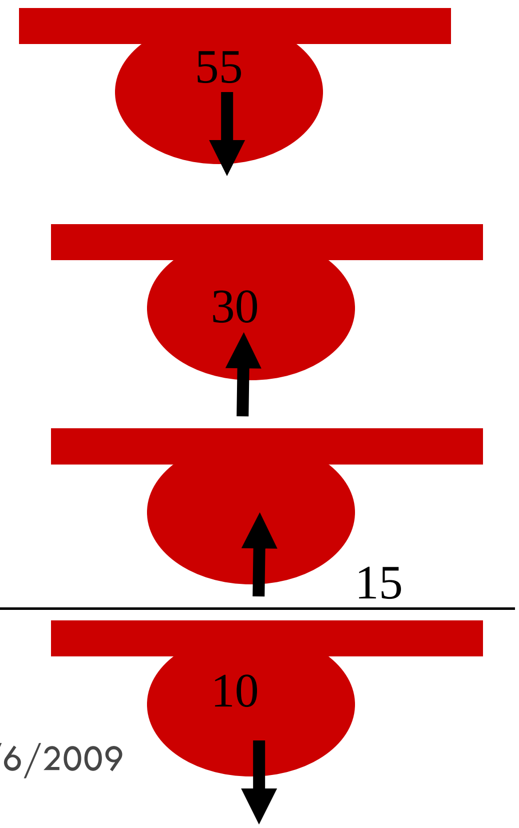
Forces Involved in Glomerular Filtration

Glomerular Capillary Blood Pressure +

Plasma Colloid Osmotic Pressure -

Bowman's Capsule Hydrostatic Pressure -

Net Filtration Pressure +



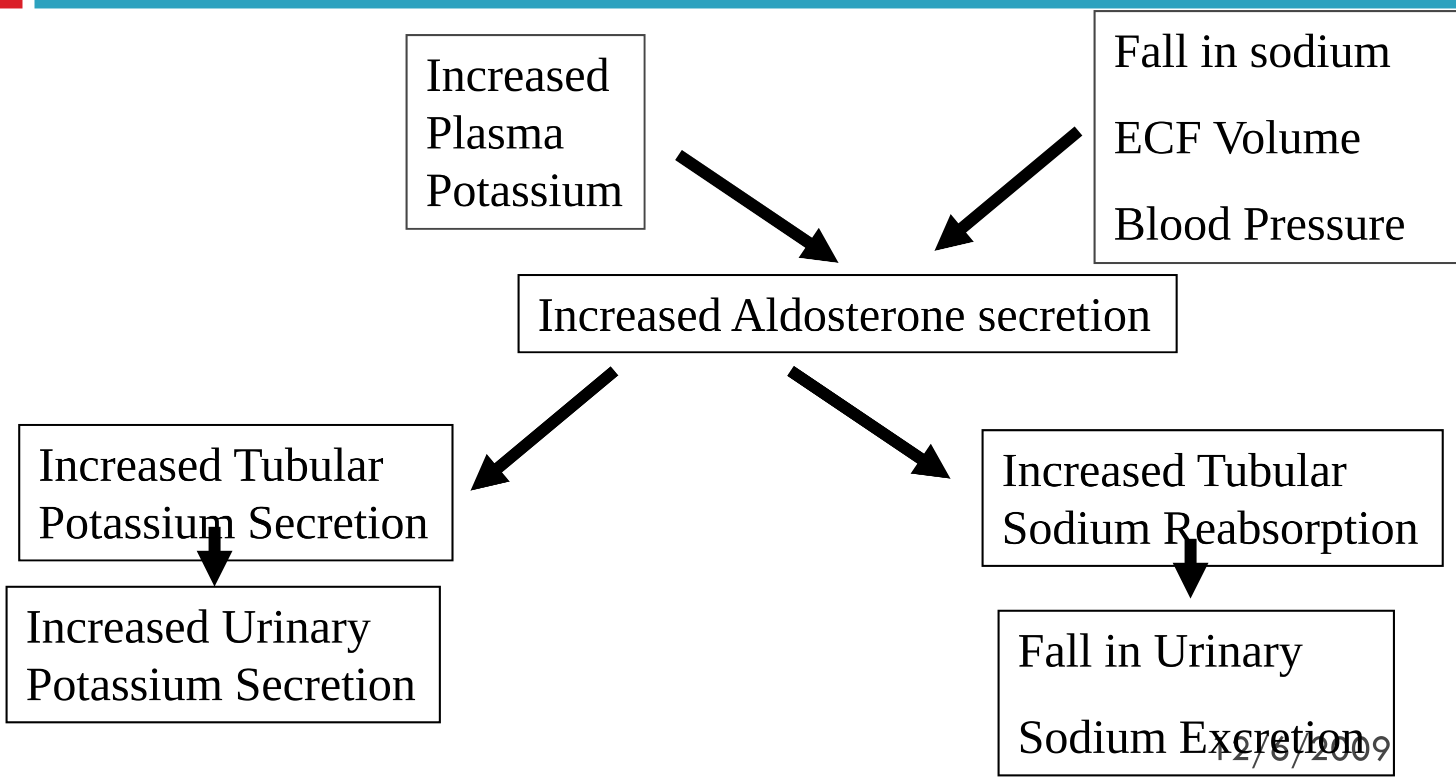
Tubular Reabsorption

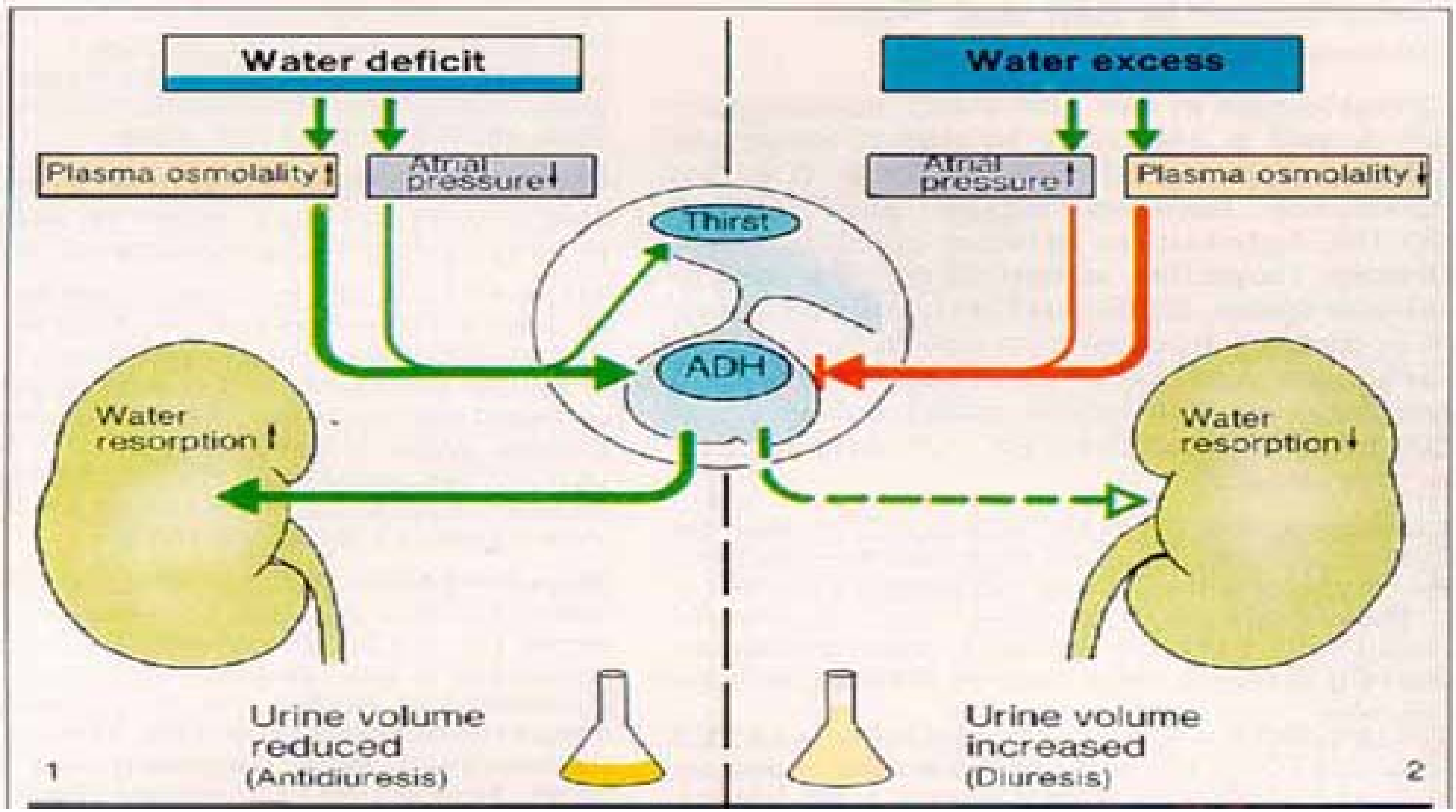
- Water: 99% reabsorbed
- Sodium: 99.5% reabsorbed
- Urea: 50% reabsobed
- Phenol: 0% reabsorbed

Tubular Reabsorption

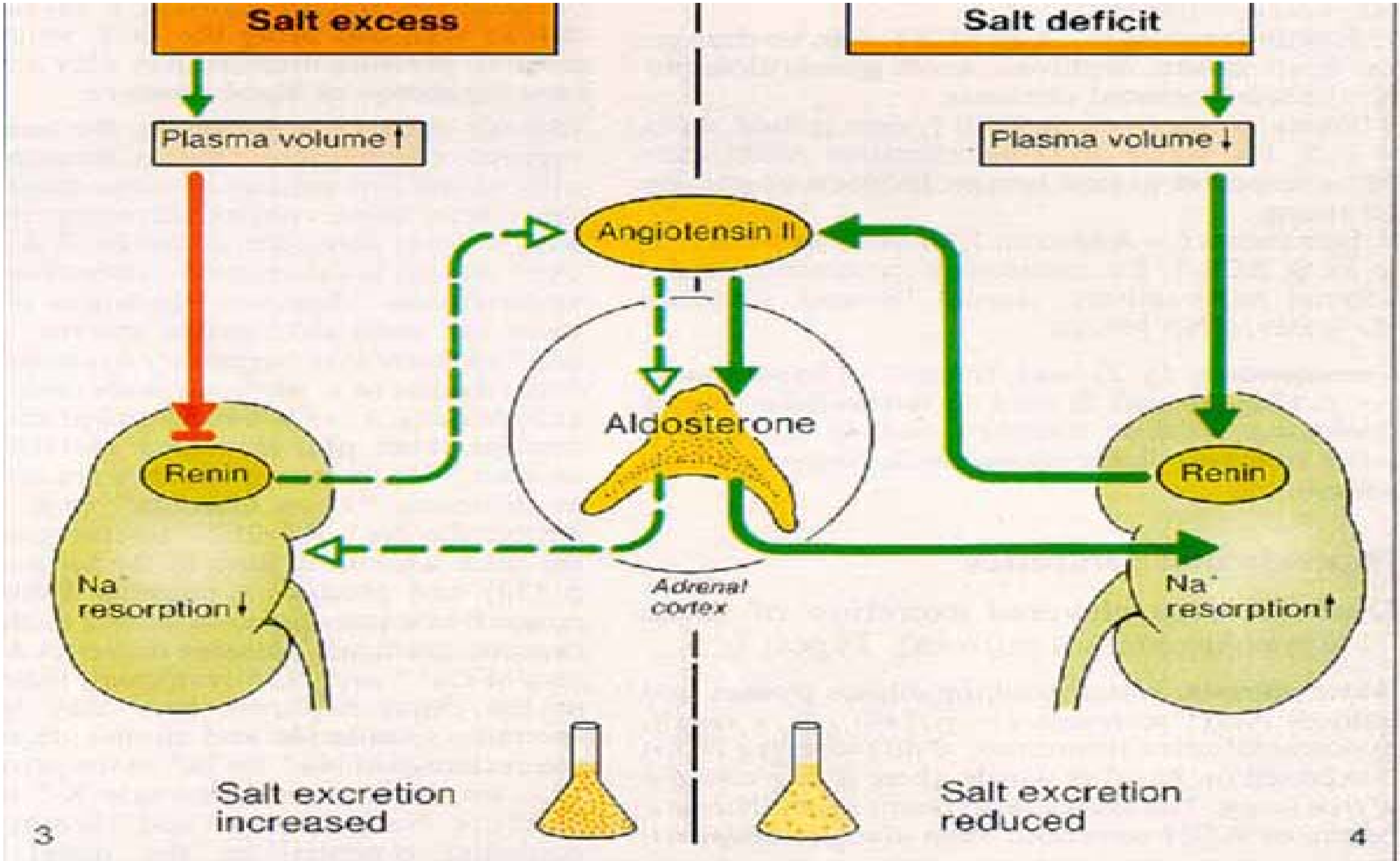
- By passive diffusion
- By primary active transport: Sodium
- By secondary active transport: Sugars and Amino Acids

DUAL CONTROL OF ALDOSTERONE SECRETION

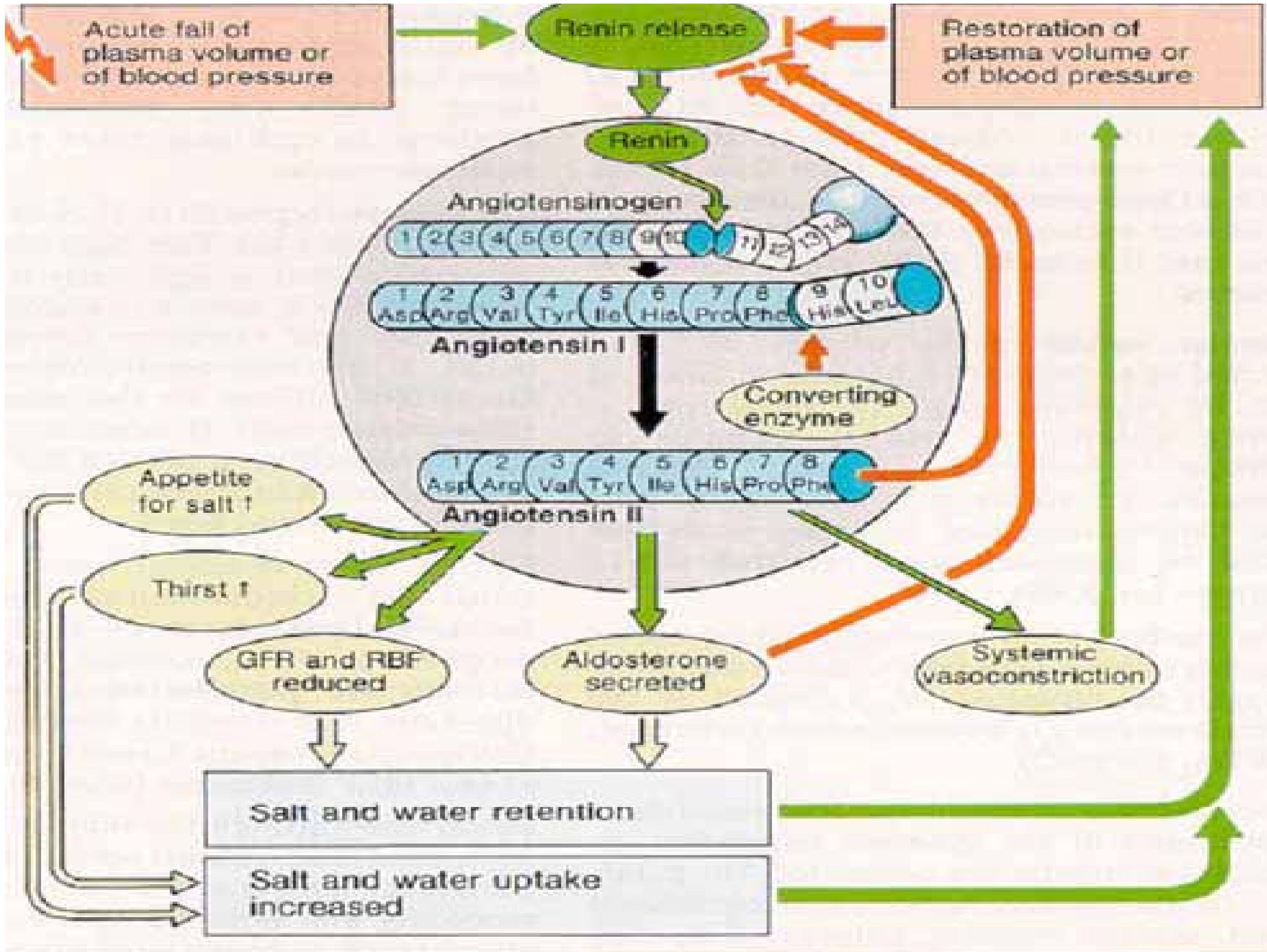




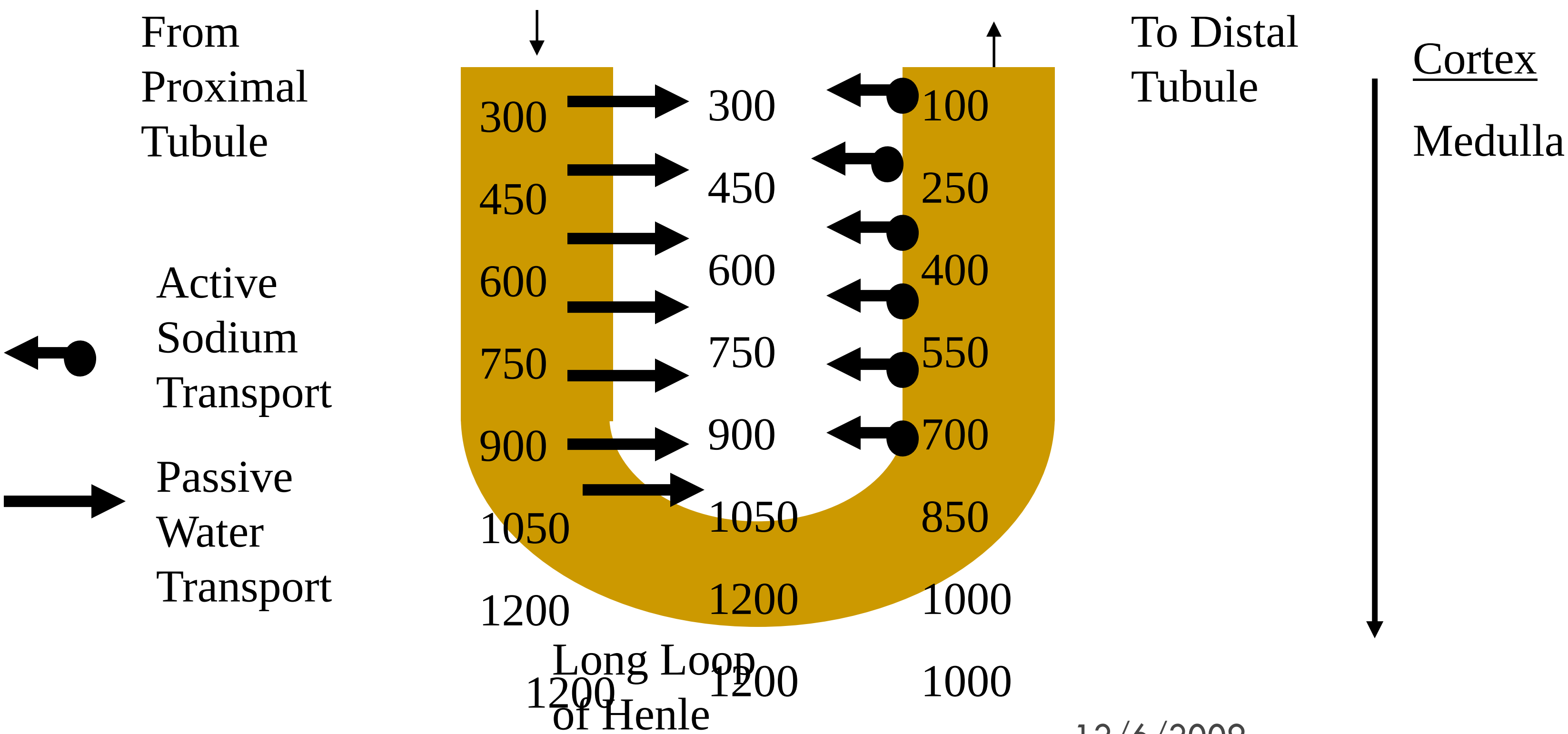
Water deficit
Plasma osmolality ↑
Atrial pressure ↓
Thirst
ADH
Water resorption ↑
Urine volume reduced (Antidiuresis)
1
Water excess
Atrial pressure ↑
Plasma osmolality ↓
Water resorption ↓
Urine volume increased (Diuresis)
2


Salt excess
Plasma volume ↑
Renin
Na⁺
resorption ↓
Angiotensin II
Aldosterone
Adrenal
cortex
Salt deficit
Plasma volume ↓
Renin
Na⁺
resorption ↑
Salt excretion
increased
Salt excretion
reduced
3
4

Renin-Angiotensin System

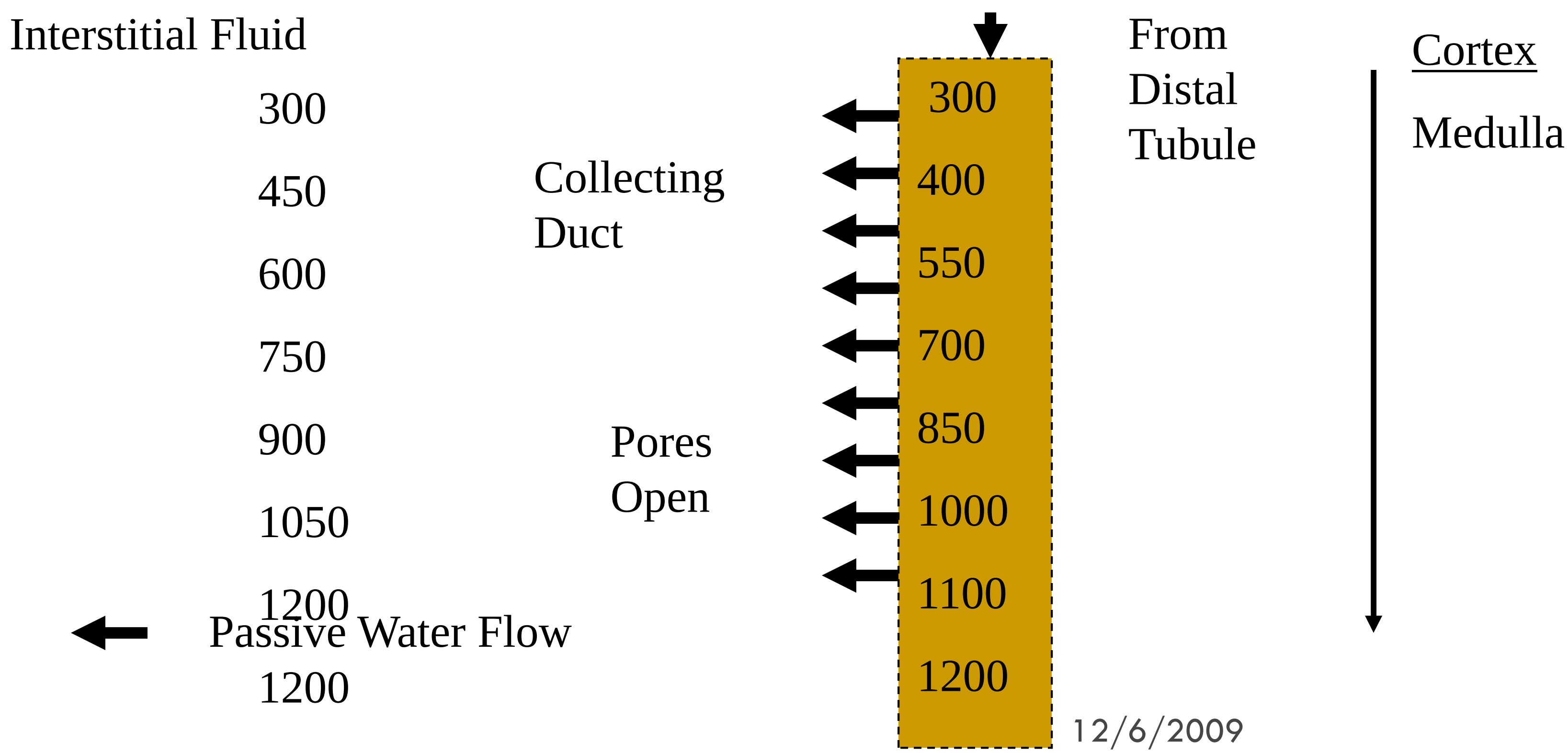


COUNTERCURRENT MAKES THE OSMOTIC GRADIENT

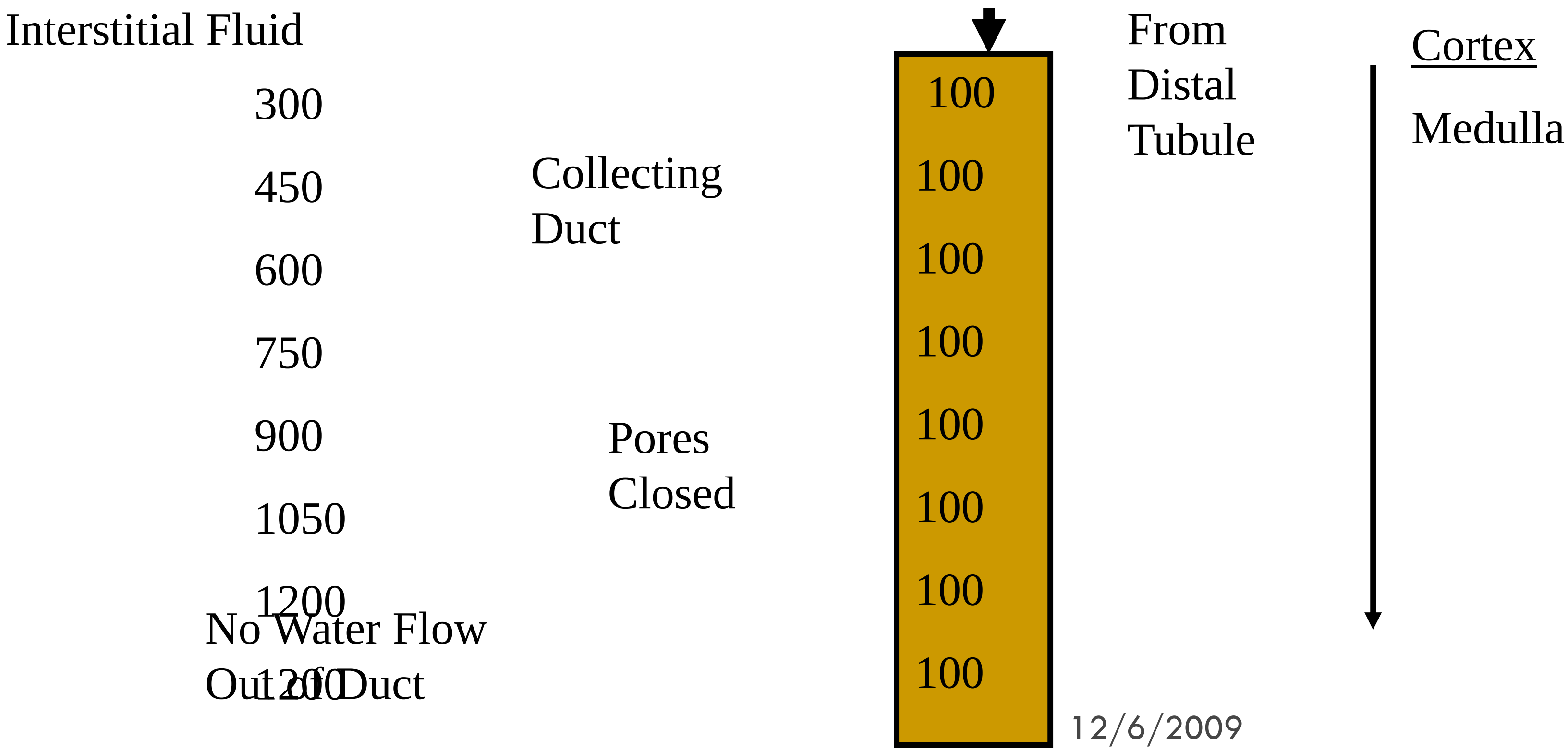


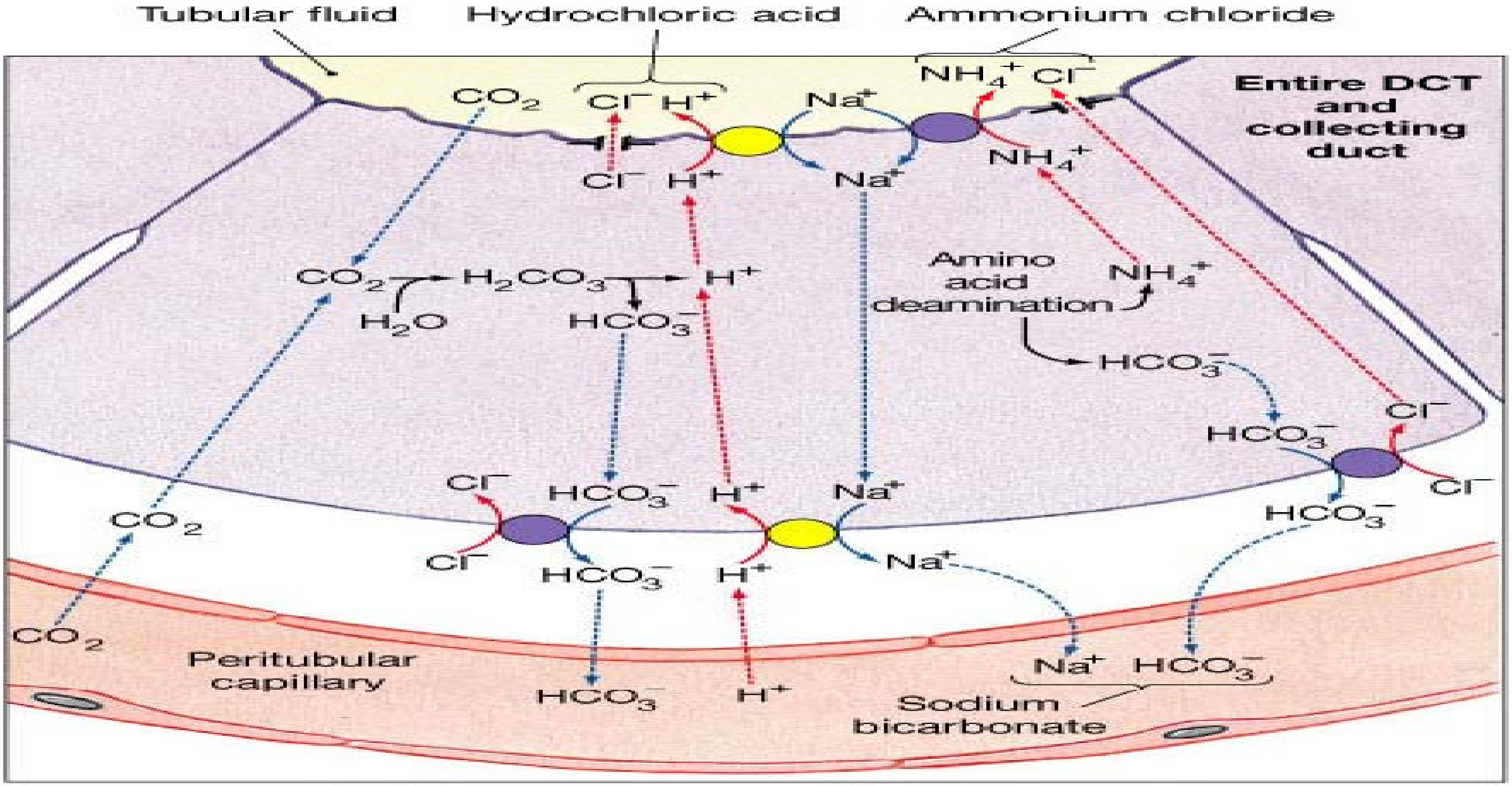
12/6/2009

THE OSMOTIC GRADIENT CONCENTRATES THE URINE WHEN VASOPRESSIN (ANTI DIURETIC HORMONE [ADH]) IS PRESENT



WHEN VASOPRESSIN (ANTI DIURETIC HORMONE [ADH]) IS ABSENT A DILUTE URINE IS PRODUCE





(c) H^+ secretion and HCO_3^- reabsorption

Secretion of Aldosterone regulated by:

- Angiotensin II (+)
- Plasma K (+)
- ACTH (+)
- Plasma Na (-)
- ANF (-)

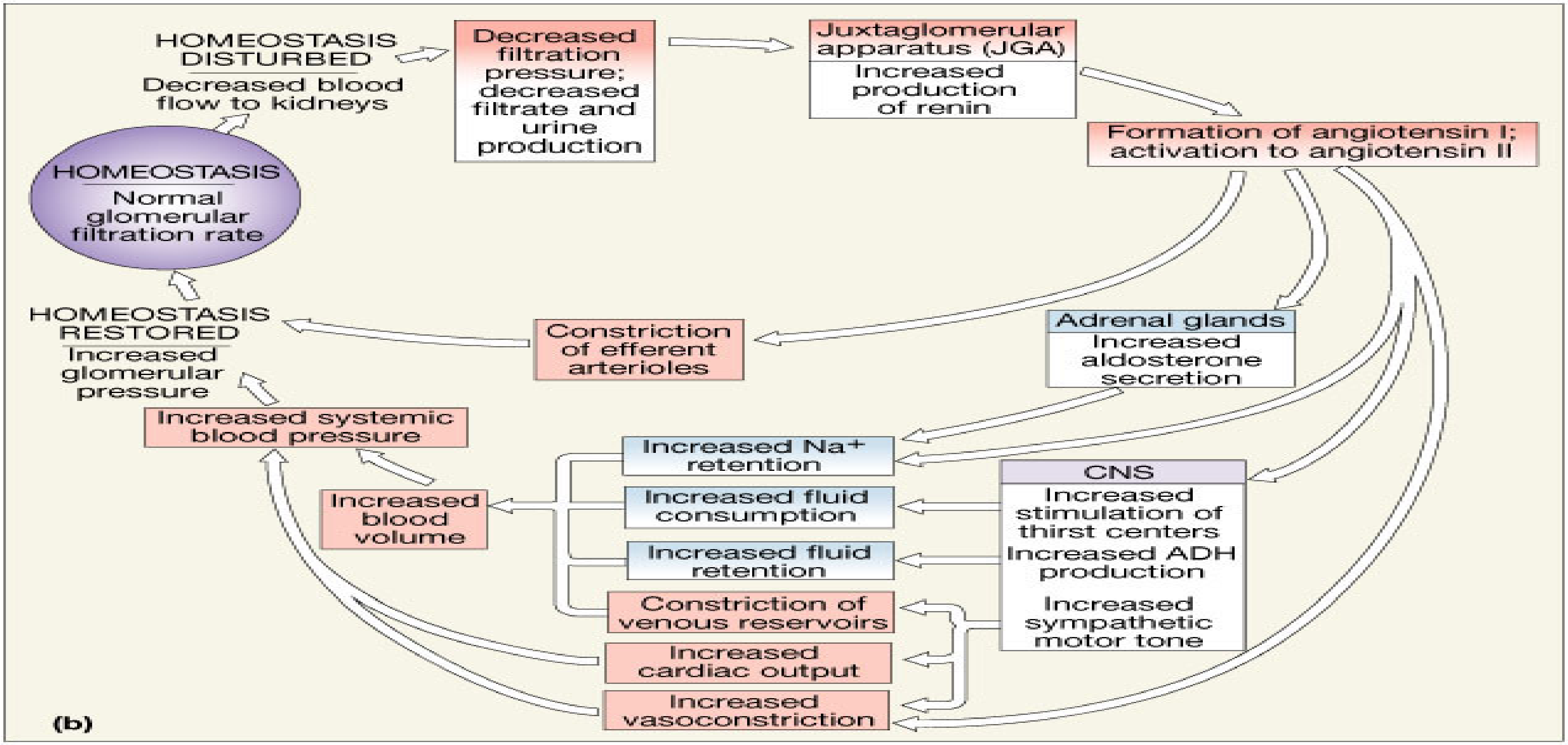
Total filtered Na/day = GFR x PNa

= 180 L/day x 145 mmol/L = 26,100 mmol/day

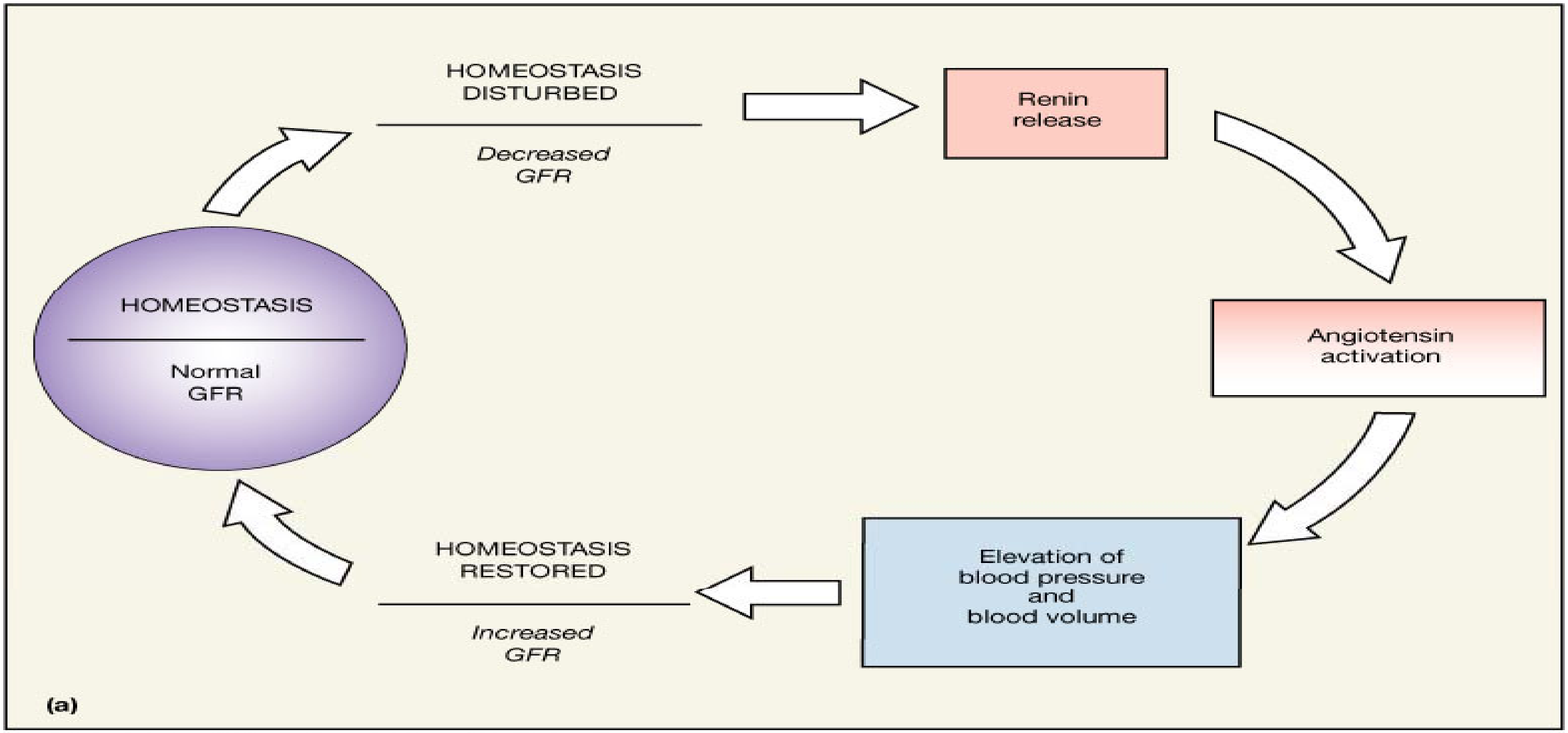
= ~ 15 g NaCl!

- **GLOMERULAR FILTRATION RATE (GFR):** The rate, in mL/min, at which blood is filtered through the glomerulus: **GFR = K_f (P_{gc} - P_t - PI_b) = (K_f)x(P_f)**
- **K_f = FILTRATION COEFFICIENT:** A constant representing the permeability of the glomerular filter.
  - You can calculate a value for K_f by measuring GFR and P_f.
- **<u>REGULATION OF GFR and RBF:</u>** In general, GFR changes in the same direction as RBF, RBF usually changes more profoundly.
  - *Lower K_f (less permeability) ------> lower GFR*
    - This is somewhat compensated by a *slower rate of rise of oncotic pressure* which is a direct consequence of the lower GFR. That leads to a slightly higher P_f, which balances off the GFR a little.
  - ARTERIOLAR CHANGES:
    - ***Efferent Arteriolar Vasoconstriction ------>***
      - LOWER RBF
      - HIGHER GFR, because of higher P_{gc}
    - ***Afferent Arteriolar Vasoconstriction ------>***
      - LOWER RBF
      - LOWER GFR, because of lower RBF
    - ***Afferent Arteriolar Vasodilation ------>***
      - HIGHER RBF
      - HIGHER GFR, because of higher RBF
    - COMBINED CHANGES: When two or more factors both change, RBF is generally affected more than GFR. GFR remains relatively stable.

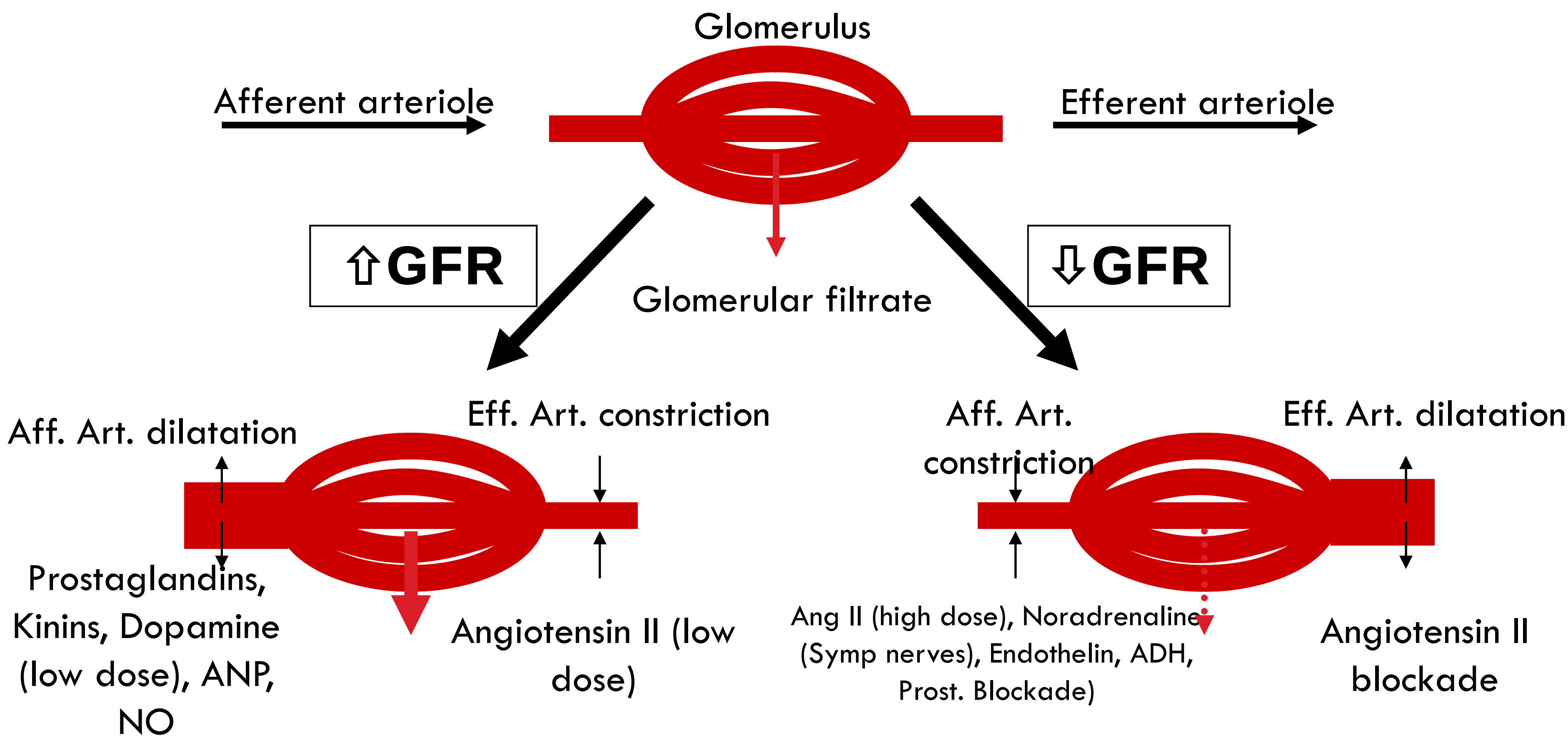
The Response to a Reduction in the GFR



The Response to a Reduction in the GFR



GFR depends on diameters of afferent and efferent arterioles



Extrinsic Controls: Renin-Angiotensin Mechanism

- Triggered when the granular cells of the JGA release renin

angiotensinogen (a plasma globulin)

resin → ↓

angiotensin I

angiotensin converting enzyme (ACE) → ↓

angiotensin II

Effects of Angiotensin II

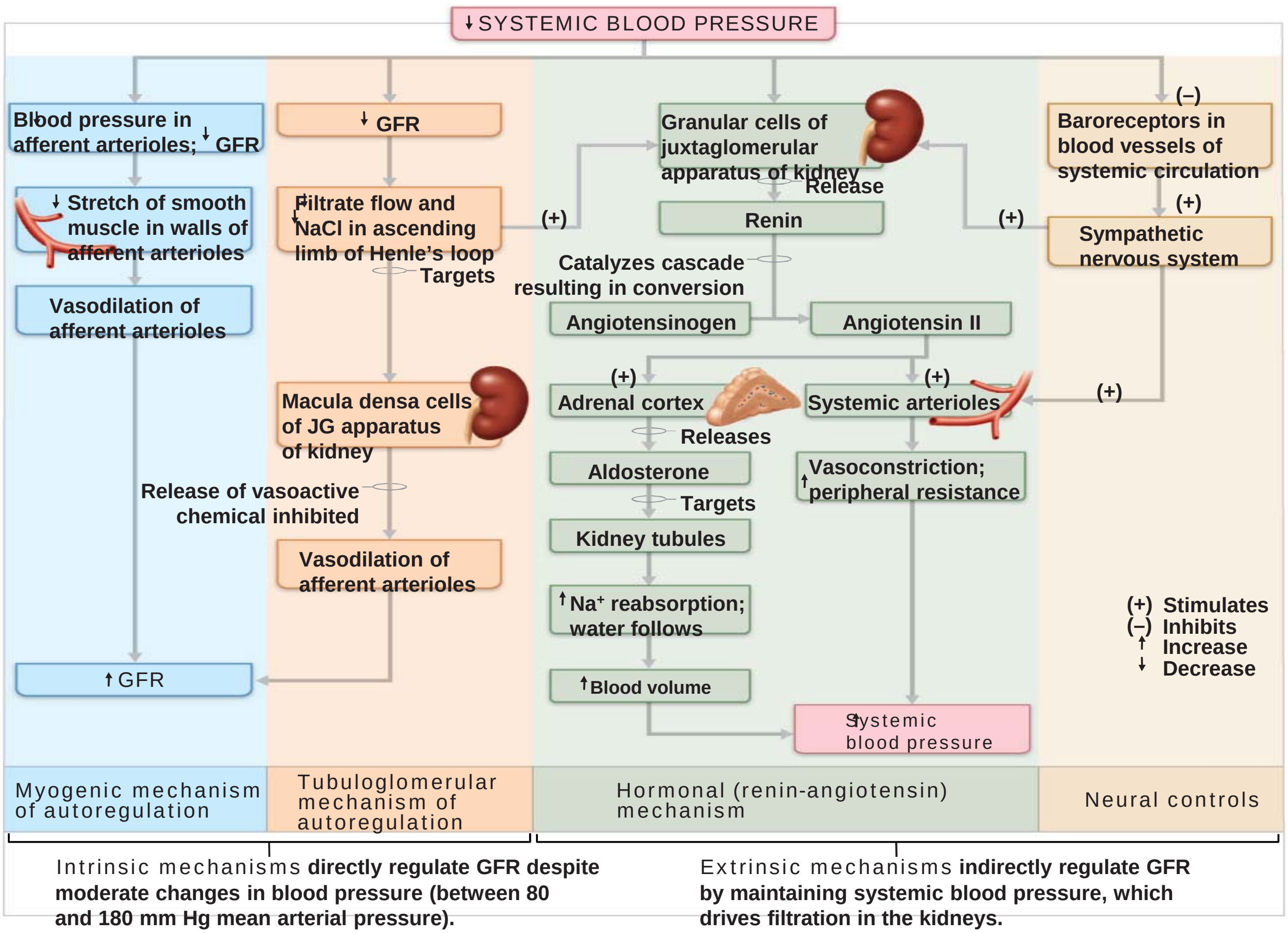
1. Constricts arteriolar smooth muscle, causing MAP to rise
2. Stimulates the reabsorption of Na^+
   - Acts directly on the renal tubules
   - Triggers adrenal cortex to release aldosterone
3. Stimulates the hypothalamus to release ADH and activates the thirst center

Effects of Angiotensin II

4. Constricts efferent arterioles, decreasing peritubular capillary hydrostatic pressure and increasing fluid reabsorption
5. Causes glomerular mesangial cells to contract, decreasing the surface area available for filtration

Extrinsic Controls: Renin-Angiotensin Mechanism

- Triggers for renin release by granular cells
  - Reduced stretch of granular cells (MAP below 80 mm Hg)
  - Stimulation of the granular cells by activated macula densa cells
  - Direct stimulation of granular cells via β1-adrenergic receptors by renal nerves



↓ SYSTEMIC BLOOD PRESSURE
Blood pressure in afferent arterioles; ↓ GFR
↓ Stretch of smooth muscle in walls of afferent arterioles
Vasodilation of afferent arterioles
↑ GFR
↓ GFR
↓ Filtrate flow and NaCl in ascending limb of Henle's loop
Targets
Macula densa cells of JG apparatus of kidney
Release of vasoactive chemical inhibited
Vasodilation of afferent arterioles
(+)
Granular cells of juxtaglomerular apparatus of kidney
Release
Renin
Catalyzes cascade resulting in conversion
Angiotensinogen
Angiotensin II
(+)
Adrenal cortex
Releases
Aldosterone
Targets
Kidney tubules
↑ Na+ reabsorption; water follows
↑ Blood volume
(+)
Systemic arterioles
Vasoconstriction; ↑ peripheral resistance
↑ Systemic blood pressure
(–)
Baroreceptors in blood vessels of systemic circulation
(+)
Sympathetic nervous system
(+)
(+)
(+) Stimulates
(–) Inhibits
↑ Increase
↓ Decrease
Myogenic mechanism of autoregulation
Tubuloglomerular mechanism of autoregulation
Hormonal (renin-angiotensin) mechanism
Neural controls
Intrinsic mechanisms directly regulate GFR despite moderate changes in blood pressure (between 80 and 180 mm Hg mean arterial pressure).
Extrinsic mechanisms indirectly regulate GFR by maintaining systemic blood pressure, which drives filtration in the kidneys.

Figure 25.12

•FACTORS AFFECTING ARTERIOLES:

- Resting tone in the arterioles, maintained by intrinsic myogenic activity.

- **SYMPATHETICS**
- innervate both afferent and efferent arterioles to cause vasoconstriction.
  - Epinephrine and Norepinephrine *both cause* ***vasoconstriction*** *in the kidneys*,
    - Moderate sympathetic increase ------> decrease RBF with little change in GFR.
    - Large increase in sympathetics ------> stop glomerular filtration entirely.
  - ATRIAL STRETCH RECEPTORS have a more significant effect on the kidneys than the baroreceptors.

- **RENIN / ANGIOTENSIN II** leads to vasoconstriction.
  - Biosynthetic Pathway: JGA Cells secrete Renin in response to low tubular osmolarity.
    - Renin converts **Angiotensinogen ------> Angiotensin I** in the kidney.
    - **ACE** converts **Angiotensin I ------> Angiotensin II** in the lungs.
    - **ANGIOTENSIN II:** It causes water retention (reabsorption) by two mechanisms:
    - Direct action on tubules to promote Na^+ and water reabsorption
    - Indirect action on kidneys by stimulating **Aldosterone** secretion in adrenal cortex.
- **PROSTAGLANDIN E_2 (PGE_2):** *Vasodilator*. Its release is stimulated by Angiotensin II, and it acts primarily on the *afferent arteriole.*

- **ENDOTHELIN** is released locally and causes vasoconstriction of primarily the efferent arteriole ------> reduce RBF

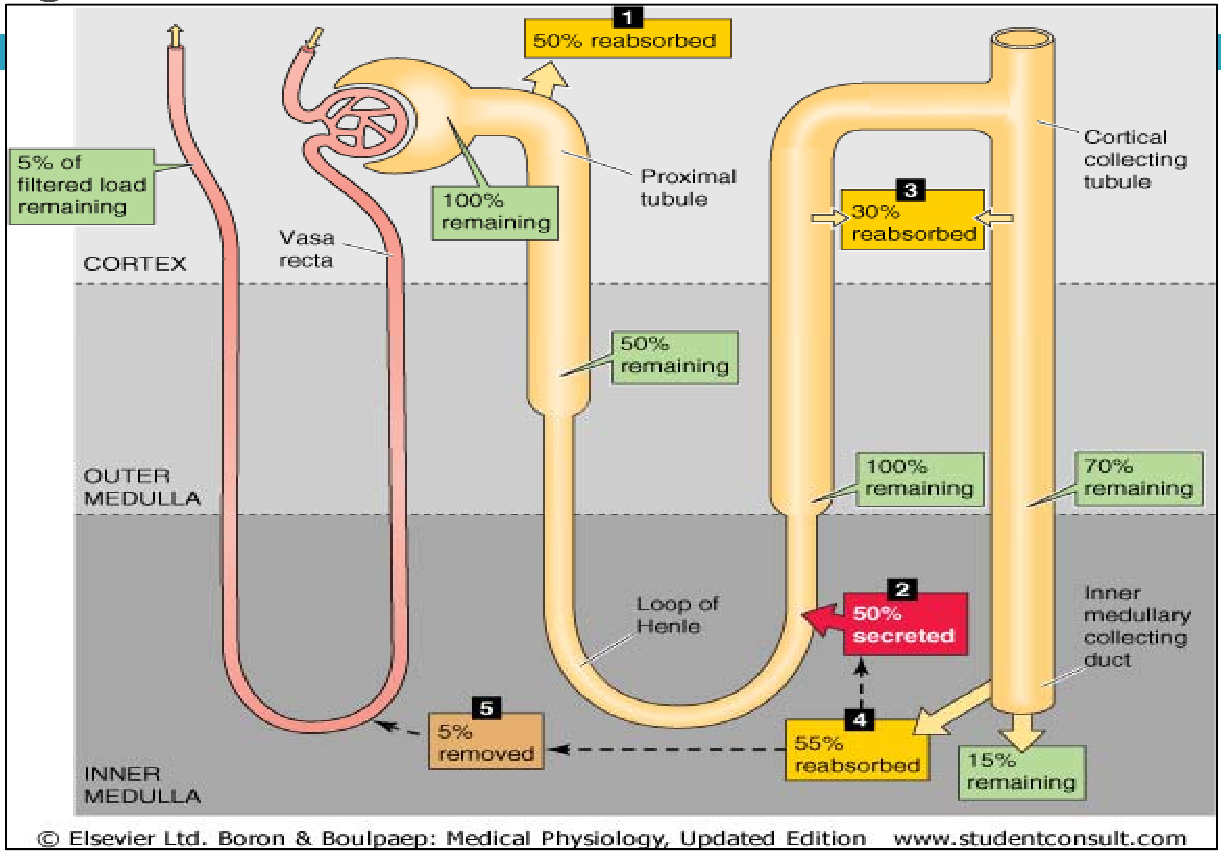
- **RENAL AUTOREGULATION:** The intrinsic response of the kidney to **changes in blood pressure**, independent of innervation.
  - ***Smooth Muscle Myogenic Response:*** The smooth muscle response to pressure accounts for some of this autoregulation.
  - **TUBULO-GLOMERULAR FEEDBACK:** *Macula Densa* senses changes in the **tubular fluid flow rate** and modifies the arterioles accordingly.
    - A higher arterial blood pressure will lead to higher tubular fluid flow: MABP ------> Capillary Pressure ------> Tubular Flow ------> Macula Densa senses the higher tubular flow ------> Resistance in Afferent Arteriole ------>Blood pressure
    - This feedback is on a per-nephron basis. Macula Densa cells will affect the resistance *only in the afferent arteriole of that local nephron*.
    - Macula Densa may sense Na^+ or Cl^- concentration. We don't know for sure what it senses

Role of urea in concentrating urine

- Urea very useful in concentrating urine.
- High protein diet = more urea = more concentrated urine.
- Kidneys filter, reabsorb and secrete urea.
- Urea excretion rises with increasing urinary flow.

Urea recycling

- Urea toxic at high levels, but can be useful in small amounts.
- Urea recycling causes buildup of high [urea] in inner medulla.
- This helps create the osmotic gradient at loop of Henle so H_2O can be reabsorbed.



A Summary of Renal Function

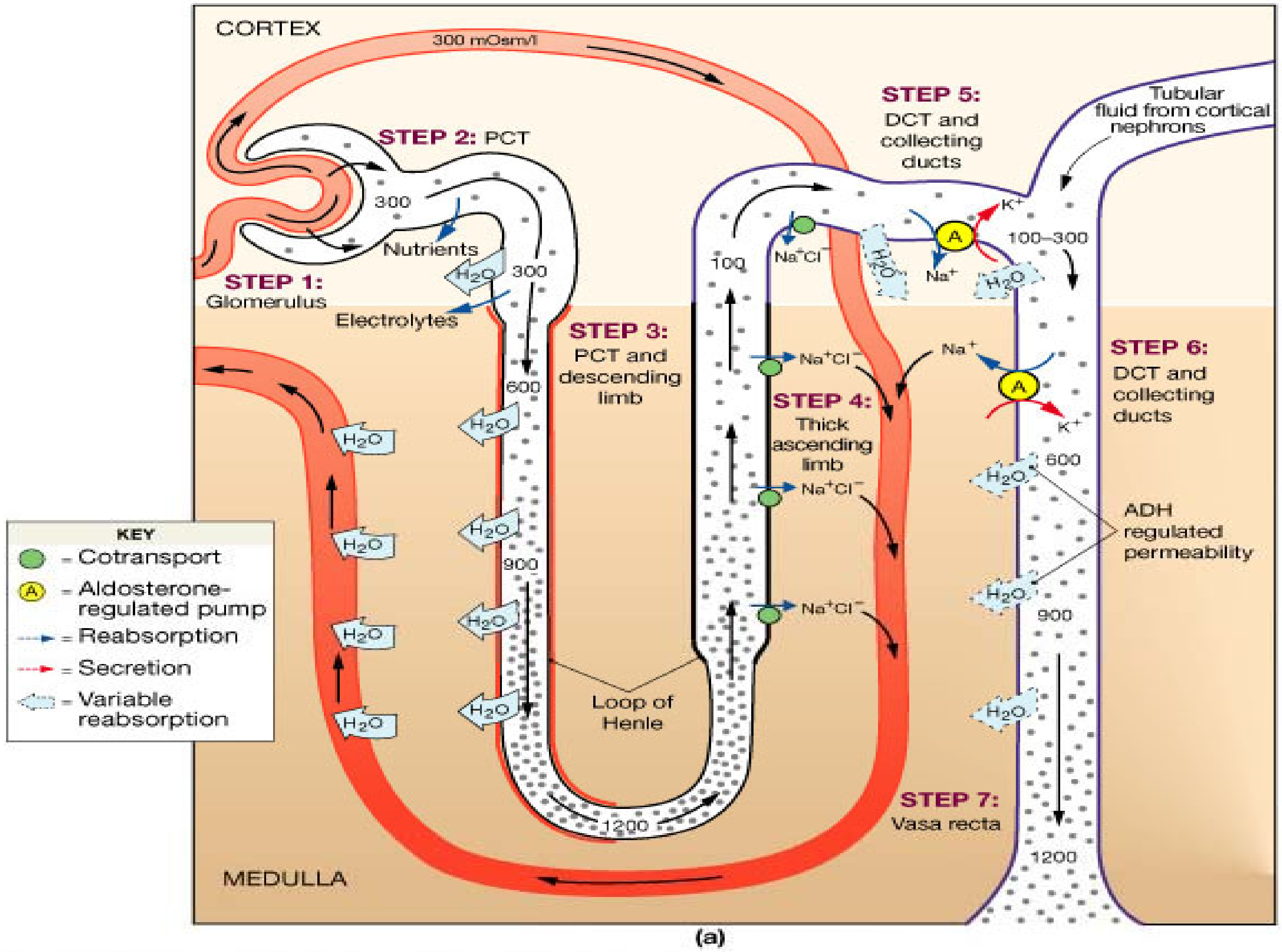
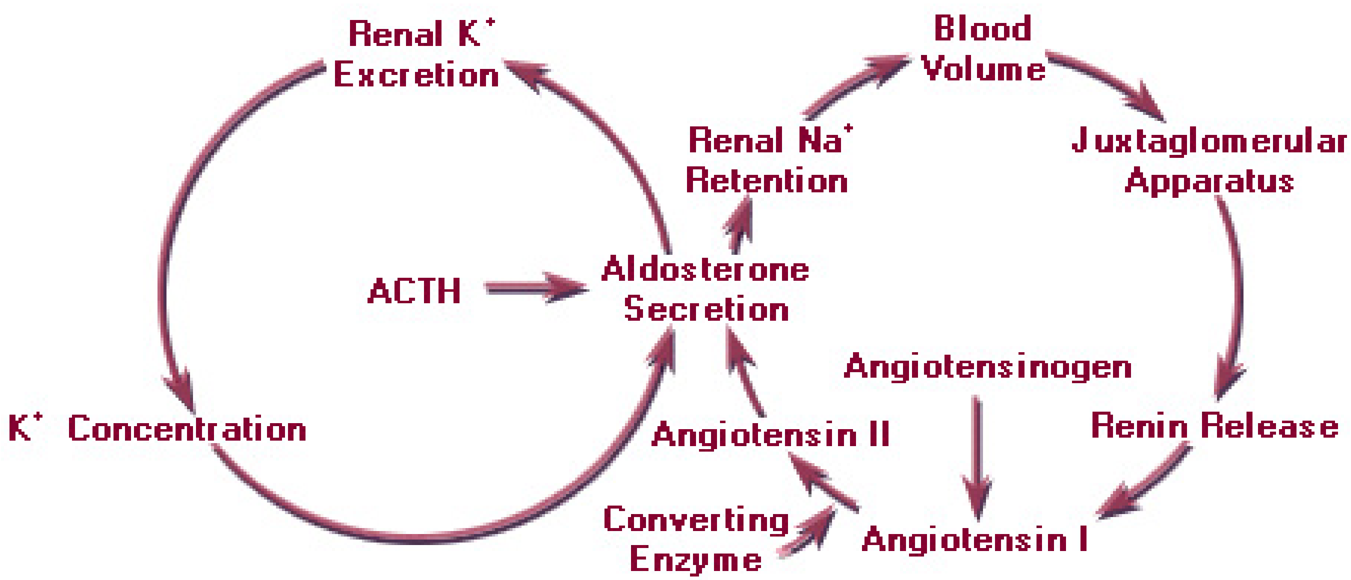


Figure 26.16a

Stimuli for Renin Secretion

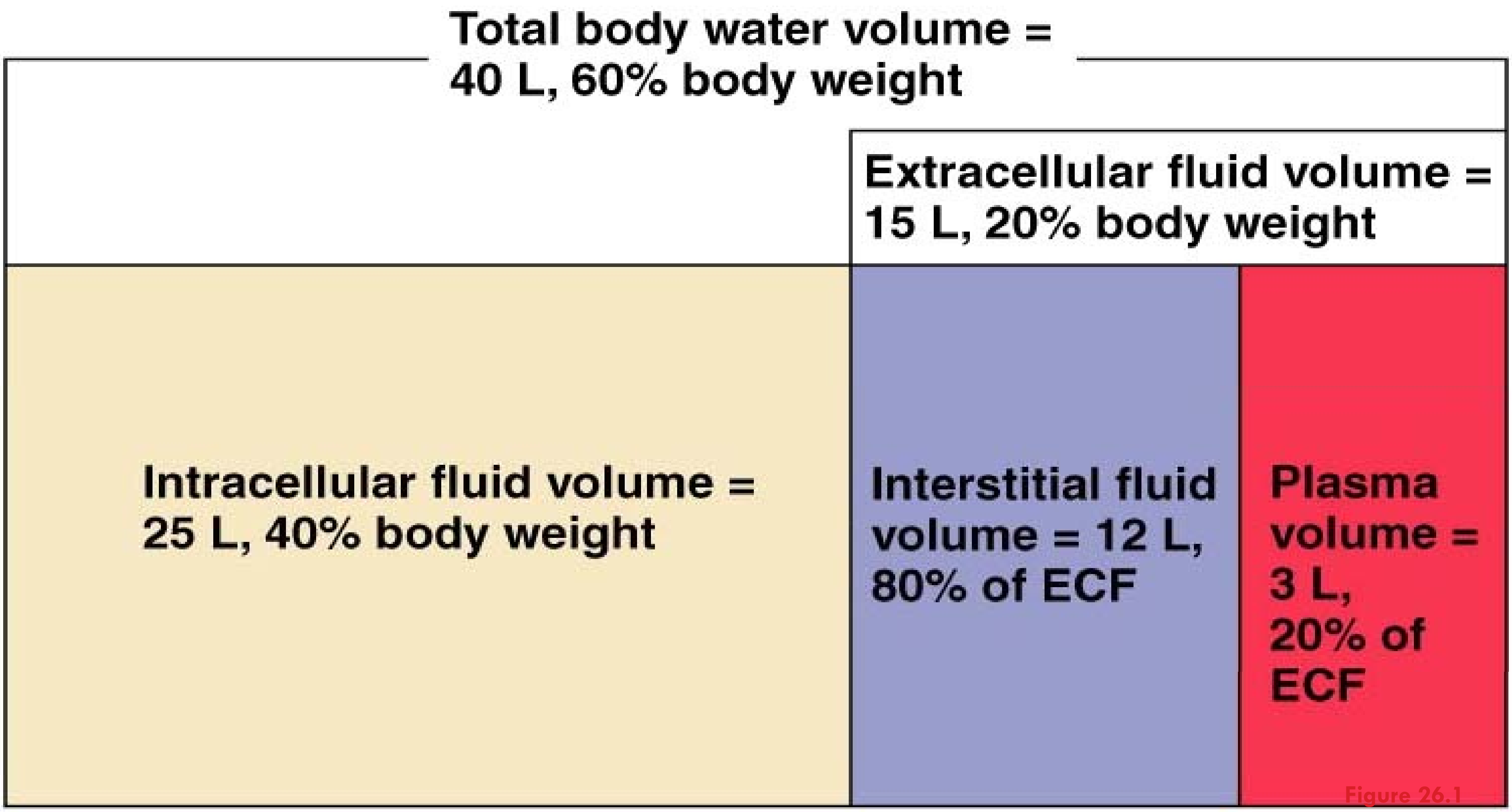
1. ⇩ blood pressure
2. ⇩ serum Na
3. ⇩ blood volume
4. ANS stimulation

Regulation-Mineralocorticoids



Actions of Angiotensin II

1. Direct arteriolar vasoconstrictor
2. Stimulus to aldosterone secretion


Total body water volume =
40 L, 60% body weight
Extracellular fluid volume =
15 L, 20% body weight
Intracellular fluid volume =
25 L, 40% body weight
Interstitial fluid
volume = 12 L,
80% of ECF
Plasma
volume =
3 L,
20% of
ECF
Figure 26.1

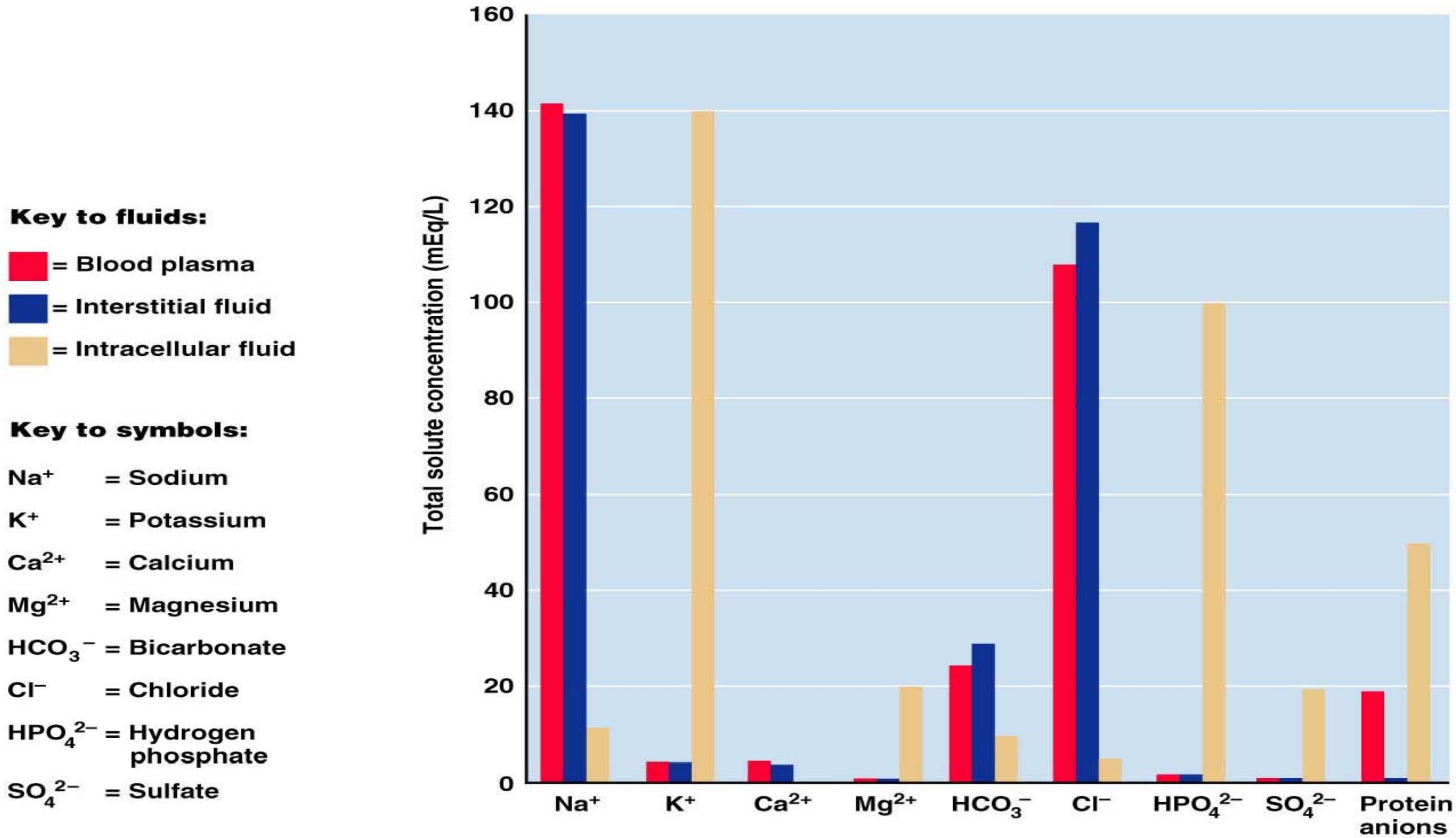

Key to fluids:
= Blood plasma
= Interstitial fluid
= Intracellular fluid
Key to symbols:
Na^+ = Sodium
K^+ = Potassium
Ca^{2+} = Calcium
Mg^{2+} = Magnesium
HCO_3^- = Bicarbonate
Cl^- = Chloride
HPO_4^{2-} = Hydrogen phosphate
SO_4^{2-} = Sulfate
Total solute concentration (mEq/L)
160
140
120
100
80
60
40
20
0
Na^+
K^+
Ca^{2+}
Mg^{2+}
HCO_3^-
Cl^-
HPO_4^{2-}
SO_4^{2-}
Protein anions

Figure 26.2

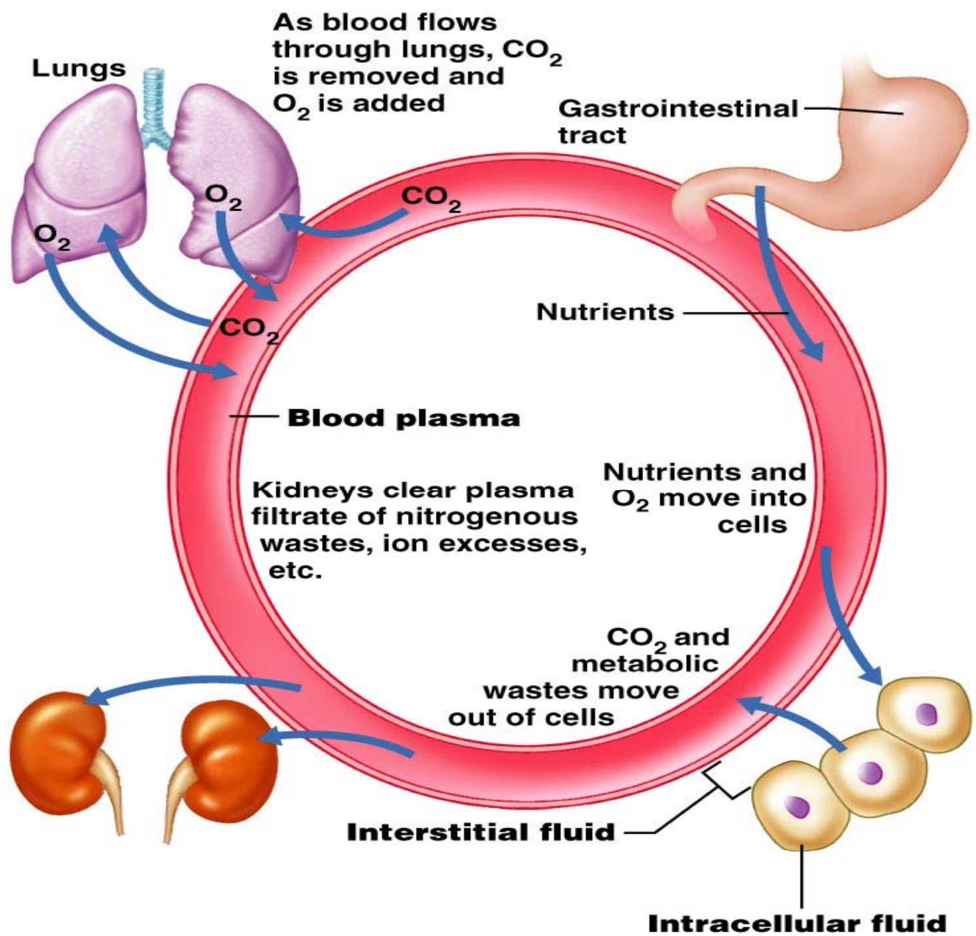

As blood flows through lungs, CO_2 is removed and O_2 is added
Lungs
O_2
O_2
CO_2
CO_2
Gastrointestinal tract
Nutrients
Blood plasma
Kidneys clear plasma filtrate of nitrogenous wastes, ion excesses, etc.
Nutrients and O_2 move into cells
CO_2 and metabolic wastes move out of cells
Interstitial fluid
Intracellular fluid

Figure 26.3

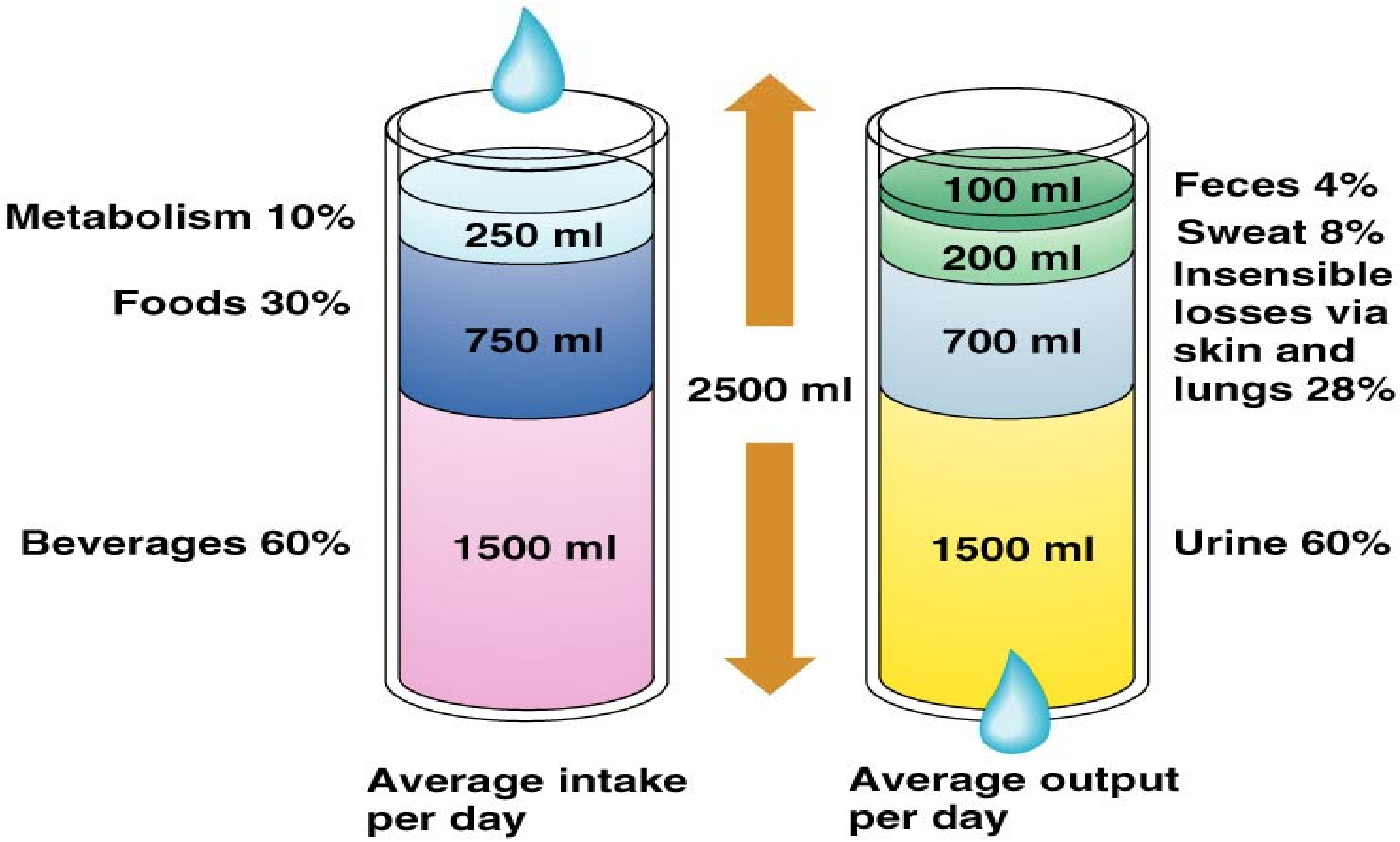

Metabolism 10%
Foods 30%
Beverages 60%
250 ml
750 ml
1500 ml
2500 ml
100 ml
200 ml
700 ml
1500 ml
Feces 4%
Sweat 8%
Insensible losses via skin and lungs 28%
Urine 60%
Average intake per day
Average output per day

Figure 26.4

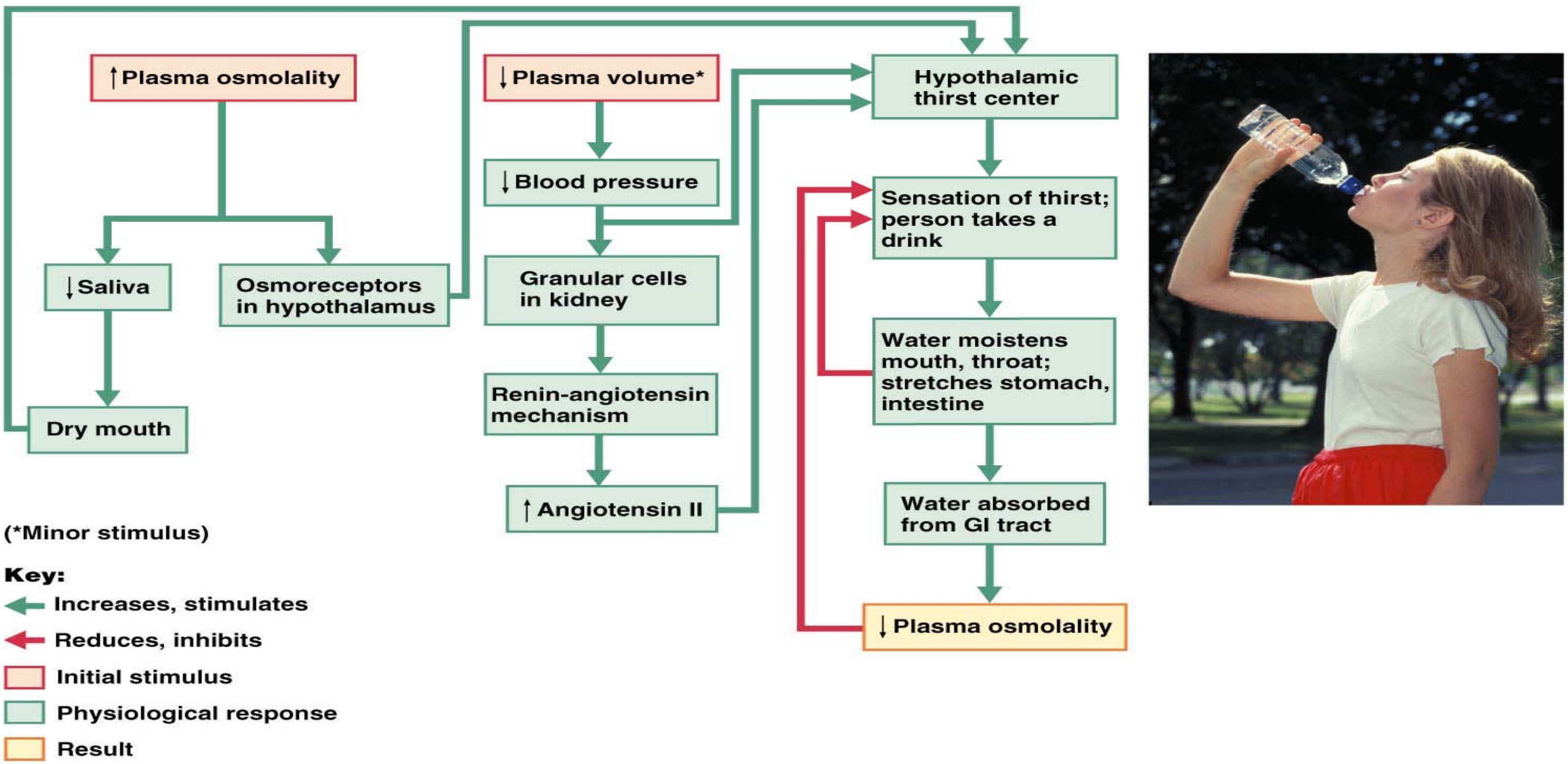
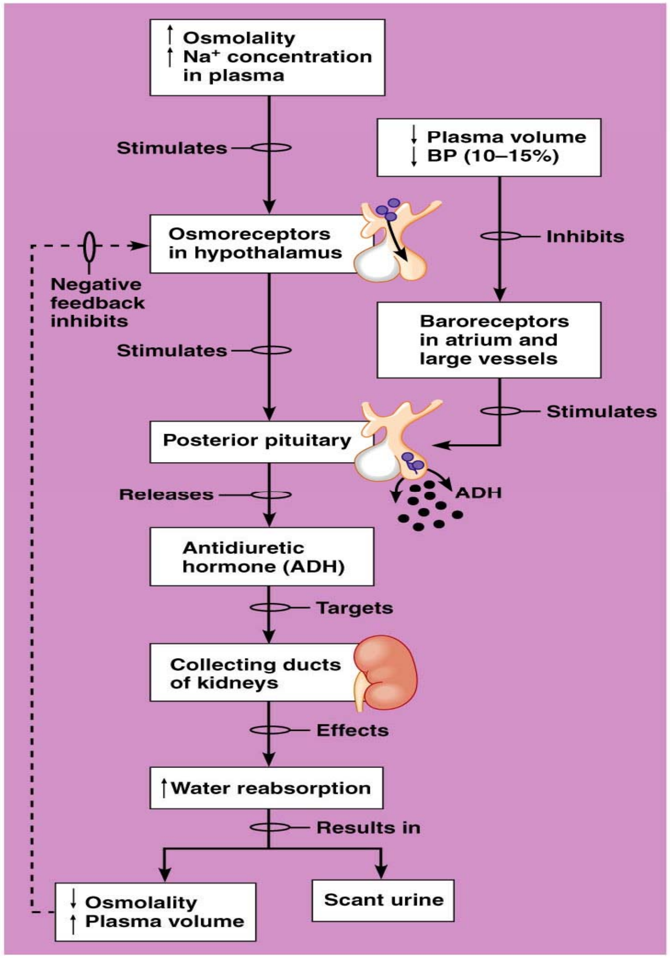
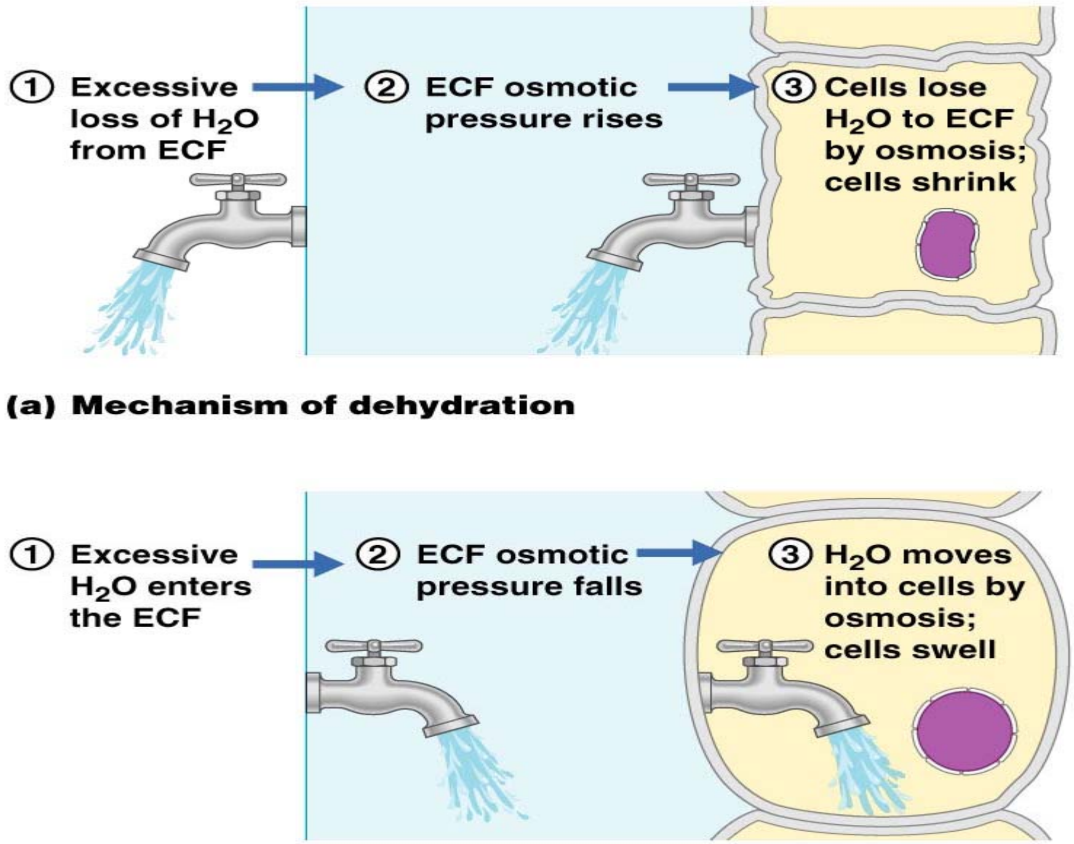

↑ Plasma osmolality
↓ Plasma volume*
Hypothalamic thirst center
↓ Blood pressure
Sensation of thirst; person takes a drink
↓ Saliva
Osmoreceptors in hypothalamus
Granular cells in kidney
Water moistens mouth, throat; stretches stomach, intestine
Dry mouth
Renin-angiotensin mechanism
↑ Angiotensin II
Water absorbed from GI tract
↓ Plasma osmolality
(*Minor stimulus)
Key:
Increases, stimulates
Reduces, inhibits
Initial stimulus
Physiological response
Result

Figure 26.5



↑ Osmolality
↑ Na^+ concentration in plasma
Stimulates
↓ Plasma volume
↓ BP (10–15%)
Osmoreceptors in hypothalamus
Inhibits
Negative feedback inhibits
Baroreceptors in atrium and large vessels
Stimulates
Stimulates
Posterior pituitary
Releases
ADH
Antidiuretic hormone (ADH)
Targets
Collecting ducts of kidneys
Effects
↑ Water reabsorption
Results in
↓ Osmolality
↑ Plasma volume
Scant urine

Figure 26.6



(a) Mechanism of dehydration

(b) Mechanism of hypotonic hydration

Figure 26.7

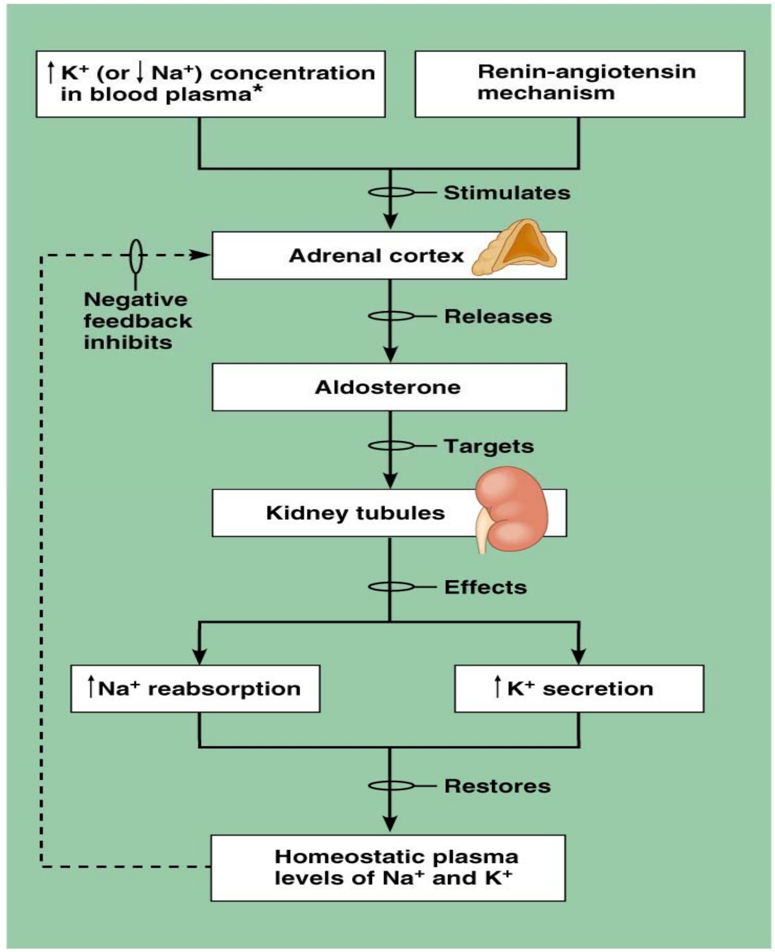

↑K+ (or ↓Na+) concentration in blood plasma*
Renin-angiotensin mechanism
Stimulates
Adrenal cortex
Negative feedback inhibits
Releases
Aldosterone
Targets
Kidney tubules
Effects
↑Na+ reabsorption
↑K+ secretion
Restores
Homeostatic plasma levels of Na+ and K+

Figure 26.8

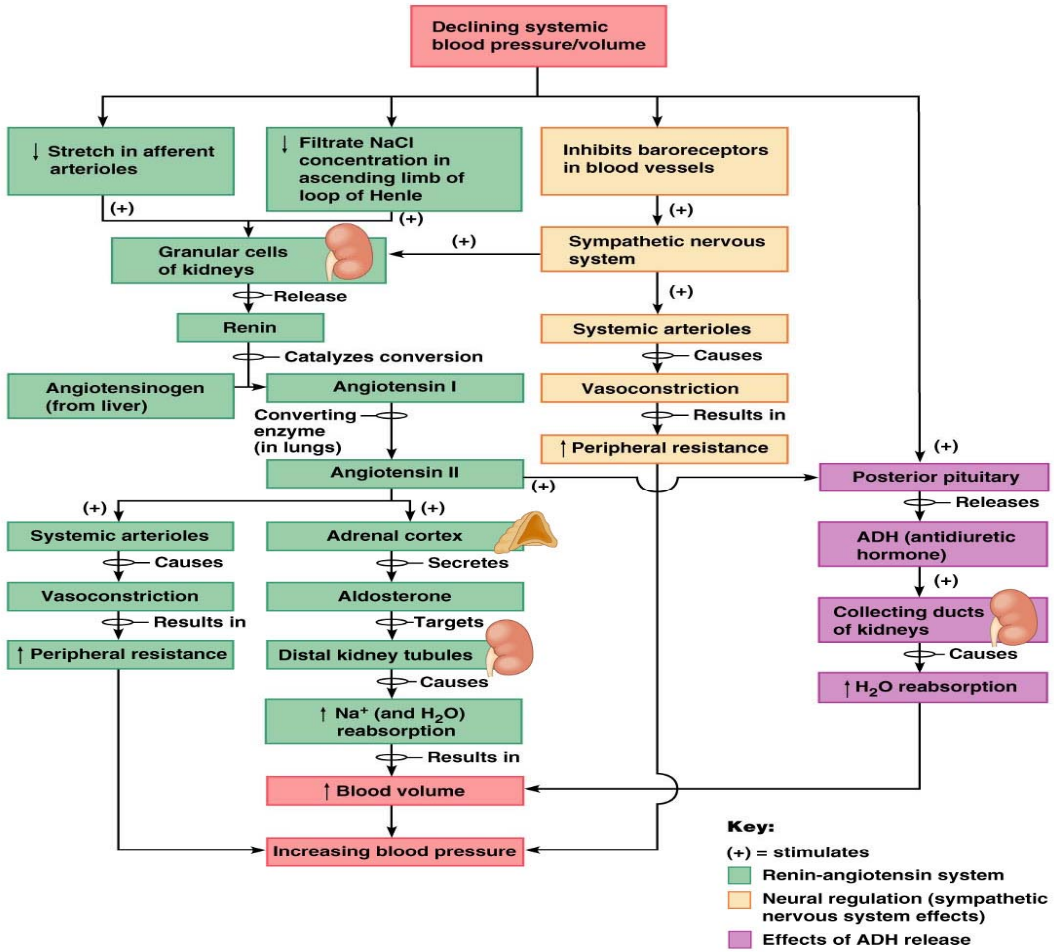

Declining systemic blood pressure/volume
↓ Stretch in afferent arterioles
↓ Filtrate NaCl concentration in ascending limb of loop of Henle
Inhibits baroreceptors in blood vessels
(+)
Granular cells of kidneys
Sympathetic nervous system
Release
Renin
Systemic arterioles
Catalyzes conversion
Causes
Angiotensinogen (from liver)
Angiotensin I
Vasoconstriction
Converting enzyme (in lungs)
Results in
↑ Peripheral resistance
Angiotensin II
Posterior pituitary
Releases
Systemic arterioles
Adrenal cortex
ADH (antidiuretic hormone)
Causes
Secretes
Vasoconstriction
Aldosterone
Collecting ducts of kidneys
Results in
Targets
Causes
↑ Peripheral resistance
Distal kidney tubules
↑ H_2O reabsorption
Causes
↑ Na^+ (and H_2O) reabsorption
Results in
↑ Blood volume
Increasing blood pressure
Key:
(+) = stimulates
Renin-angiotensin system
Neural regulation (sympathetic nervous system effects)
Effects of ADH release

Figure 26.9

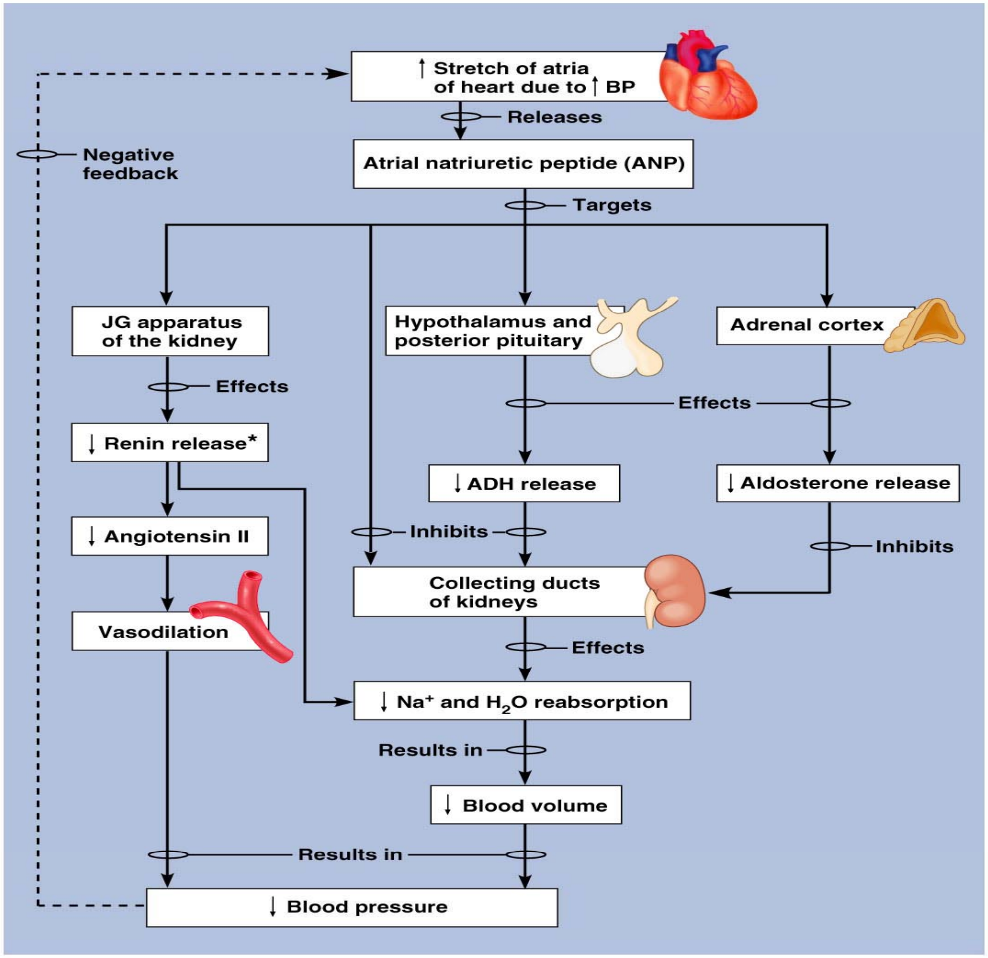

↑ Stretch of atria of heart due to ↑ BP
Releases
Atrial natriuretic peptide (ANP)
Negative feedback
Targets
JG apparatus of the kidney
Hypothalamus and posterior pituitary
Adrenal cortex
Effects
Effects
↓ Renin release*
↓ ADH release
↓ Aldosterone release
↓ Angiotensin II
Inhibits
Inhibits
Collecting ducts of kidneys
Vasodilation
Effects
↓ Na^+ and H_2O reabsorption
Results in
↓ Blood volume
Results in
↓ Blood pressure

Figure 26.10

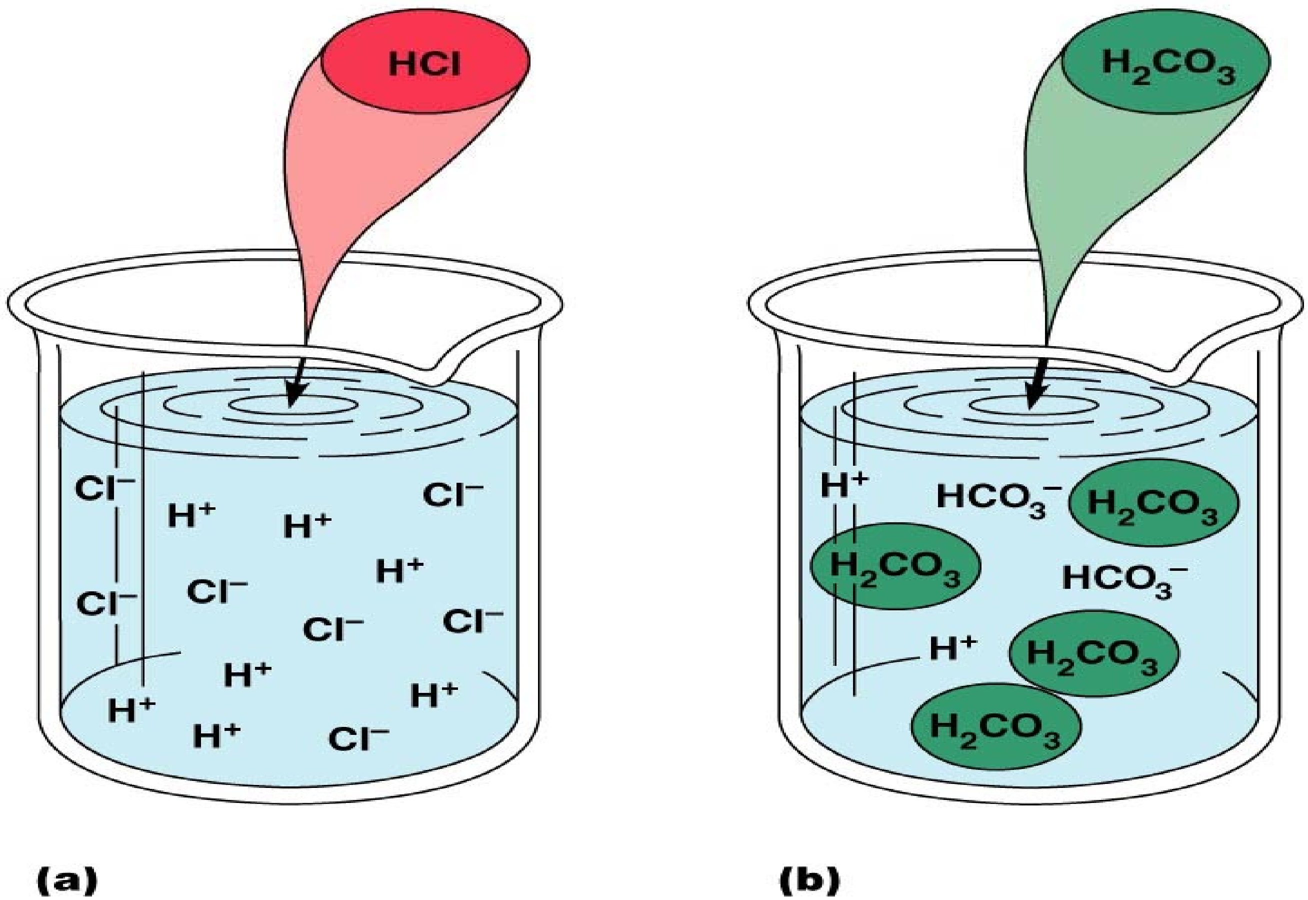
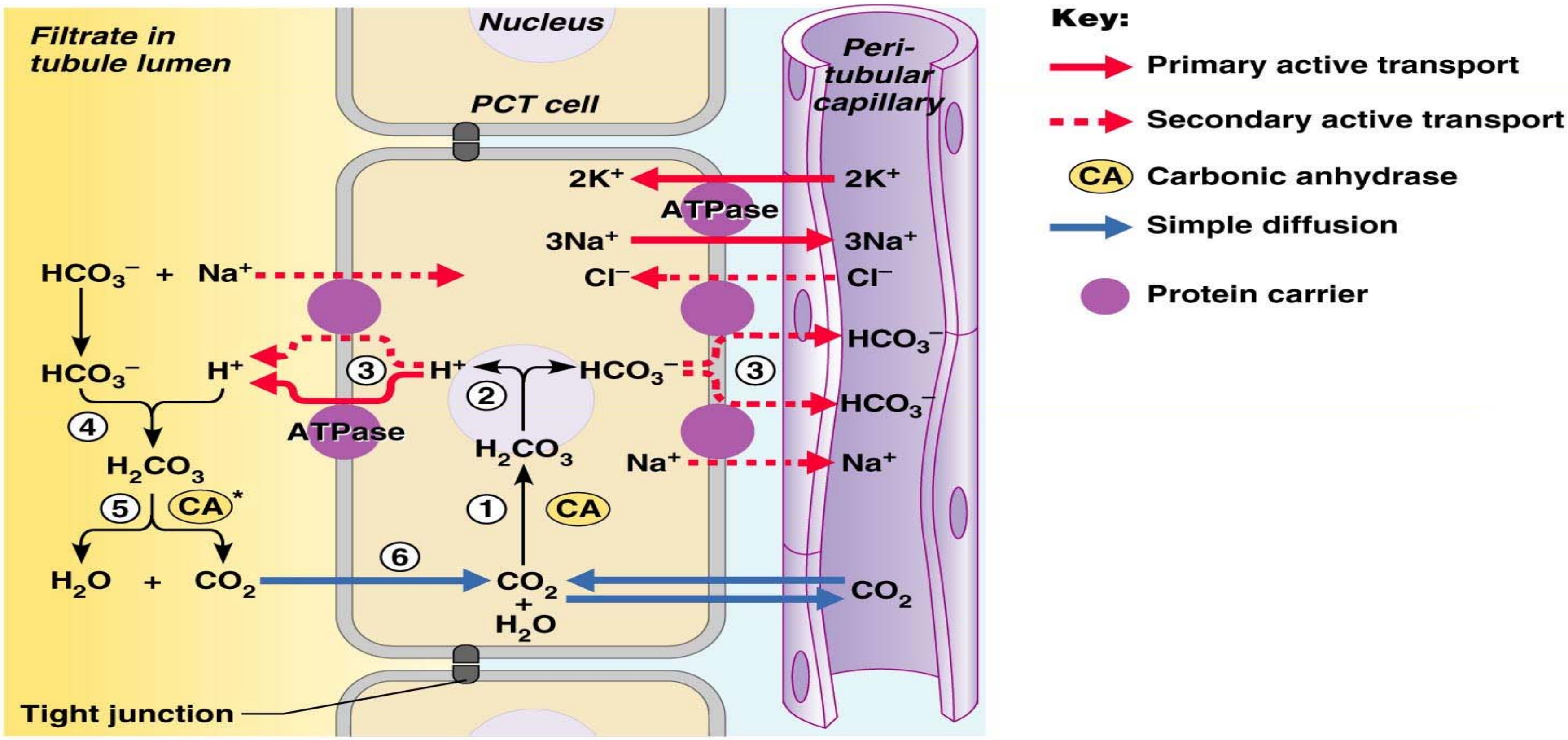
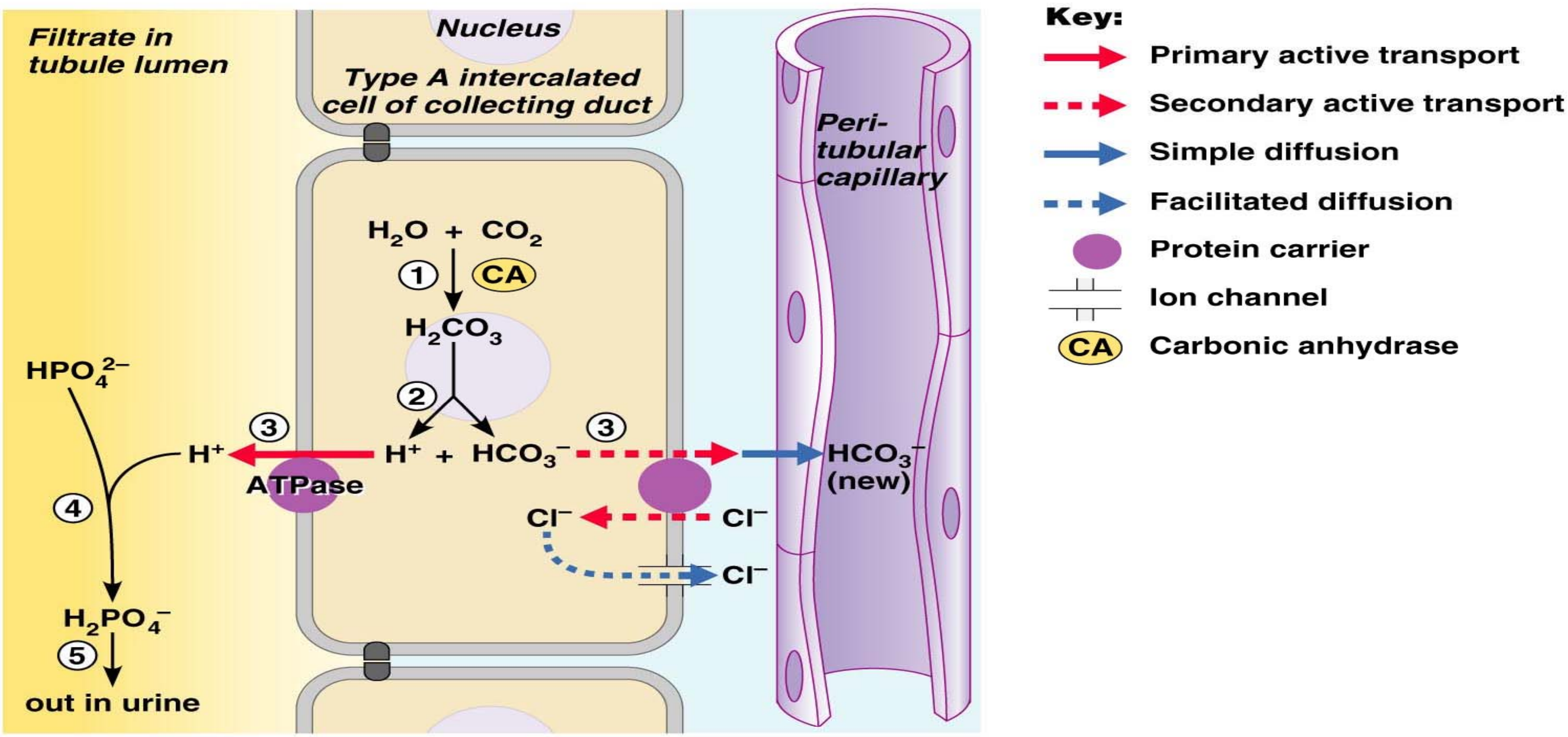

HCl
Cl⁻
H⁺
H⁺
Cl⁻
H⁺
Cl⁻
Cl⁻
Cl⁻
Cl⁻
H⁺
H⁺
H⁺
H⁺
Cl⁻
(a)
H_2CO_3
H⁺
HCO_3^-
H_2CO_3
H_2CO_3
HCO_3^-
H⁺
H_2CO_3
H_2CO_3
(b)

Figure 26.11



Filtrate in tubule lumen
Nucleus
PCT cell
Peri-tubular capillary
Key:
Primary active transport
Secondary active transport
CA Carbonic anhydrase
Simple diffusion
Protein carrier
2K+
2K+
ATPase
3Na+
3Na+
HCO3− + Na+
Cl−
Cl−
HCO3−
H+
3
H+
2
HCO3−
3
HCO3−
HCO3−
4
ATPase
H2CO3
H2CO3
Na+
Na+
5
CA*
1
CA
6
H2O + CO2
CO2 + H2O
CO2
Tight junction

Figure 26.12



Filtrate in tubule lumen
Nucleus
Type A intercalated cell of collecting duct
Peri-tubular capillary
H_2O + CO_2
1
CA
H_2CO_3
2
HPO_4^{2-}
3
H^+
ATPase
H^+ + HCO_3^-
3
HCO_3^- (new)
4
Cl^-
Cl^-
Cl^-
$H_2PO_4^-$
5
out in urine
Key:
Primary active transport
Secondary active transport
Simple diffusion
Facilitated diffusion
Protein carrier
Ion channel
CA
Carbonic anhydrase

Figure 26.13

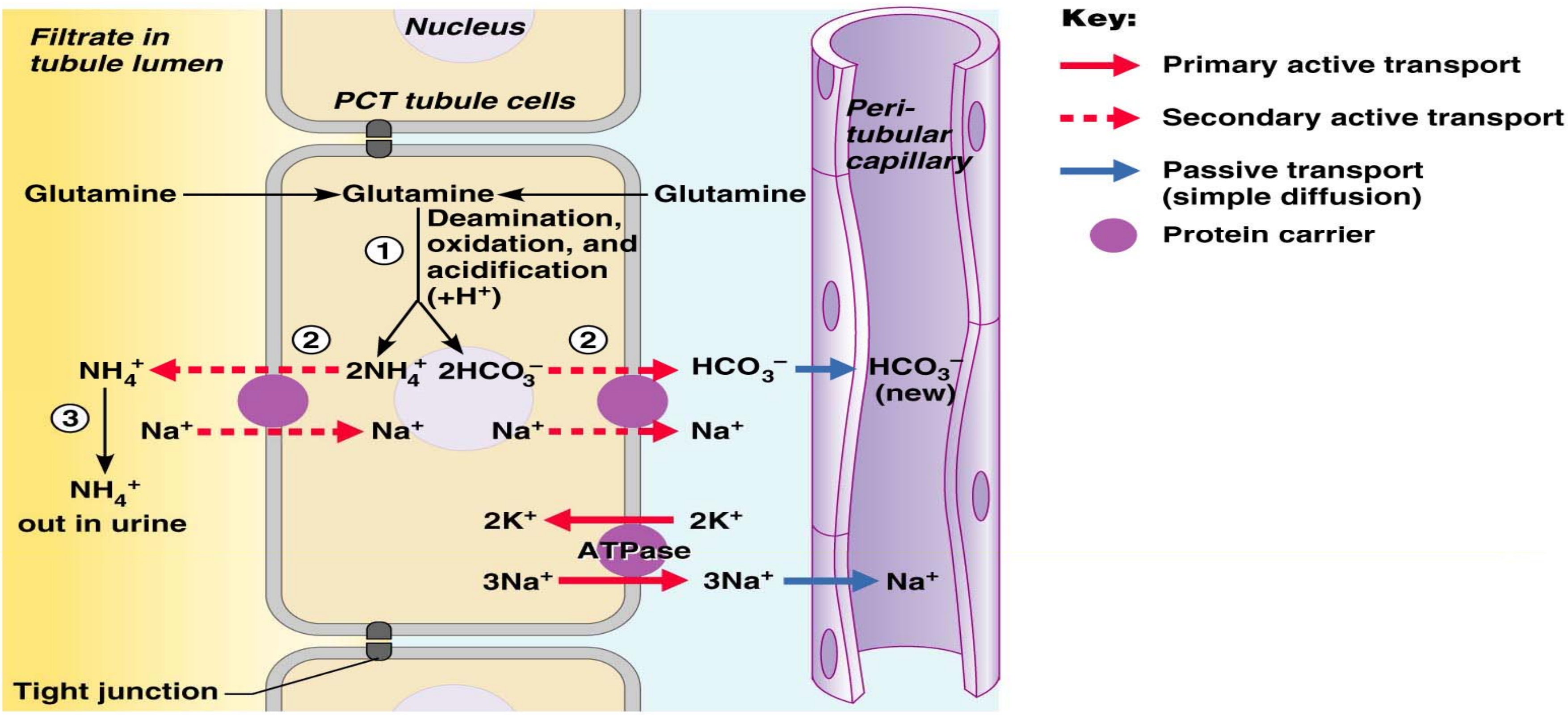

Filtrate in tubule lumen
Nucleus
PCT tubule cells
Peri-tubular capillary
Glutamine
Glutamine
Glutamine
Deamination, oxidation, and acidification (+H⁺)
1
2
2
NH_4^+
$2NH_4^+$
$2HCO_3^-$
HCO_3^-
HCO_3^- (new)
3
Na^+
Na^+
Na^+
Na^+
NH_4^+ out in urine
$2K^+$
$2K^+$
ATPase
$3Na^+$
$3Na^+$
Na^+
Tight junction
Key:
Primary active transport
Secondary active transport
Passive transport (simple diffusion)
Protein carrier

Figure 26.14

TABLE 26.1	Causes and Consequences of Electrolyte Imbalances		
ION	**ABNORMALITY (SERUM VALUE)**	**POSSIBLE CAUSES**	**CONSEQUENCES**
Sodium	Hypernatremia (Na^+ excess: >145 mEq/L)	Dehydration; uncommon in healthy individuals; may occur in infants or the confused aged (individuals unable to indicate thirst) or may be a result of excessive intravenous NaCl administration	Thirst: CNS dehydration leads to confusion and lethargy progressing to coma; increased neuromuscular irritability evidenced by twitching and convulsions
	Hyponatremia (Na^+ deficit: <135 mEq/L)	Solute loss, water retention, or both (e.g., excessive Na^+ loss through vomiting, diarrhea, burned skin, tubal drainage of stomach, and as a result of excessive use of diuretics); deficiency of aldosterone (Addison's disease); renal disease; excess ADH release; excess H_2O ingestion	Most common signs are those of neurologic dysfunction due to brain swelling. If sodium amounts are actually normal but water is excessive, the symptoms are the same as those of water excess: mental confusion; giddiness; coma if development occurs slowly; muscular twitching, irritability, and convulsions if the condition develops rapidly. In hyponatremia accompanied by water loss, the main signs are decreased blood volume and blood pressure (circulatory shock)
Potassium	Hyperkalemia (K^+ excess: >5.5 mEq/L)	Renal failure; deficit of aldosterone; rapid intravenous infusion of KCl; burns or severe tissue injuries which cause K^+ to leave cells	Nausea, vomiting, diarrhea; bradycardia; cardiac arrhythmias, depression, and arrest; skeletal muscle weakness; flaccid paralysis
	Hypokalemia (K^+ deficit: <3.5 mEq/L)	Gastrointestinal tract disturbances (vomiting, diarrhea), gastrointestinal suction; Cushing's disease; inadequate dietary intake (starvation); hyperaldosteronism; diuretic therapy	Cardiac arrhythmias, flattened T wave; muscular weakness; metabolic alkalosis; mental confusion; nausea; vomiting
Phosphate	Hyperphosphatemia (HPO_4^{2-} excess: >2.9 mEq/L)	Decreased urinary loss due to renal failure; hypoparathyroidism; major tissue trauma; increased intestinal absorption	Clinical symptoms arise because of reciprocal changes in Ca^{2+} levels rather than directly from changes in plasma phosphate concentrations
	Hypophosphatemia (HPO_4^{2-} deficit: <1.6 mEq/L)	Decreased intestinal absorption; increased urinary output; hyperparathyroidism	

Table 23.1.1

TABLE 26.1 Causes and Consequences of Electrolyte Imbalances *(continued)*

ION	ABNORMALITY (SERUM VALUE)	POSSIBLE CAUSES	CONSEQUENCES
Chloride	Hyperchloremia (Cl^- excess: >105 mEq/L)	Dehydration; increased retention or intake; metabolic acidosis; hyperparathyroidism	No direct clinical symptoms; symptoms generally associated with the underlying cause, which is often related to pH abnormalities
	Hypochloremia (Cl^- deficit: <95 mEq/L)	Metabolic alkalosis (e.g., due to vomiting or excessive ingestion of alkaline substances); aldosterone deficiency	
Calcium	Hypercalcemia (Ca^{2+} excess: >5.2 mEq/L or 10.5 mg%)*	Hyperparathyroidism; excessive vitamin D; prolonged immobilization; renal disease (decreased excretion); malignancy	Decreased neuromuscular excitability leading to cardiac arrhythmias and arrest, skeletal muscle weakness, confusion, stupor, and coma; kidney stones; nausea and vomiting
	Hypocalcemia (Ca^{2+} deficit: <4.5 mEq/L or 9 mg%)*	Burns (calcium trapped in damaged tissues); hypoparathyroidism; vitamin D deficiency; renal tubular disease; renal failure; hyperphosphatemia; diarrhea; alkalosis	Increased neuromuscular excitability leading to tingling of fingers, tremors, skeletal muscle cramps, tetany, convulsions; depressed excitability of the heart; osteomalacia; fractures
Magnesium	Hypermagnesemia (Mg^{2+} excess: >2.2 mEq/L)	Rare; occurs in renal failure when Mg is not excreted normally; excessive ingestion of Mg^{2+}-containing antacids	Lethargy; impaired CNS functioning, coma, respiratory depression; cardiac arrest
	Hypomagnesemia (Mg^{2+} deficit: <1.4 mEq/L)	Alcoholism; loss of intestinal contents, severe malnutrition; diuretic therapy	Tremors, increased neuromuscular excitability, tetany, convulsions

*1 mg% = 1 mg/100 ml

Table 26.1.2

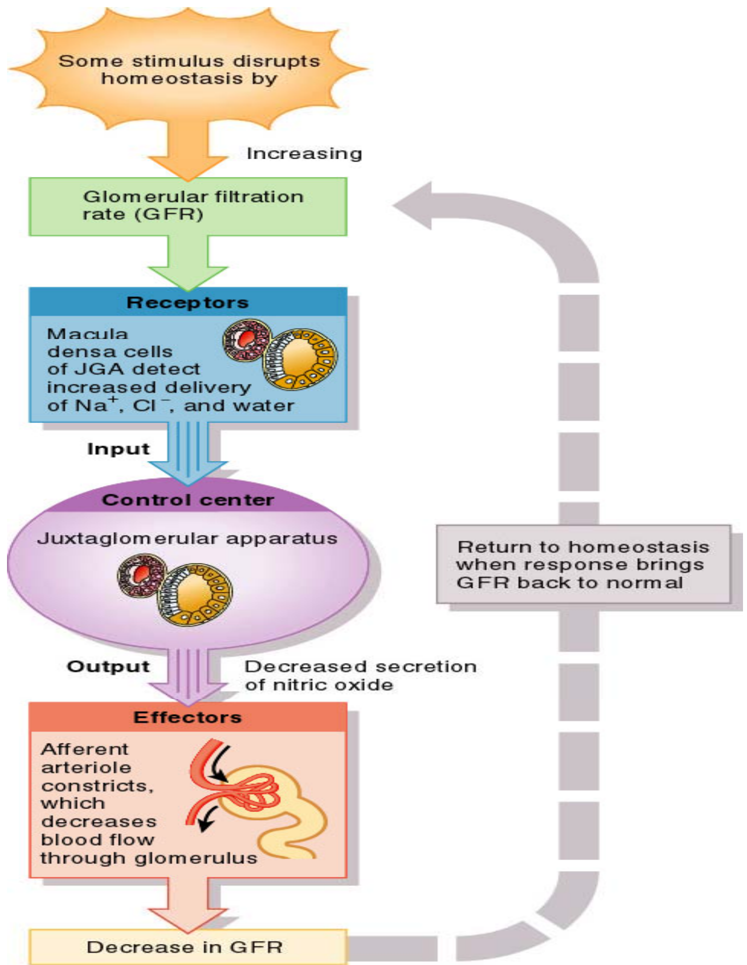
TABLE 26.2 Causes and Consequences of Acid-Base Imbalances

CONDITION AND HALLMARK	POSSIBLE CAUSES; COMMENTS
METABOLIC ACIDOSIS	
uncompensated (uncorrected) (HCO_3^- <22 mEq/L; pH <7.35)	**Severe diarrhea:** bicarbonate-rich intestinal (and pancreatic) secretions rushed through digestive tract before their solutes can be reabsorbed; bicarbonate ions are replaced by renal mechanisms that generate new bicarbonate ions **Renal disease:** failure of kidneys to rid body of acids formed by normal metabolic processes **Untreated diabetes mellitus:** lack of insulin or inability of tissue cells to respond to insulin, resulting in inability to use glucose; fats are used as primary energy fuel, and ketoacidosis occurs **Starvation:** lack of dietary nutrients for cellular fuels; body proteins and fat reserves are used for energy—both yield acidic metabolites as they are broken down for energy **Excess alcohol ingestion:** results in excess acids in blood **High ECF potassium concentrations:** potassium ions compete with H^+ for secretion in renal tubules; when ECF levels of K^+ are high, H^+ secretion is inhibited
METABOLIC ALKALOSIS	
uncompensated (HCO_3^- >26 mEq/L; pH >7.45)	**Vomiting or gastric suctioning:** loss of stomach HCl requires that H^+ be withdrawn from blood to replace stomach acid; thus H^+ decreases and HCO_3^- increases proportionately **Selected diuretics:** cause K^+ depletion and H_2O loss. Low K^+ directly stimulates the tubule cells to secrete H^+. Reduced blood volume elicits the renin-angiotensin mechanism, which stimulates Na^+ reabsorption and H^+ secretion. **Ingestion of excessive sodium bicarbonate (antacid):** bicarbonate moves easily into ECF, where it enhances natural alkaline reserve **Excess aldosterone** (e.g., adrenal tumors): promotes excessive reabsorption of Na^+, which pulls increased amount of H^+ into urine. Hypovolemia promotes the same relative effect because aldosterone secretion is increased to enhance Na^+ (and H_2O) reabsorption.

►

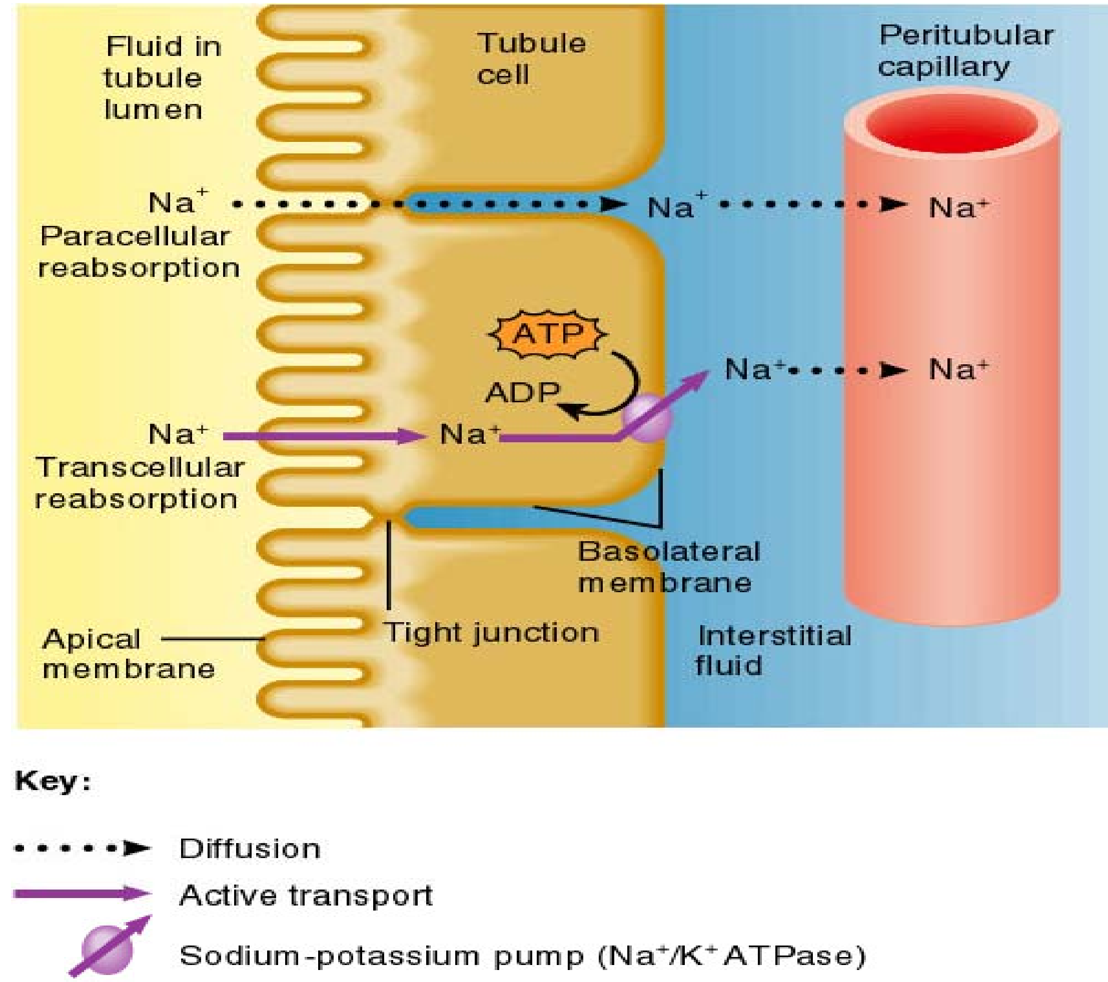
TABLE 26.2	Causes and Consequences of Acid-Base Imbalances *(continued)*
CONDITION AND HALLMARK	**POSSIBLE CAUSES; COMMENTS**
RESPIRATORY ACIDOSIS (HYPOVENTILATION)	
uncompensated (>45 mm Hg; pH <7.35)	**Impaired lung function** (e.g., in chronic bronchitis, cystic fibrosis, emphysema): impaired gas exchange or alveolar PCO_2 ventilation **Impaired ventilatory movement:** paralysis of respiratory muscles, chest injury, extreme obesity **Narcotic or barbiturate overdose or injury to brain stem:** depression of respiratory centers, resulting in hypoventilation and respiratory arrest
RESPIRATORY ALKALOSIS (HYPERVENTILATION)	
uncompensated (P_{CO_2} <35 mm Hg; pH >7.45)	**Strong emotions**: pain, anxiety, fear, panic attack **Hypoxia:** asthma, pneumonia, high altitude; represents effort to raise P_{O_2} at the expense of excessive CO_2 excretion **Brain tumor or injury**: abnormality of respiratory controls

Table 26.2.2



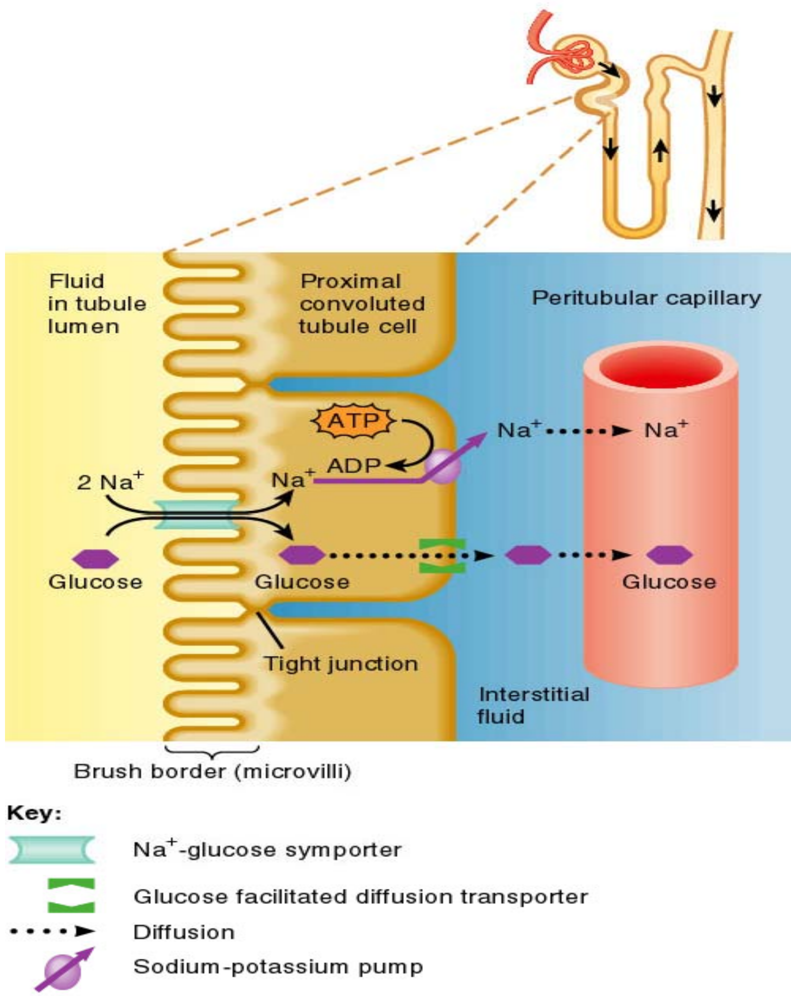
Some stimulus disrupts homeostasis by
Increasing
Glomerular filtration rate (GFR)
Receptors
Macula densa cells of JGA detect increased delivery of Na+, Cl−, and water
Input
Control center
Juxtaglomerular apparatus
Output
Decreased secretion of nitric oxide
Effectors
Afferent arteriole constricts, which decreases blood flow through glomerulus
Decrease in GFR
Return to homeostasis when response brings GFR back to normal

26.10

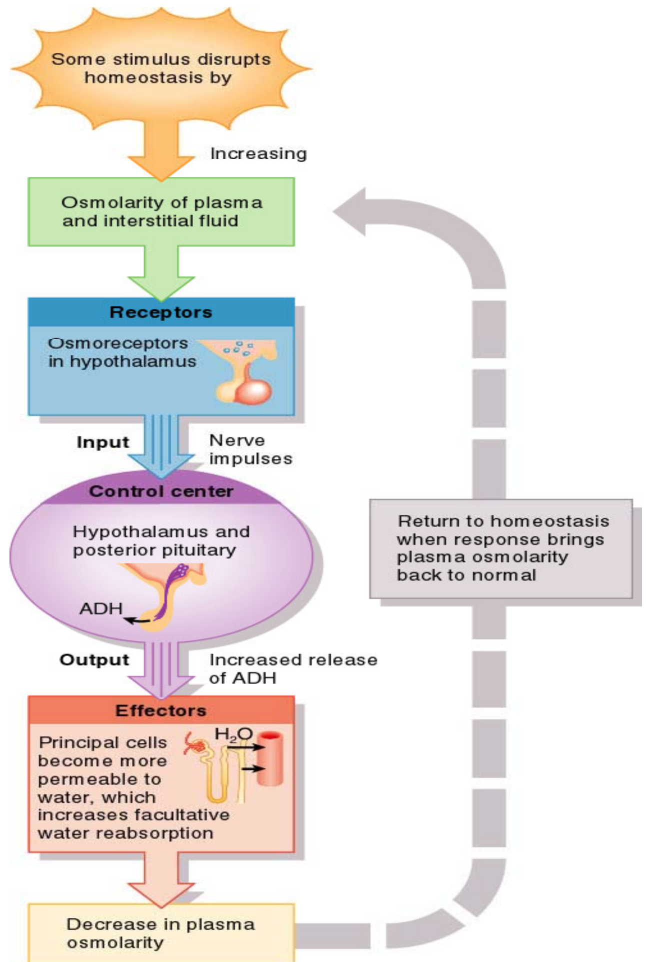


Fluid in tubule lumen
Tubule cell
Peritubular capillary
Na+
Paracellular reabsorption
Na+
Na+
ATP
ADP
Na+
Na+
Na+
Transcellular reabsorption
Na+
Basolateral membrane
Apical membrane
Tight junction
Interstitial fluid
Key:
Diffusion
Active transport
Sodium-potassium pump (Na+/K+ ATPase)

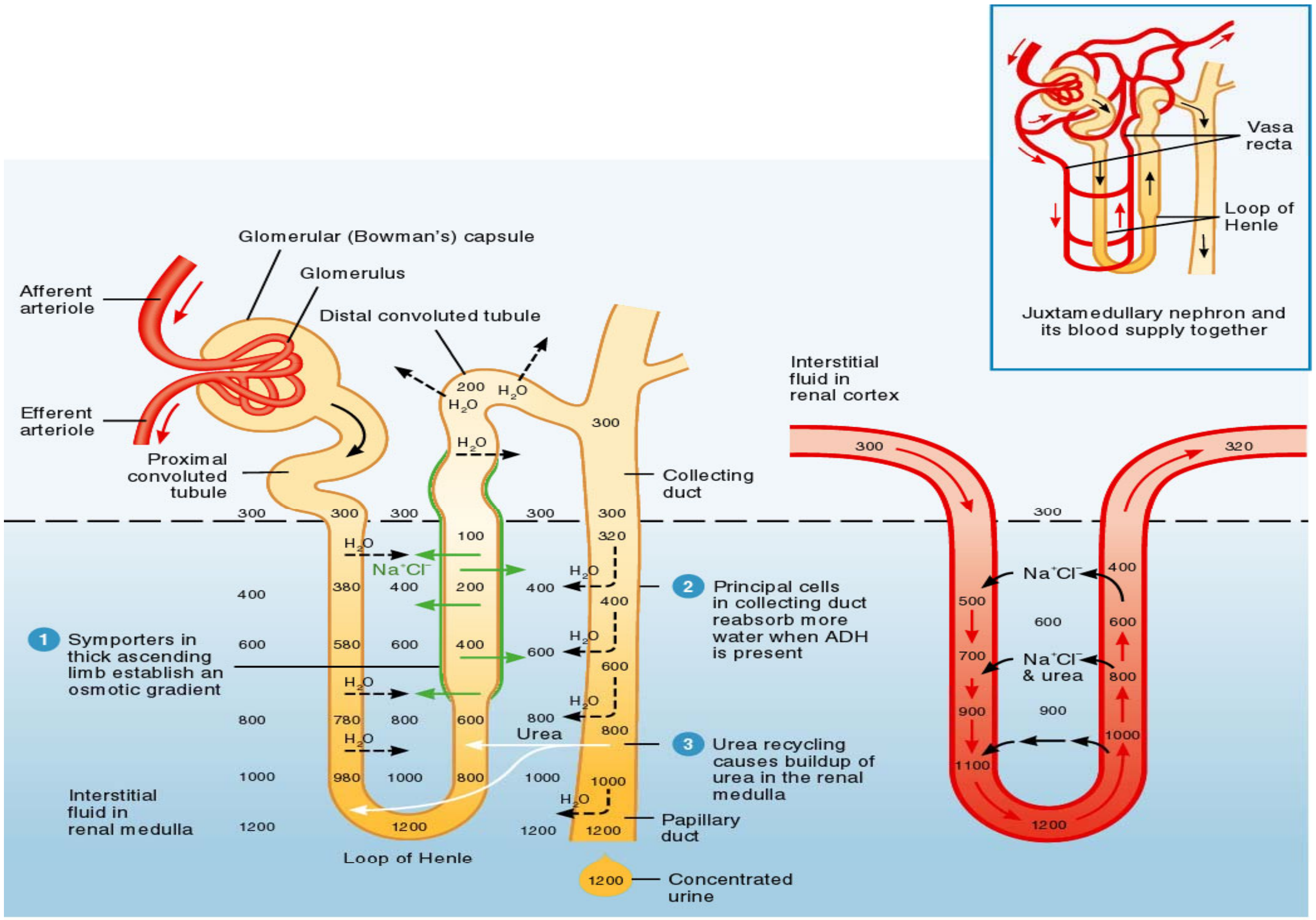
26.11


Fluid in tubule lumen
Proximal convoluted tubule cell
Peritubular capillary
ATP
ADP
Na^+
Na^+
Na^+
2 Na^+
Glucose
Glucose
Glucose
Tight junction
Interstitial fluid
Brush border (microvilli)
Key:
Na^+-glucose symporter
Glucose facilitated diffusion transporter
Diffusion
Sodium-potassium pump

26.12


Some stimulus disrupts homeostasis by
Increasing
Osmolarity of plasma and interstitial fluid
Receptors
Osmoreceptors in hypothalamus
Input
Nerve impulses
Control center
Hypothalamus and posterior pituitary
ADH
Output
Increased release of ADH
Effectors
H_2O
Principal cells become more permeable to water, which increases facultative water reabsorption
Decrease in plasma osmolarity
Return to homeostasis when response brings plasma osmolarity back to normal

26.17



(a) Reabsorption of Na^+, Cl^- and water in a long-loop juxtamedullary nephron

(b) Recycling of salts and urea in the vasa recta

26.19

PROXIMAL CONVOLUTED TUBULE

Reabsorption (into blood) of filtered:

Water	65% (osmosis)
Na^+	65% (sodium-potassium pumps, symporters, antiporters)
K^+	65% (diffusion)
Glucose	100% (symporters and facilitated diffusion)
Amino acids	100% (symporters and facilitated diffusion)
Cl^-	50% (diffusion)
HCO_3^-	80–90% (facilitated diffusion)
Urea	50% (diffusion)
Ca^{2+}, Mg^{2+}	variable (diffusion)

Secretion (into urine) of:

H^+	variable (antiporters)
NH_4^+	variable, increases in acidosis (antiporters)
Urea	variable (diffusion)
Creatinine	small amount

At end of PCT, tubular fluid is still isotonic to blood (300 mOsm/liter).

LOOP OF HENLE

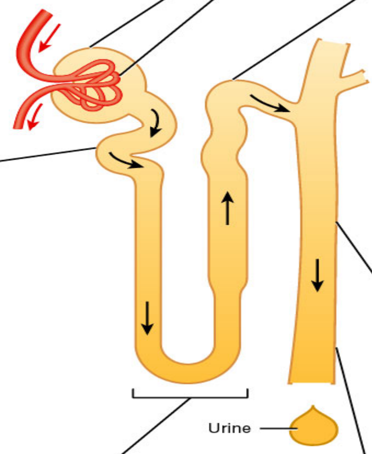
Reabsorption (into blood) of:

Water	15% (osmosis in descending limb)
Na^+	20–30% (symporters in ascending limb)
K^+	20–30% (symporters in ascending limb)
Cl^-	35% (symporters in ascending limb)
HCO_3^-	10–20% (facilitated diffusion)
Ca^{2+}, Mg^{2+}	variable (diffusion)

Secretion (into urine) of:

Urea	variable (recycling from collecting duct)

At end of loop of Henle, tubular fluid is hypotonic (100–150 mOsm/liter).



RENAL CORPUSCLE

Glomerular filtration rate: 105–125 mL/min of fluid that is isotonic to blood

Filtered substances: water and all solutes present in blood (except proteins) including ions, glucose, amino acids, creatinine, uric acid

DISTAL CONVOLUTED TUBULE

Reabsorption (into blood) of:

Water	10–15% (osmosis)
Na^+	5% (symporters)
Cl^-	5% (symporters)
Ca^{2+}	variable (stimulated by parathyroid hormone)

PRINCIPAL CELLS IN LATE DISTAL TUBULE AND COLLECTING DUCT

Reabsorption (into blood) of:

Water	5–9% (insertion of water channels stimulated by ADH)
Na^+	1–4% (sodium-potassium pumps)
Urea	variable (recycling to loop of Henle)

Secretion (into urine) of:

K^+	variable amount to adjust for dietary intake (leakage channels)

Tubular fluid leaving the collecting duct is dilute when ADH level is low and concentrated when ADH level is high.

INTERCALATED CELLS IN LATE DISTAL TUBULE AND COLLECTING DUCT

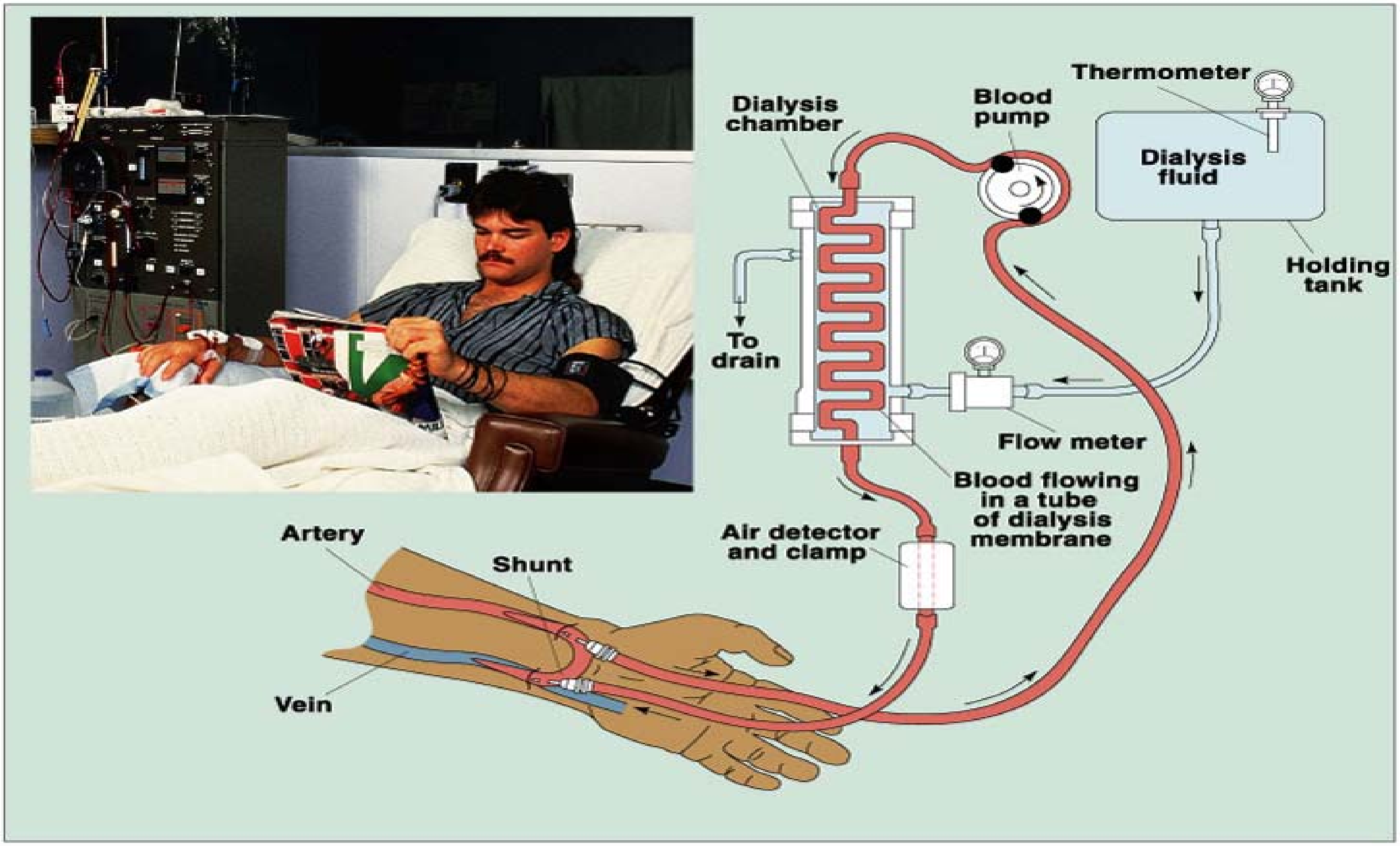
Reabsorption (into blood) of:

HCO_3^- (new)	varible amount, depends on H^+ secretion (antiporters)
Urea	variable (recycling to loop of Henle)

Secretion (into urine) of:

H^+	variable amounts to maintain acid-base homeostasis (H^+ pumps)

26.20

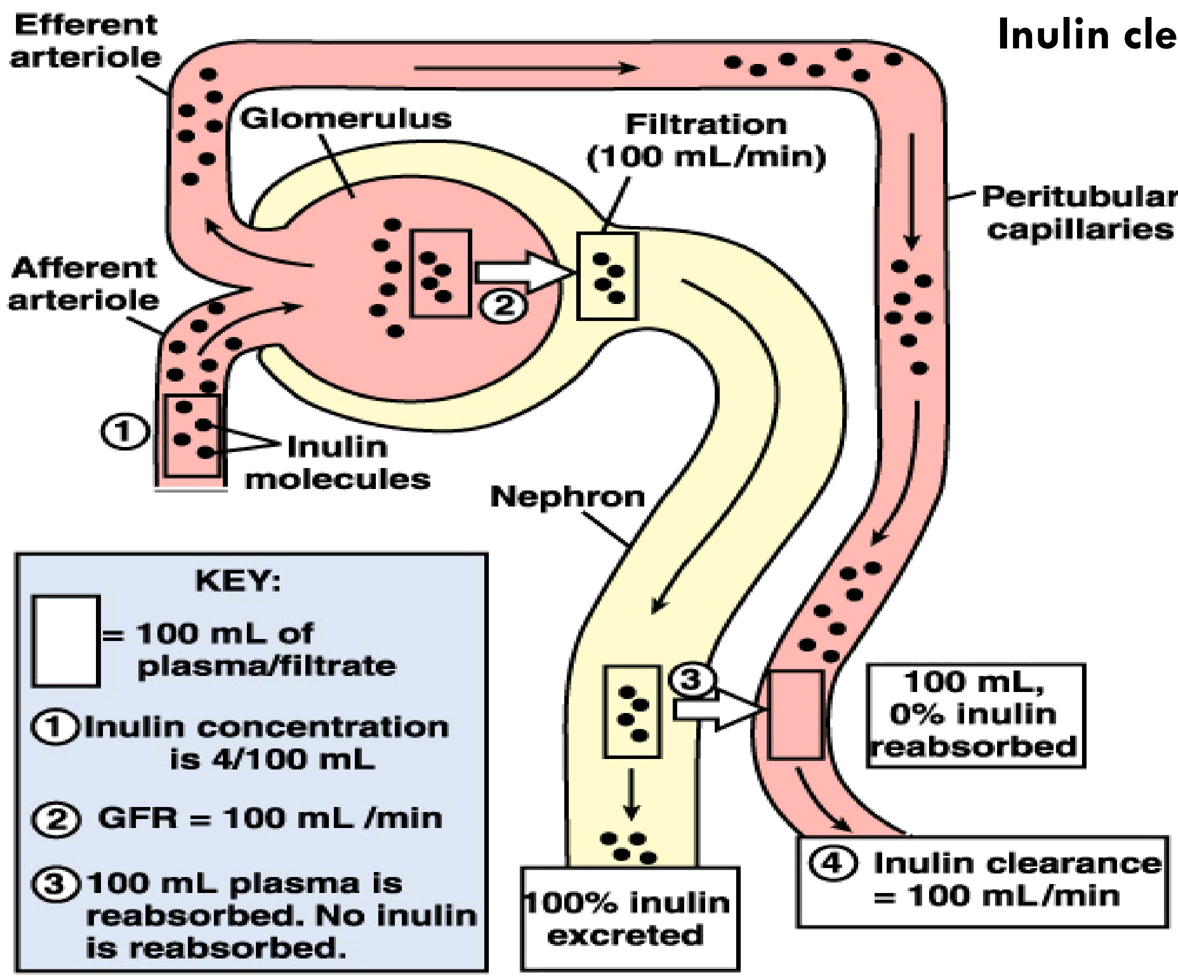


Thermometer
Dialysis chamber
Blood pump
Dialysis fluid
Holding tank
To drain
Flow meter
Blood flowing in a tube of dialysis membrane
Air detector and clamp
Artery
Shunt
Vein

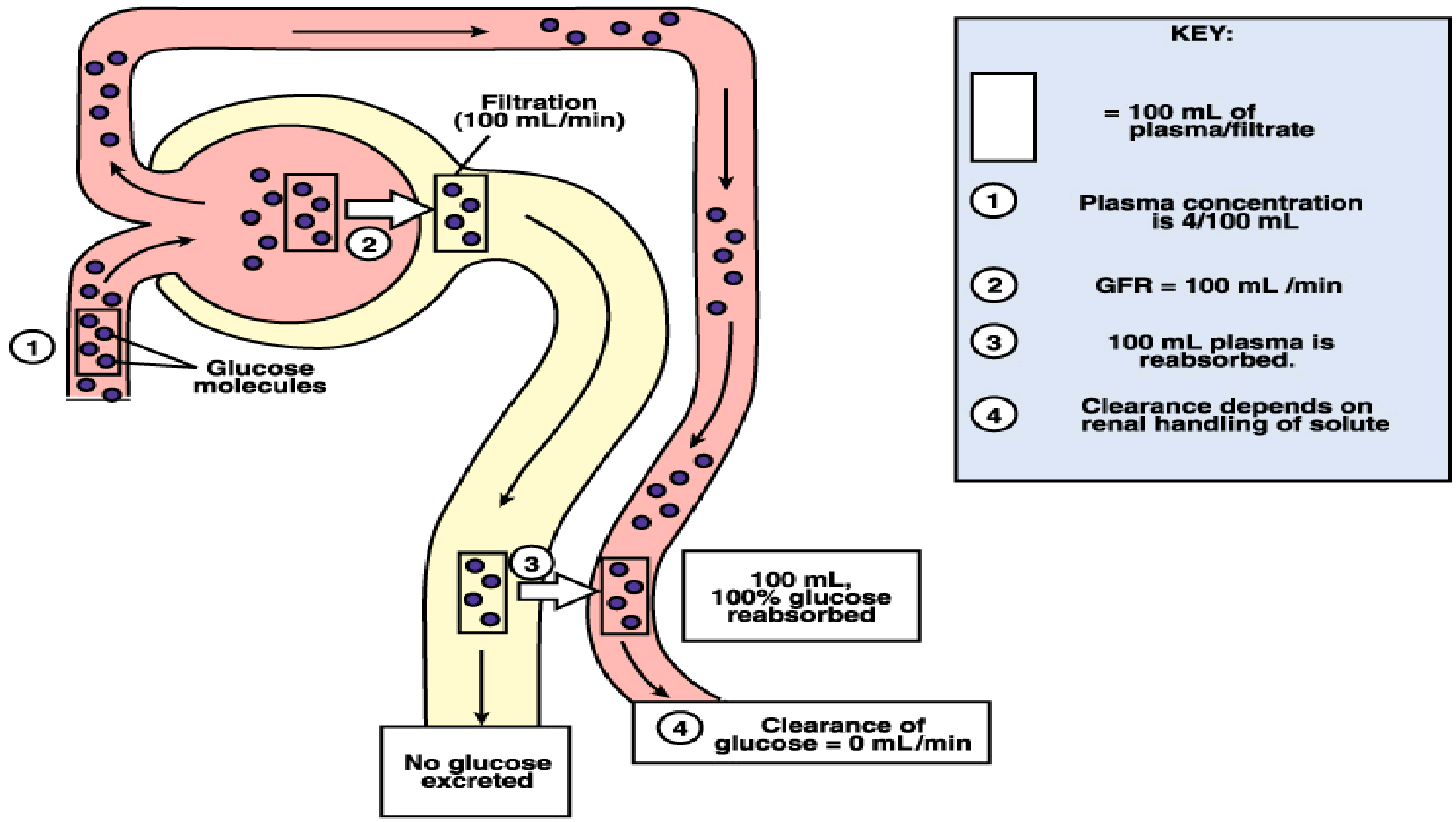
Normal Constituents of Urine

- Urea – from metabolism of amino acids
- Creatinine – from creatine metabolism
- Uric acid – from catabolism of nucleic acids
- Urobilinogen – breakdown of hemoglobin
- Hippuric acid, indican, and ketone bodies
- Other substances and inorganic molecules

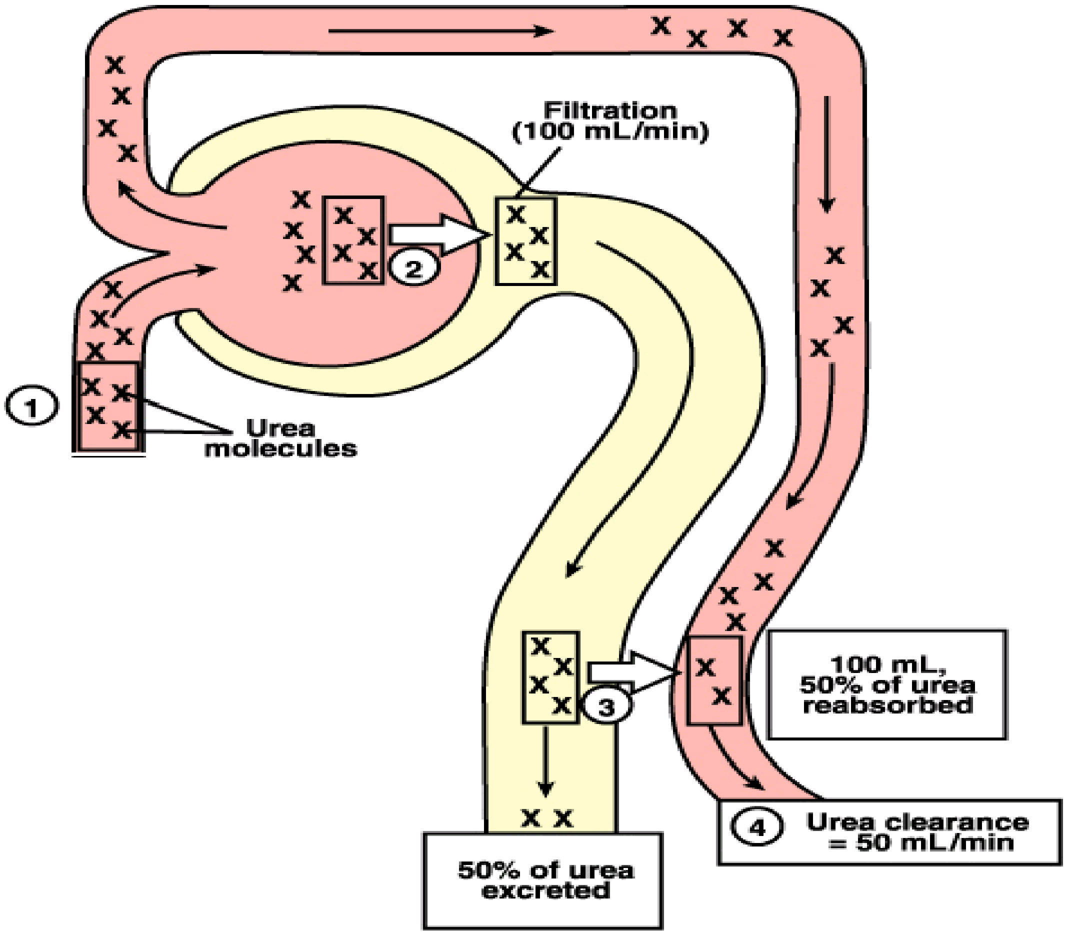
Inulin clearance



Glucose clearance



Urea clearance



KEY:

- ▭ = 100 mL of plasma/filtrate
- (1) Plasma concentration is 4/100 mL
- (2) GFR = 100 mL /min
- (3) 100 mL plasma is reabsorbed.
- (4) Clearance depends on renal handling of solute