Renal physiology

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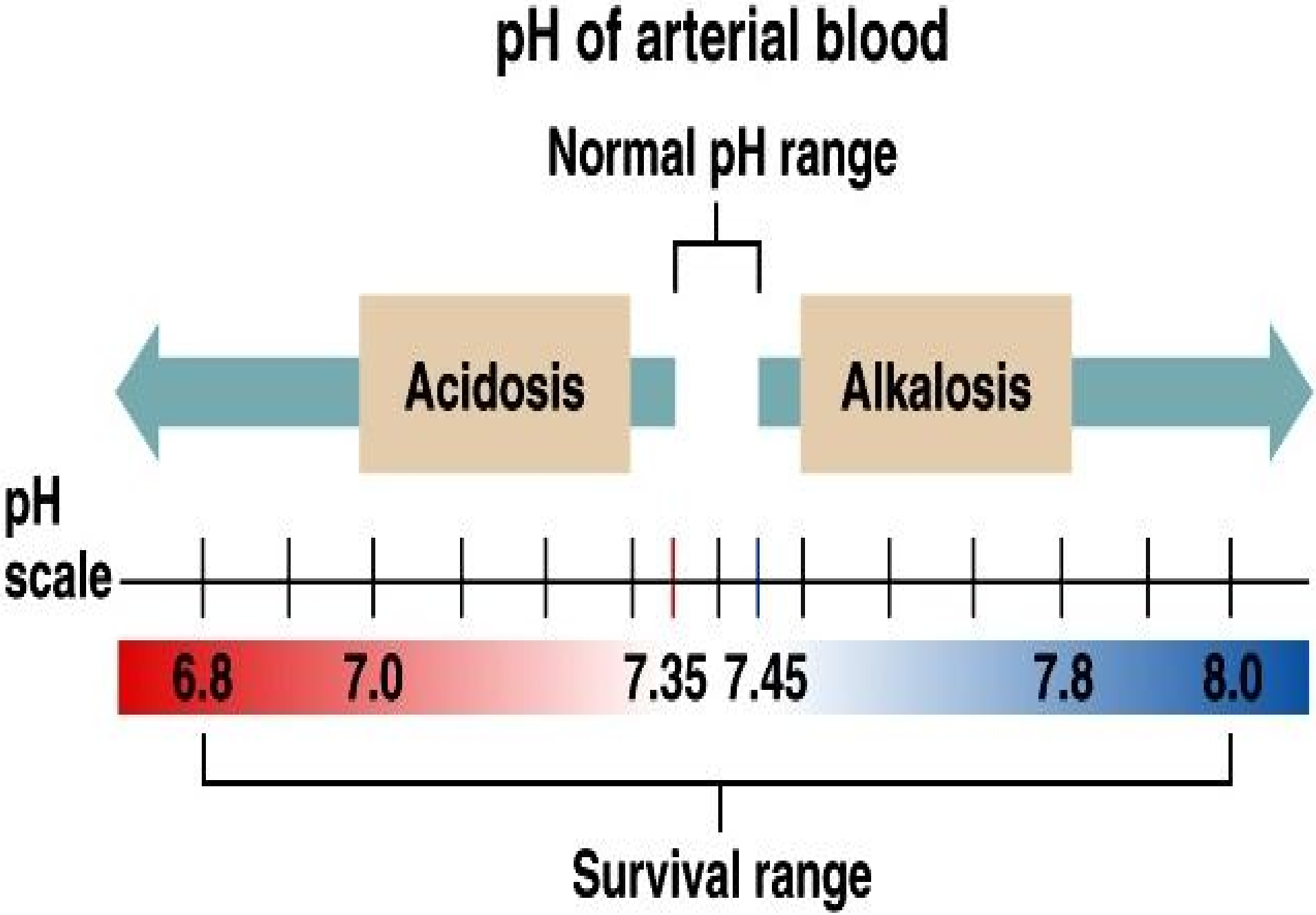
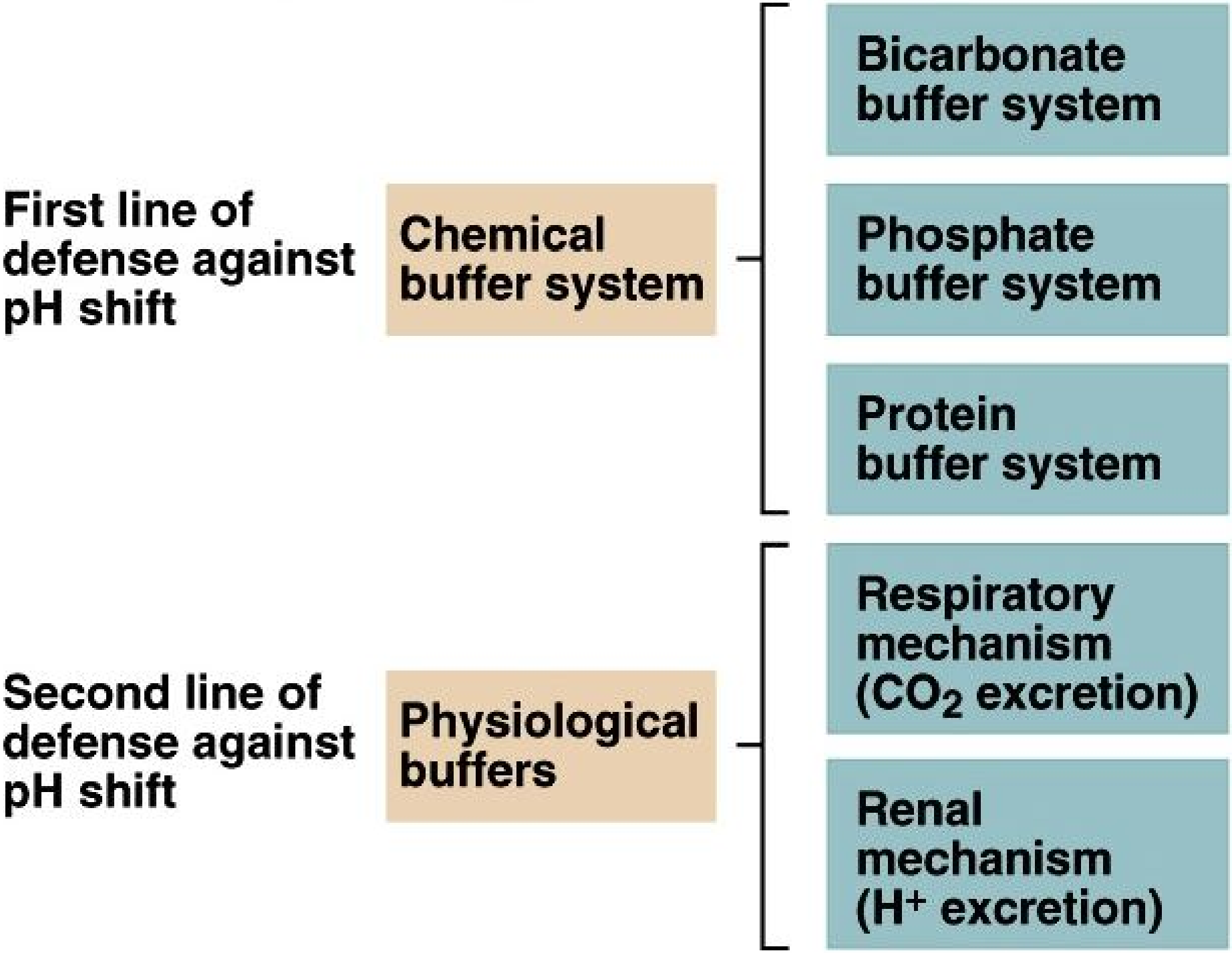
Functions

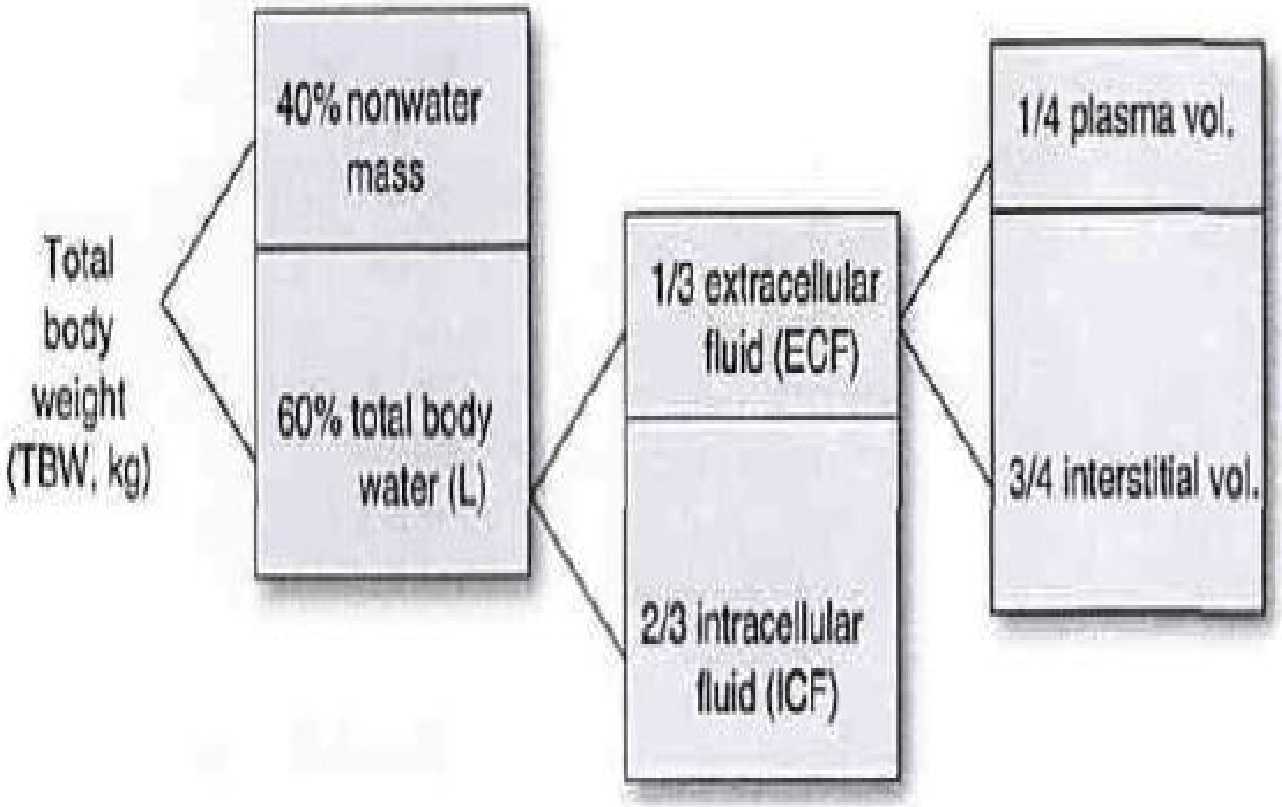
- **Regulating blood ionic composition**
- **Regulating blood pH**
- **Regulating blood volume**
- **Regulating blood pressure**
- **Produce calcitrol and erythropoietin**
- **Regulating blood glucose**
- **Excreting wastes**

Urinary excretion rate = Filtration rate -Reabsorption rate + Secretion rate


pH of arterial blood
Normal pH range
Acidosis
Alkalosis
pH
scale
6.8
7.0
7.35
7.45
7.8
8.0
Survival range


First line of defense against pH shift
Chemical buffer system
Bicarbonate buffer system
Phosphate buffer system
Protein buffer system
Second line of defense against pH shift
Physiological buffers
Respiratory mechanism (CO_2 excretion)
Renal mechanism (H^+ excretion)

Fluid compartments



ECF: ↑ NaCl, ↓ K^+.

ICF: ↑ K^+, ↓ NaCl

(HIKIN': HIgh K INtracellular).

TBW – ECF = ICF.

ECF – PV = interstitial volume.

60–40–20 rule (% of body weight):

60% total body water

40% ICF

20% ECF

Plasma volume measured by radiolabeled albumin.

Extracellular volume measured by inulin.

Osmolarity = 290 mOsm.

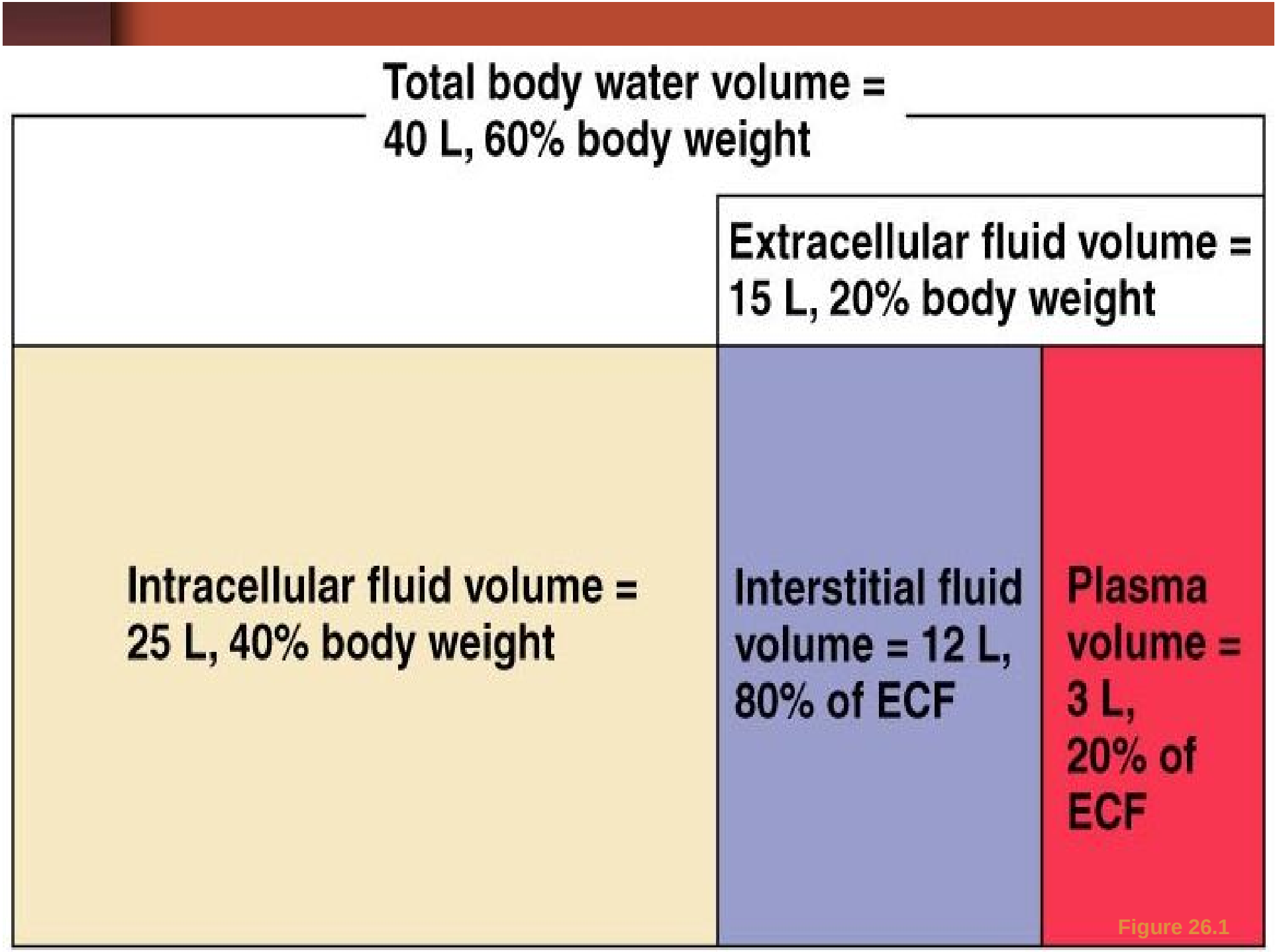
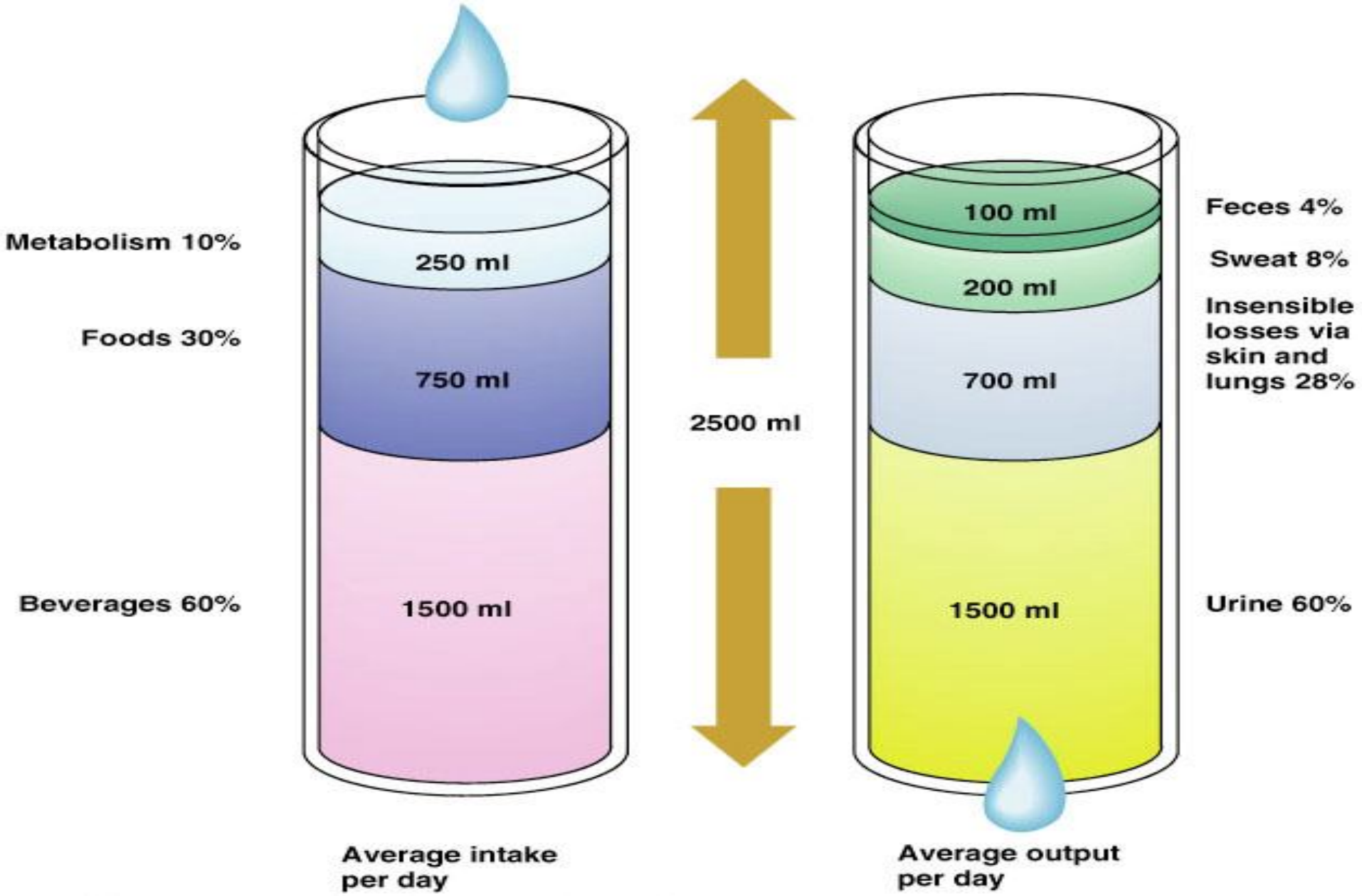
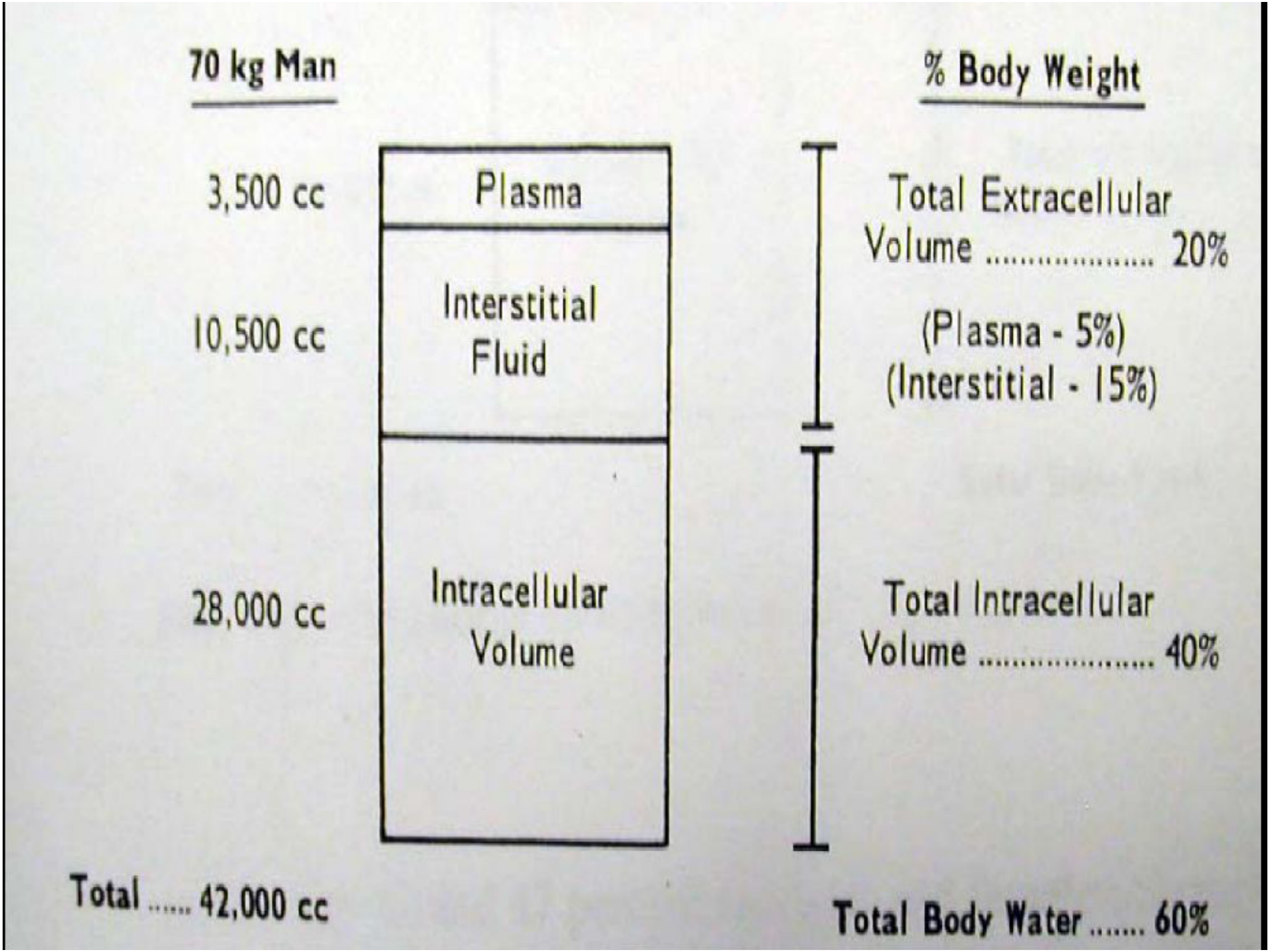
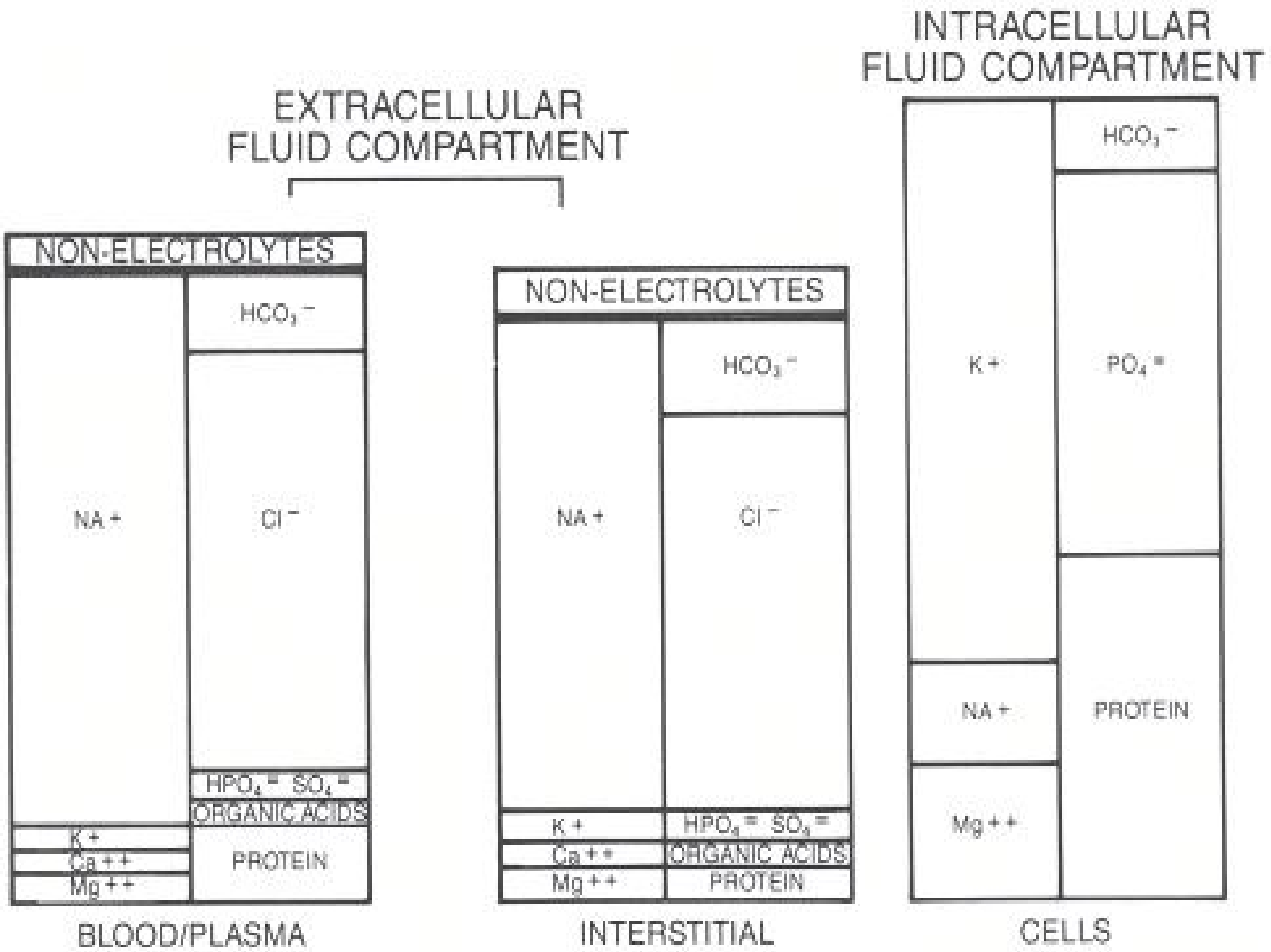

Total body water volume =
40 L, 60% body weight
Extracellular fluid volume =
15 L, 20% body weight
Intracellular fluid volume =
25 L, 40% body weight
Interstitial fluid volume = 12 L, 80% of ECF
Plasma volume = 3 L, 20% of ECF

Figure 26.1

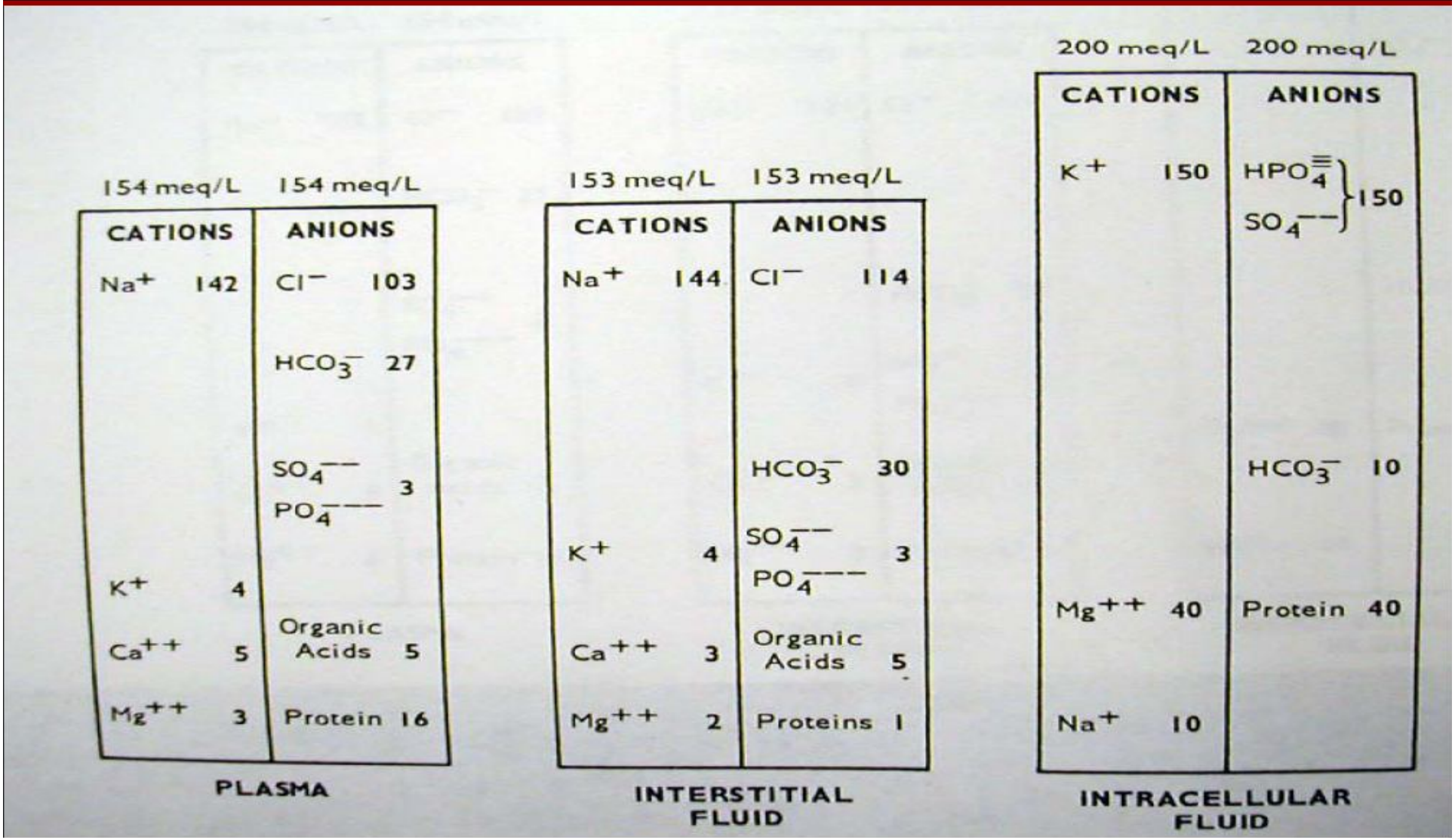
Fluid Balance



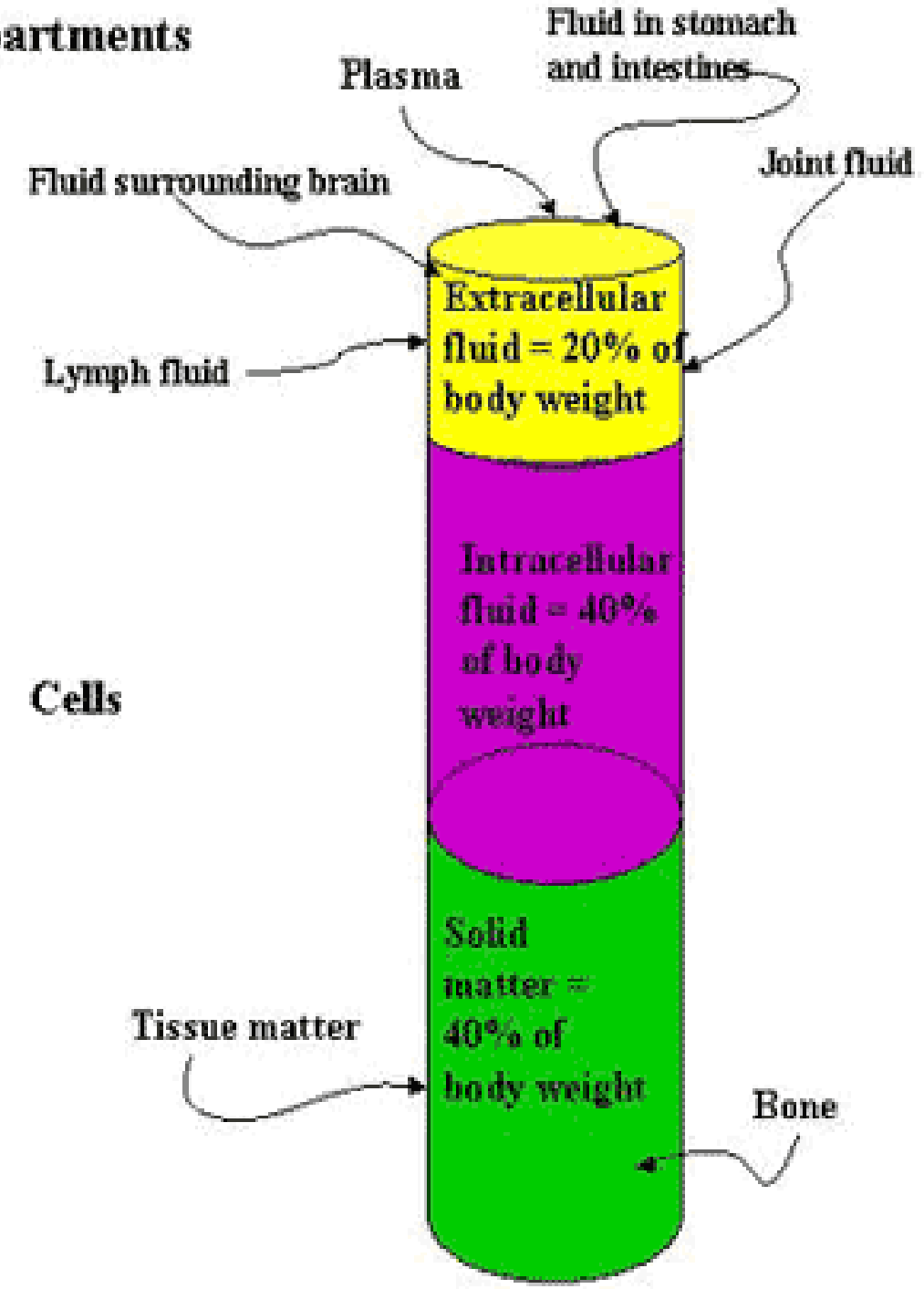

70 kg Man
% Body Weight
3,500 cc
Plasma
10,500 cc
Interstitial Fluid
28,000 cc
Intracellular Volume
Total Extracellular Volume 20%
(Plasma - 5%)
(Interstitial - 15%)
Total Intracellular Volume 40%
Total ..... 42,000 cc
Total Body Water 60%


EXTRACELLULAR FLUID COMPARTMENT
INTRACELLULAR FLUID COMPARTMENT
NON-ELECTROLYTES
HCO3 -
NA +
Cl -
HPO4 = SO4 =
ORGANIC ACIDS
K +
Ca ++
Mg ++
PROTEIN
BLOOD/PLASMA
NON-ELECTROLYTES
HCO3 -
NA +
Cl -
K +
Ca ++
Mg ++
HPO4 = SO4 =
ORGANIC ACIDS
PROTEIN
INTERSTITIAL
HCO3 -
K +
PO4 =
NA +
Mg ++
PROTEIN
CELLS

FLUID COMPARTMENT COMPOSITION

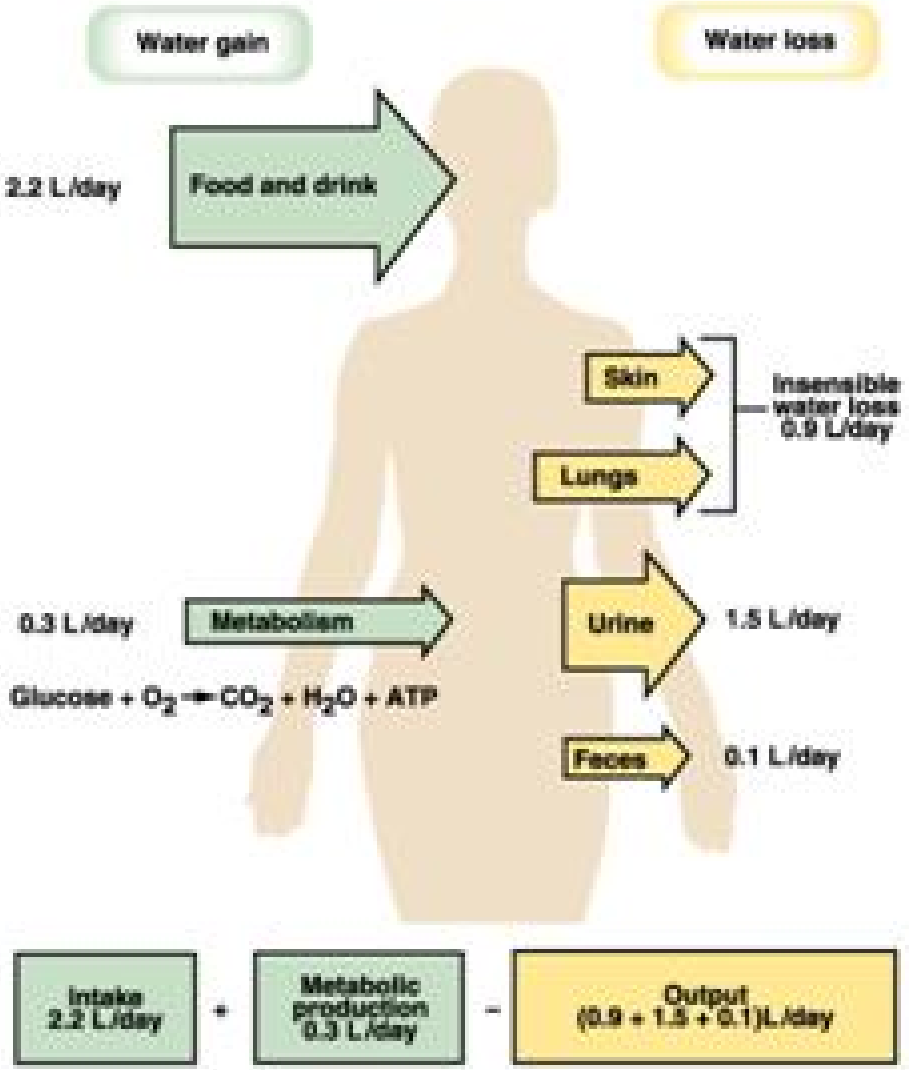


Body Fluid Compartments



Water Steady State

- Amount Ingested = Amount Eliminated



- Pathological losses
  - ✓vascular bleeding (H20, Na+)
  - ✓vomiting (H20, H+)
  - ✓diarrhea (H20, HCO3-).

OSMOLARITY, HYDROSTATIC, ONCOTIC THOSE WHO DECIDE WHICH WAY FLUIDS GO

- 2 X NA + = INDEX OF EC OSMOLARITY

- OSMOLALITY=

2[NA +K] + BUN/2.8 GLUCOSE/18

WHEN ECF OSMOLARITY INCREASES CELLS SHRINK
WHEN ECF OSMOLARITY DECREASES CELLS SWELL

IN A NORMAL WORLD [H2O] INTRACELLULAR = EC [H2O]
CAN KILL GIVING IV WATER CELL BURST NO NA IN WATER.

Body Fluid Compartments

- **Total body water - 50-60 % of body weight**
  - **decrease with age, gender and obesity**
- **Intracellular water - 40% of body weight**
  - **75 trillion cells**
  - **Similar composition in different species**
- **Extracellular water - 20% of body weight**
  - **% is important in fluid therapy**
  - **Transcellular accounts for ~ 1-2 liters**

- BODY WATER DEFICIT = DESIRED TBW – CURRENT TBW
- DESIRED TBW = $\frac{\text{measured serum } Na^+ \text{ x current TBW}}{\text{NORMAL SERUM } Na^+}$
- CURRENT TBW = 0.6 X CURRENT BODY WEIGHT [KG]

Serum Values of Electrolytes

Cations (+)	**Concentration**
Sodium	**135 – 145 mEq/L**
Potassium	**3.5 - 4.5 mEq/L**
Calcium	**9-10.5 mg/dL**
Magnesium	**1.5 - 2.5 mEq/L**
Anions (-)	
Chloride	**95 – 107 mEq/L**
CO2	**24 – 30 mEq/L**
Phosphate	**2.5 - 4.5 mEq/L**
HCO_3	**22 – 26 mEq/L**

Daily Requirements for Electrolytes

- **Sodium: 1-2 mEq/kg/d**
- **Potassium: 0.5-1 mEq/kg/d**
- **Calcium: 800 - 1200 mg/d**
- **Magnesium: 300 - 400 mg/d**
- **Phosphorus: 800 - 1200 mg/d**

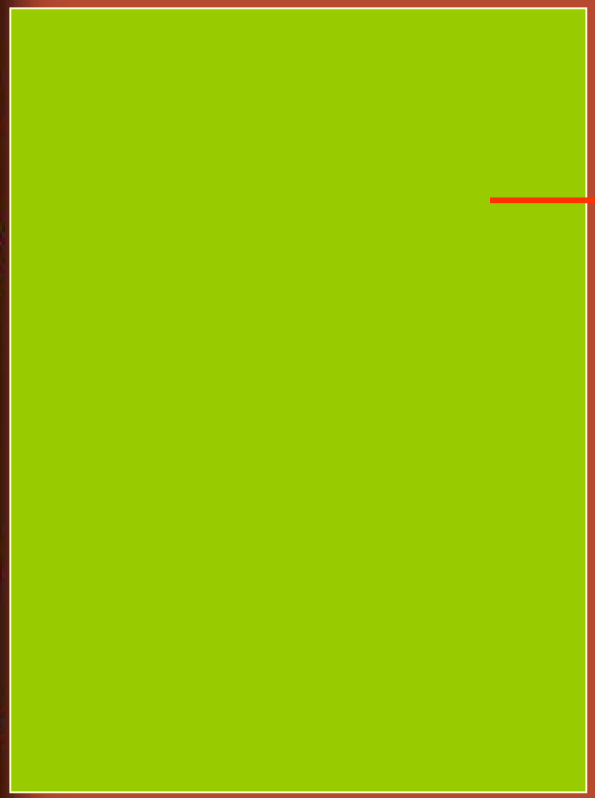
Function	Mechanism	Affected Elements
•Waste Excretion	Glomerular filtration	Nitrogenous products of protein metabolism (urea, Cr)
	Tubular secretion	Organic acids (urate) Organic bases (Cr)
	Tubular catabolism	Drugs (antibiotics, diuretics) Peptide hormones (most pituitary hormones, insulin, glucagon)
•Electrolyte Balance	Tubular NaCl absorption	Volume status, osmolar balance
	Tubular water reabsorption	Osmolar balance
	Tubular K secretion	Potassium concentration
	Tubular H secretion	Acid-base balance
	HCO_3 synthesis and reabsorption	
	Tubular Ca, Mg, PO_4 transport	Ca, Mg, PO_4 homeostasis

•Hormonal Synthesis	Erythropoietin production (cortex)	Red blood cell mass
	Vitamin D activation	Calcium homeostasis
	Renin production (JG apparatus)	Vascular resistance, aldosterone secretion
•Blood Pressure Regulation	Altered sodium excretion	ECF volume
	Renin production	Vascular resistance
•Glucose Homeostasis	Gluconeogenesis (from lactate, pyruvate, amino acids)	Glucose supply maintained in prolonged starvation

Osmolality and Osmotic Pressure

- Fluid concentration (osmolality) create osmotic pressure (pull)
- Normal
  - Serum osmolality 275 to 295 mOsm/L
  - Urine osmolality

Osmotic / oncotic pressure

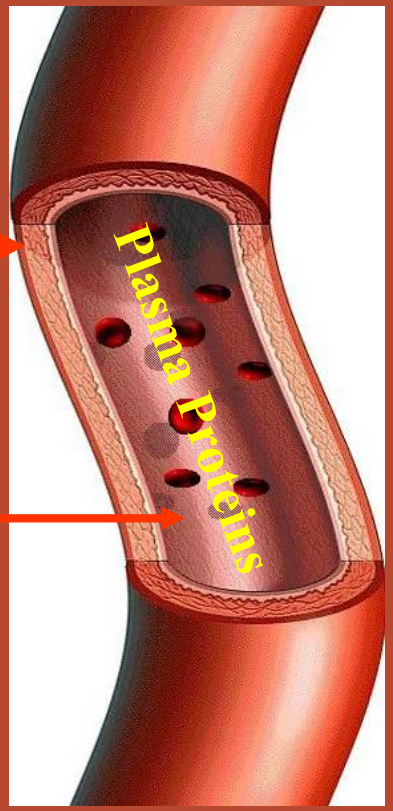


H_2O

Colloidal Osmotic Pressure

Na

Diffusion allows Na to move freely between intravascular and interstial spaces



PP

Intracellular Interstitial Intravascular

Body Systems Controlling Fluid and Electrolyte Balance

- Renal
- Endocrine
  - ADH
  - Aldosterone
- Gastrointestinal

Components of Glomerular Filtration Barrier

1. Capillary endothelial cells
2. Glomerular basement membrane
3. Visceral epithelial cells (podocytes)

Filtration is based on charge and pore size.

Urine production maintains homeostasis

- Regulating blood volume and composition
- Excreting waste products
  - Urea
  - Creatinine
  - Uric acid

Basic processes of urine formation

- Filtration
  - Blood pressure
  - Water and solutes across glomerular capillaries
- Reabsorption
  - The removal of water and solutes from the filtrate
- Secretion
  - Transport of solutes from the peritubular fluid into the tubular fluid

Carrier Mediated Transport

- Filtration in the kidneys modified by carrier mediated transport
  - Facilitated diffusion
  - Active transport
  - Cotransport
  - Countertransport
- Carrier proteins have a transport maximum (T_m)
  - Determines renal threshold

Reabsorption and secretion

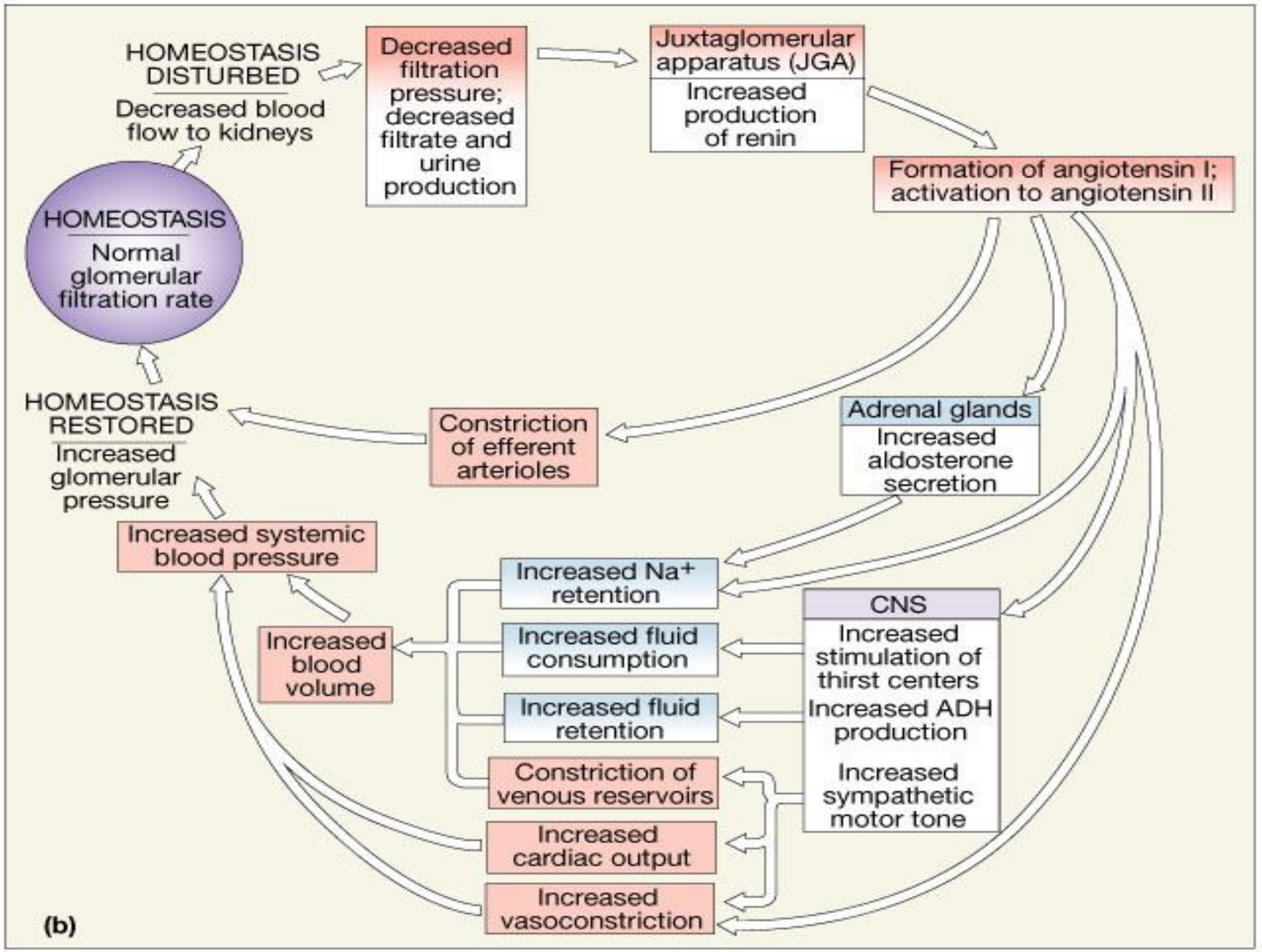
- Accomplished via diffusion, osmosis, and carrier-mediated transport
- T_m determines renal threshold for reabsorption of substances in tubular fluid

Urine Concentration

- Isothenuric- Urine concentration equal to blood plasma concentration
- **Concentrated** - urine concentration greater than that of the blood plasma
- **Dilute** - urine less concentrated than the blood plasma

Urine production maintains homeostasis

- Regulating blood volume and composition
- Excreting waste products
  - Urea
  - Creatinine
  - Uric acid


HOMEOSTASIS DISTURBED
Decreased blood flow to kidneys
Decreased filtration pressure; decreased filtrate and urine production
Juxtaglomerular apparatus (JGA)
Increased production of renin
Formation of angiotensin I; activation to angiotensin II
HOMEOSTASIS
Normal glomerular filtration rate
HOMEOSTASIS RESTORED
Increased glomerular pressure
Constriction of efferent arterioles
Adrenal glands
Increased aldosterone secretion
Increased systemic blood pressure
Increased Na+ retention
CNS
Increased blood volume
Increased fluid consumption
Increased stimulation of thirst centers
Increased fluid retention
Increased ADH production
Constriction of venous reservoirs
Increased sympathetic motor tone
Increased cardiac output
Increased vasoconstriction
(b)

Secretion of hormones

- **Secretion of *erythropoietin*,** which regulates red blood cell production in the bone marrow.

- **Secretion of *renin***, which is a key part of the renin-angiotensin-aldosterone system. (Technically, though, renin is not a hormone, it is an enzyme.)

- **Secretion of the active form of vitamin D (calcitriol) and prostaglandins.**

aldosterone, which stimulates active sodium reabsorption (and water as a result)

antidiuretic hormone, which stimulates passive water reabsorption

Both hormones exert their effects principally on the collecting ducts.

Antidiuretic hormone and the mineralcorticoids

Synthesis of ADH

- ADH synthesized in the cell bodies of hypothalamic neurons in the supraoptic nucleus
- ADH is stored in the neurohypophysis (posterior pituitary)—forms the most readily released ADH pool

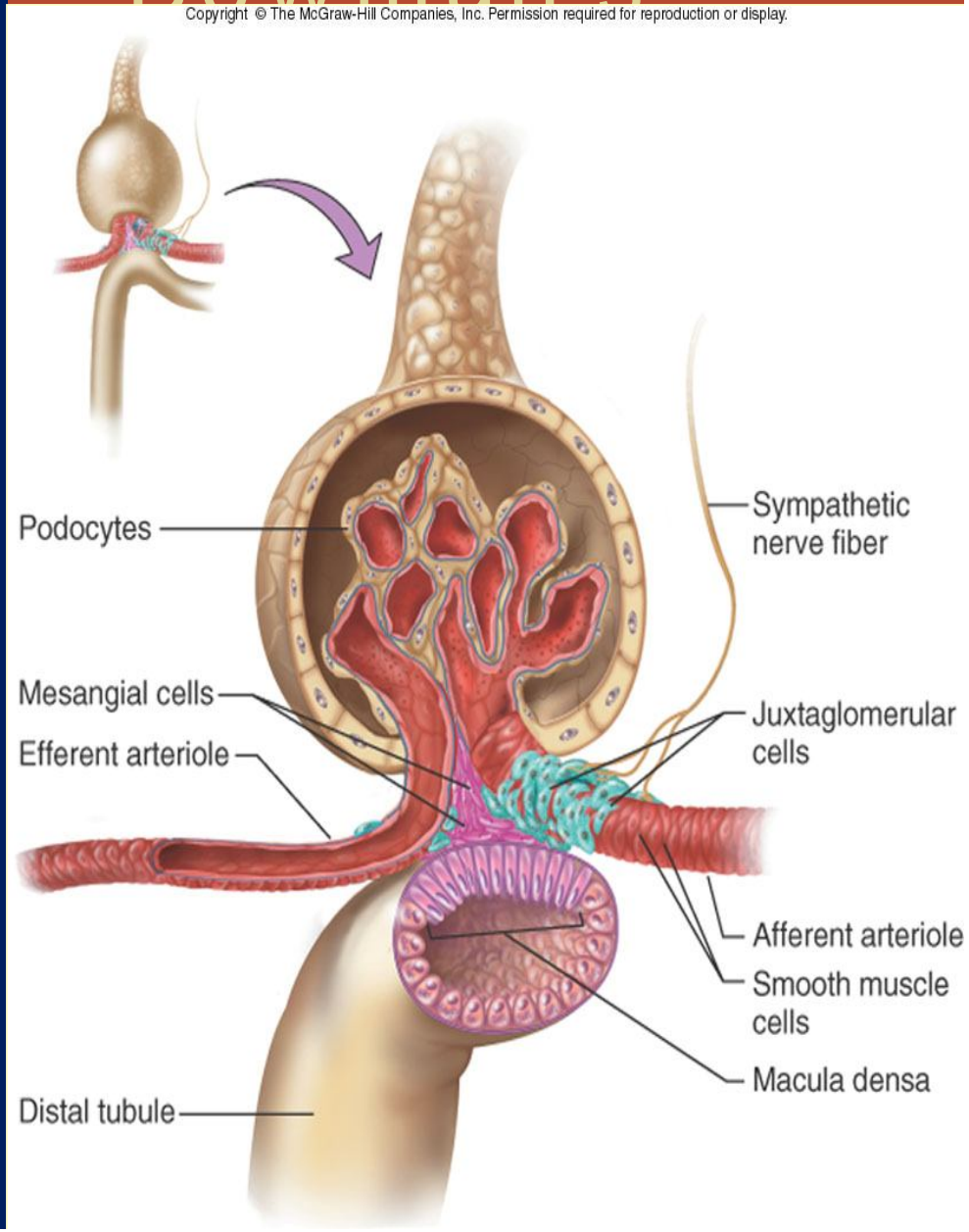
ADH is also known as arginine vasopressin (AVP = ADH) because of its vasopressive activity, but its major effect is on the kidney in preventing water loss.

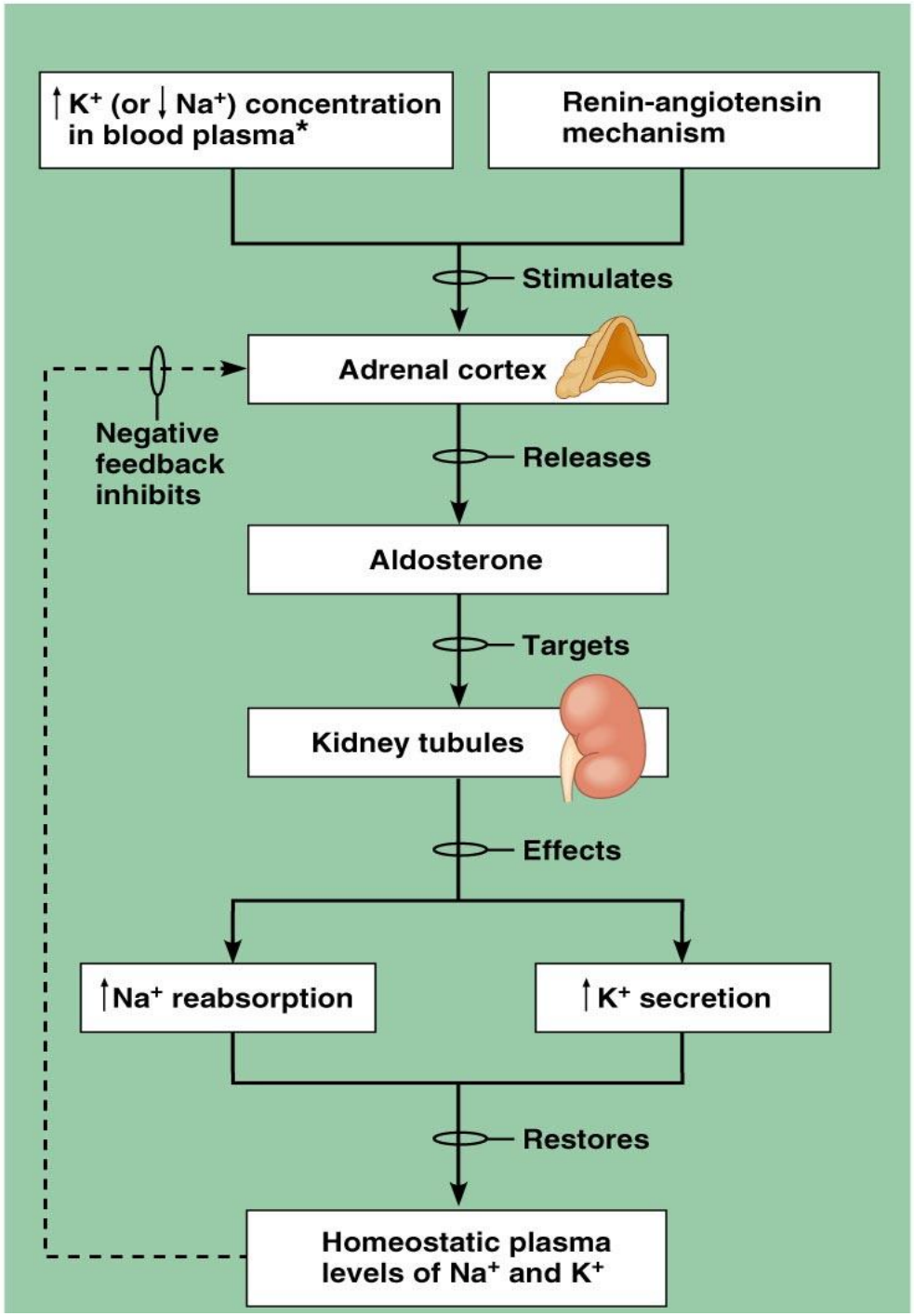
ADH

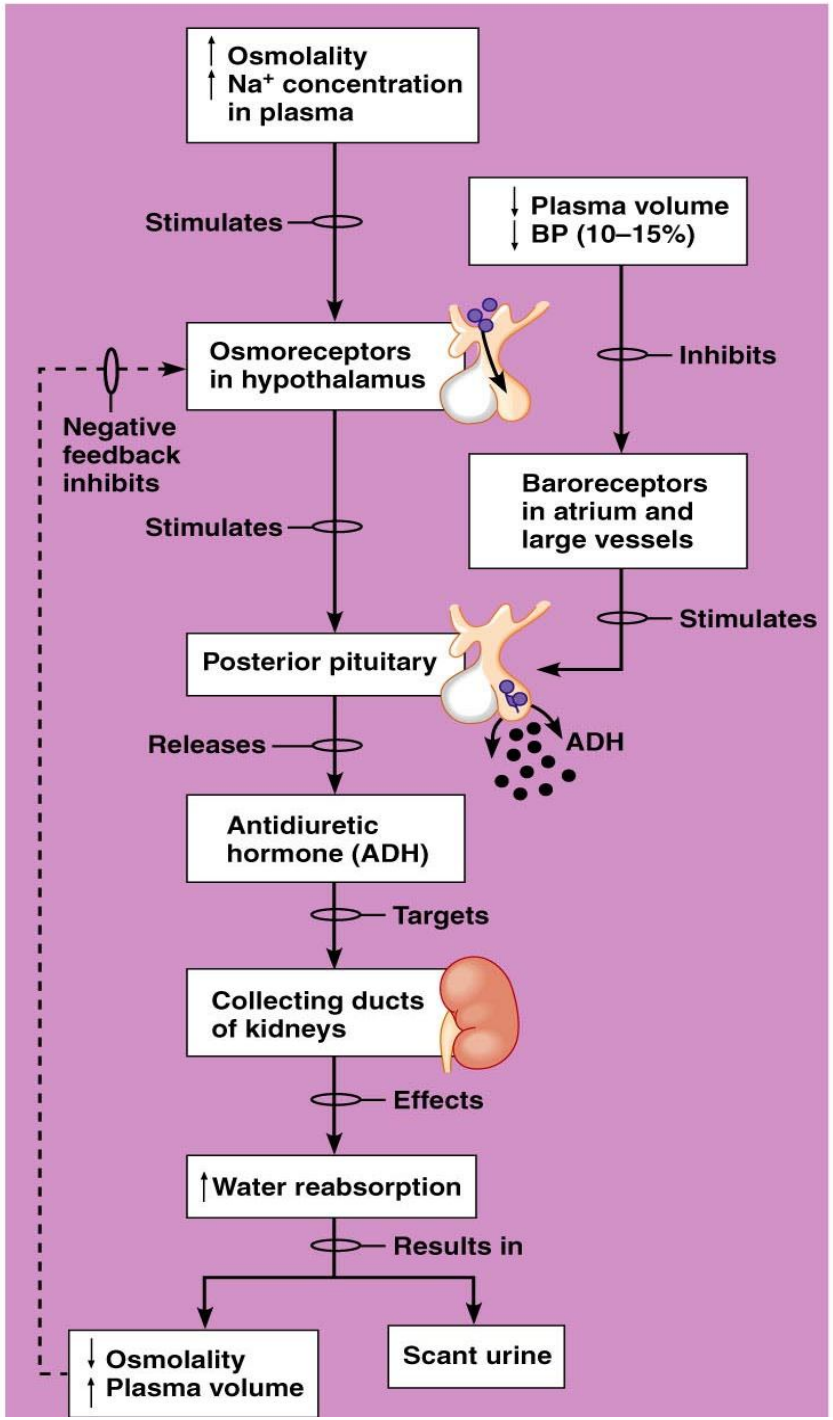
- **Regulated by osmotic and volume stimuli**
- **Water deprivation increases osmolality of plasma which activates hypothalmic osmoreceptors to stimulate ADH release**

Glomerulus and Bowman's

- Glomerular filtrate drains into Bowman's space, and then into proximal convoluted tubule.
- Endothelium has pores to allow small molecules through.
- Podocytes have negative charge. This and the basement membrane stops proteins getting through into tubular fluid.
- **Macula densa senses GFR by [Na^+]**
- **Juxtaglomerular (JG) apparatus includes JG cells that secrete renin**.
- JGA helps regulate renal blood flow, GFR and also indirectly, modulates Na^+ balance and systemic BP




↑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+


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

(a) Mechanism of dehydration

(b) Mechanism of hypotonic hydration

Figure 26.7

$$GFR = \frac{\text{Urine Concentration} \times \text{Urine Flow}}{\text{Plasma Concentration}}$$

Filtration

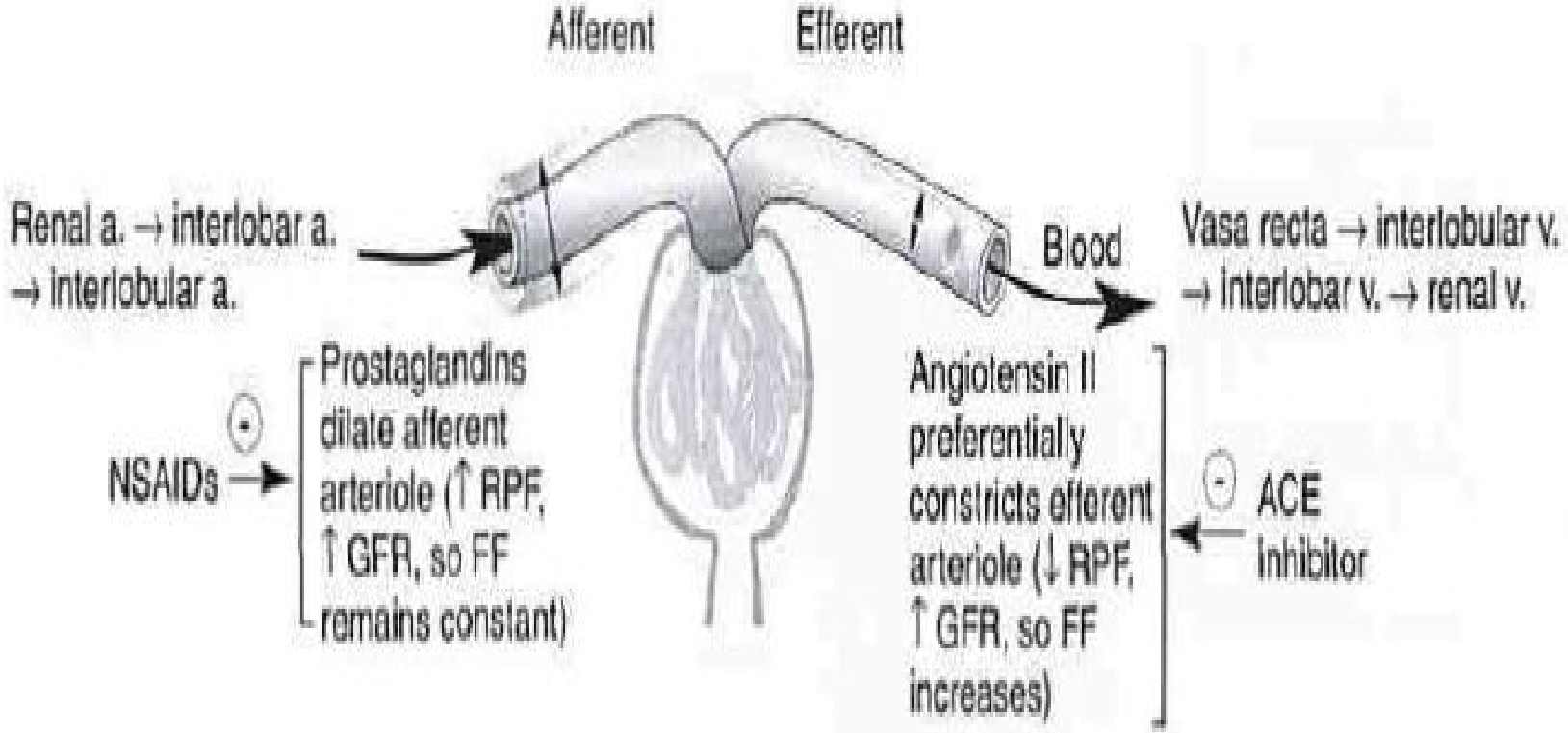
Filtration fraction (FF) = GFR/RPF.

Normal FF = 20%.

Filtered load = GFR × plasma concentration.

GFR can be estimated with creatinine.

RPF is best estimated with PAH.

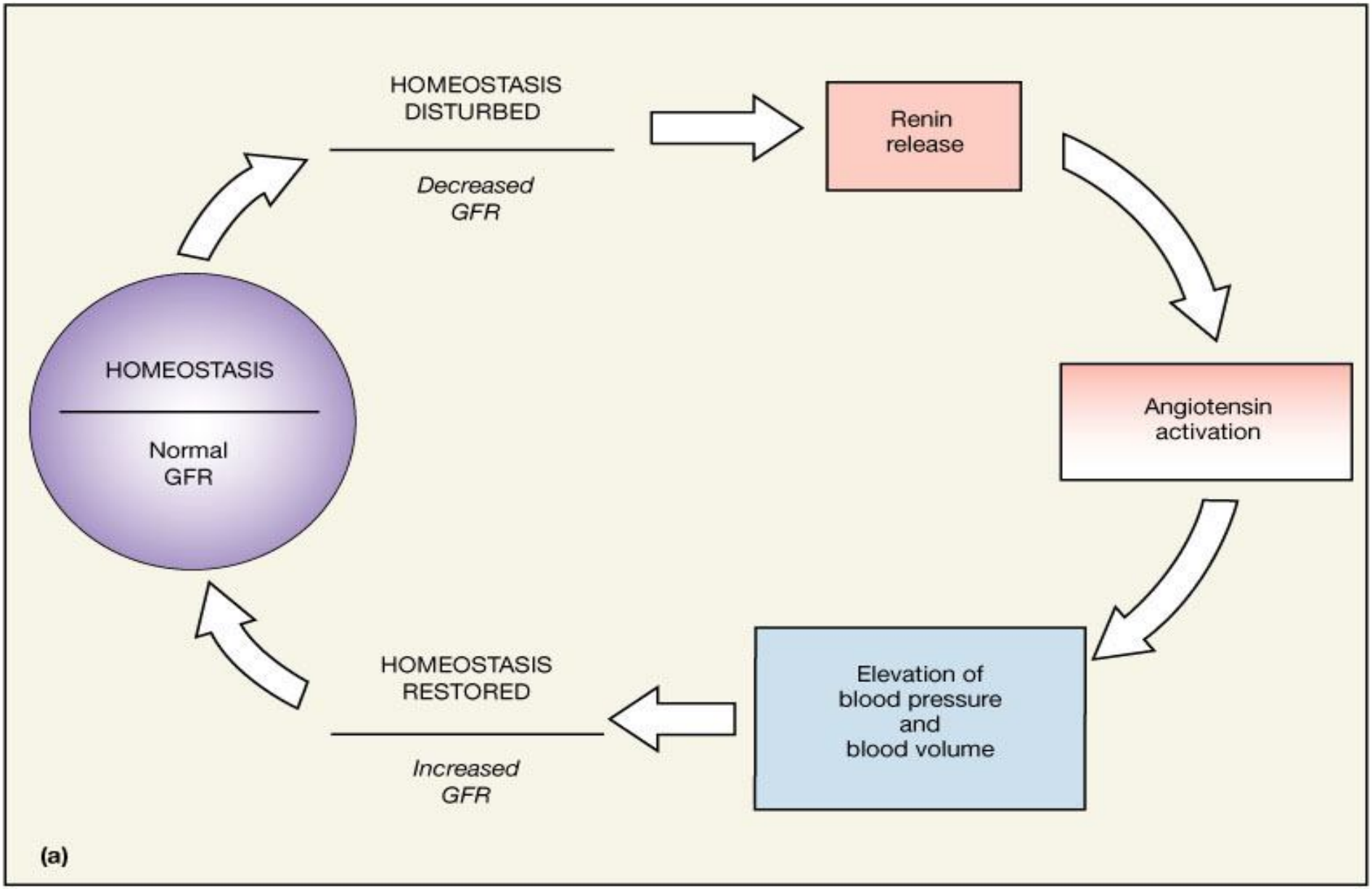


Effective Renal Plasma Flow (FIT-RPF)

Changes in glomerular dynamics

Effect	RPF	GFR	FF (GFR/RPF)
Afferent arteriole constriction	↓	↓	NC
Efferent arteriole constriction	↓	↑	↑
↑ plasma protein concentration	NC	↓	↓
↓ plasma protein concentration	NC	↑	↑
Constriction of ureter	NC	↓	↓

The Response to a Reduction in the GFR



Dynamics of Glomerular Filtration

- Forces Opposing Filtration (tends to keep fluid in the glomerulus)
  - tubular pressure
    - 18mmHg back pressure
  - osmotic pressure of plasma proteins (OPPP)
    - 32mmHg
    - higher than systemic
    - concentration of plasma proteins

Dynamics of Glomerular Filtration

- Effective Filtration Pressure

  EFP= CP - (OPPP + Tubular Pressure)

  10mmHg= 60 – (32 +18)

  – driving force that pushes fluid

Inulin is such a substance, thus we can measure what we call the clearance of inulin, C_{in}, and for this "special" substance

$$C_{in} = GFR = \frac{[U]_{in} \times V}{[P]_{in}} \quad \text{(units are ml/min)}$$

We now have a standard in inulin clearance. If we measure the clearance of any substance, x, and compare it to C_{in}, if

$C_x > C_{in}$, substance must be added to the tubule (i.e., secreted)

$C_x < C_{in}$, substance must be removed from tubule (i.e., absorbed)

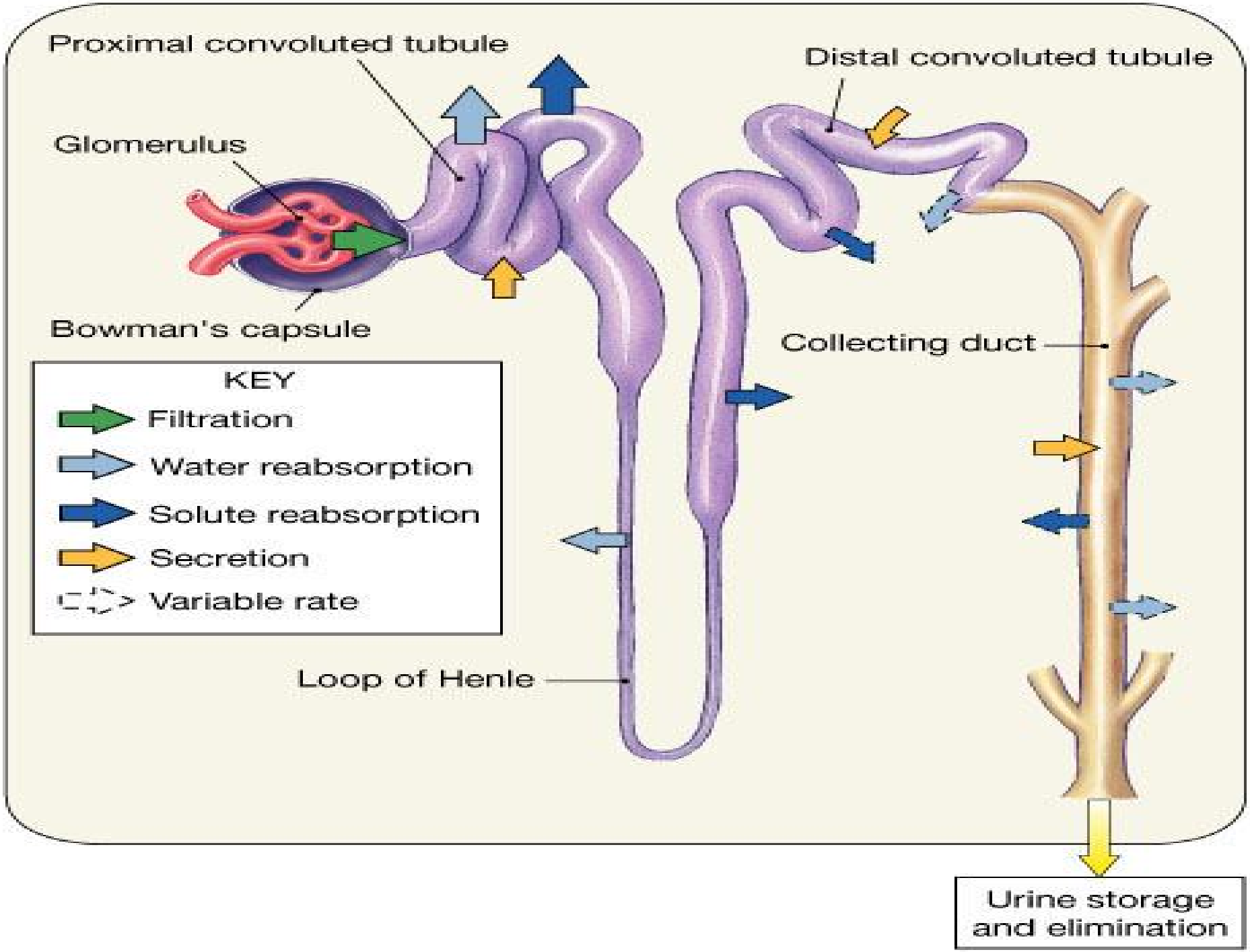
$$GFR = \frac{5mg/ml \times 5ml/\min}{0.2mg/ml}$$

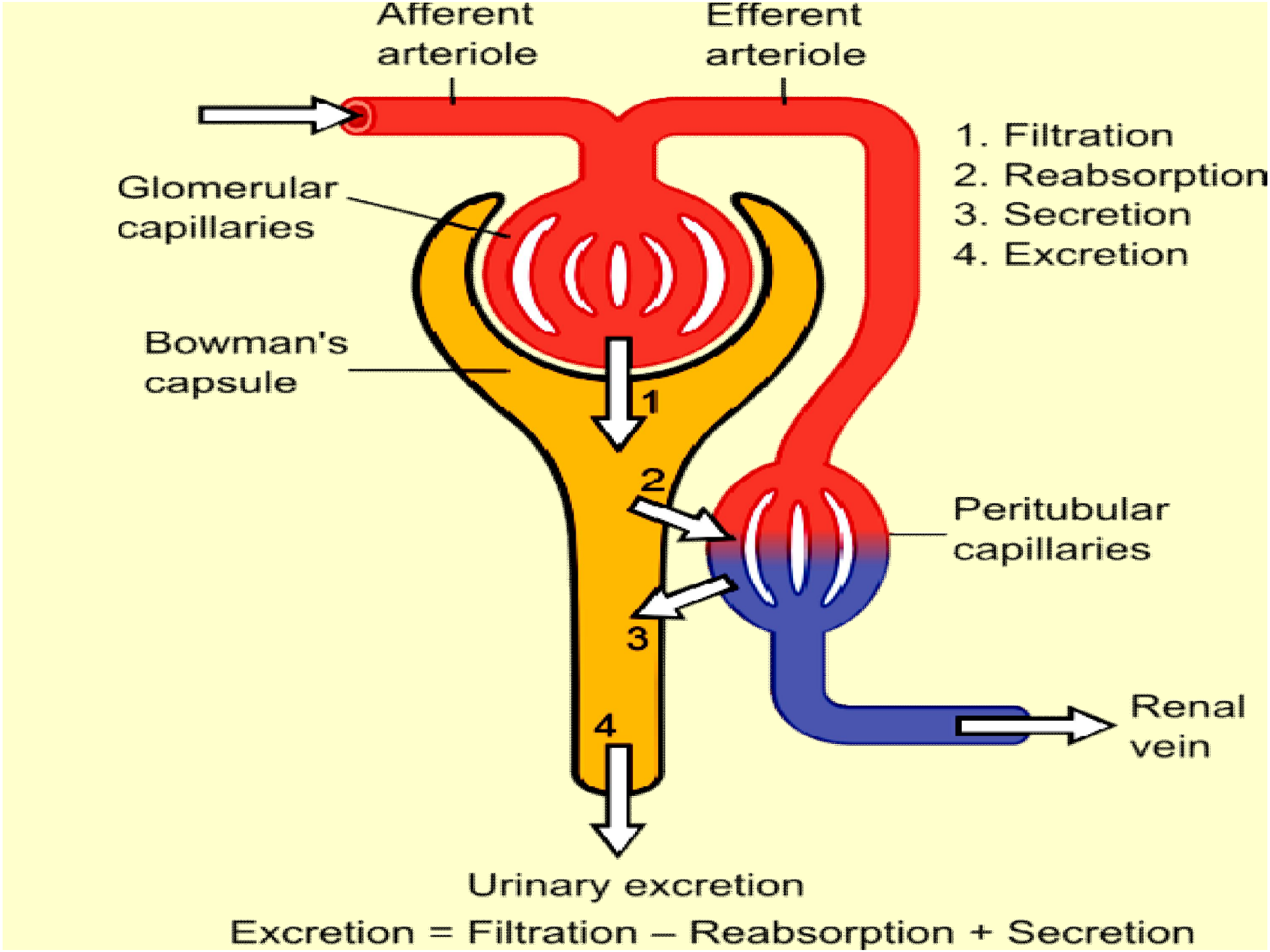
125ml/min

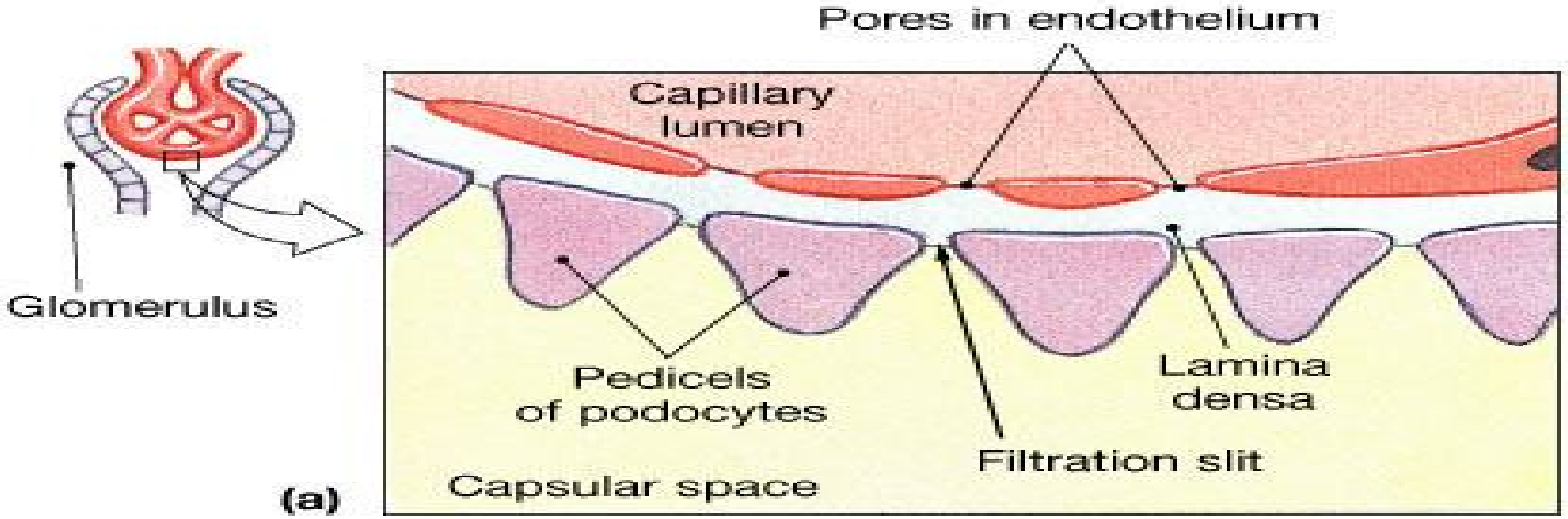
- If the amount excreted is less than the filtered amount= filtered and reabsorbed
- If in excess of what has been filtered= filtration and secretion

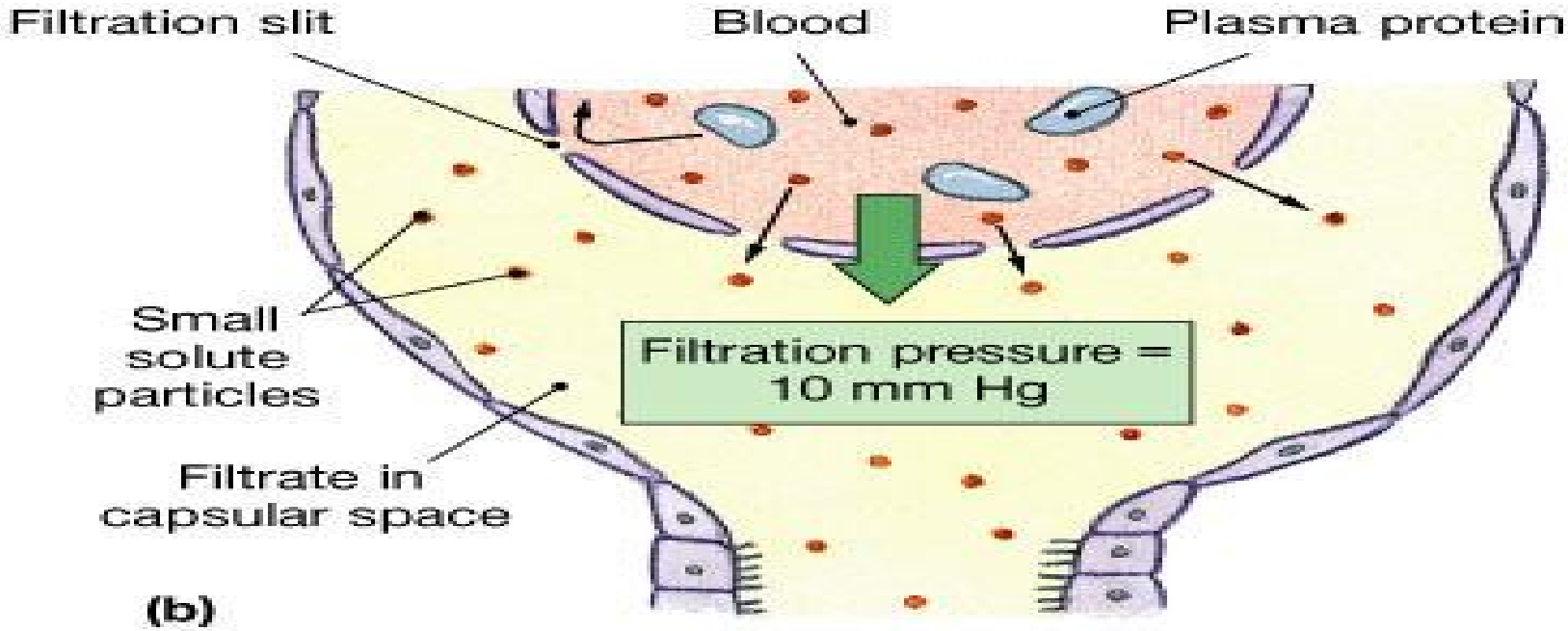
Factors Affecting the GFR

- Changes in glomerular capillary hydrostatic pressure
  - systemic blood pressure
  - afferent or efferent arteriolar constriction
- Changes in hydrostatic pressure in bowmans capsule
  - ureteral obstruction
  - edema of kidney inside tight renal capsule
- Changes in oncotic pressure of plasma proteins
  - dehydration
  - hypoproteinemia
- Increased permeability of glomerular filter
  - various disease
- Decrease in total area of glomerular capillary bed
  - disease which destroy glomeruli with or without destruction of tubules
  - partial nephrectomy


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


Afferent arteriole
Efferent arteriole
1. Filtration
2. Reabsorption
3. Secretion
4. Excretion
Glomerular capillaries
Bowman's capsule
1
2
3
4
Peritubular capillaries
Renal vein
Urinary excretion
Excretion = Filtration – Reabsorption + Secretion

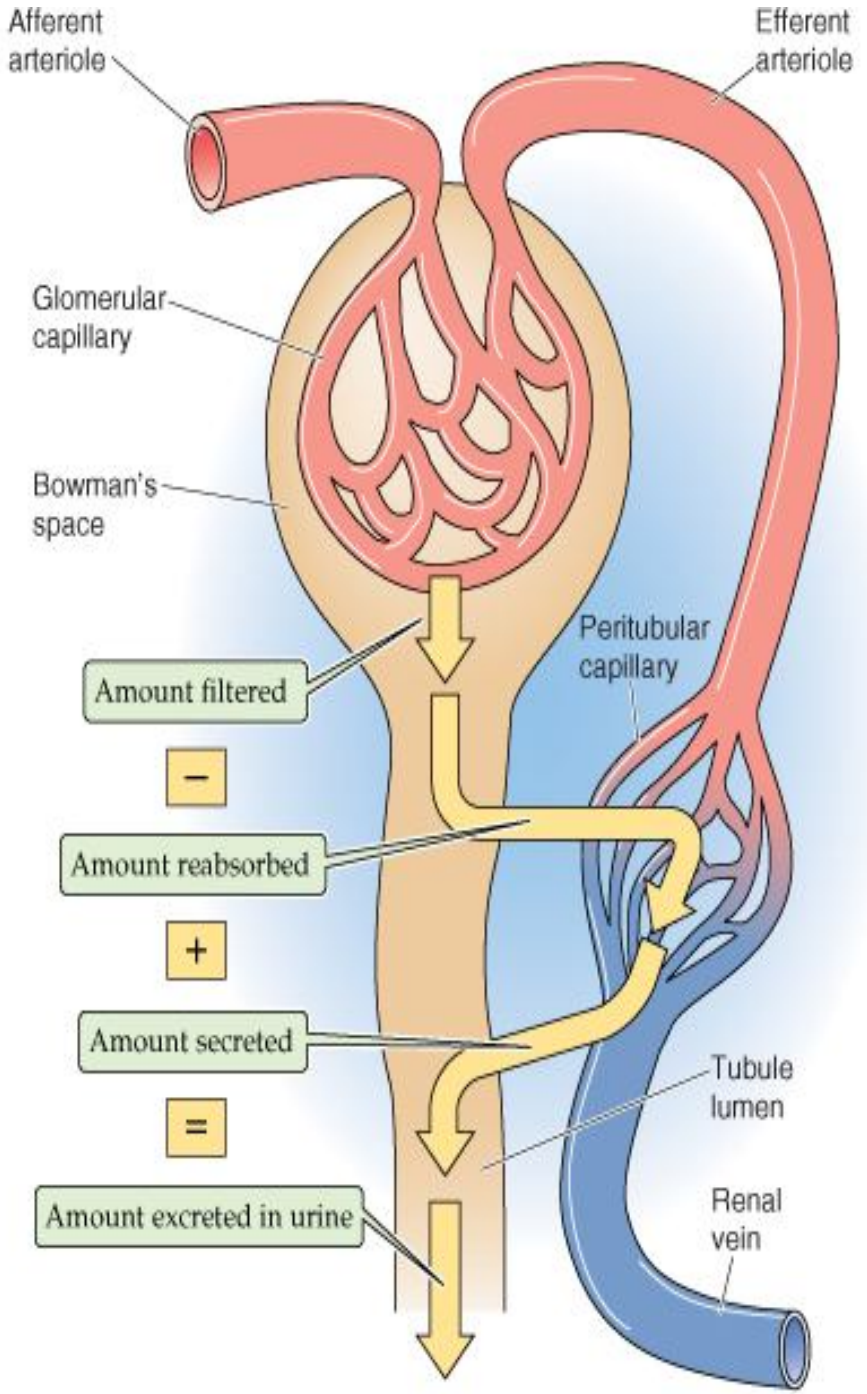

Pores in endothelium
Capillary lumen
Glomerulus
Pedicels of podocytes
Lamina densa
Filtration slit
Capsular space
(a)


Filtration slit
Blood
Plasma protein
Small solute particles
Filtration pressure = 10 mm Hg
Filtrate in capsular space
(b)

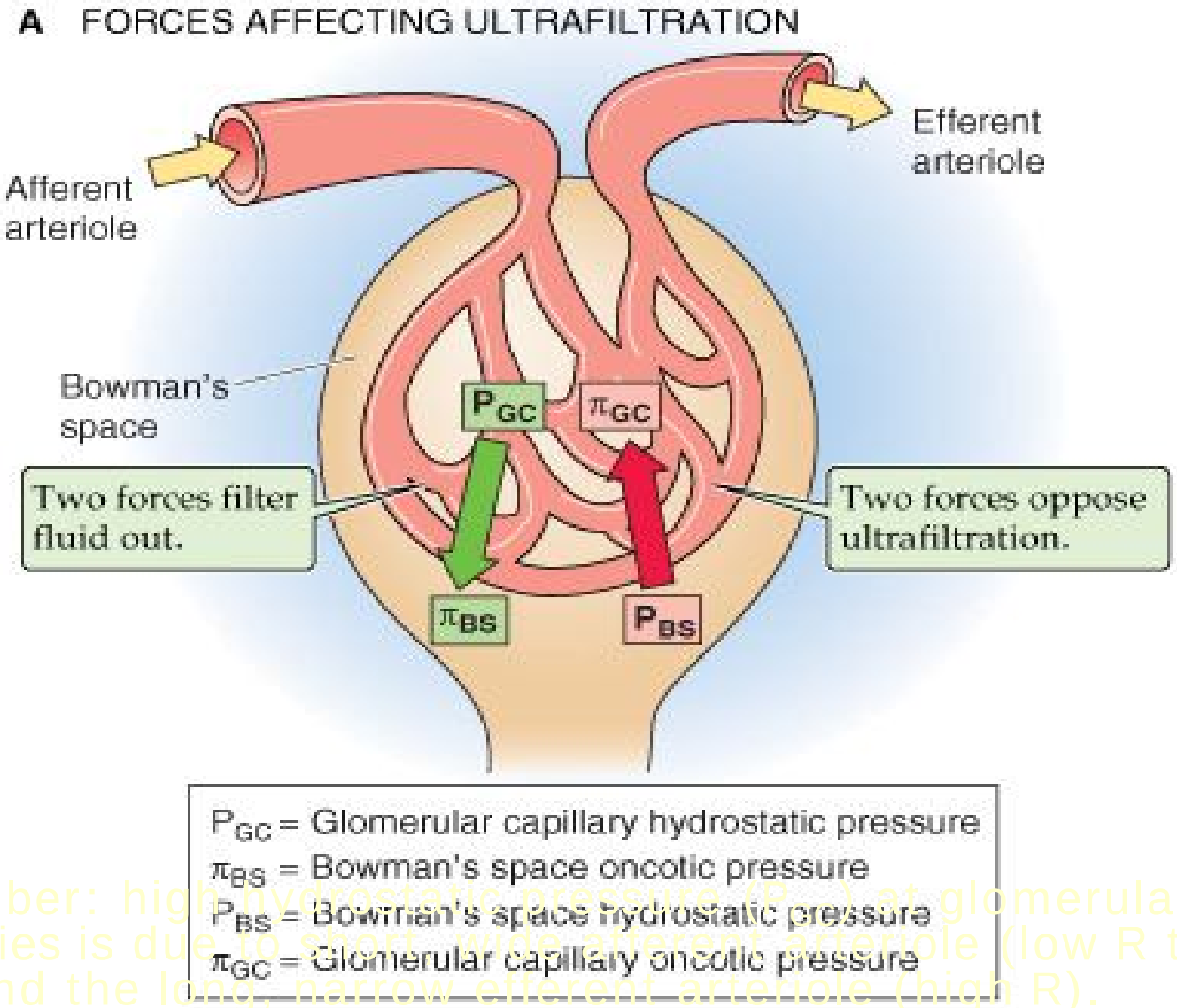
The three basic renal processes

- **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.

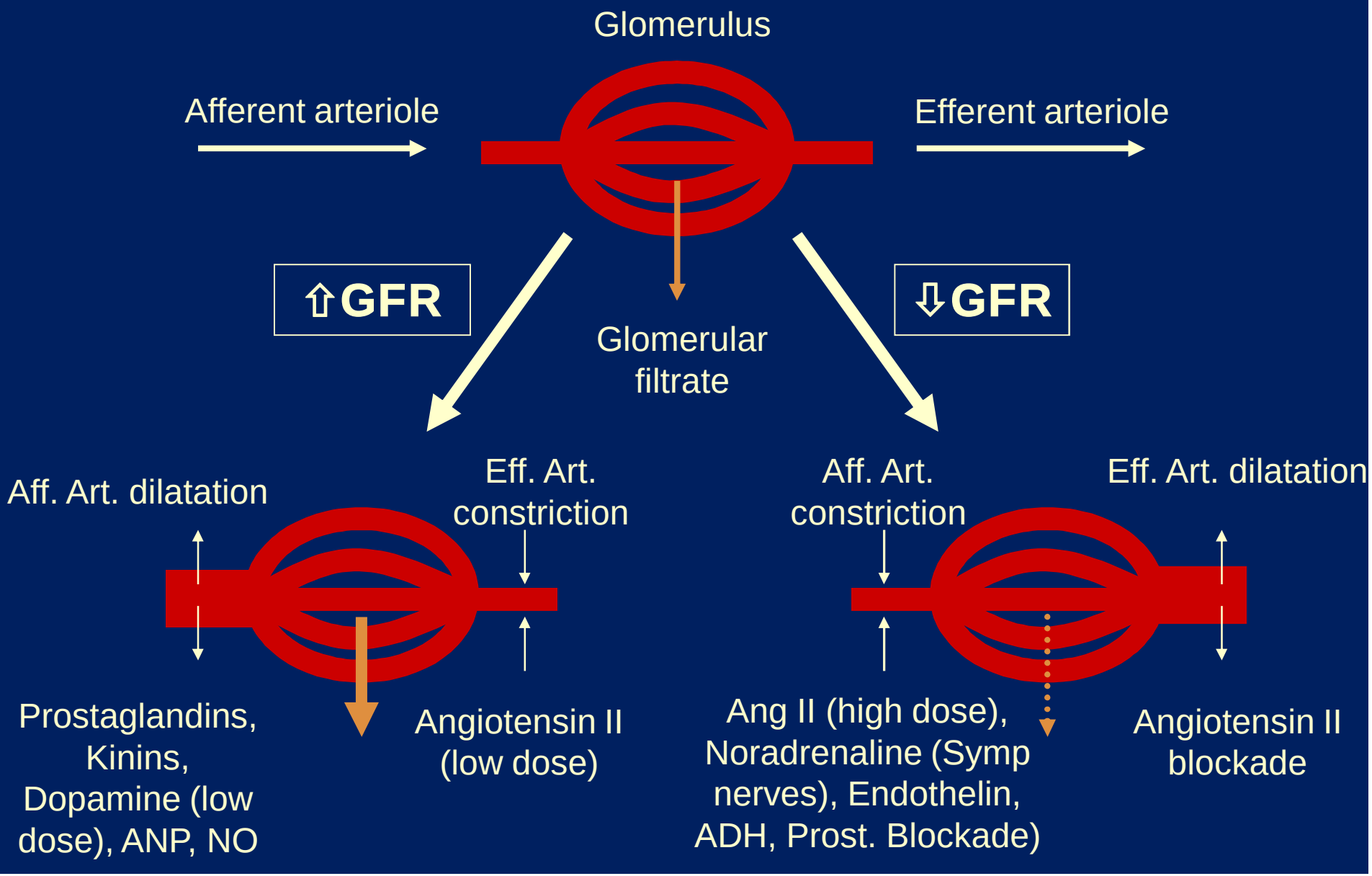


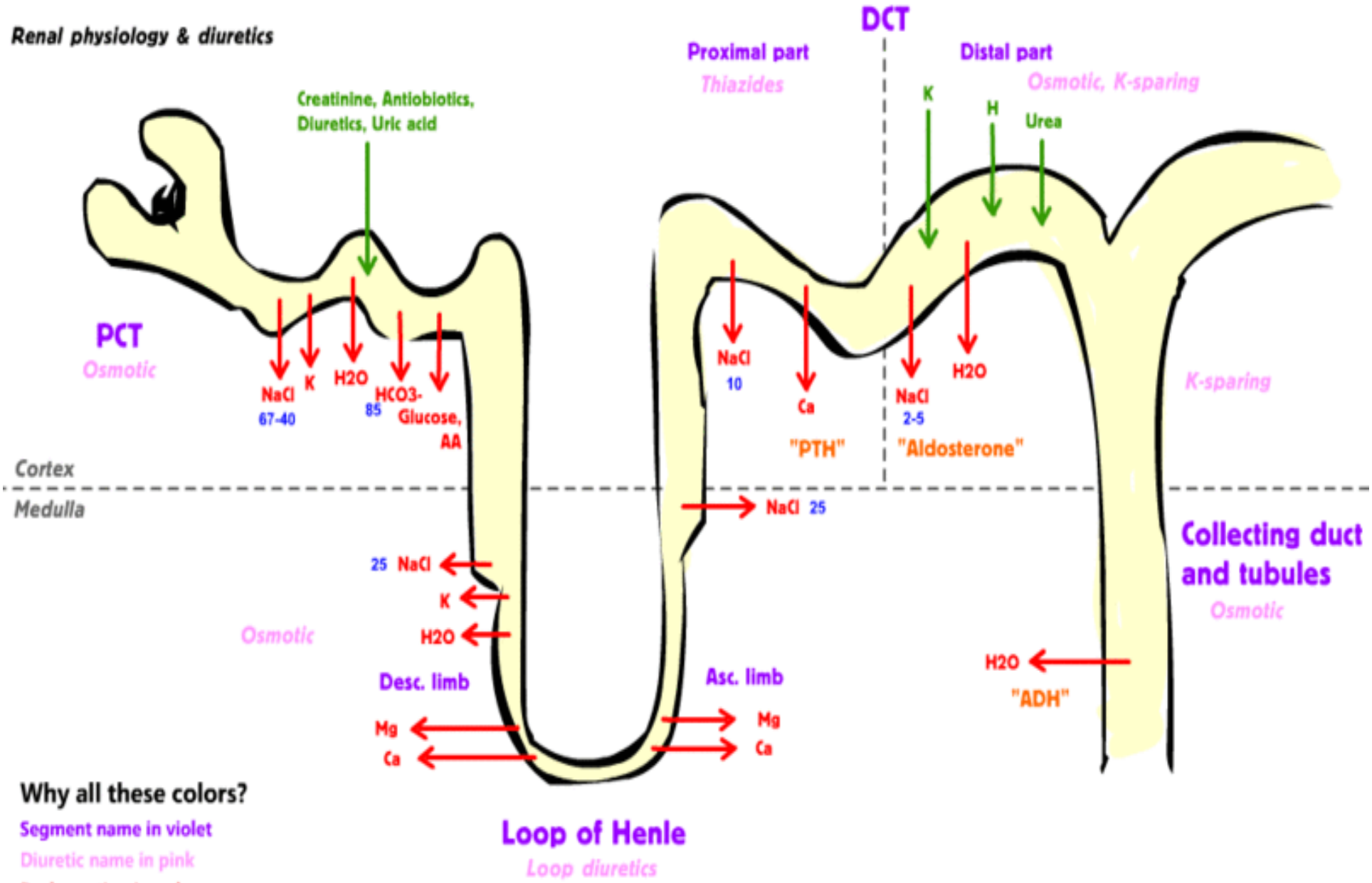
Glomerular filtration



- Remember: high hydrostatic pressure (P_{GC}) at glomerular capillaries is due to short, wide afferent arteriole (low R to flow) and the long, narrow efferent arteriole (high R).

GFR depends on diameters of afferent and efferent arterioles





Why all these colors?

Segment name in violet

Diuretic name in pink

Reabsorption in red

Secretion in green

Percentage in blue

Hormone in orange

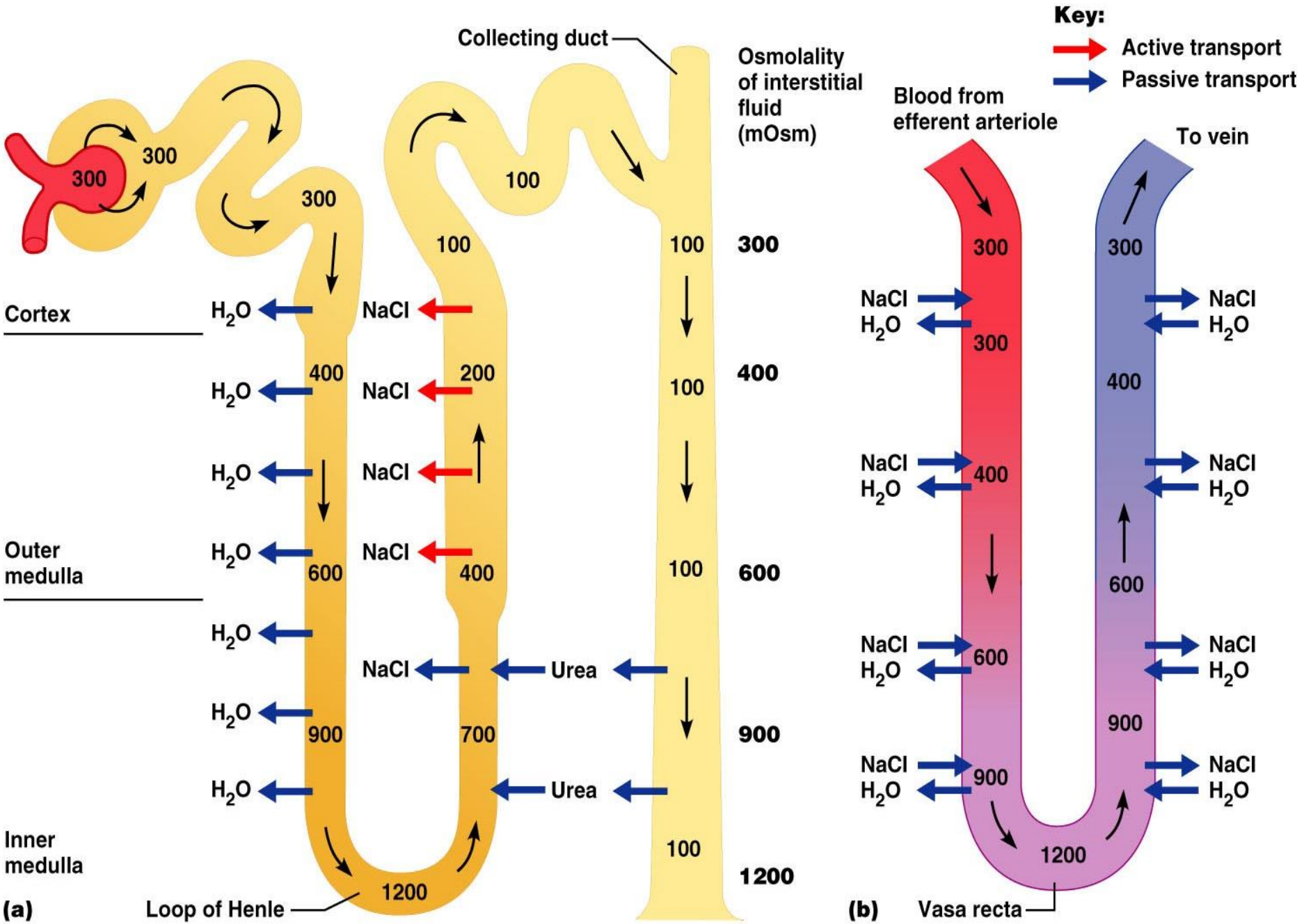


Figure 25.14

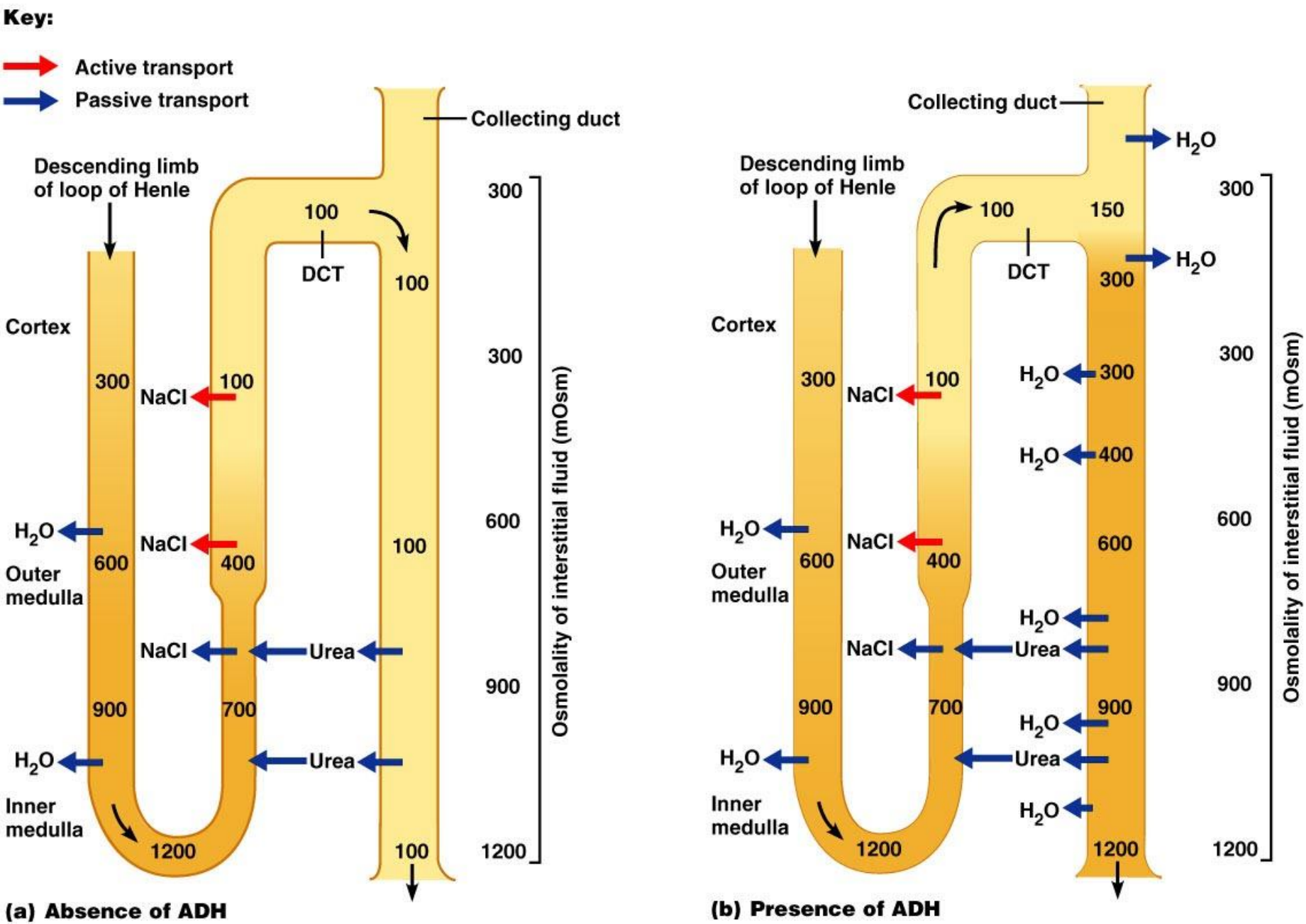


Figure 25.15

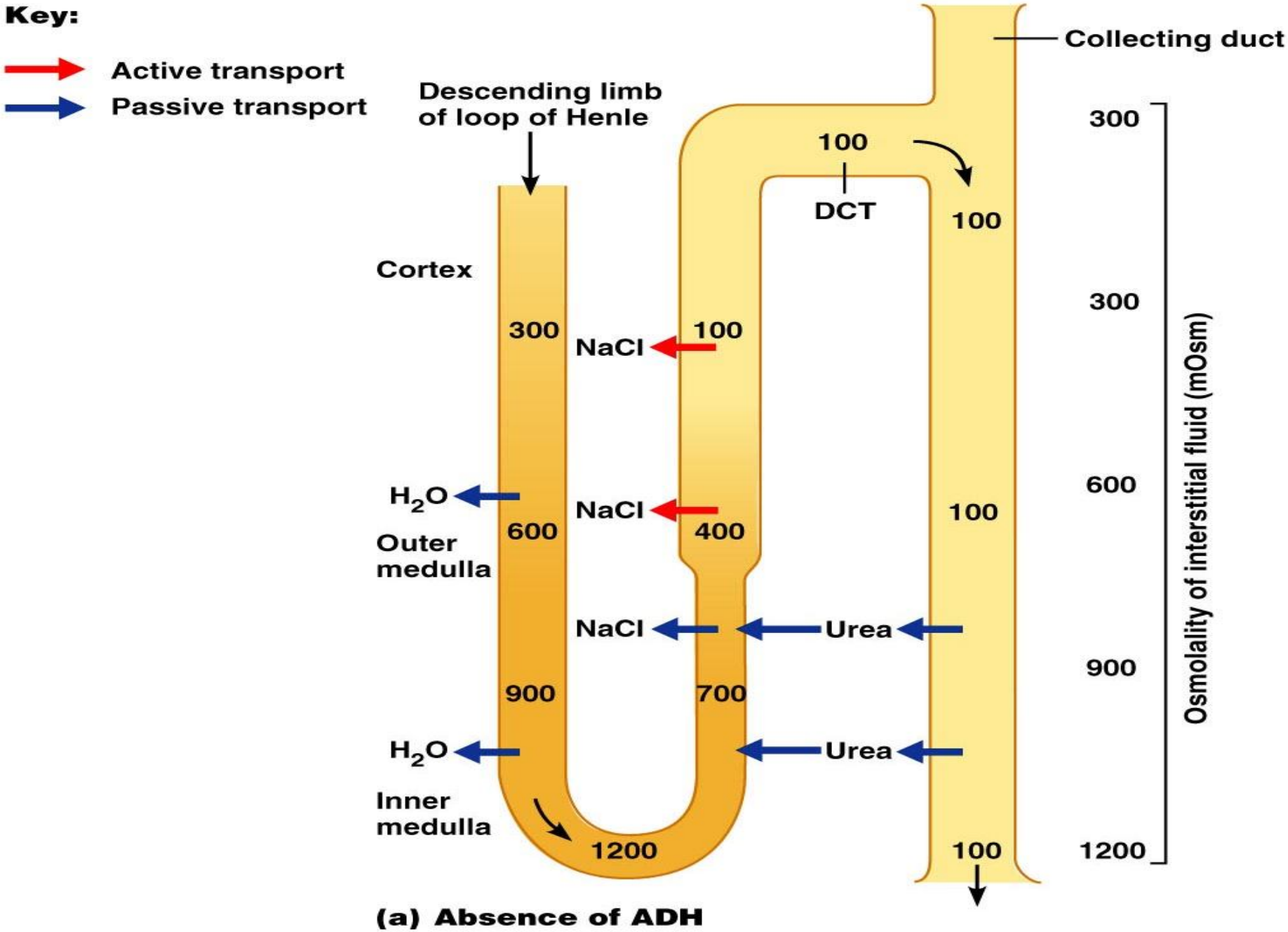


Figure 25.15a

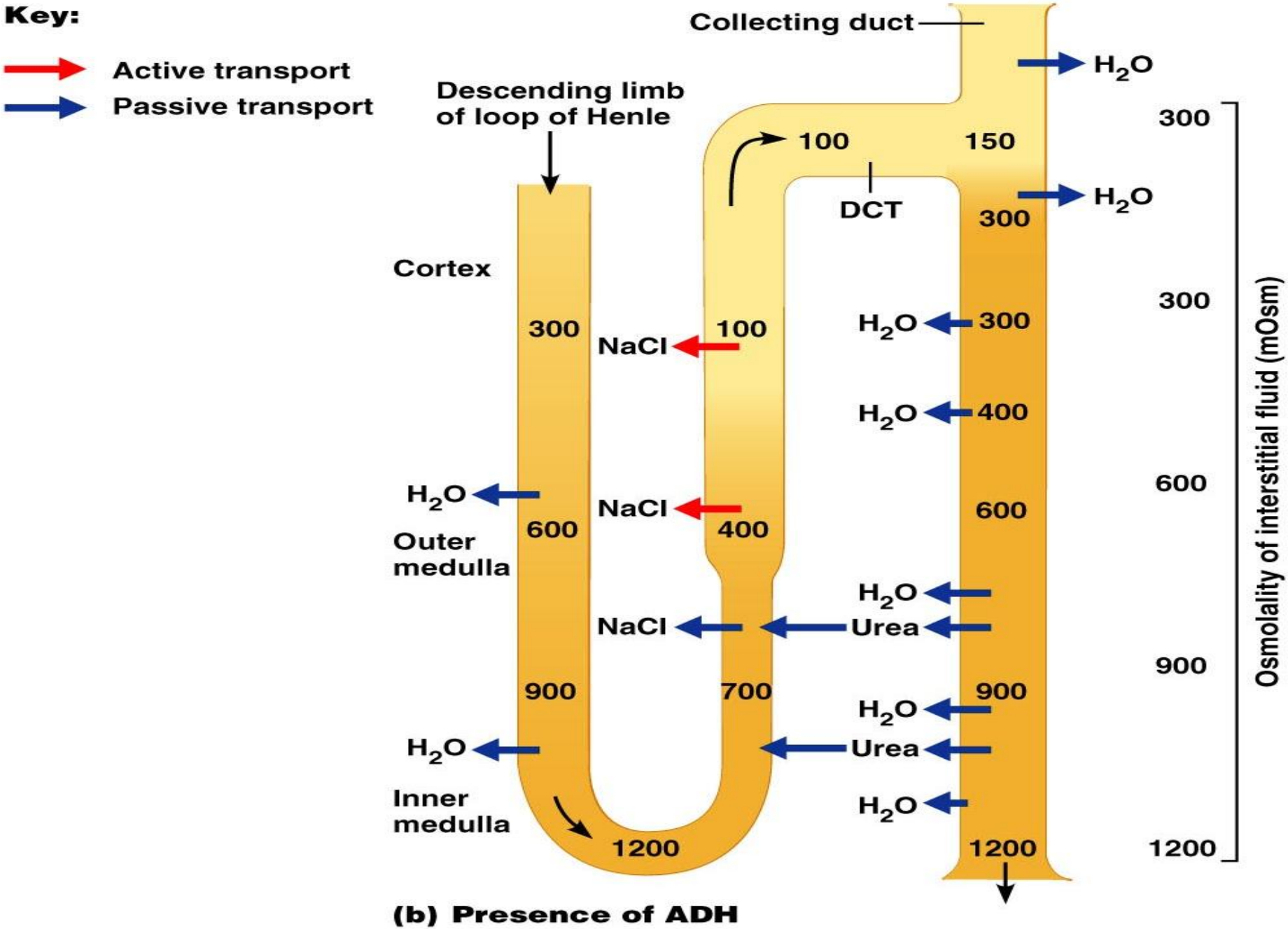


Figure 25.15b

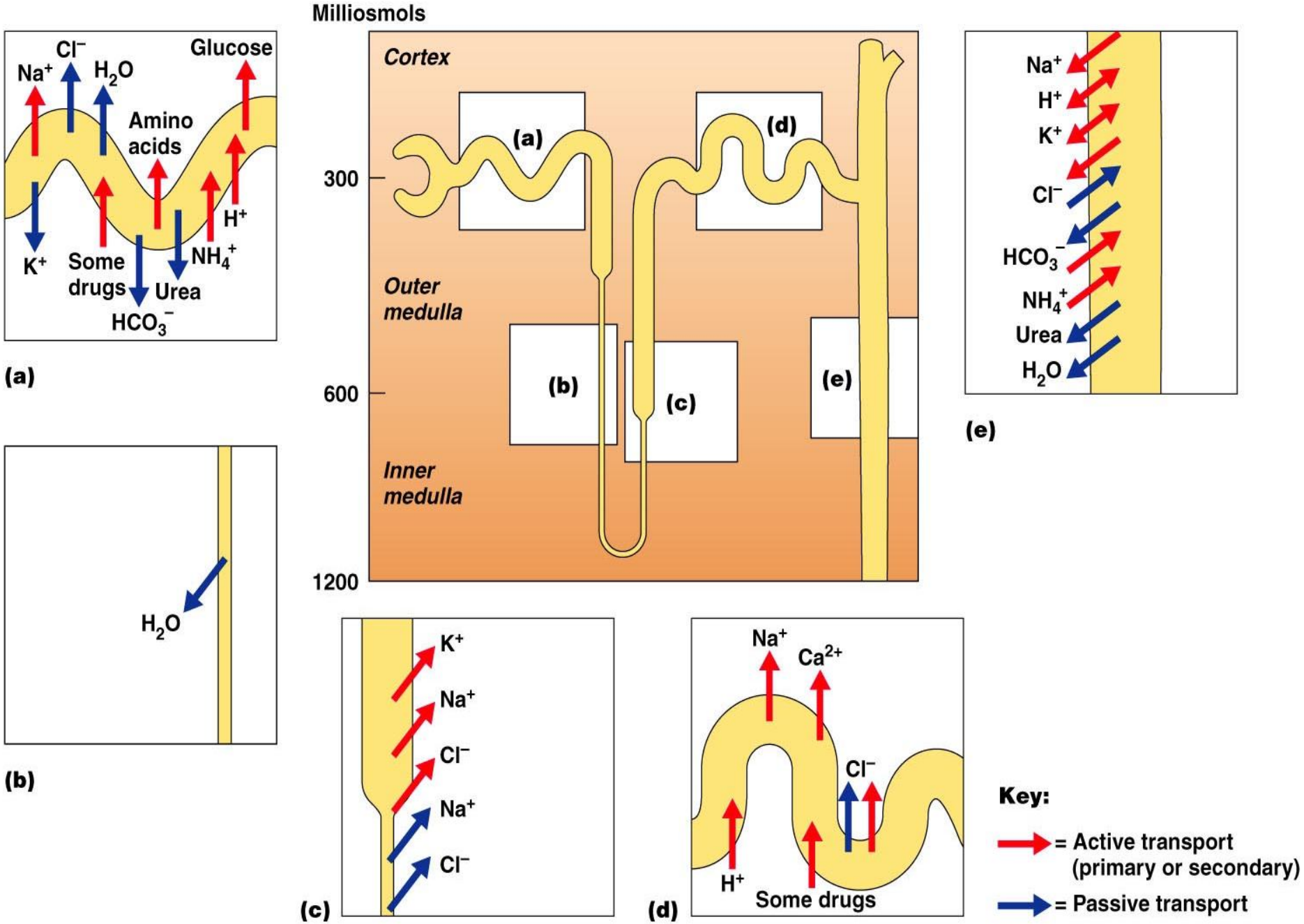
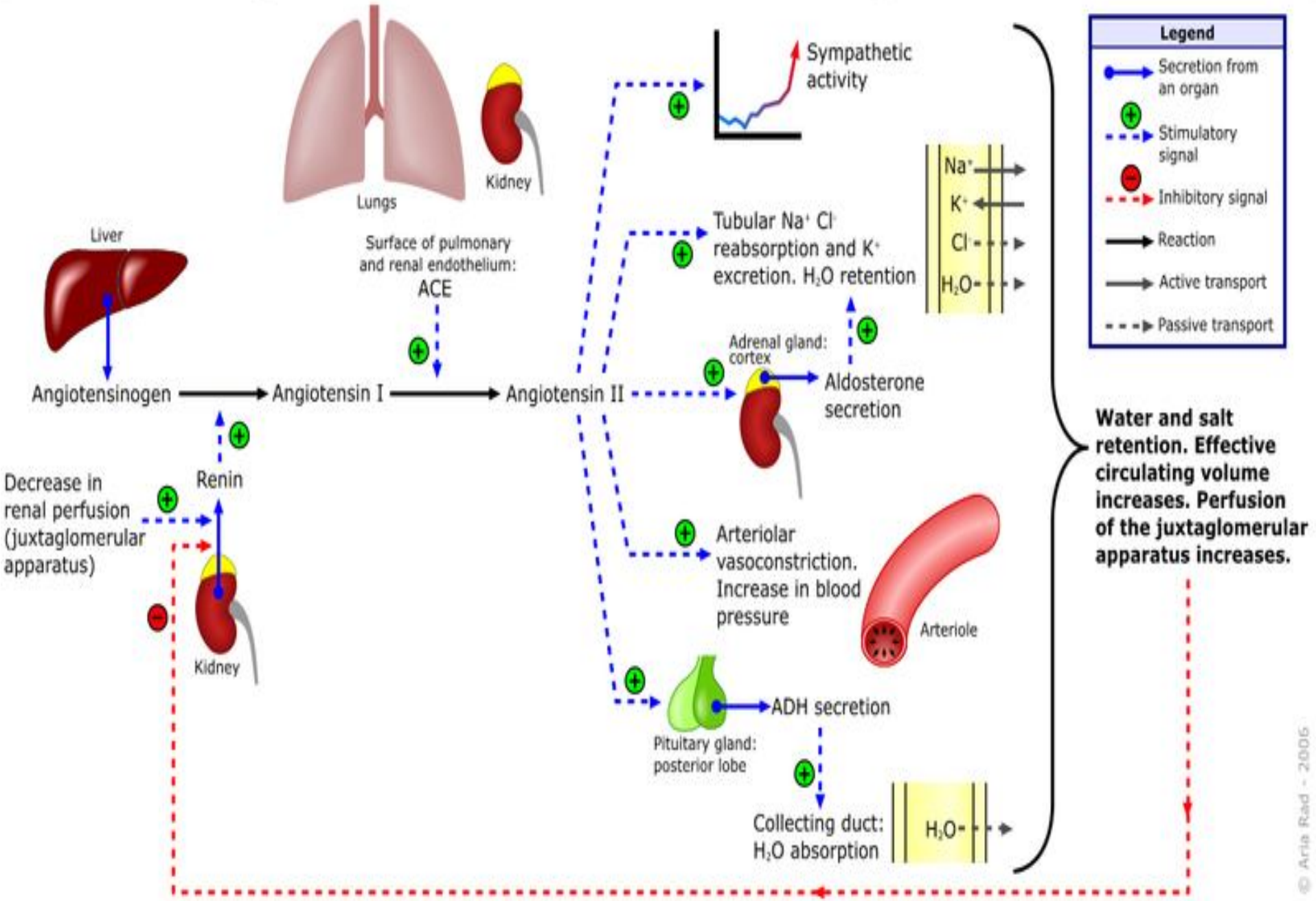
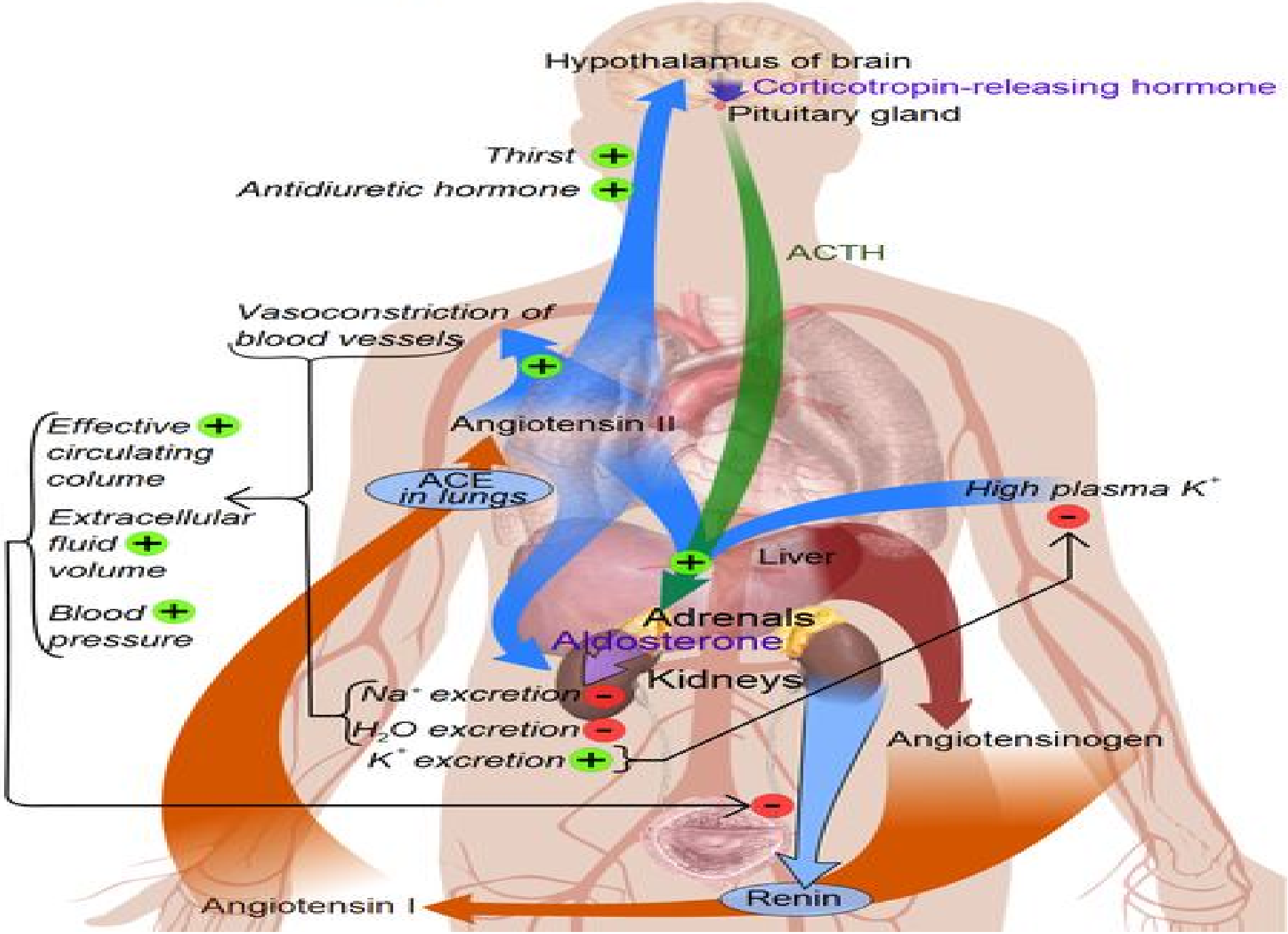


Figure 25.16

Renin-angiotensin-aldosterone system



Renin-angiotensin-aldosterone system



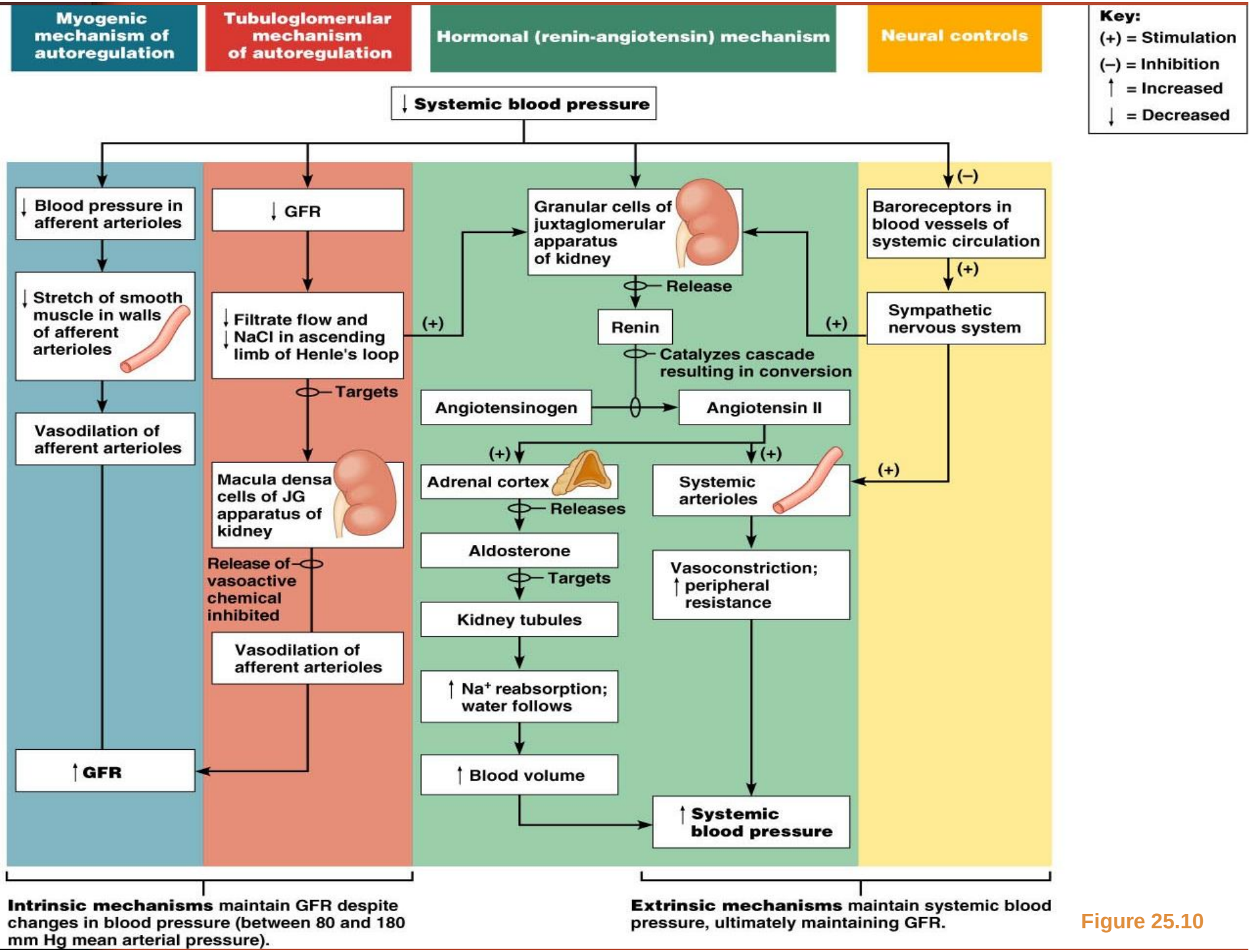
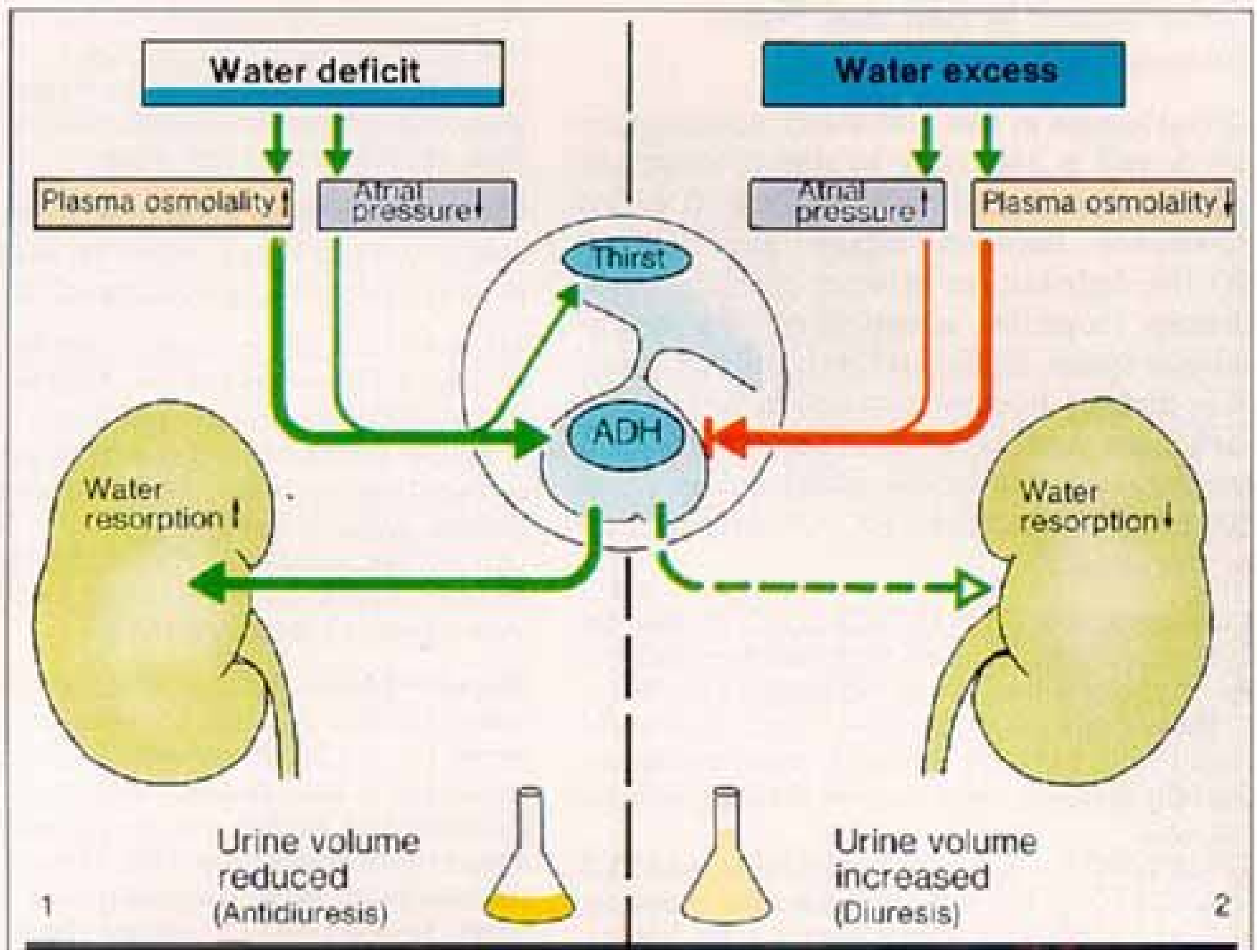
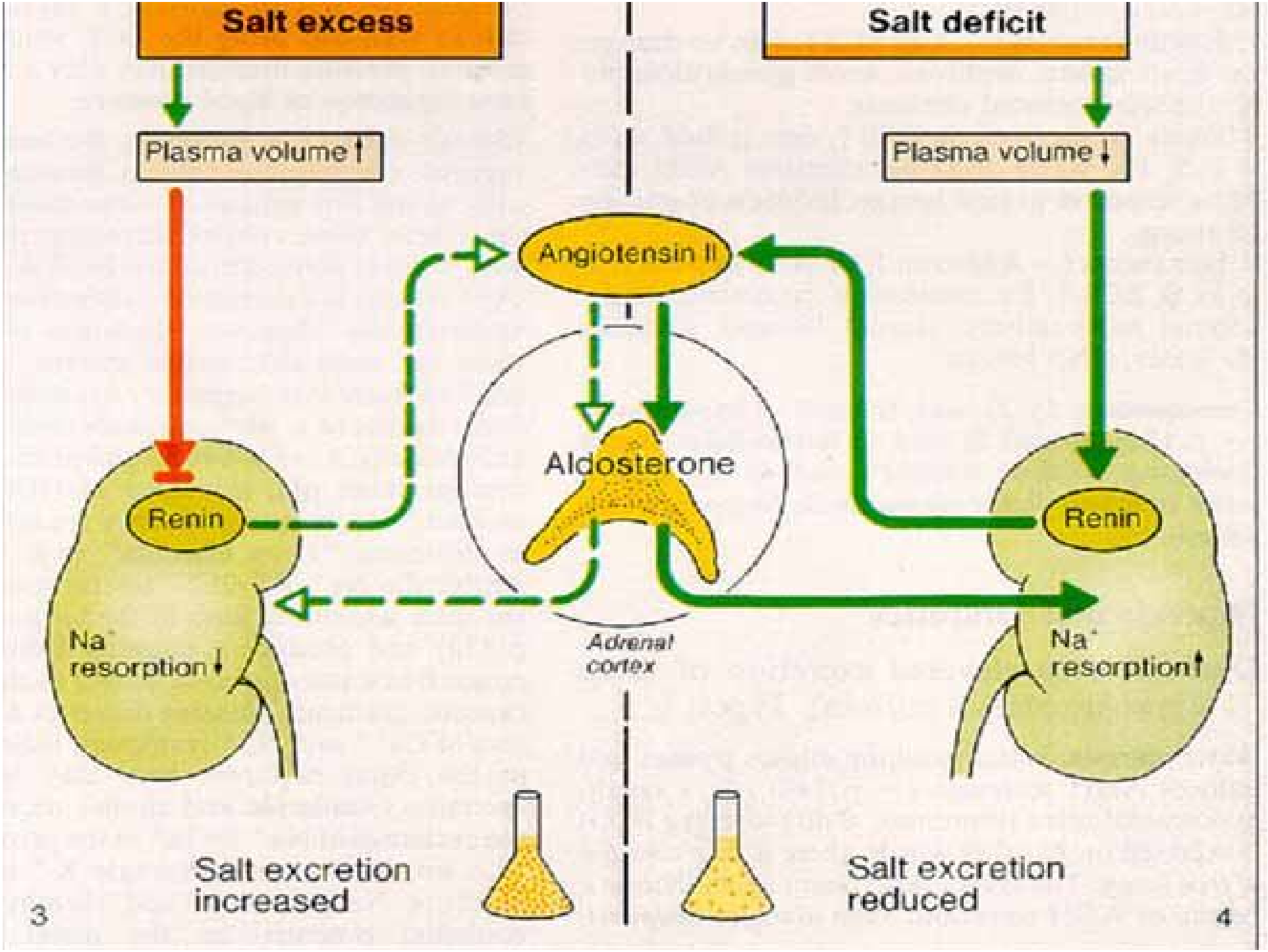
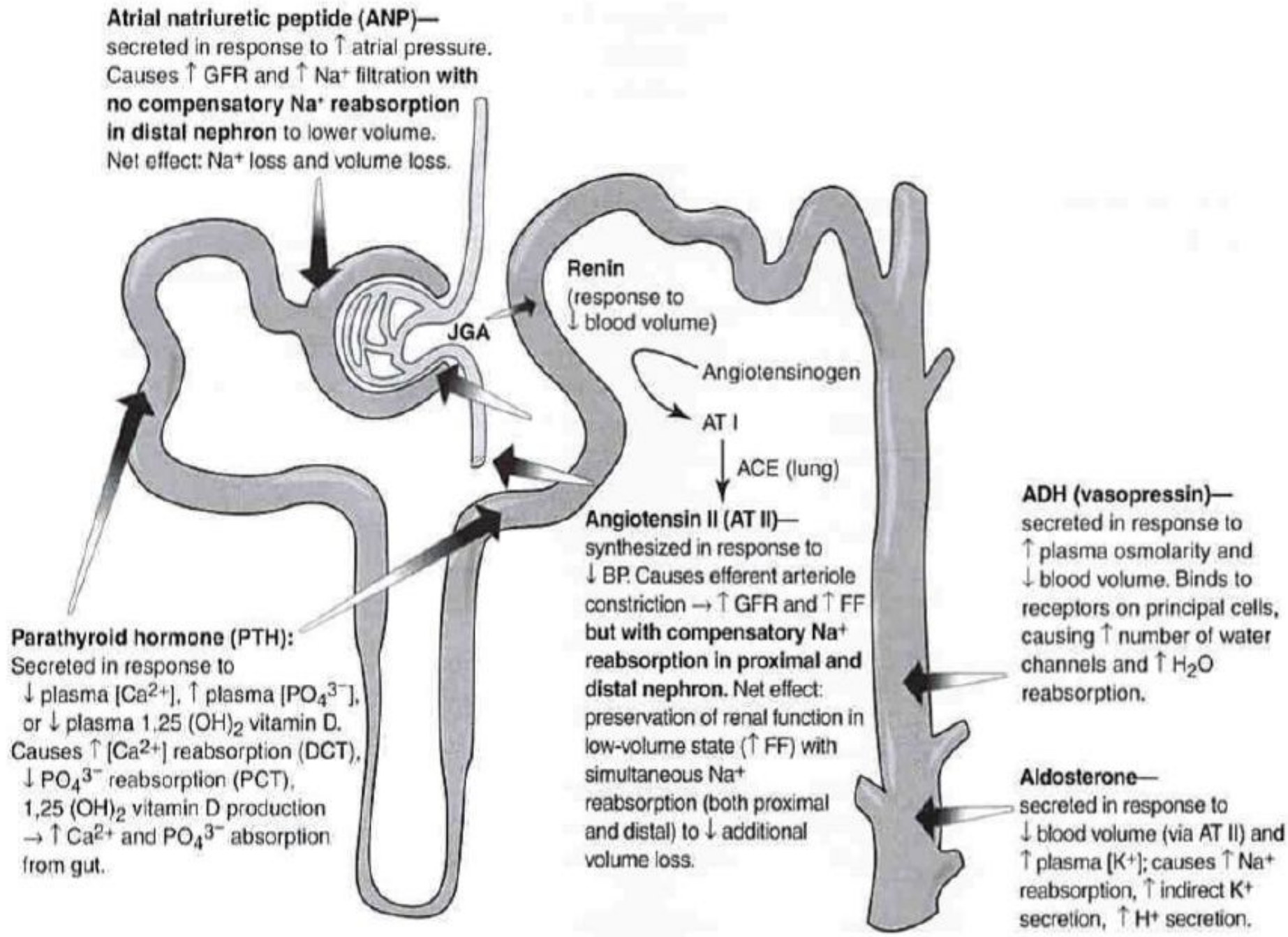

Myogenic mechanism of autoregulation
Tubuloglomerular mechanism of autoregulation
Hormonal (renin-angiotensin) mechanism
Neural controls
Key:
(+) = Stimulation
(–) = Inhibition
↑ = Increased
↓ = Decreased
↓ Systemic blood pressure
↓ Blood pressure in afferent arterioles
↓ Stretch of smooth muscle in 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
(+)
(+)
Intrinsic mechanisms maintain GFR despite changes in blood pressure (between 80 and 180 mm Hg mean arterial pressure).
Extrinsic mechanisms maintain systemic blood pressure, ultimately maintaining GFR.

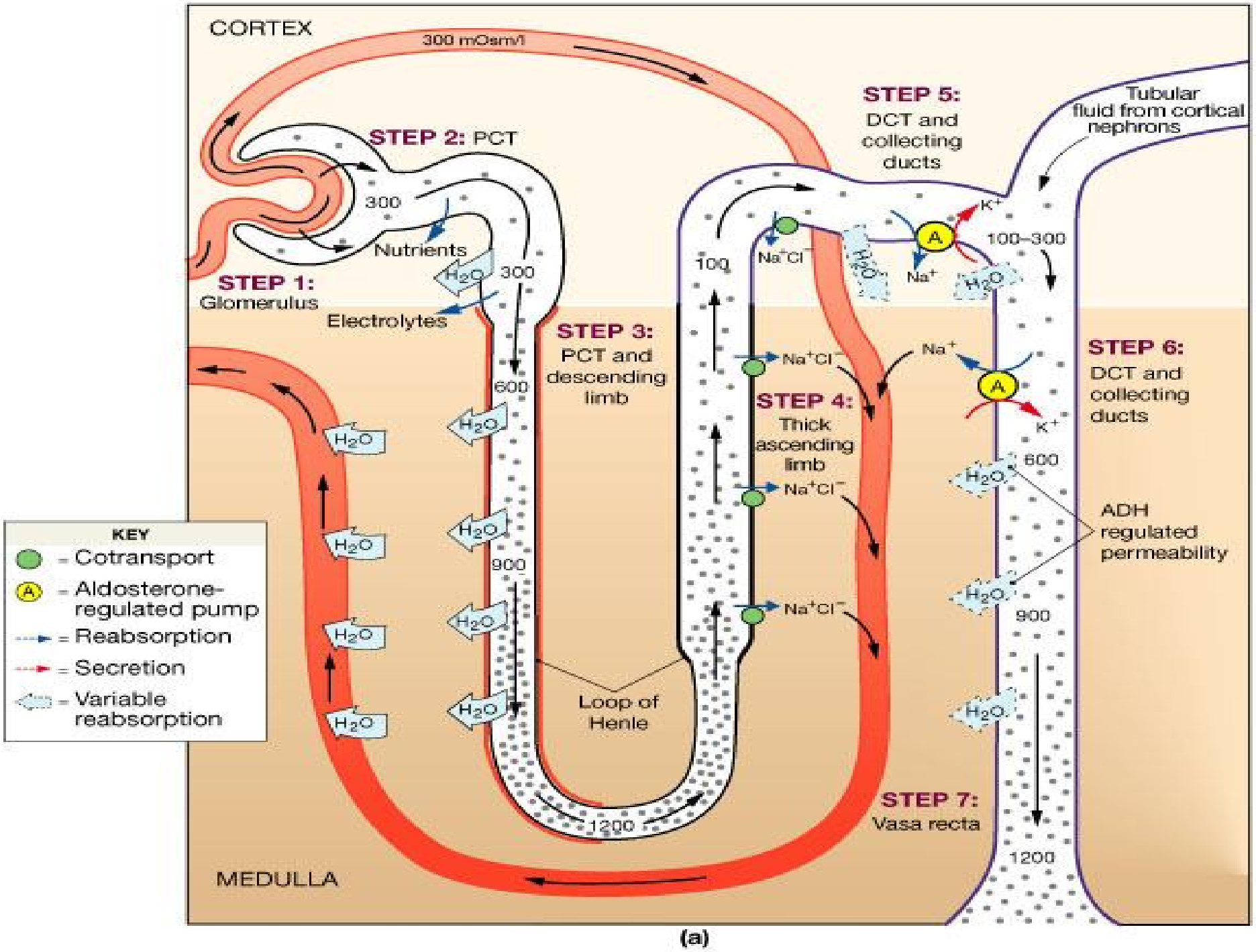
Figure 25.10


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


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

Hormones acting on kidney




CORTEX
300 mOsm/l
STEP 1:
Glomerulus
STEP 2: PCT
300
Nutrients
Electrolytes
300
600
900
1200
STEP 3:
PCT and
descending
limb
Loop of
Henle
STEP 4:
Thick
ascending
limb
100
STEP 5:
DCT and
collecting
ducts
Tubular
fluid from cortical
nephrons
100–300
STEP 6:
DCT and
collecting
ducts
ADH
regulated
permeability
STEP 7:
Vasa recta
MEDULLA
KEY
= Cotransport
= Aldosterone-regulated pump
= Reabsorption
= Secretion
= Variable reabsorption

(a)

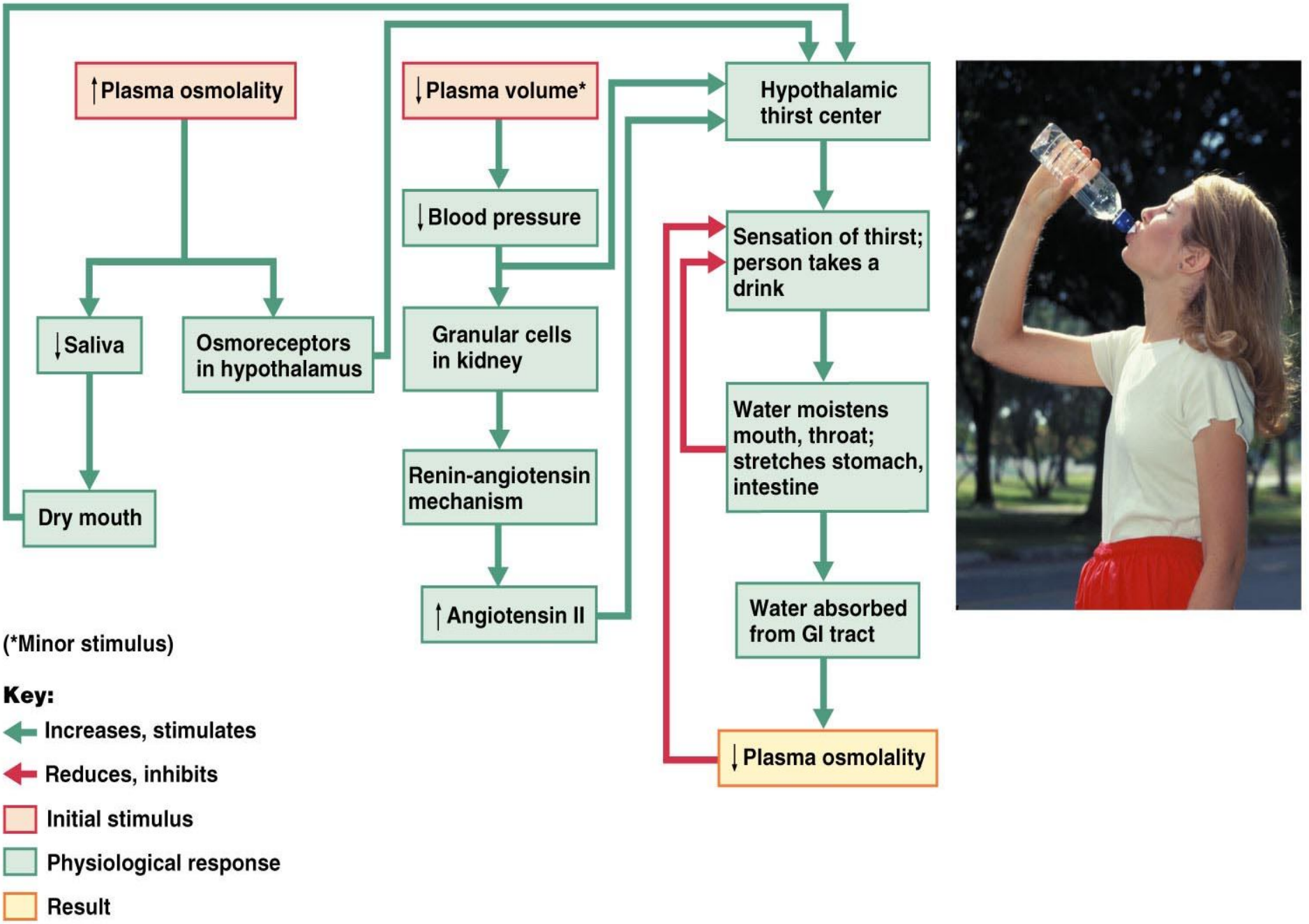


Figure 26.5

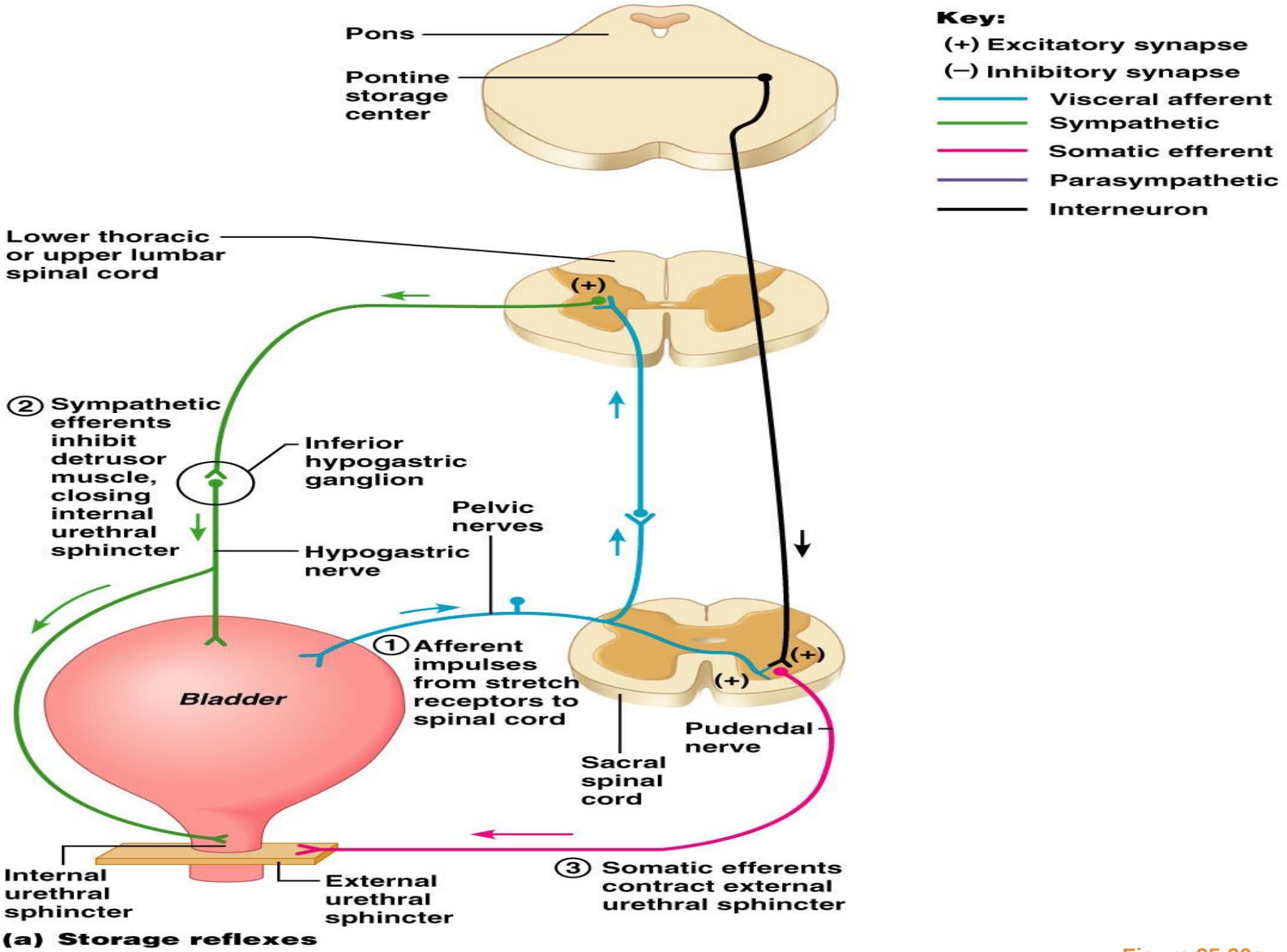


Figure 25.20a

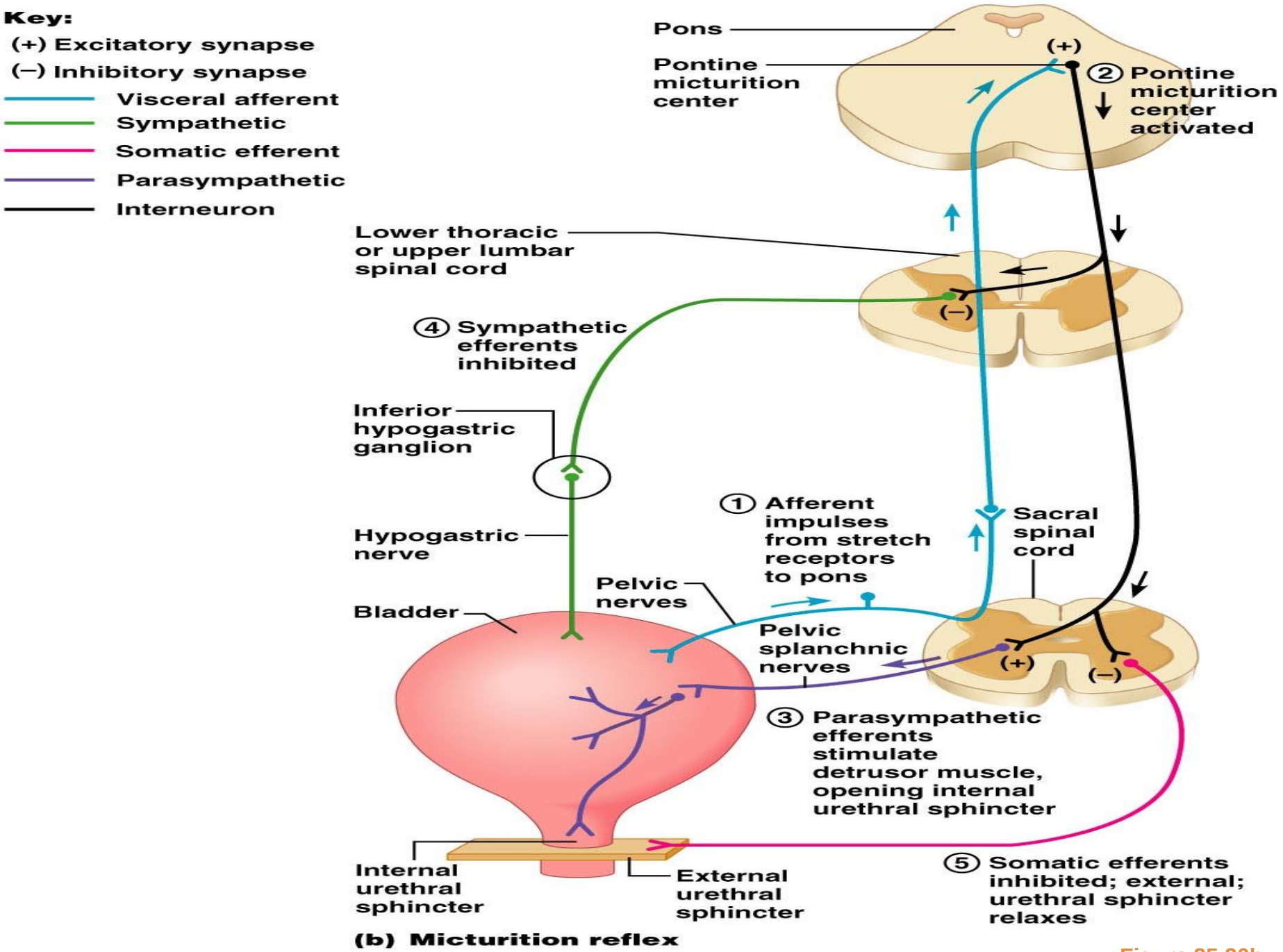
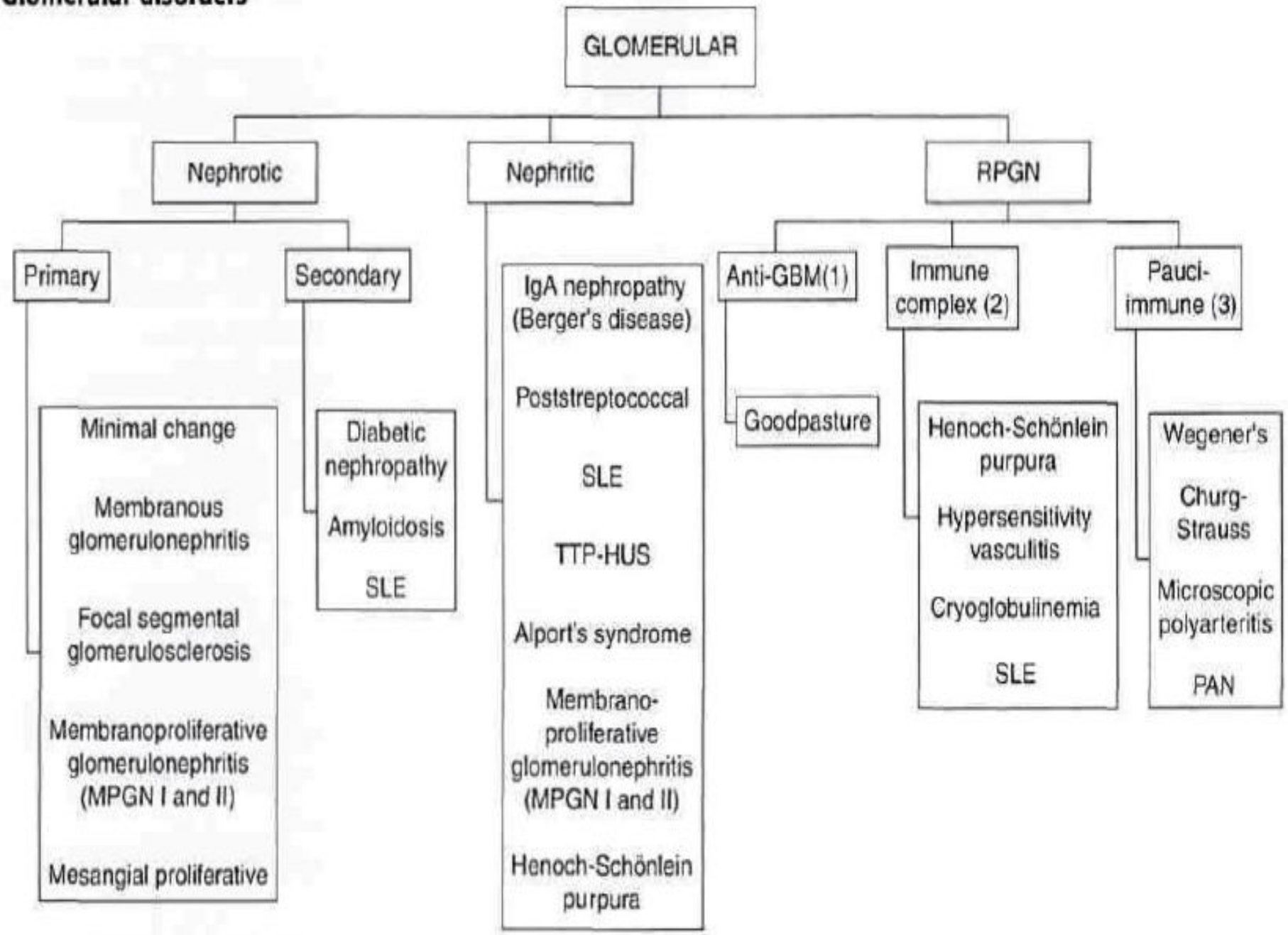


Figure 25.20b

Glomerular disorders



Kidney stones	Can lead to severe complications, such as hydronephrosis and pyelonephritis. Treat and prevent by encouraging fluid intake.	
Calcium	Most common kidney stones (75–85%). Calcium oxalate (see Image 88), calcium phosphate, or both. Conditions that cause hypercalcemia (cancer, ↑ PTH, ↑ vitamin D, milk-alkali syndrome) can lead to hypercalciuria and stones. Tend to recur.	Radiopaque. Oxalate crystals can result from ethylene glycol (antifreeze) or vitamin C abuse.
Ammonium magnesium phosphate (**struvite**)	2nd most common kidney stone. Caused by infection with urease-positive bugs (*Proteus vulgaris*, *Staphylococcus*, *Klebsiella*). Can form **staghorn calculi** that can be a nidus for UTIs.	Radiopaque or radiolucent. Worsened by alkaluria.
Uric acid	Strong association with hyperuricemia (e.g., gout). Often seen as a result of diseases with ↑ cell turnover, such as leukemia and myeloproliferative disorders.	RadiolUcent.
Cystine	Most often 2° to cystinuria. Hexagonal shape. Rarely, may form cystine staghorn calculi.	Faintly radiopaque. Treat with alkalinization of urine.

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 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 26.2 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