

4.4 Demonstrate understanding of the role of the kidneys in fluid & electrolyte balance (Ch. 26)

4.4.1 define the fluid compartments

Intracellular fluid compartment (ICF) – within cells 60% total body fluid

Extracellular fluid compartment (ECF) – 40% body fluid; 2 areas

(a) plasma: ~20% ECF

(b) interstitial space: ~80% ECF – includes???

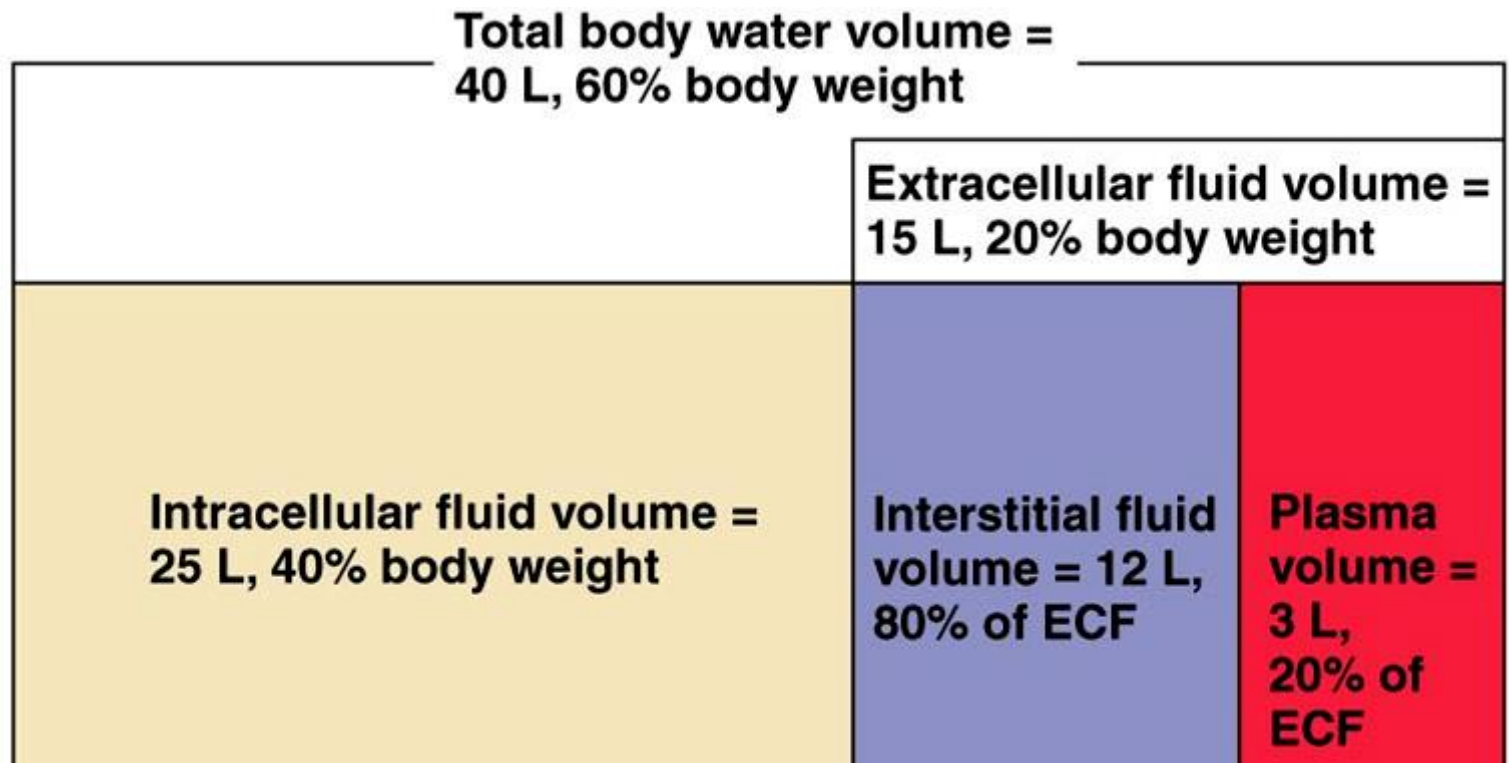


Fig. 26.1

4.4.2 remind yourselves of the differences between electrolytes & non-electrolytes and of the key electrolytes in ICF & ECF

- electrolytes have greater osmotic power than non-electrolytes – Why?
- **in ECF:** chief cation is _____ and chief anion is _____
- **in ICF:** chief cation is _____ and chief anion is _____
- Na^+ and K^+ are **opposite**, when comparing ECF & ICF \Rightarrow ATP-dependent Na/K pumps keep intracellular $[\text{Na}^+]$ low and maintain high intracellular $[\text{K}^+]$

renal mechanisms can reinforce these ion distributions by secreting K^+ as Na^+ is reabsorbed from filtrate

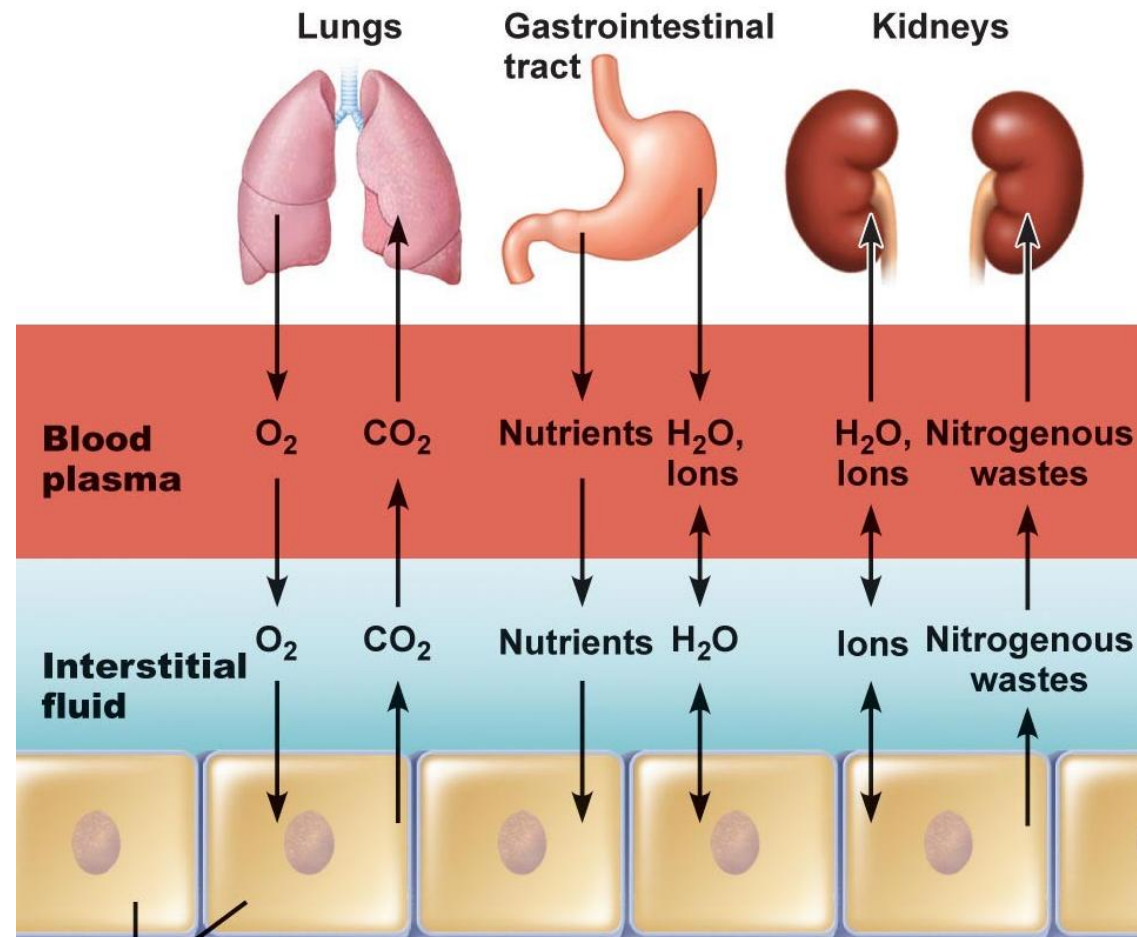


Fig. 26.3

$\text{mEq/L} = [\text{mg/L}] / \text{atomic weight} \times \text{number electrical charges/atom}$
 $\text{Na}^+ : 3300 / 23 \times 1 = 143 \text{ mEq/L}$; $\text{Ca}^{2+} : 100 / 40 \times 2 = 5 \text{ mEq/L}$

- Blood plasma
- Interstitial fluid
- Intracellular fluid

- Na^+ Sodium
- K^+ Potassium
- Ca^{2+} Calcium
- Mg^{2+} Magnesium
- HCO_3^- Bicarbonate
- Cl^- Chloride
- HPO_4^{2-} Hydrogen phosphate
- SO_4^{2-} Sulfate

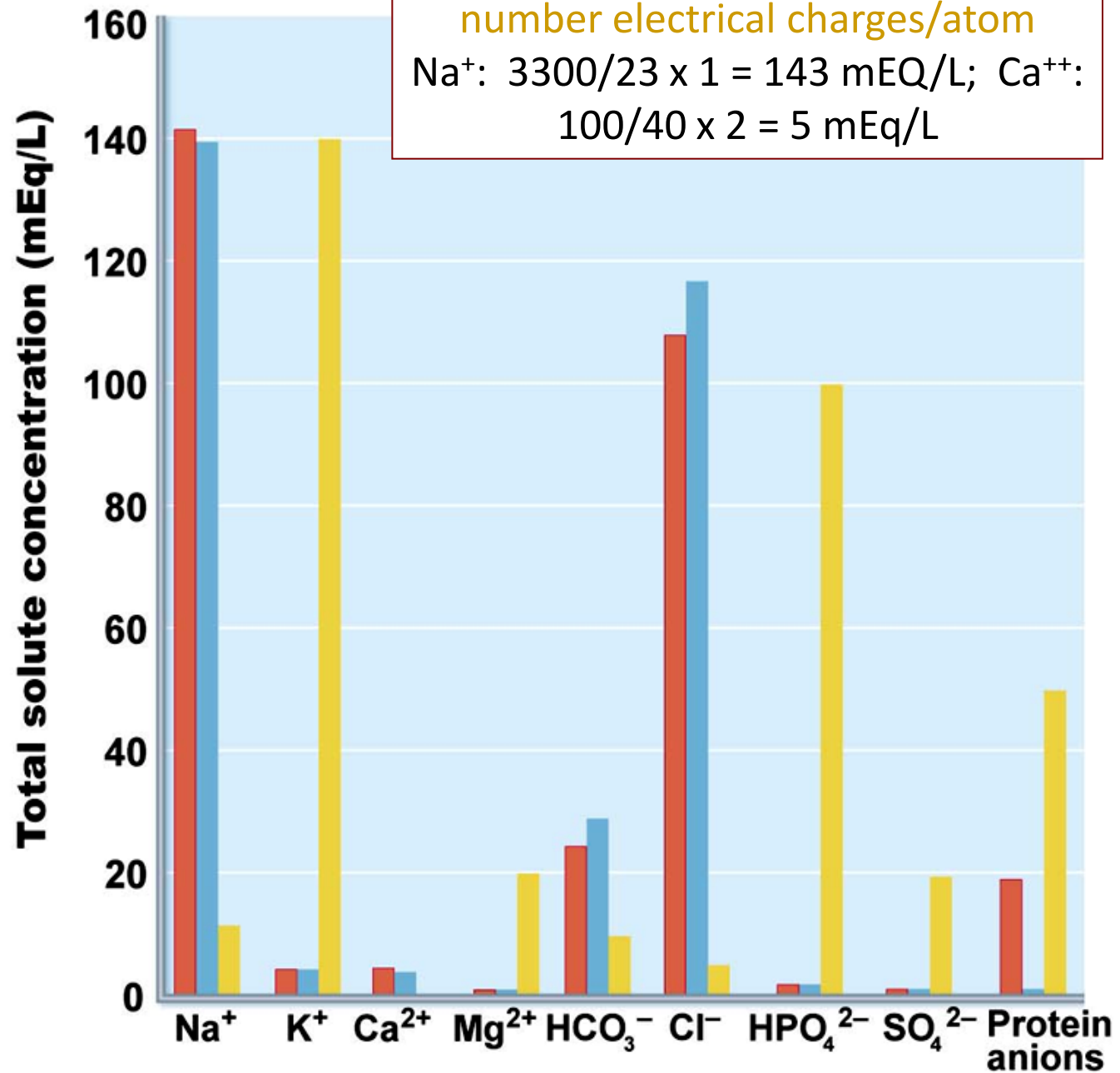


Fig. 26.2

4.4.3 define water balance

- water intake must = water output

Intake: liquids, foods, cellular metabolism

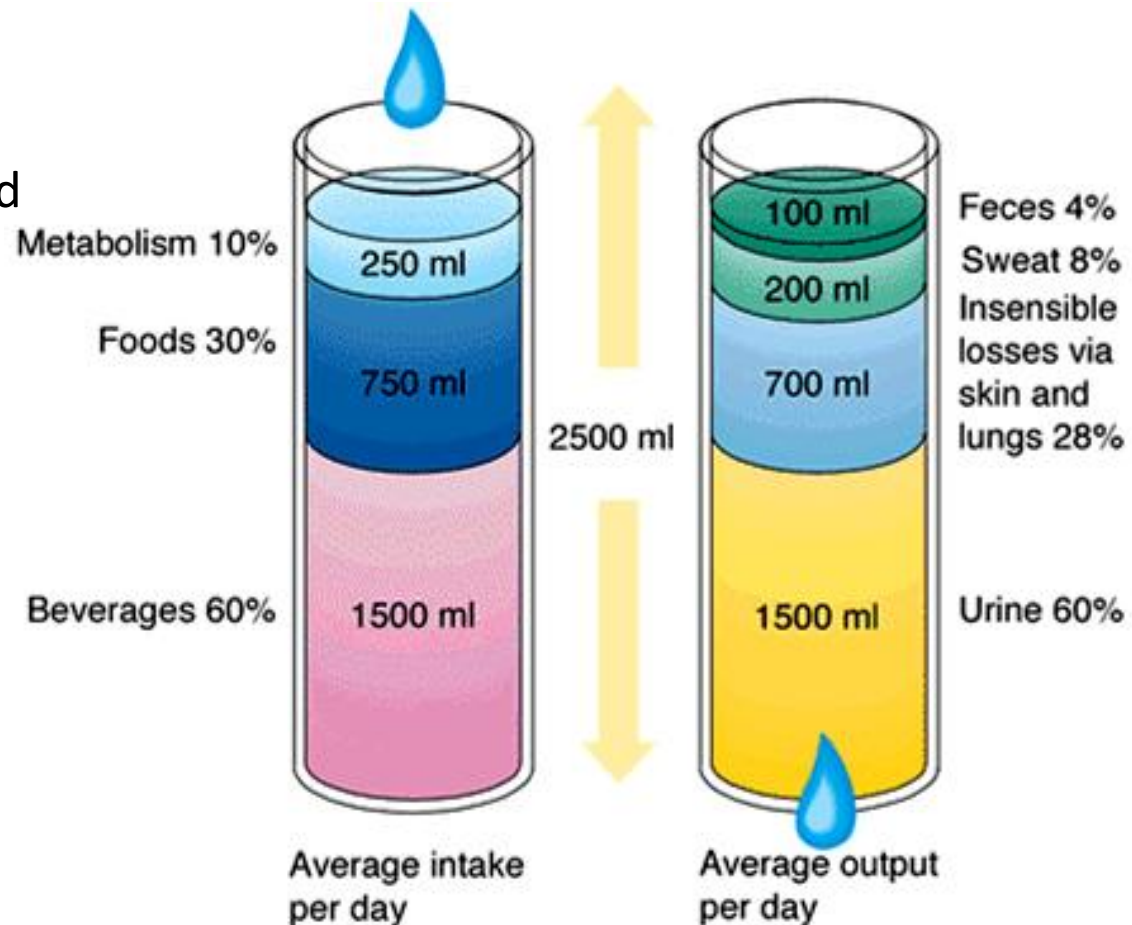
Output: ~60% via kidneys; also lungs, skin, sweat, feces

Increased plasma osmolality (usu 285-300 mOsm):

- (1) **thirsty** → increase water intake
- (2) **ADH** stimulates renal water reabsorption

Decreased plasma osmolality:

- (1) thirst **not** stimulated
- (2) ADH secretion **not** stimulated



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Fig. 26.4

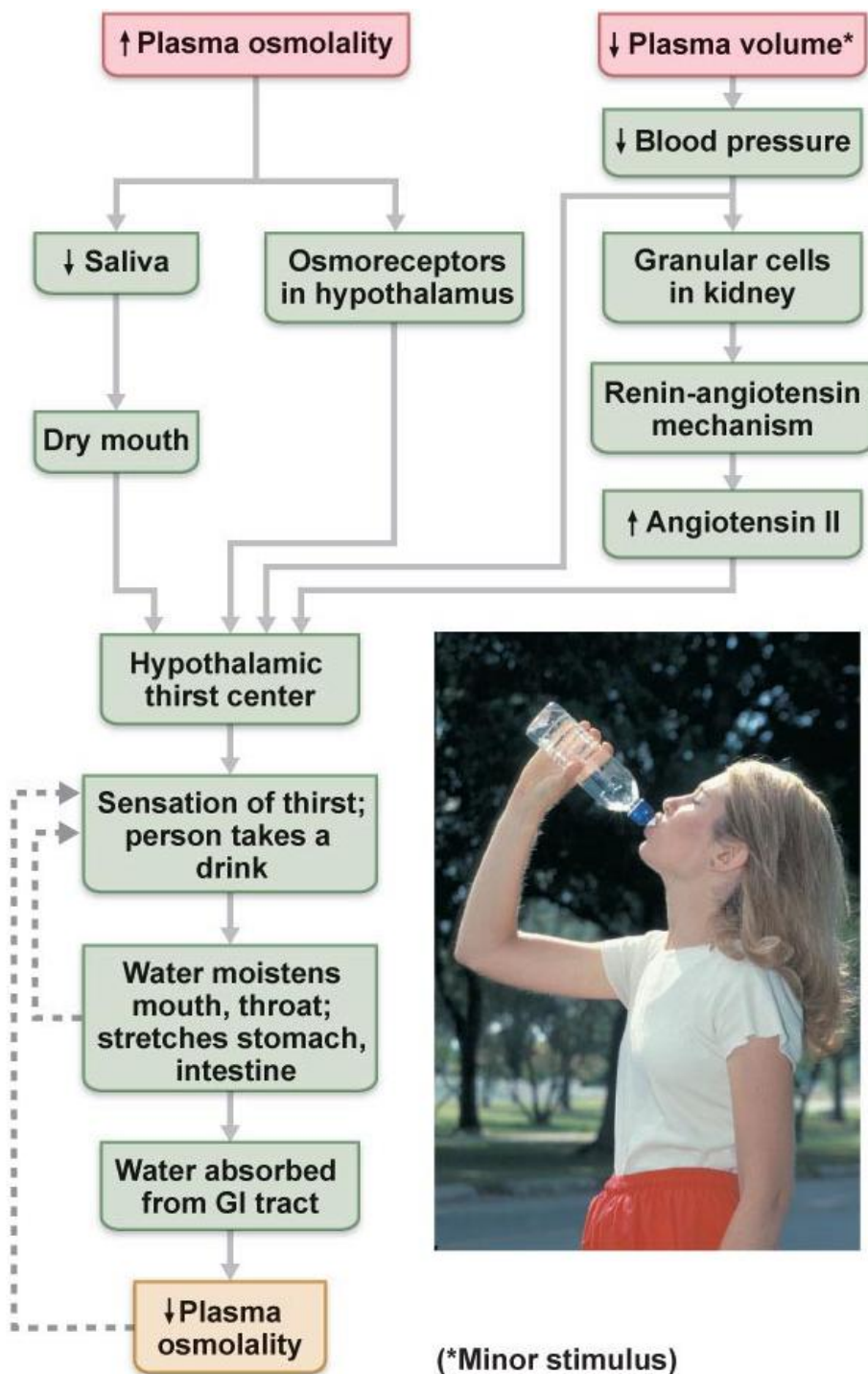
4.4.3 (cont) describe the thirst mechanism

- (1) ↓ in plasma volume of $\geq 10\%$ or 1-2% ↑ in plasma osmolarity \Rightarrow dry mouth
- (2) osmoreceptors of hypothalamic thirst centre lose water to hypertonic ECF \rightarrow become irritable & depolarize

dampening of thirst begins once mucosa of mouth & throat moistened \rightarrow prevents overdrinking while water moves to ECF

Obligatory water losses:

- (i) insensible water loss via lungs/skin
- (ii) via feces
- (iii) min sensible urinary loss = 500 ml/day



(*Minor stimulus)

Fig. 26.5 The thirst mechanism for regulating water intake

- Initial stimulus
- Physiological response
- Result
- ← Increases, stimulates
- ← - - - Reduces, inhibits

Disorders of water balance:

(i) Dehydration:

(ii) Hypotonic hydration:

(iii) Edema:



(a) Mechanism of dehydration



Fig. 26.7

(b) Mechanism of hypotonic hydration

4.4.4 justify the role of sodium as the only solute exerting significant osmotic pressure and describe the influences on sodium balance of: aldosterone, cardiovascular baroreceptors, ADH and ANF

water follows salt!!!

- salt content of body can vary due to: diet, loss via sweating, vomiting, etc

1. Sodium

- 90-95% of ECF solute; NaCl & NaHCO₃ contribute 280/300 mOsm solute concentration; the only solute exerting significant osmotic pressure
- regulating Na⁺ balance one of most important functions of kidneys
- *sodium content of body may change, but its concentration in ECF remains stable due to **immediate** adjustments in water volume (what happens to bp after salty meal?)*

Factors influencing [Na⁺]

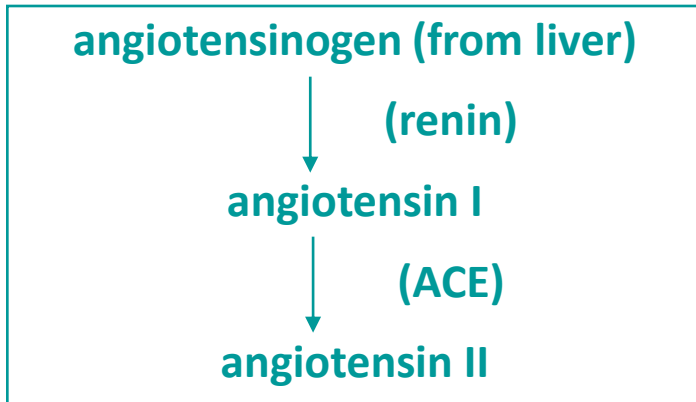
(a) Aldosterone

- most influential agent wrt kidney; acts slowly
- even without aldosterone, 65% Na⁺ in filtrate reabsorbed in PCT & 25% in loop of Henle; aldosterone secretion essential to life
- high aldosterone: virtually all remaining Na⁺ (chloride co-transported) actively reabsorbed by DCT & collecting ducts

2 pathways to aldosterone secretion:

- (i) *renin-angiotensin system*
- (ii) *direct effect of high K^+ or low Na^+ renin secretion in response to:*

- (i) *symp ns*
- (ii) *decreased filtrate osmolarity*
- (iii) *decreased stretch (bp)*



Addison's disease

hyopsecretion of aldosterone
excess loss of Na^+ & water in
urine

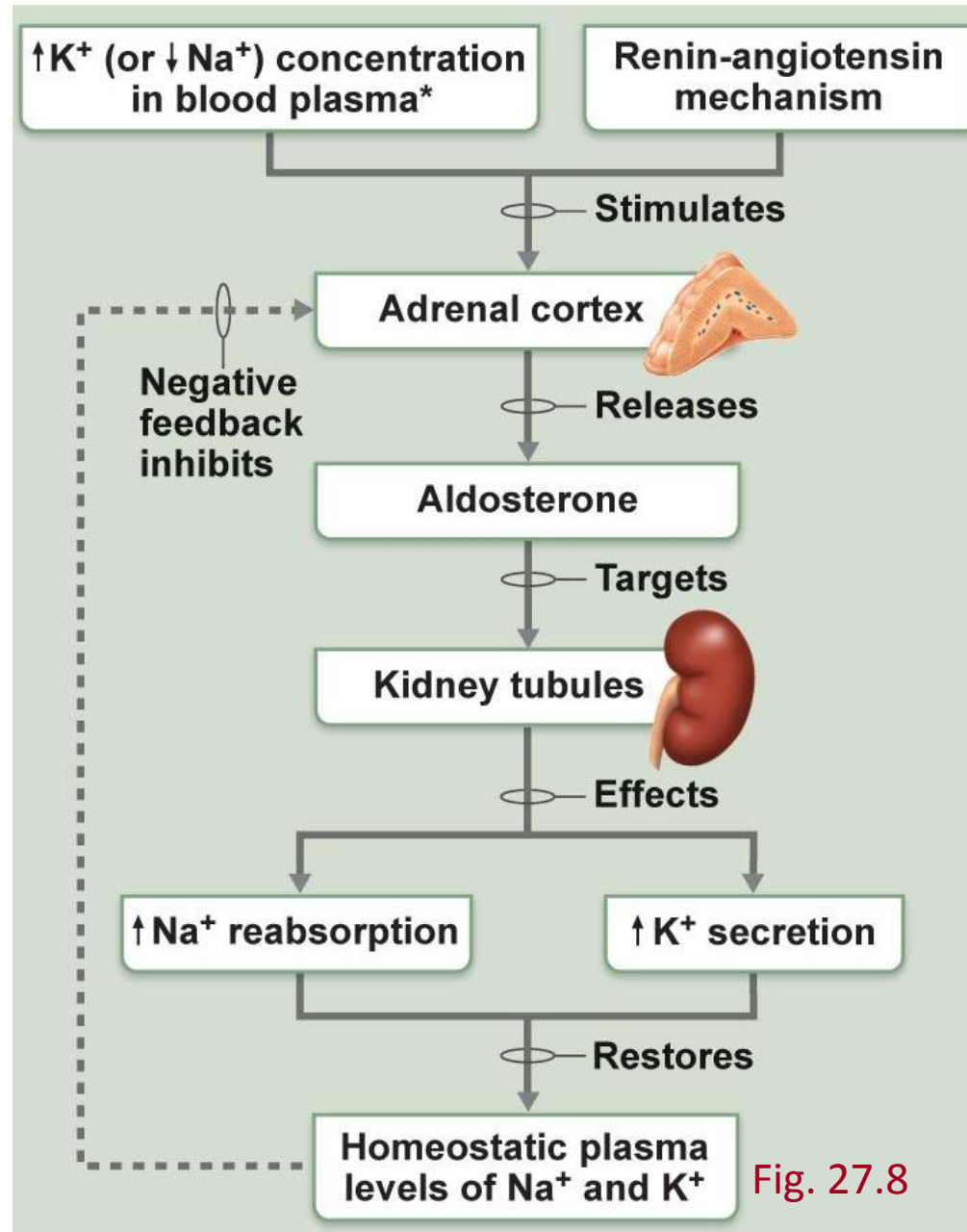


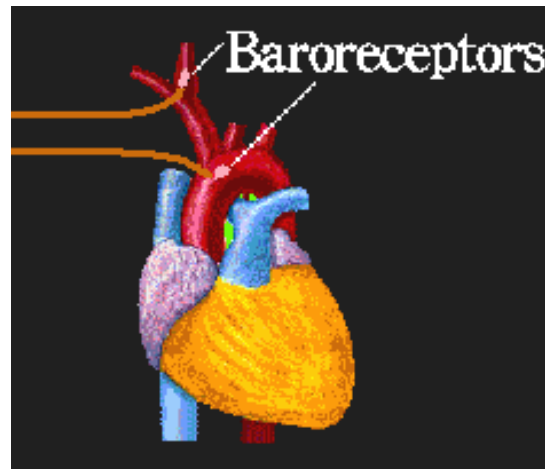
Fig. 27.8

(b) Cardiovascular Baroreceptors

- **pressure diuresis:**

when blood volume and/or pressure \uparrow , symp input to kidney $\downarrow \Rightarrow \Rightarrow$ result is dilation of afferent arterioles & \uparrow GFR --- overall result is???

- not that effective – why????
- $[\text{Na}^+]$ **determines** blood volume



<http://user.gru.net/clawrence/vccl/chpt6/local.htm>

(c) ADH

water reabsorption in collecting ducts relies on ADH secretion

osmoreceptors in hypothalamus:

- (i) **low $[Na^+]$** = excess fluid → reduced ADH secretion & dilute urine
- (ii) **high $[Na^+]$** = decreased blood volume → ADH & reduced urine volume

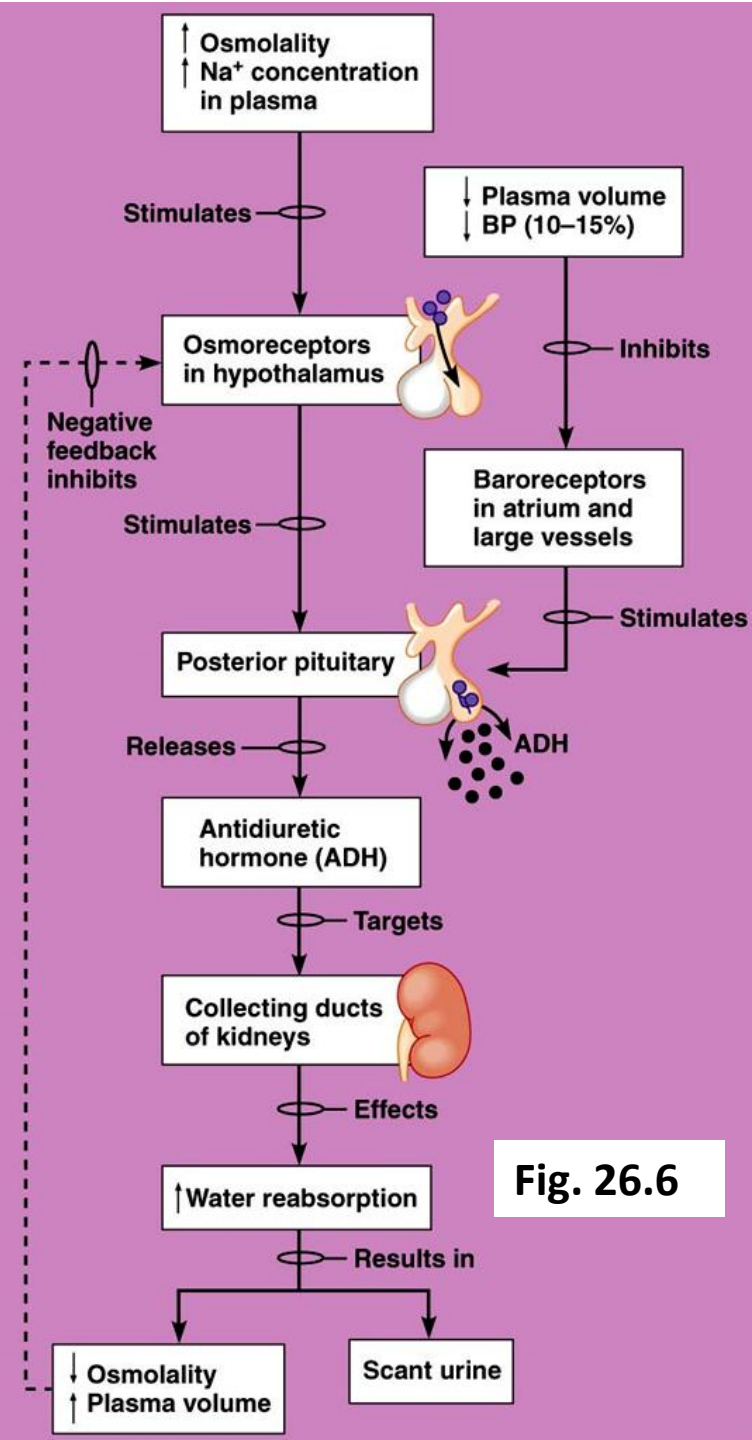


Fig. 26.6

(d) Atrial Natriuretic Factor

- released by certain cardiac cells when bp ↑
- potent **diuretic** & **natriuretic** hormone:
 - (i) inhibits Na^+ reabsorption by DCT & collecting duct
 - (ii) ↓ release of ADH, renin & aldosterone
 - (iii) induces vasodilationoverall effect is to **reduce** bp

(e) Other Hormones

- (i) Estradiol
- (ii) Progesterone
- (iii) Cortisol

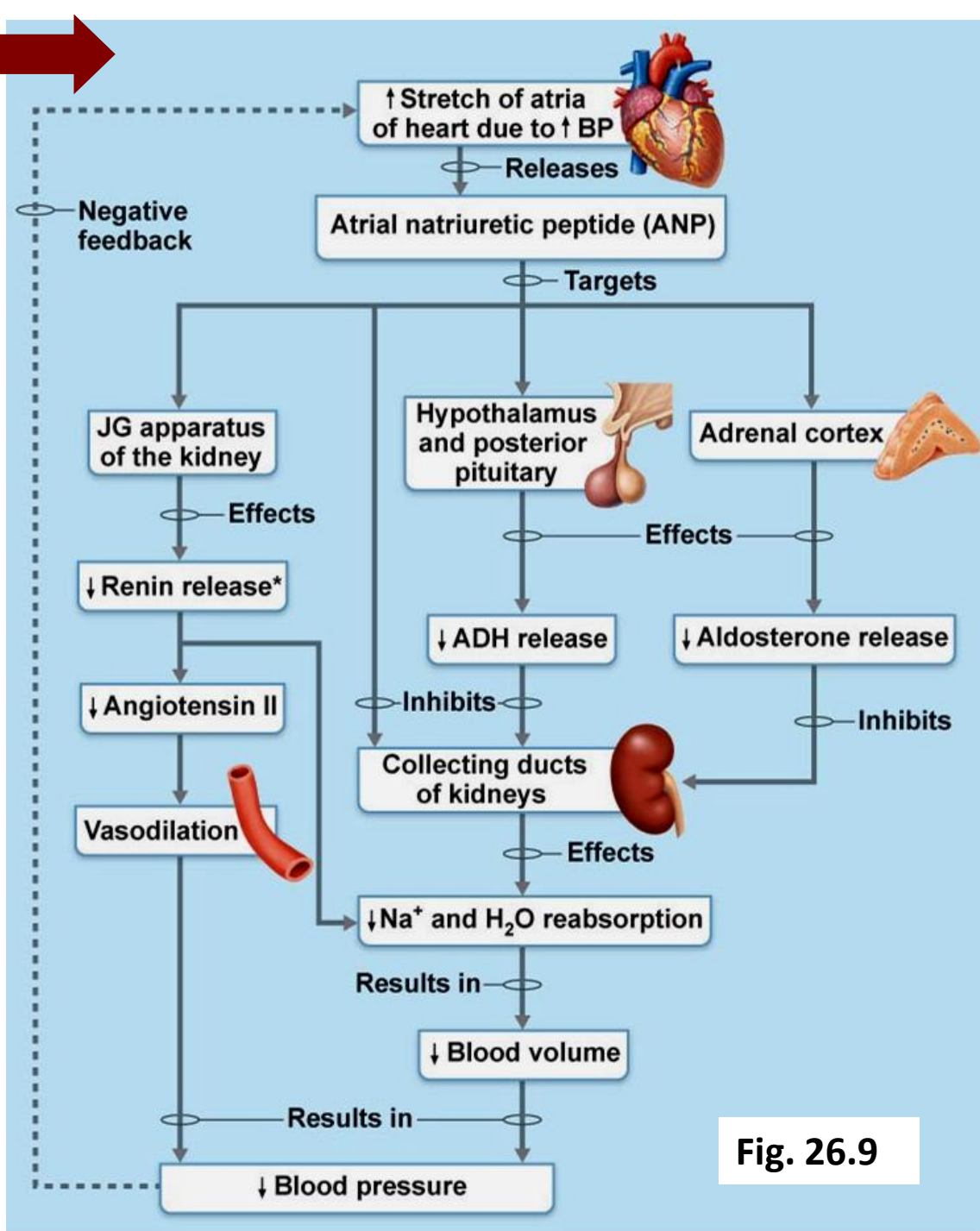


Fig. 26.9

4.4.5 outline the main features of potassium balance

- high $[K^+]$ in ECF is **toxic**
 - √ reduces membrane excitability
 - √ involved in acid-base balance
- usu 10% K^+ in filtrate lost (90% _____)
- if $[K^+]$ in ECF high, tubular **secretion** (principal cells of cortical collecting ducts)
- dietary K^+ important – why??



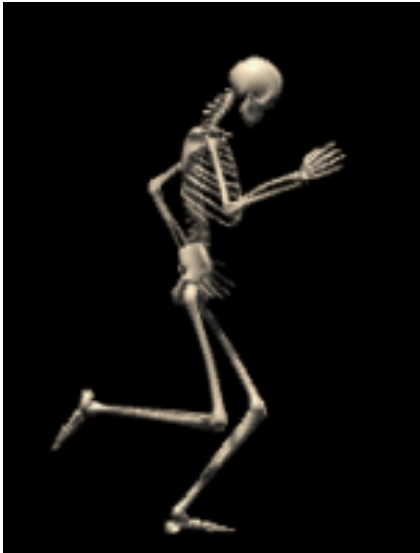
2 factors determine rate & extent of K^+ excretion:

(i) *plasma $[K^+]$*

(ii) *[aldosterone]*

4.4.6 outline the main features of calcium and phosphate balance

- 99% of body's calcium found in bone
- Ca^{++} important for: _____, _____, _____ --
hence must be **closely regulated**
- 2 hormones:
 - (i) **PTH**: primary, from parathyroid glands; **increases** blood Ca^{++}
 - (ii) **calcitonin**: parafollicular cells of thyroid gland; **decreases** blood calcium
- usu ~98% filtered Ca^{++} is reabsorbed



<http://www.edb.utexas.edu/faculty/dingwell/>

(a) PTH:

- stimulus for secretion is **drop** in blood Ca^{++}
 - (i) **bone** (osteoclasts)
 - (ii) **small intestine**
 - (iii) **kidneys** – **opposite** effects on Ca^{++} vs **phosphate**
- most (~75%) of filtered **phosphate** reabsorbed in proximal tubules by AT
 - (1) **no PTH:** **phosphate** reabsorbed to T_m
 - (2) **high PTH:** reduced AT of **phosphate**

(b) calcitonin:

- stimulus for secretion is rising blood Ca^{++}

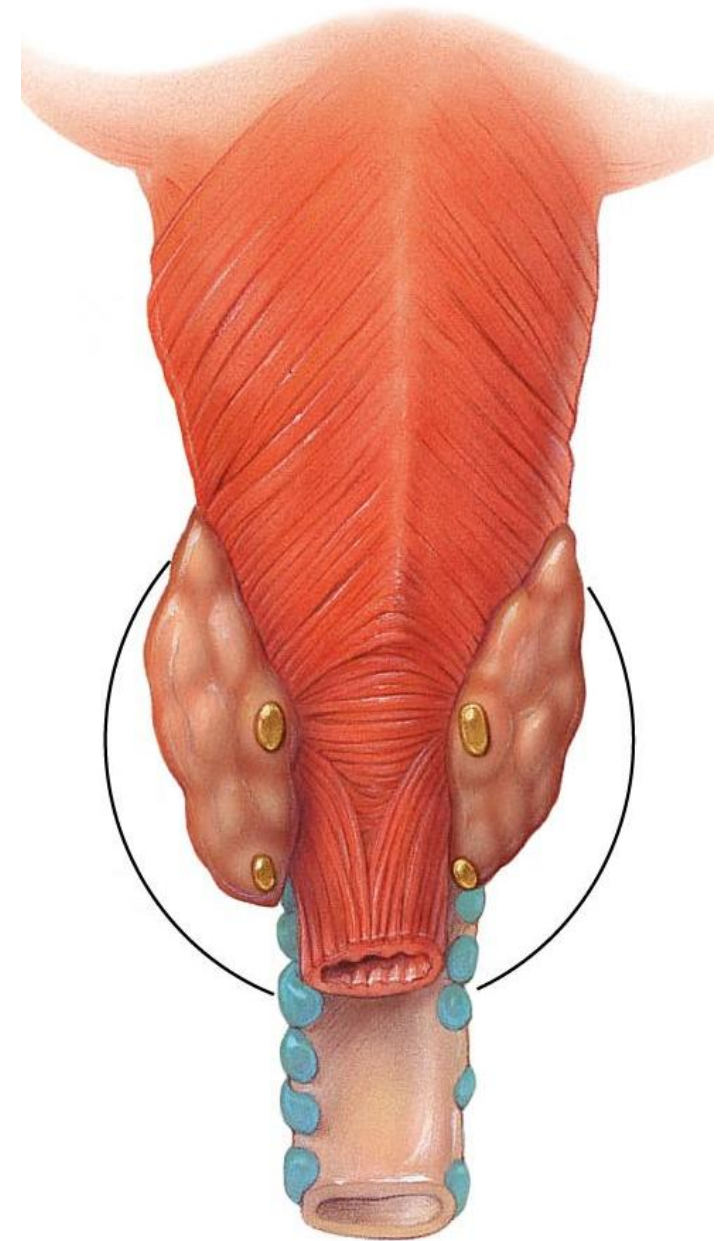


Fig. 16.11 – Posterior view of Thyroid Gland

4.4.7 describe the 3 mechanisms of acid-base balance used in the body; describe in detail the 3rd mechanism – the role of the kidneys

- **very important:** activity of functional ptns depends on pH (7.4 arterial, 7.35 venous, 7.0 intracellular)

What is alkalosis? What is acidosis?

Sources of acid:

- (i) Breakdown of phosphorus-containing ptns → phosphoric acid
- (ii) Anaerobic metabolism of glucose →
- (iii) Fat metabolism → fatty acids & ketone bodies
- (iv) Loading & transport of CO₂ as bicarbonate → H⁺ ions
- (v) HCl released during digestion stays in GI tract but must be buffered

Blood [H⁺] is regulated by:

(1) Chemical buffer systems: (H₂CO₃ ⇌ HCO₃⁻, Na₂HPO₄ ⇌ NaH₂PO₄, protein buffers)

pro:

con:

(2) Respiratory centre in brain stem:

pro:

con:

(3) Renal mechanisms:

pro:

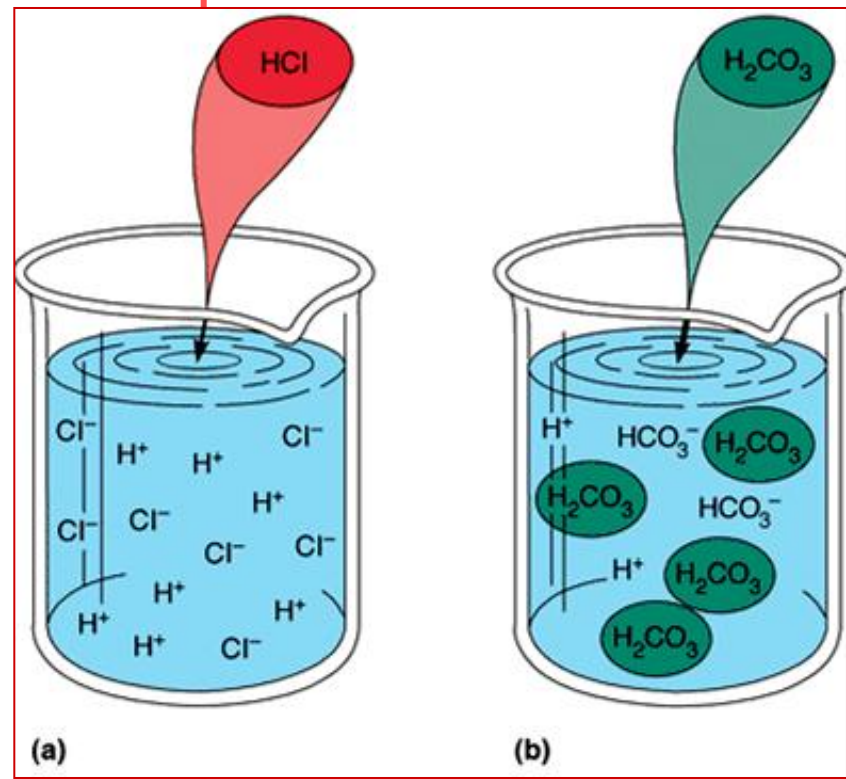
con:

• renal mechanism involves:

(1) excreting bicarbonate (= gaining H⁺)

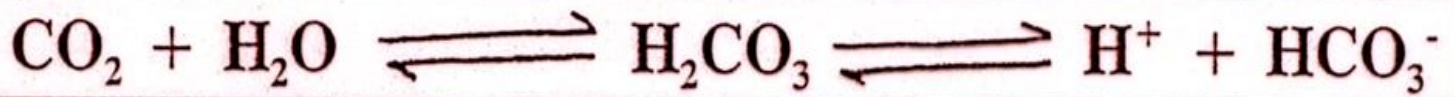
(2) reabsorbing or generating new bicarbonate (= getting rid of H⁺)

Fig. 26.11



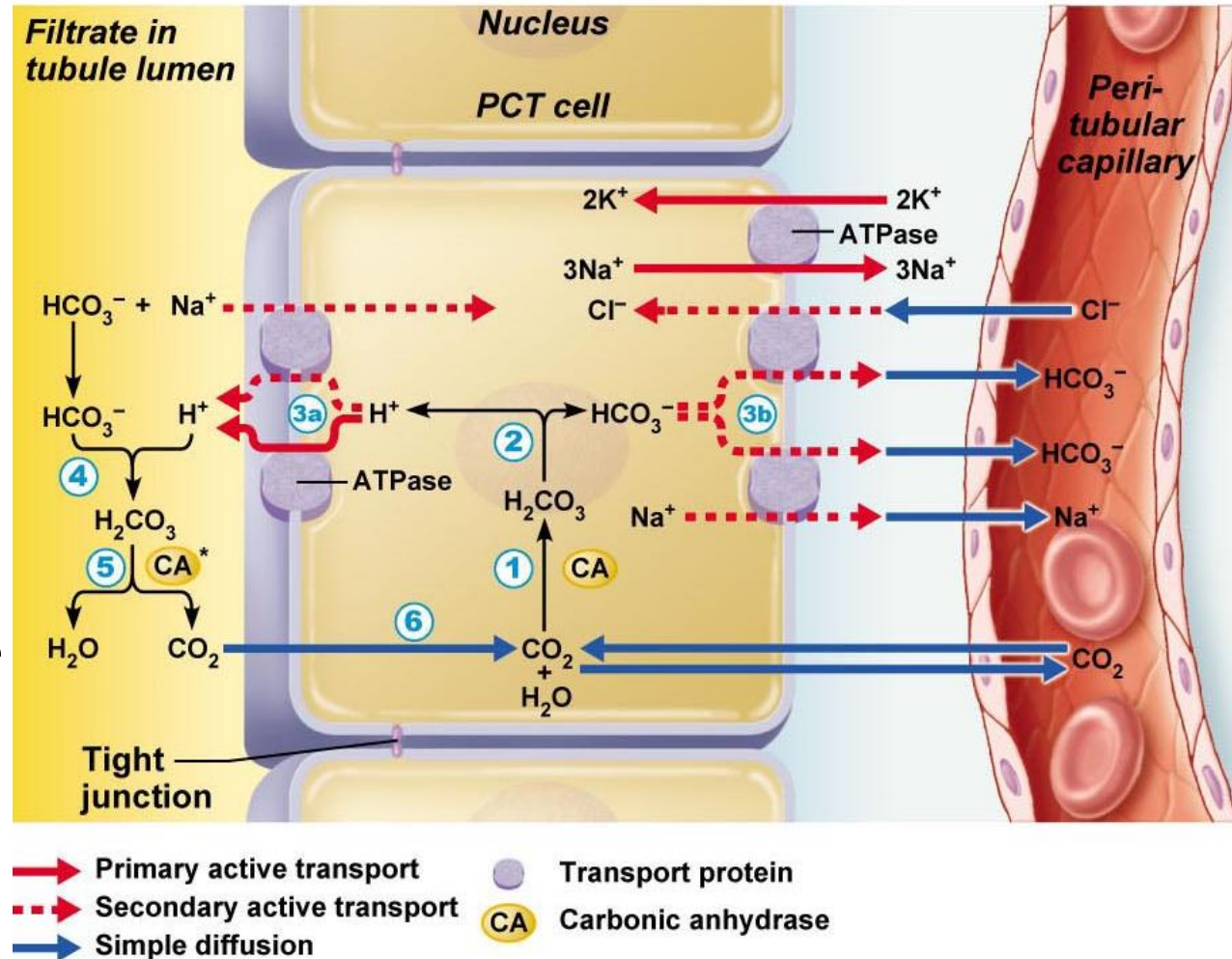
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H⁺ Secretion:

- (1) tubule & collecting duct respond to pH of ECF & alter rate of H⁺ secretion
- (2) Secreted H⁺ comes from carbonic acid
- (3) For each H⁺ actively secreted into tubule lumen, one Na⁺ is reabsorbed, maintaining electrochemical balance
- (4) H⁺ can combine with HCO₃⁻ producing CO₂ & H₂O; CO₂ returns to tubule cell & promotes more H⁺ secretion



Bicarbonate reabsorption:

Problem: tubule cells almost completely impermeable to bicarbonate in filtrate

- need to constantly replenish body's stores of bicarbonate

(why?? how is it lost??)

- bicarbonate ions are reabsorbed **indirectly** from bicarbonate made in tubule cells
- Na^+ accompanies HCO_3^- into peritubular capillaries

Generating new bicarbonate ions:

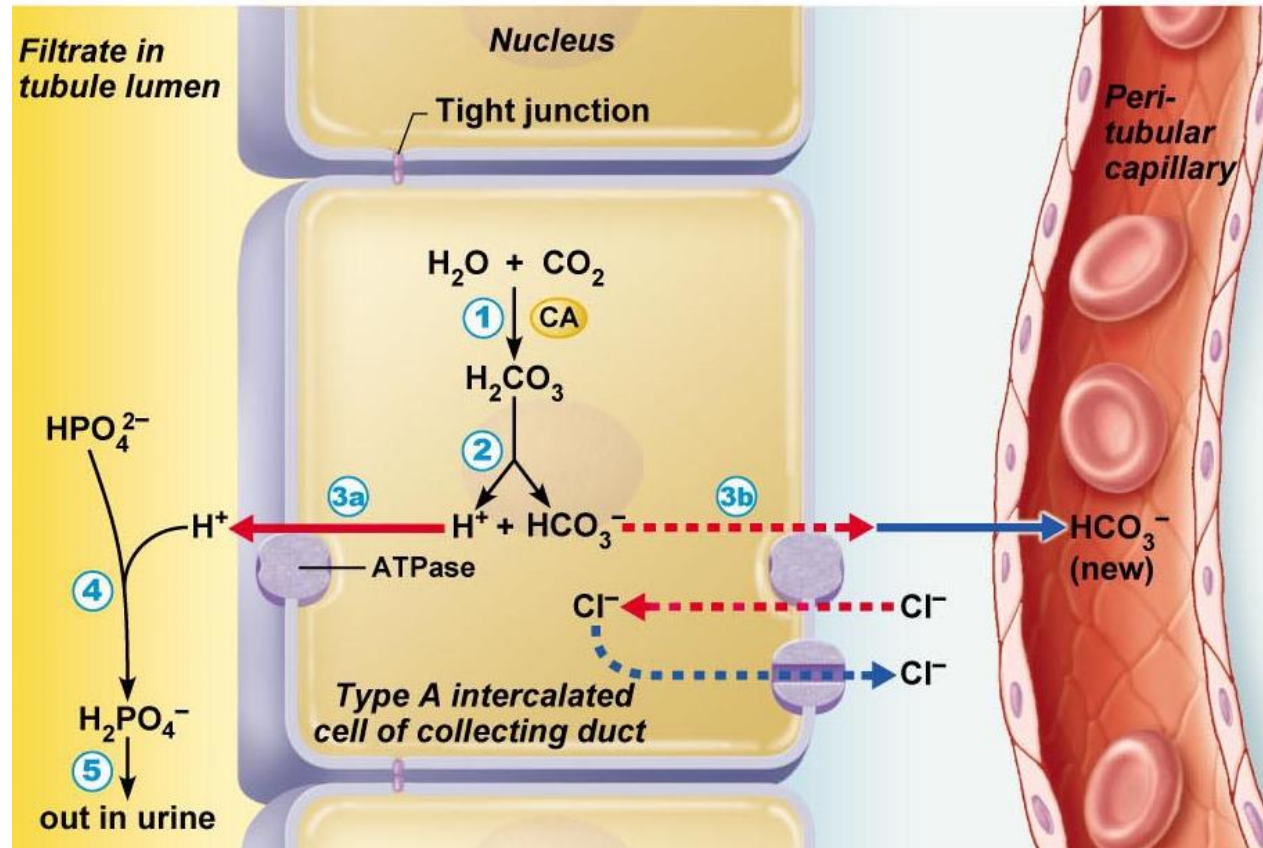
- bicarb reabsorption just recycles bicarb already present in body
- **new** H^+ enters via diet ➤ must generate **new** bicarb to maintain pH
 - (i) phosphate buffer system
 - (ii) NH_4^+ excretion

Phosphate buffer system:

weak base is HPO_4^{2-}

components freely filter into tubules; usually ~75% reabsorbed, except during acidosis

type A intercalated cells actively secrete H^+ (**new** HCO_3^- generated as byproduct; $\text{HCO}_3^-/\text{Cl}^-$ antiport)



- Primary active transport
- Secondary active transport
- Simple diffusion
- Facilitated diffusion
- Transport protein
- Ion channel
- Carbonic anhydrase

Fig. 26.13: Phosphate buffer system

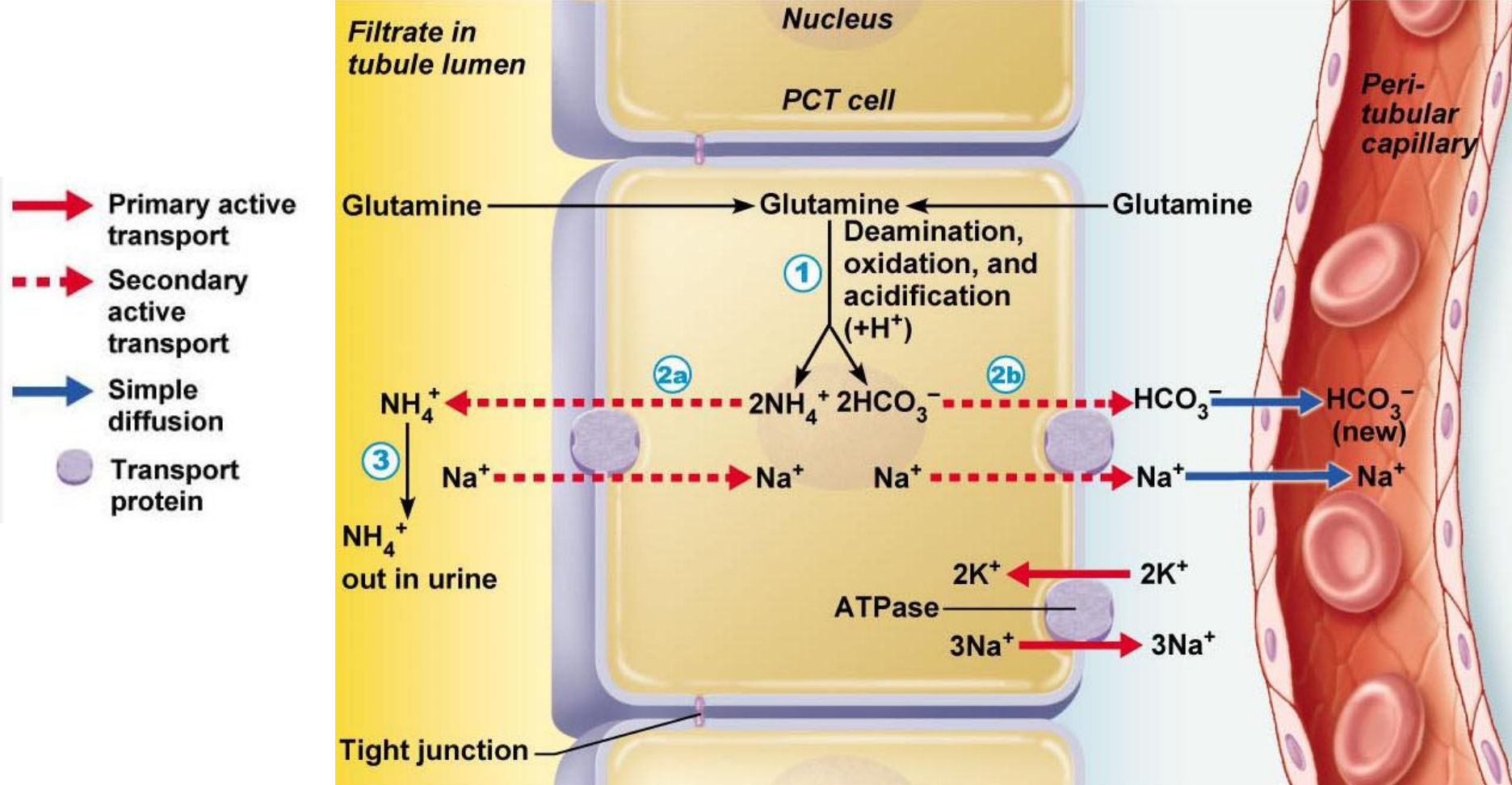


Fig. 26.14: NH₄⁺ excretion

NH₄⁺ Excretion:

- generated in PCT cells by metabolism of glutamine
- HCO₃⁻ moves into blood; NH₄⁺ is a very weak acid – lost via urine

Bicarbonate ion excretion:

- more rare occurrence; type B intercalated cells; reverse of reabsorption

TABLE 26.2

Causes and Consequences of Acid-Base Imbalances

| CONDITION AND HALLMARK | POSSIBLE CAUSES; COMMENTS |
|---|--|
| Metabolic Acidosis | |
| If uncompensated (uncorrected): $\text{HCO}_3^- < 22$ mEq/L; $\text{pH} < 7.35$ | <p>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</p> <p>Renal disease: failure of kidneys to rid body of acids formed by normal metabolic processes</p> <p>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</p> <p>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</p> <p>Excess alcohol ingestion: results in excess acids in blood</p> <p>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</p> |
| Metabolic Alkalosis | |
| If uncompensated: $\text{HCO}_3^- > 26$ mEq/L; $\text{pH} > 7.45$ | <p>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</p> <p>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.</p> <p>Ingestion of excessive sodium bicarbonate (antacid): bicarbonate moves easily into ECF, where it enhances natural alkaline reserve</p> <p>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.</p> |

TABLE 26.2

Causes and Consequences of Acid-Base Imbalances (continued)

CONDITION
AND HALLMARK

POSSIBLE CAUSES; COMMENTS

Respiratory Acidosis (Hypoventilation)

If uncompensated:
 $P_{CO_2} > 45$ mm Hg;
 $pH < 7.35$

Impaired lung function (e.g., in chronic bronchitis, cystic fibrosis, emphysema): impaired gas exchange or alveolar P_{CO_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)

If 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

Normal range in plasma

pH 7.35–7.45

P_{CO_2} 35–45 mm Hg

HCO_3^- 22–26 mEq/L

Acid-base disturbance

| | | | |
|-----------------------|---|-------------------|-------------------|
| Respiratory acidosis | ↓ | ↑ | ↑ if compensating |
| Respiratory alkalosis | ↑ | ↓ | ↓ if compensating |
| Metabolic acidosis | ↓ | ↓ if compensating | ↓ |
| Metabolic alkalosis | ↑ | ↑ if compensating | ↑ |

Problem #1

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UofO*

Blood values: pH 7.6, $P(\text{CO}_2)$ 24 mm Hg, $\text{HCO}_3^- = 23$ mEq/L

Problem #2

Blood values: pH 7.48, $P(\text{CO}_2)$ 46 mm Hg, $\text{HCO}_3^- = 33$ mEq/L





1. Effects of aldosterone include:

- a) increase in sodium ion excretion
- b) increase in water retention
- c) increase in $[K^+]$ in the urine
- d) higher blood pressure
- e) b), c) and d)

2. To calculate renal clearance, one must know:

- a) the concentration of the substance in the plasma
- b) the concentration of the substance in the urine
- c) the glomerular filtration rate
- d) a) and b)
- e) a), b) and c)

3. TR was standing at a urinal in a crowded public rest room and a long line was forming behind him. He became anxious and found he could not micturate. Use logic to deduce TR's problem.

- a) his internal urethral sphincter would not relax
- b) his external urethral sphincter would not relax
- c) his detrusor muscle was contracting too forcefully
- d) he almost certainly had a burst bladder

3. Inhibition of ADH secretion:

- a) is caused by alcohol consumption
- b) results in edema
- c) disturbs acid-base balance
- d) is triggered by hyponatremia
- e) a) and d)

