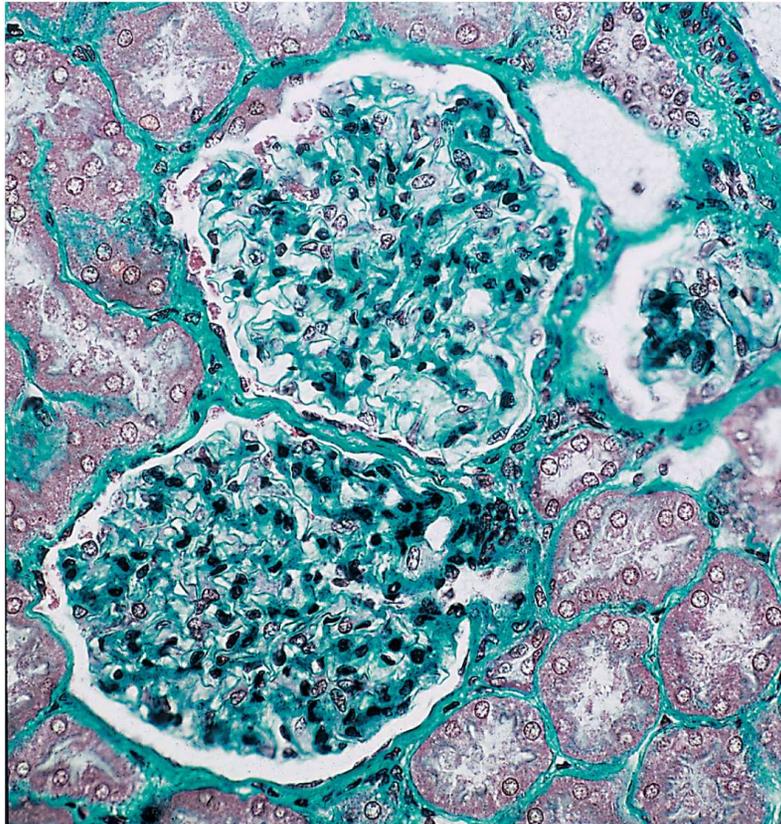


Chapter 27

Homeostatic Balance

Water / Electrolytes / pH



What in Our Body Fluids Needs to be “Balanced”?



Three “essential fluid components” need to be controlled by homeostatic mechanisms

water balance // average daily water intake and loss are equal

electrolyte balance // the amount of electrolytes absorbed by the small intestine balance with the amount lost from the body, usually in urine

acid-base balance // the body ability to rids itself of acid (hydrogen ion – H^+) at a rate that balances metabolic production

Fluid Compartments



- Major fluid compartments of the body
 - 65% **intracellular fluid** (ICF)
 - 35% **extracellular fluid** (ECF)
 - 25% tissue (**interstitial**) fluid
 - 8% blood plasma and lymphatic fluid (**vascular**)
 - 2% **transcellular fluid** 'catch-all' category ///
cerebrospinal, synovial, peritoneal, pleural, and pericardial
fluids /// vitreous and aqueous humors of the eye /// bile,
and fluids of the digestive, urinary, and reproductive tracts

Body Water

- **Total body water** (TBW) of a 70kg (150 lb) young male is about **40 liters**
 - newborn baby's body weight is about **75%** water
 - young men average **55% - 60%**
 - women average **slightly less** (higher fat content)
 - obese and elderly people as little as **45%** by weight

Fluid Homeostasis Requires Functional Integration of Many Systems

- Cellular function requires a **fluid medium** with a carefully controlled composition
- These fluid compartments must be “balanced” and maintained by the **collective action of the following systems:**
 - Urinary
 - Respiratory
 - Digestive
 - Integumentary
 - Endocrine
 - Nervous
 - Cardiovascular
 - Lymphatic

How Does Water Move Between Fluid Compartments?



- fluid continually exchanged between compartments
- water moves across membranes by osmosis
- Water molecules also follow ions able to cross through the semipermeable membrane
- because water moves easily through plasma membranes, osmotic gradients never last for very long
- if an imbalance arises, osmosis restores balance within seconds so the osmolarity in the intracellular and extracellular osmolarity is equal
 - *if osmolarity in extracellular fluid rises then water moves out of the cell*
 - *if osmolarity in extracellular fluid falls then water moves into the cell*

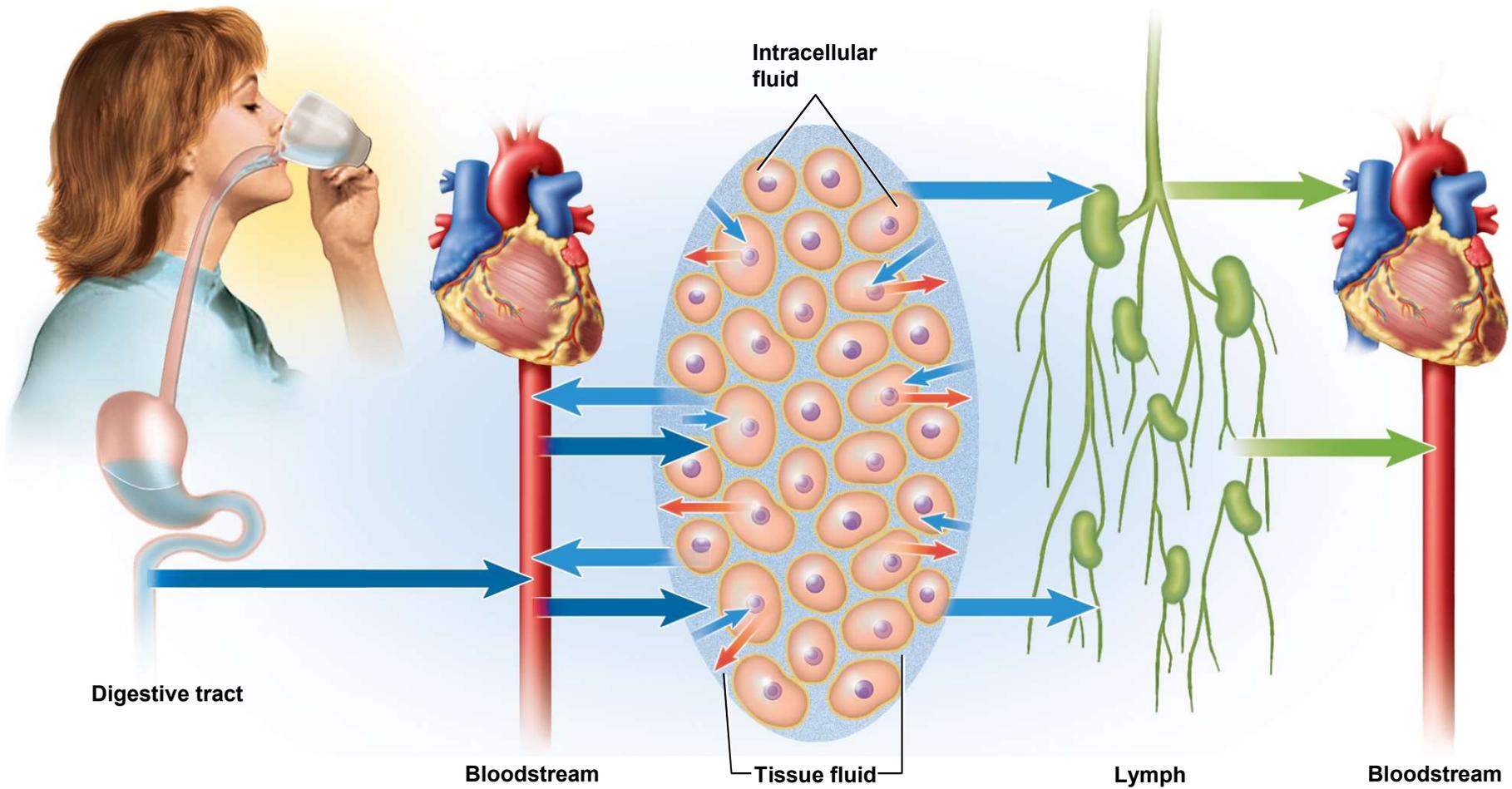
Water Movement Between Fluid Compartments

- The movement of water (i.e. osmosis) from one fluid compartment to another is determined by the relative concentrations of solutes that are large enough to be restricted by the membranes between the compartments
- Electrolytes play the principal role in governing the body's water distribution and total water content
- Electrolytes – they are the most abundant solute particles / water must follow (i.e. obligate) electrolyte movement!

sodium salts in ECF

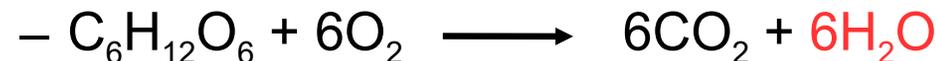
potassium salts in ICF

Water Movement Between Fluid Compartments



Fluid Balance Requires That the Loss = Gain

- Fluid balance is when daily gains and losses are equal /// **about 2,500 mL/day**
- Gains come from two sources
 - **preformed water** (2,300 mL/day)
 - ingested in food (700 mL/day)
 - drink (1600 mL/day)
 - **metabolic water** (200 mL/day)
 - made during aerobic metabolism and dehydration synthesis



How do we lose water?



Two Types of Water Losses

Sensible water loss /// this is observable

1,500 mL/ day is in urine

200 mL/day is in feces

100 mL/day is sweat in resting adult

Insensible water loss /// this is unnoticed

300 mL/day in expired breath

400 mL/day is cutaneous transpiration // diffuses through epidermis and evaporates // does not come from sweat glands

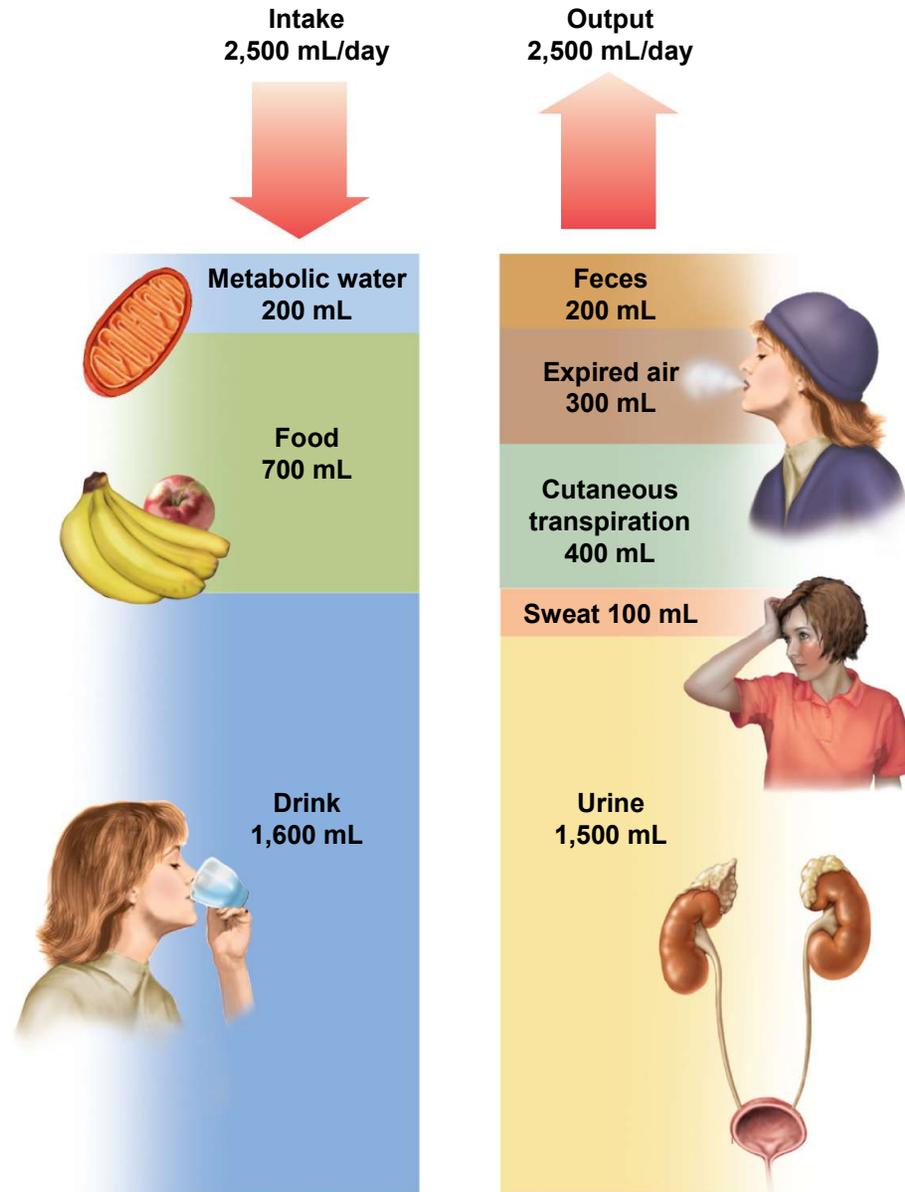
loss varies greatly with environment and activity

Obligatory water loss is output that is relatively unavoidable /// expired air, cutaneous transpiration, sweat, fecal moisture, and urine output

Fluid Balance



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Regulation of Fluid Intake

- **Thirst is a conscious sensation to a subconscious stimuli.** This changes our behavior so we seek fluid intake. What stimuli triggers thirst? 1) dehydration and 2) increase osmolarity
 - **dehydration** results in increase blood osmolarity accompanied by low blood volume “linked to” low blood pressure
 - **osmoreceptors** in hypothalamus sense increase in osmolarity
 - osmoreceptors communicate with the hypothalamus and cerebral cortex (conscious and unconscious responses) /// hypothalamus produces antidiuretic hormone /// promotes water conservation
 - cerebral cortex dictates our behaviour so we seek water intake

Regulation of Fluid Intake

Tissue in kidneys (juxamedullary cells) **sense reduced blood pressure**

activates the renin – angiotensin - aldosterone mechanism

BP drops (concurrent rise in osmolarity of ECF) with a drop in blood volume

Cerebral cortex produces conscious sense of thirst /// receptors in brain for Angiotensin and ADH - regulate systemic tissues and brain

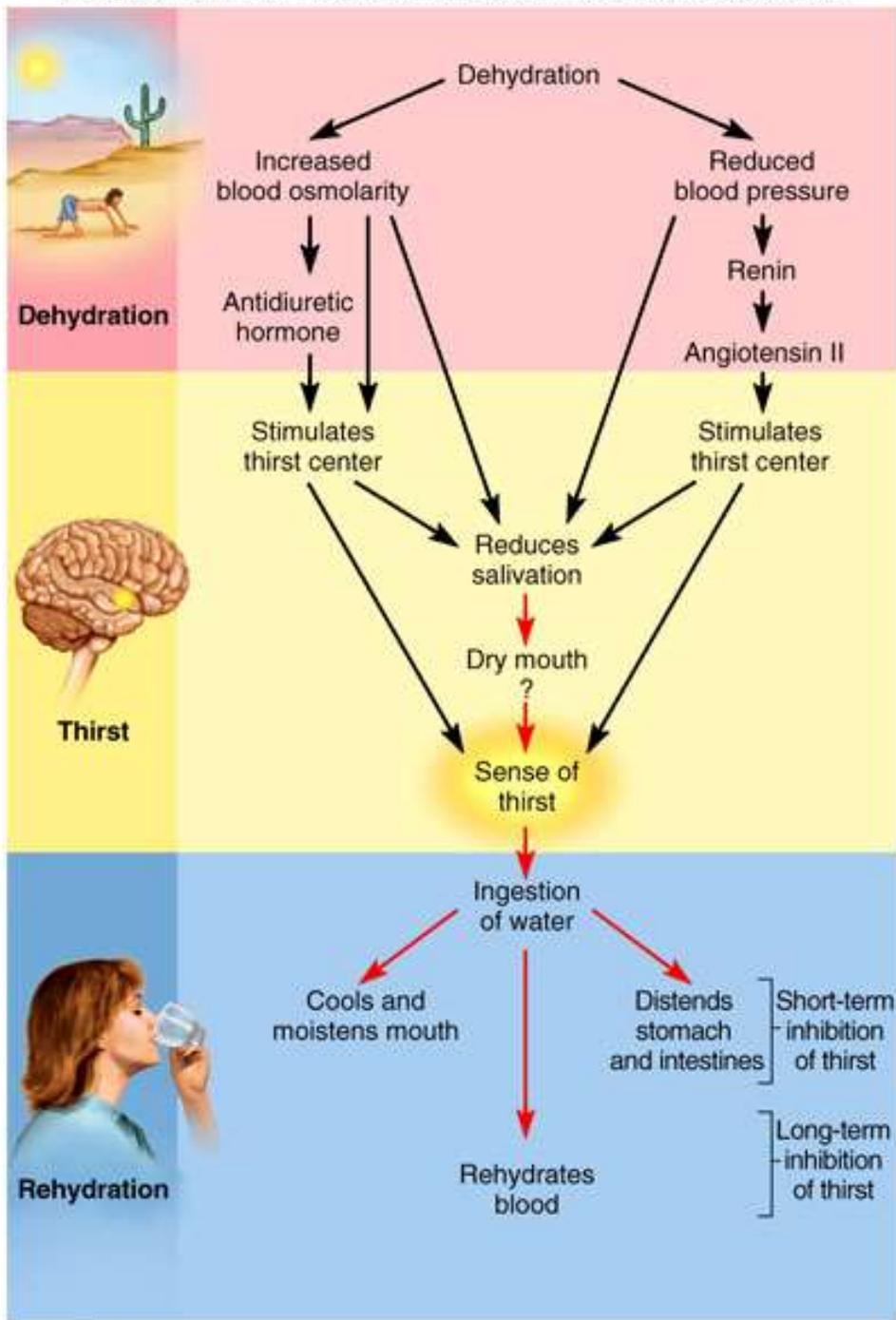
intense sense of thirst occurs with 2-3% increase in plasma osmolarity

or 10-15% of blood loss

salivation is inhibited with thirst /// sympathetic signals from thirst center to salivary glands



Dehydration, Thirst, and Rehydration



You become intensely thirsty with a 2% to 3% increase in osmolarity or a 10% to 15% blood volume loss.

Thirst Satiation Mechanisms

- Long term inhibition of thirst
 - absorption of water from small intestine
 - reduces osmolarity of blood
 - stops the osmoreceptor response
 - promotes capillary filtration
 - makes the saliva more abundant and watery
 - changes require **30 minutes** or longer to take effect

Thirst Satiation Mechanisms

- Short term inhibition of thirst
 - cooling and moistening of mouth quenches thirst
 - distension of stomach and small intestine
 - 30 to 45 min of satisfaction // must be followed by water being absorbed into the bloodstream or thirst returns
 - short term response designed to prevent overdrinking

Regulation of Water Output (1 of 2)

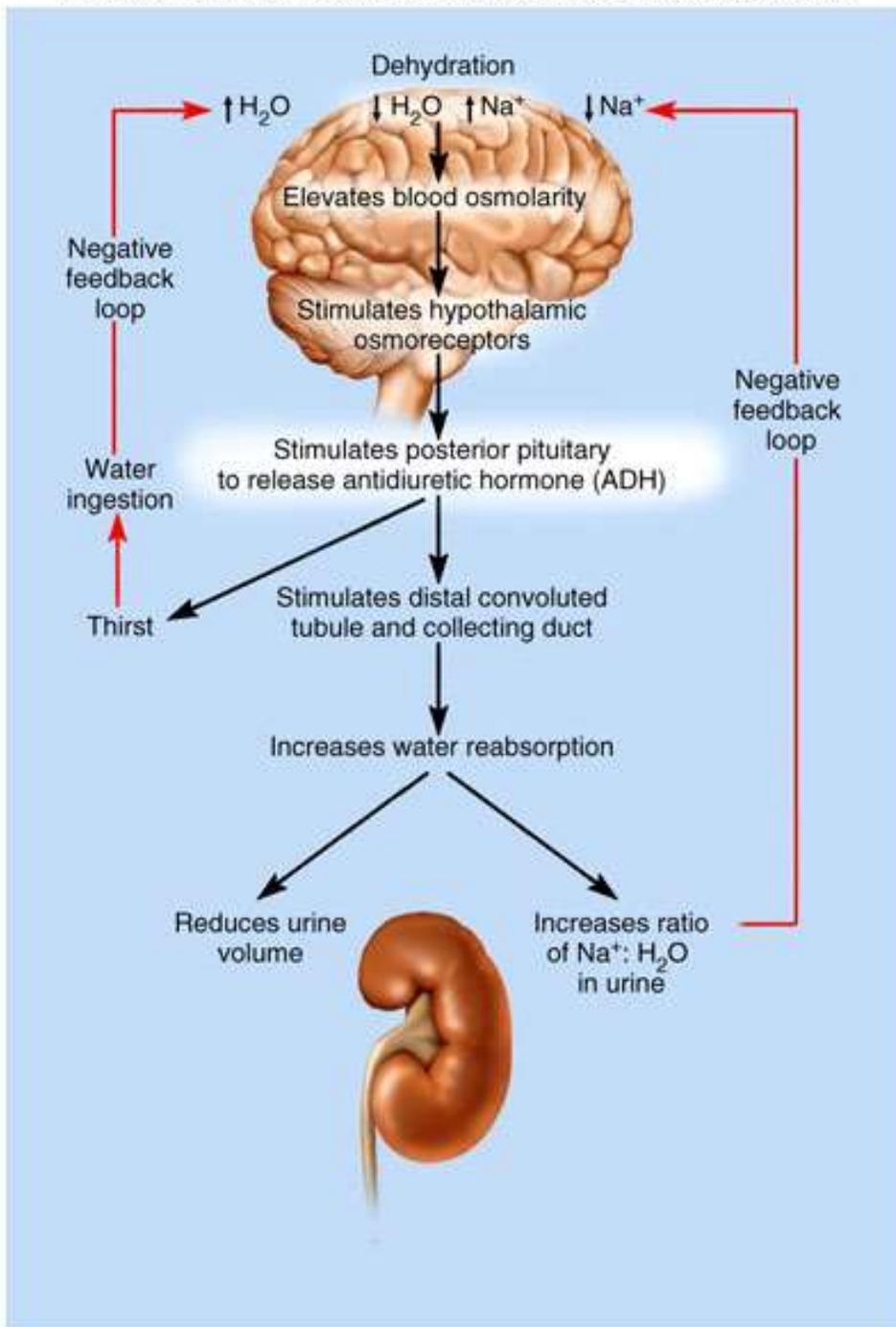


- The only way to control water output in a significant way is through variation in urine volume
 - kidneys can't replace water or electrolytes
 - kidneys can only slow rate of water and electrolyte loss until water and electrolytes can be ingested
- Two mechanisms regulated by hormones:
 - 1st = Aldosterone hormone (minor role)
 - changes in urine volume linked to adjustments in **Na⁺ reabsorption**
 - as Na⁺ is reabsorbed water follows but increases blood pressure so GFR also increases which increases water loss!

Regulation of Water Output (2 of 2)



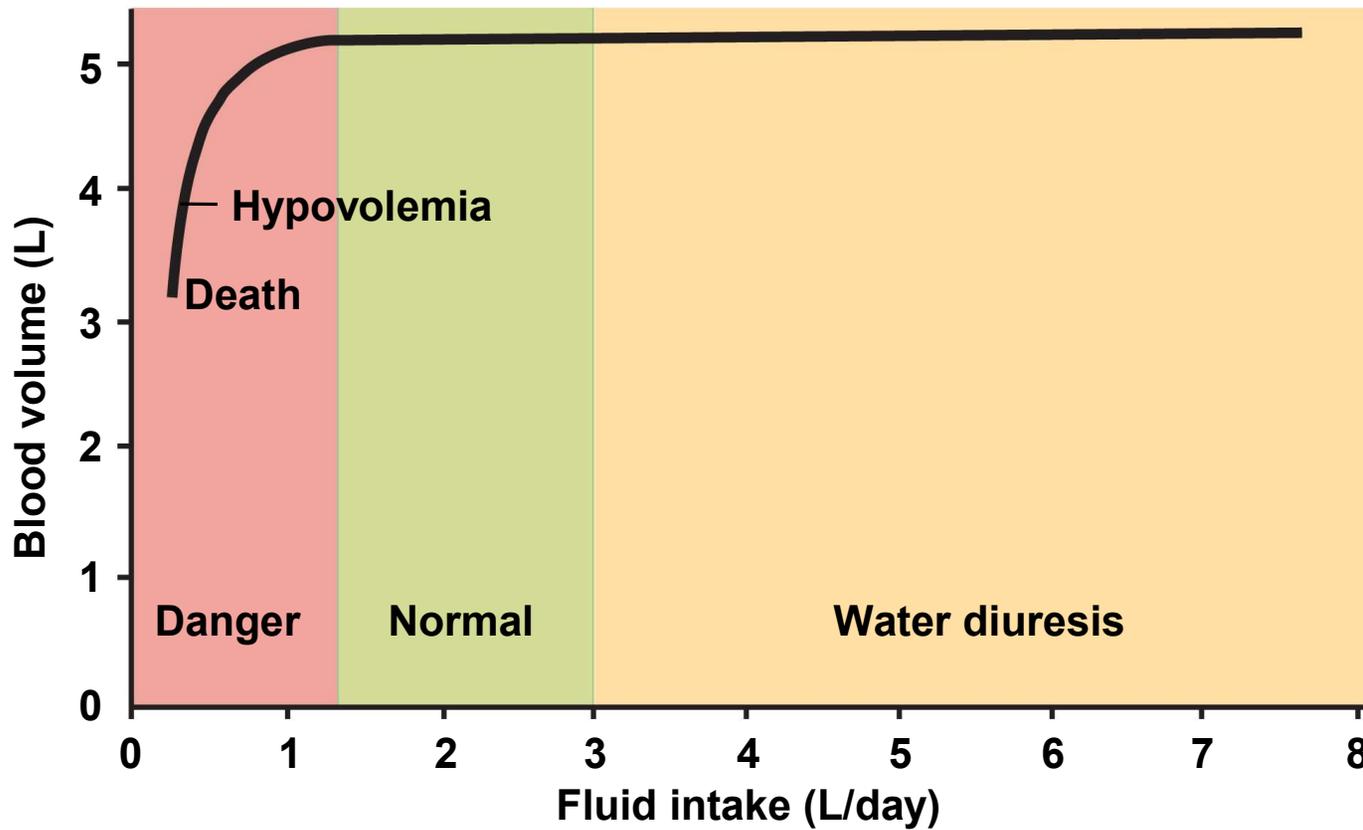
- 2nd = Anitdiuretic hormone
 - concentrates the urine / becomes darker color
 - ADH secretion stimulated by hypothalamic osmoreceptors in response to dehydration
 - **aquaporins** synthesized in response to ADH
 - membrane proteins in renal collecting ducts whose job is to channel water back into renal medulla, Na⁺ is still excreted
 - slows decrease in water volume and increased osmolarity – concentrates urine
 - ADH release inhibited when blood volume and pressure is too high or blood osmolarity too low // effective way to compensate for hypertension



ADH Secretion

Note: dehydration or high sodium concentration in plasma will cause release of antidiuretic hormone

Blood Volume and Fluid Intake



What is the danger caused by water intoxication from hypotonic hydration?

kidneys compensate very well for excessive fluid intake, but not for inadequate fluid intake

Acid-Base Balance



- This is one of the more critical fluid components for life regulated by homeostatic mechanisms
 - metabolism depends on enzymes, and enzymes are sensitive to pH
 - slight deviation from the normal pH can shut down entire metabolic pathways
 - slight deviation from normal pH can alter the structure and function of macromolecules
 - failed pH balance will result in death

Acid-Base Balance



- 7.35 to 7.45 is the normal pH range of blood and tissue fluid // only able to live couple hours if pH below 7 or above 7.7, and pH below 6.8 and above 8 is quickly fatal.
- challenges to acid-base balance:
 - metabolism constantly produces acid
 - lactic acids from anaerobic fermentation
 - phosphoric acid from nucleic acid catabolism
 - fatty acids and ketones from fat catabolism
 - carbonic acid from carbon dioxide



Acids and Bases

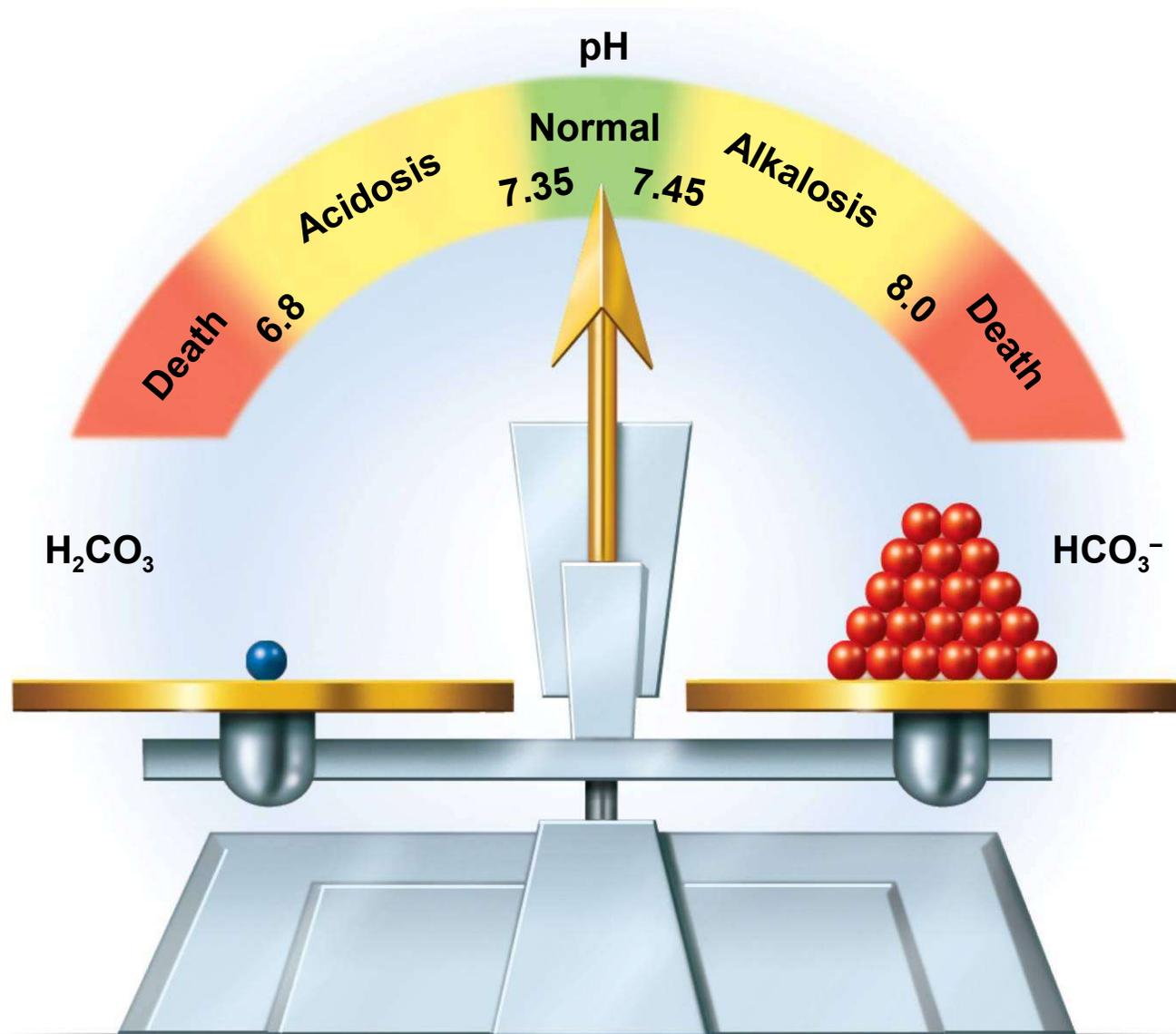
- pH of a solution is determined solely by its **hydrogen ions (H^+)**
- **acids** – any chemical that can release H^+ into the solution
 - **strong acids** like hydrochloric acid (HCl) ionize freely /// gives up most of its H^+ // markedly lower pH of a solution
 - **weak acids** like carbonic acid (H_2CO_3) ionize only slightly /// keeps most H^+ chemically bound // does not affect pH
- *Review: What is the difference between a salt and an acid or base.*



Acids and Bases

- **bases** – any chemical that accepts H^+
 - **strong bases**, like the hydroxide ion (OH^-), has a strong tendency to bind H^+ , markedly raising pH
 - **weak bases**, such as the bicarbonate ion (HCO_3^-) bind less available H^+ and has less effect on pH

Acid-Base Balance



Buffers



- any mechanism that **resists changes in pH**
- convert strong acids or bases to weak acids and bases
- **physiological buffer** - system that controls output of acids, bases, or CO₂
 - **urinary system** buffers greatest quantity of acid or base /// takes several hours to days to exert its effect
 - **respiratory system** buffers within minutes /// cannot alter pH as much as the urinary system

Buffers



- **chemical buffer** = a substance that binds H^+ and removes it from solution as its concentration begins to rise, or releases H^+ into solution as its concentration falls
 - restore normal pH in fractions of a second
 - function as mixtures called **buffer systems** composed of weak acids and weak bases
 - **three major chemical buffers : bicarbonate, phosphate, and protein systems**
 - amount of acid or base neutralized depends on the concentration of the buffers and the pH of the working environment

Bicarbonate Buffer System

- **bicarbonate buffer system** – a solution of carbonic acid and bicarbonate ions.
 - **carbonic acid and bicarbonate ions**
 - $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+$
 - **reversible reaction** important in ECF
 - $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+$
 - lowers pH by releasing H^+
 - $\text{CO}_2 + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{HCO}_3^- + \text{H}^+$
 - raises pH by binding H^+
-
- functions best in the **lungs and kidneys** to constantly remove CO_2
 - to lower pH, kidneys excrete HCO_3^-
 - to raise pH, kidneys excrete H^+ and lungs excrete CO_2

Phosphate Buffer System

- a solution of HPO_4^{2-} and H_2PO_4^-
- $\text{H}_2\text{PO}_4^- \leftrightarrow \text{HPO}_4^{2-} + \text{H}^+$
 - as in the bicarbonate system, reactions that proceed to the right liberating H^+ and decreasing pH, and those to the left increase pH
- more important **buffering the ICF and renal tubules**
 - where phosphates are more concentrated and function closer to their optimum pH of 6.8
 - constant production of metabolic acids creates pH values from 4.5 to 7.4 in the ICF, avg. 7.0

Protein Buffer System

- **proteins** are more concentrated than bicarbonate or phosphate systems, especially in the ICF
- **protein buffer system** accounts for about **three-quarters of all chemical buffering in the body fluids**
- protein buffering ability is due to certain side groups of their amino acid residues
- **carboxyl (-COOH) side groups** which releases H⁺ when pH begins to rise
- **others have amino (-NH₂) side groups** that bind H⁺ when pH gets too low

Respiratory Control of pH

- This is the basis for the strong buffering capacity of the respiratory system.
 - the addition of CO₂ to the body fluids raises the H⁺ concentration and lowers pH
 - the removal of CO₂ has the opposite effects
- neutralizes 2 to 3 times as much acid as chemical buffers

Respiratory Control of pH

- CO₂ is constantly produced by aerobic metabolism
 - normally eliminated by the lungs at an equivalent rate
 - $\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+$
 - lowers pH by releasing H⁺
 - $\text{CO}_2 \text{ (expired)} + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{HCO}_3^- + \text{H}^+$
 - raises pH by binding H⁺
- increased CO₂ and a decrease in the pH number (i.e. more acidic) **stimulate pulmonary ventilation**
- Decreased CO₂ and an increase in the pH number (i.e. more alkaline or basic) **inhibits pulmonary ventilation**

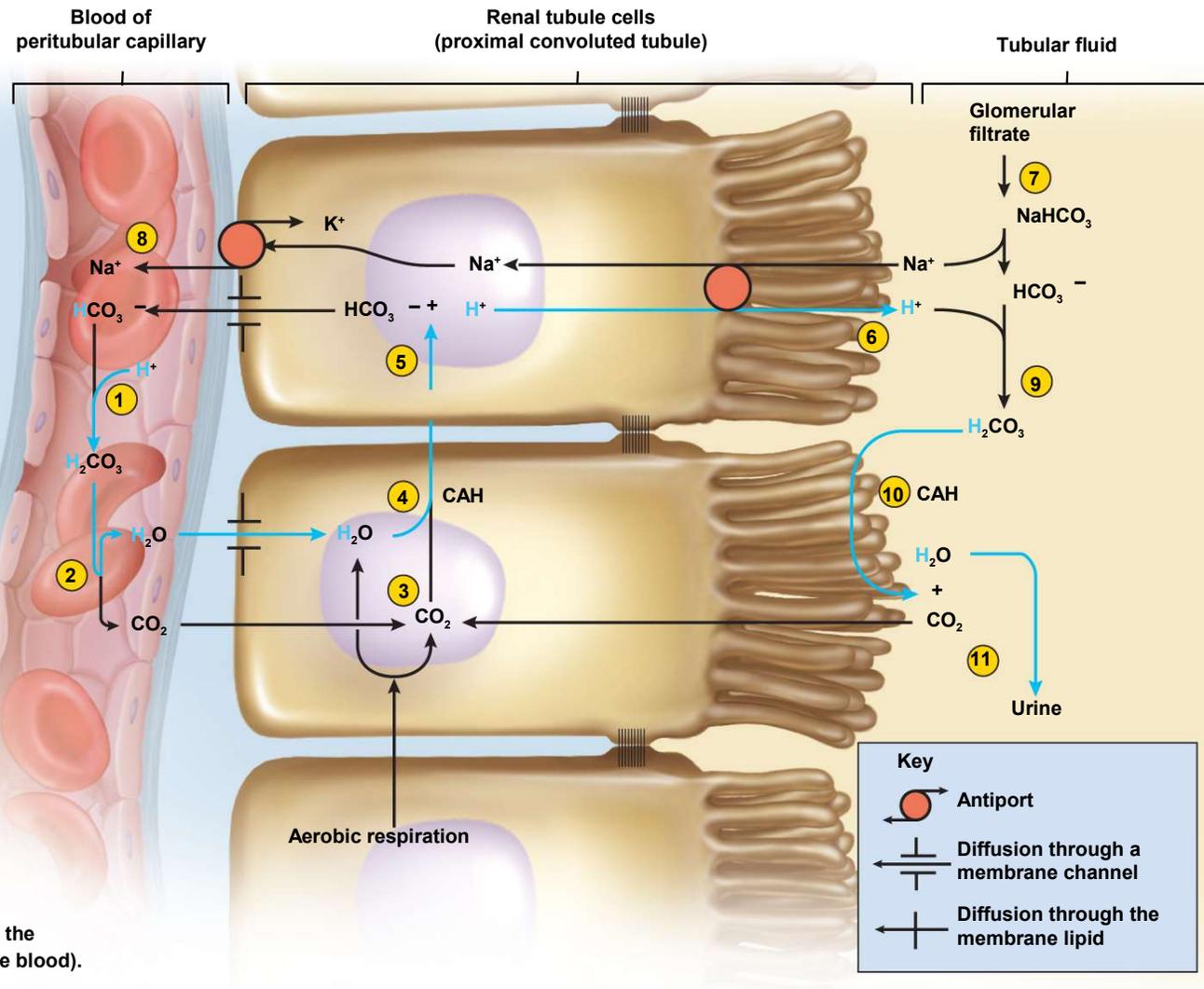
Renal Control of pH

- the kidneys can neutralize more acid or base than either the respiratory system or chemical buffers
- renal tubules secrete H^+ into the tubular fluid
 - most binds to bicarbonate, ammonia, and phosphate buffers
 - bound and free H^+ are excreted in the urine
 - Kidney actually expelling H^+ from the body, not just “binding it to another molecule
 - other buffer systems only reduce its concentration by binding it to other chemicals

H⁺ Secretion and Excretion in Kidney

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- 1 H⁺ in blood reacts with HCO₃⁻ to form H₂CO₃.
- 2 H₂CO₃ decomposes into H₂O and CO₂, which enter the tubule cell.
- 3 Tubule cells acquire CO₂ from blood, tubular fluid, and their own aerobic respiration.
- 4 Carbonic anhydrase (CAH) combines H₂O and CO₂ to re-form H₂CO₃.
- 5 H₂CO₃ ionizes to form HCO₃⁻ (which returns to the blood) and H⁺.
- 6 Na⁺-H⁺ antiport exchanges H⁺ for Na⁺.
- 7 NaHCO₃ from glomerular filtrate decomposes into Na⁺ and HCO₃⁻. Na⁺ is pumped into tubule cell.
- 8 Na⁺ is removed by Na⁺-K⁺ pump at the base of the cell.
- 9 HCO₃⁻ reacts with H⁺ from tubule cell to form H₂CO₃.
- 10 CAH on brush border decomposes H₂CO₃ into H₂O and CO₂ again.
- 11 CO₂ enters the tubular cell and H₂O passes in the urine (carrying the H⁺ that was originally in the blood).



Limiting pH

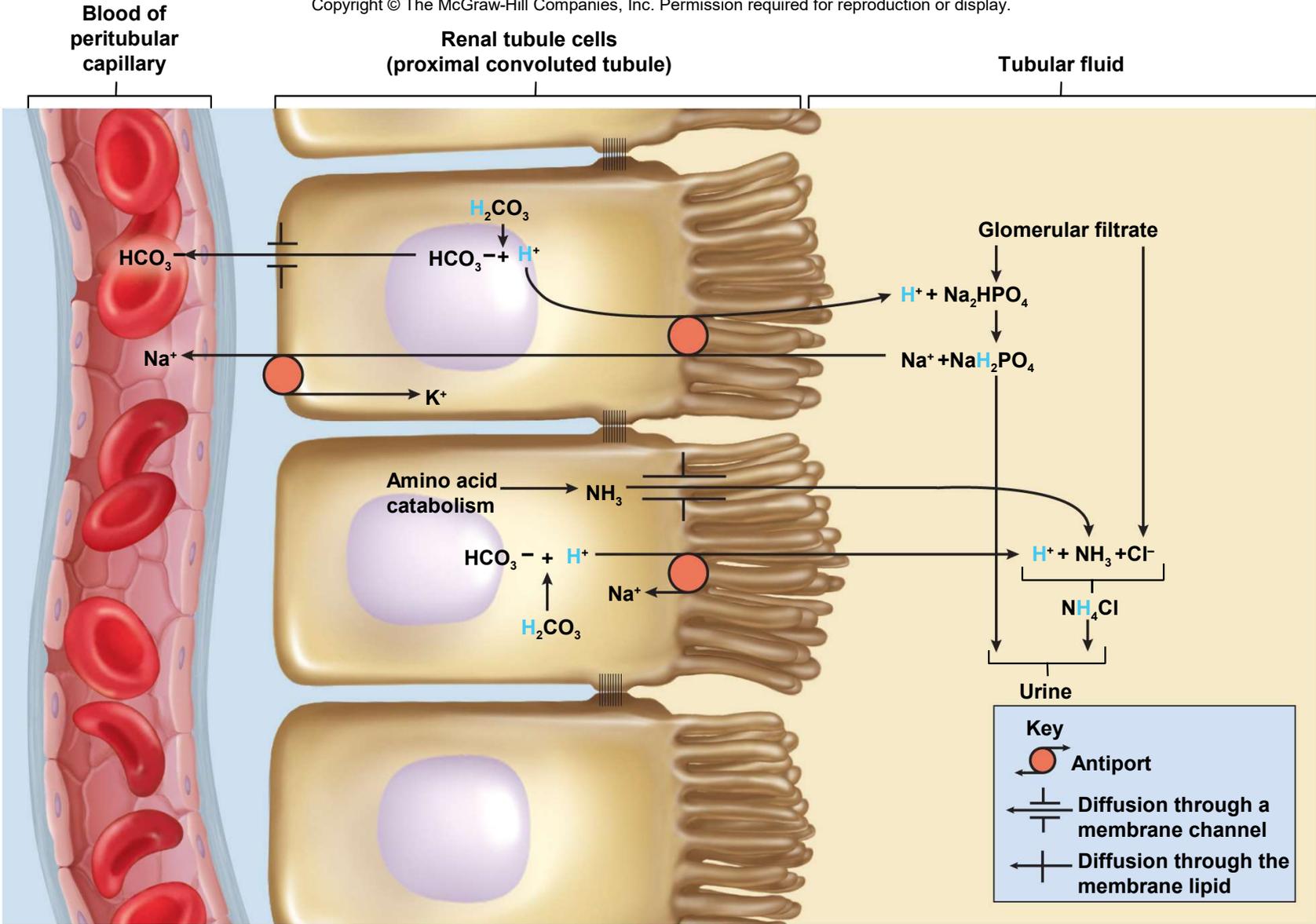
- tubular secretion of H^+ (step 6)
 - continues only with a steep concentration gradient of H^+ between tubule cells and tubular fluid
 - if H^+ concentration increased in tubular fluid, lowering pH to 4.5, secretion of H^+ stops – **limiting pH**

Limiting pH

- this is prevented by buffers in tubular fluid
 - **bicarbonate system** – all bicarbonate ions in tubular fluid are consumed neutralizing H^+
 - so there is no HCO_3^- in the urine
 - the more acid the kidneys secrete, less sodium is in the urine
 - **phosphate system** - dibasic sodium phosphate is contained in glomerular filtrate
 - reacts with some of the H^+ replacing a Na^+ in the buffer which passes into the urine
 - $Na_2HPO_4 + H^+ \rightarrow NaH_2PO_4 + Na^+$
 - **ammonia** (NH_3) - from amino acid catabolism acts as a base to neutralize acid
 - $NH_3 + H^+ \text{ and } Cl^- \rightarrow NH_4Cl$ (ammonium chloride – a weak acid)

Buffering Mechanisms in Urine

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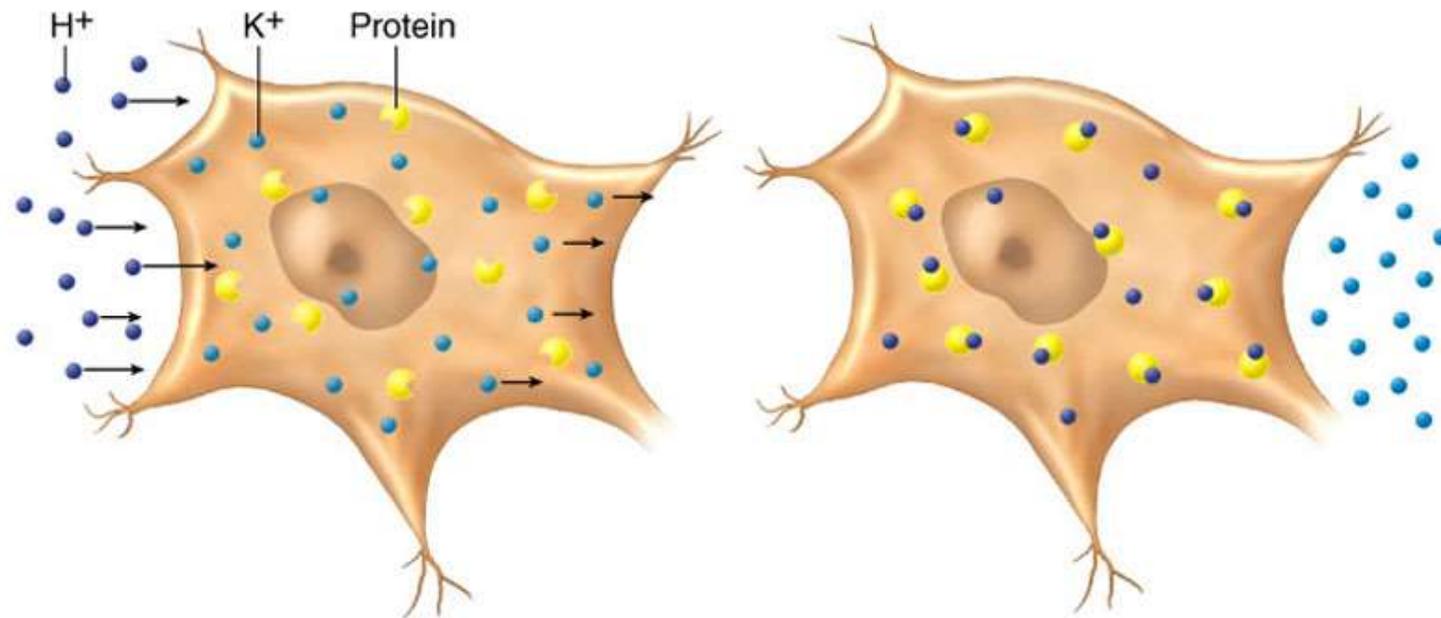
Disorders of Acid-Base Balance / Acidosis



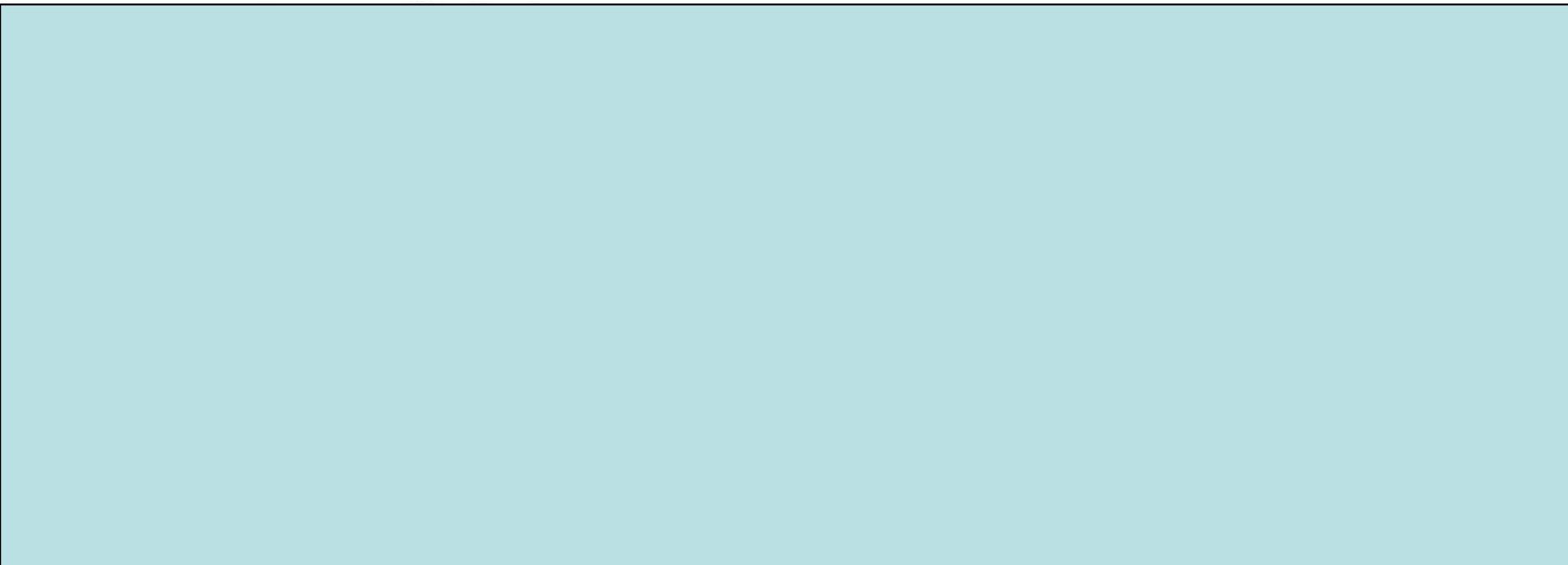
- **In acidosis**

- pH below **7.35**
- H^+ diffuses into cells and drives out K^+
- elevating K^+ concentration in ECF = hyperkalemia
 - H^+ buffered by protein in ICF
 - as K^+ leaves ICF it causes membrane **hyperpolarization**
 - moves cells away from their threshold
 - nerve and muscle cells are hard to stimulate
 - CNS depression may lead to confusion, disorientation, coma, and possibly death

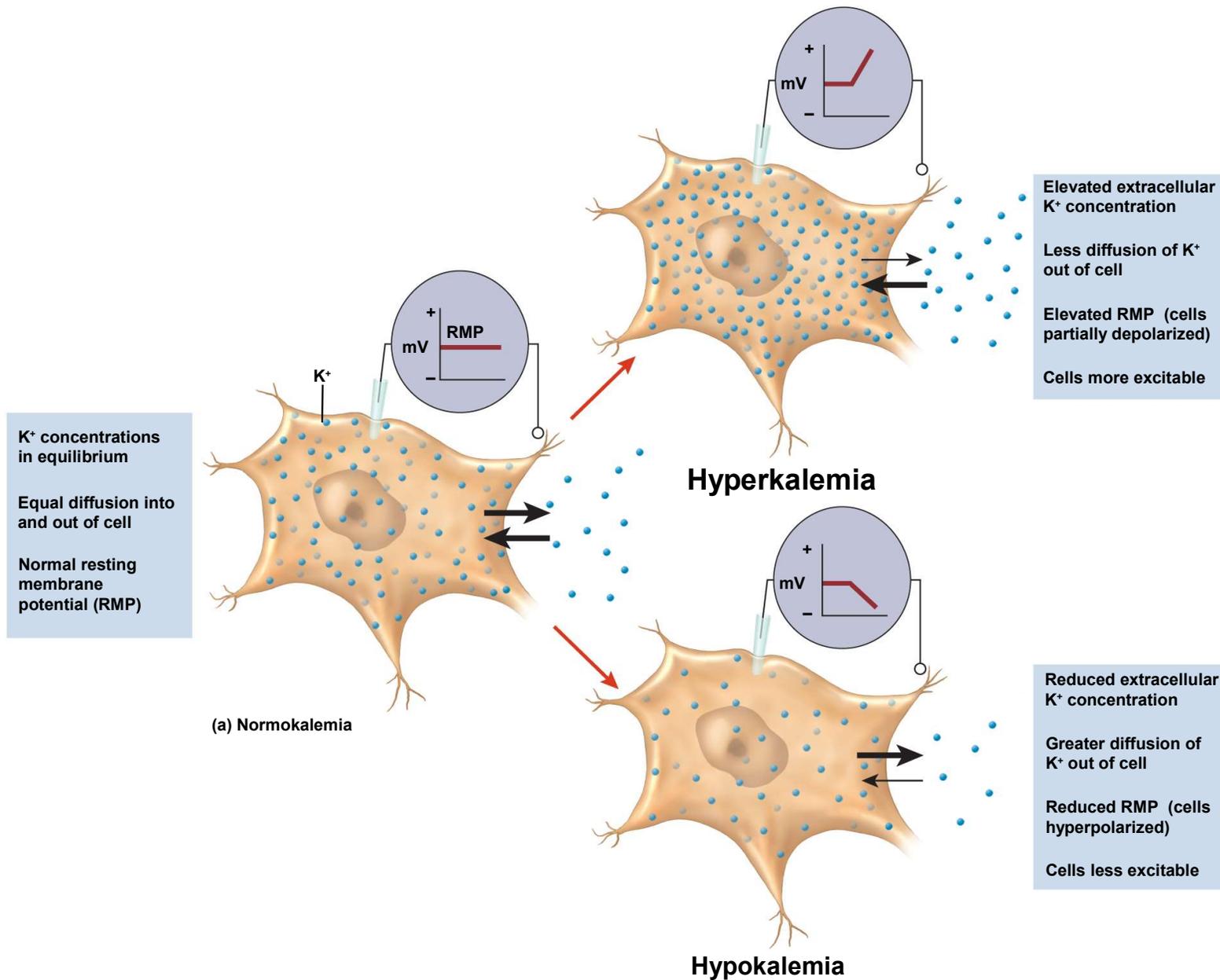
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(a) Acidosis → leading to → Hyperkalemia



Potassium & Membrane Potentials



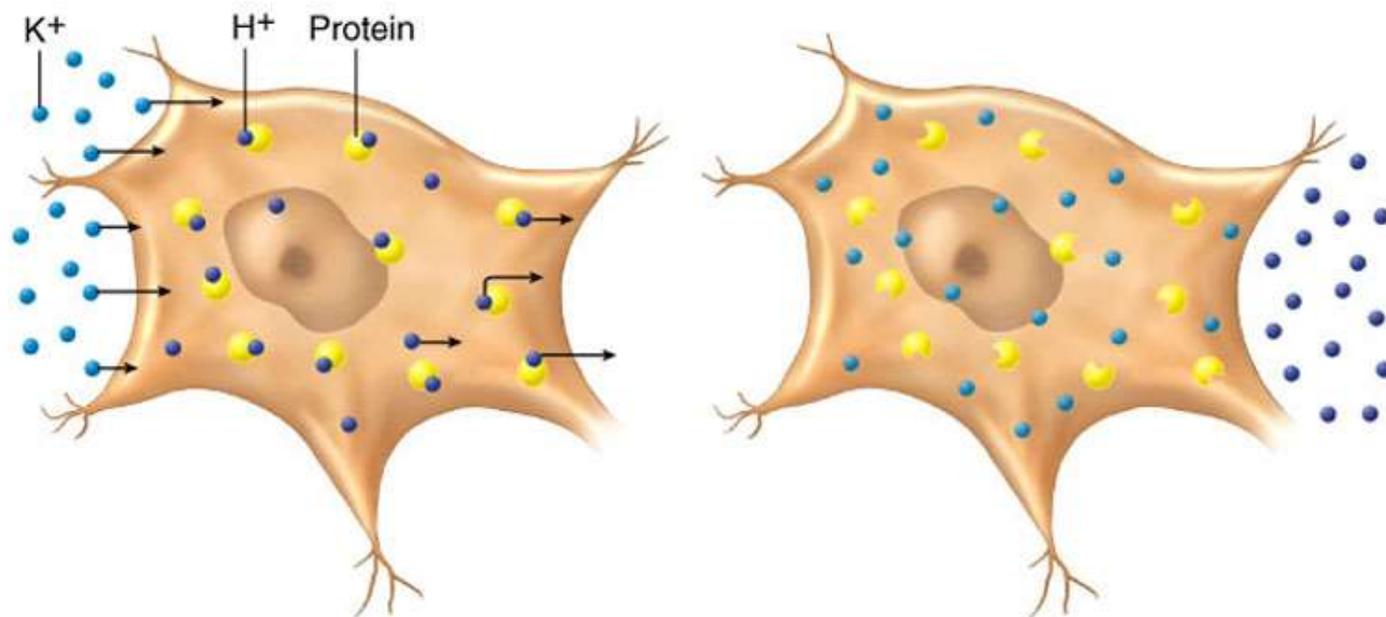


- **In alkalosis**

- pH above **7.45**
- H^+ diffuses out of cells
- K^+ diffuses in

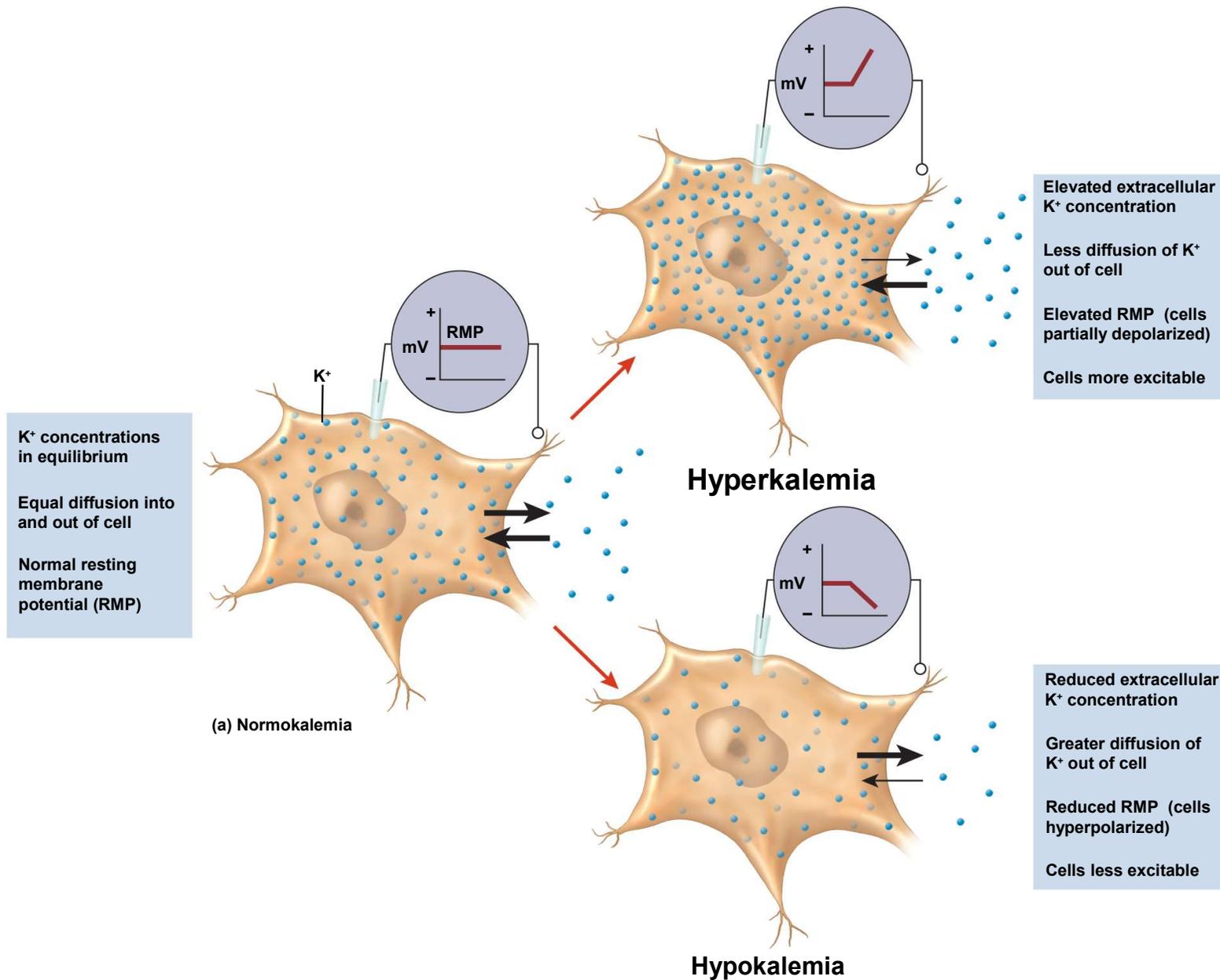
- membranes depolarized, moves closer to threshold, nerves overstimulated, muscles causing spasms, tetany, convulsions, respiratory paralysis

See Next Slides



(b) Alkalosis → leading to → Hypokalemia

Potassium & Membrane Potentials



Disorders of Acid-Base Balances

- Acid-base imbalances fall into one of two categories:
 - **Respiratory cause**
 - **Metabolic cause**
- **Respiratory acidosis**
 - occurs when rate of alveolar ventilation fails to keep pace with the body's rate of CO₂ production
 - carbon dioxide accumulates in the ECF and lowers its pH
 - occurs in emphysema where there is a severe reduction of functional alveoli
- **Respiratory alkalosis**
 - results from hyperventilation
 - CO₂ eliminated faster than it is produced

Disorders of Acid-Base Balances

- **Metabolic acidosis**

- increased production of organic acids such as lactic acid in anaerobic fermentation, and ketone bodies seen in alcoholism, and diabetes mellitus
- ingestion of acidic drugs (aspirin)
- loss of base due to chronic diarrhea, laxative overuse

- **Metabolic alkalosis**

- rare, but can result from:
 - overuse of bicarbonates (antacids and IV bicarbonate solutions)
 - loss of stomach acid (chronic vomiting)

Compensation for Acid-Base Imbalances



- Compensated acidosis or alkalosis
 - the kidneys compensate for pH imbalances of respiratory origin
 - the respiratory system compensates for pH imbalances of metabolic origin
- Uncompensated acidosis or alkalosis = a pH imbalance that the body cannot correct without clinical intervention
- A person cannot live for more than a few hours if the blood pH is below 7.0 or above 7.7
- A person dies almost immediately if pH below 6 or above 8

Compensation for Acid-Base Imbalances

- **Respiratory compensation**
 - **changes in pulmonary ventilation** to correct changes in pH of body fluids by expelling or retaining CO₂
 - **hypercapnia** (excess CO₂) - stimulates pulmonary ventilation eliminating CO₂ and allowing pH to rise
 - **hypocapnia** (deficiency of CO₂) reduces ventilation and allows CO₂ accumulate lowering pH

Compensation for Acid-Base Imbalances (cont.)

- **Renal compensation**

- an adjustment of pH by changing the rate of H^+ secretion by the renal tubules
- slow, but better at restoring a fully normal pH
- in **acidosis**, urine pH may fall as low as 4.5 due to excess H^+
 - renal tubules increase rate of H^+ secretion elevating pH
- in **alkalosis** as high as 8.2 because of excess HCO_3^-
 - renal tubules decrease rate of H^+ secretion, and allows neutralization of bicarbonate, lowering pH
- *kidneys cannot act quickly enough to compensate for short-term pH imbalances*
- effective at compensating for pH imbalances that lasts for a few days or longer

Electrolytes Balance in Body Fluids

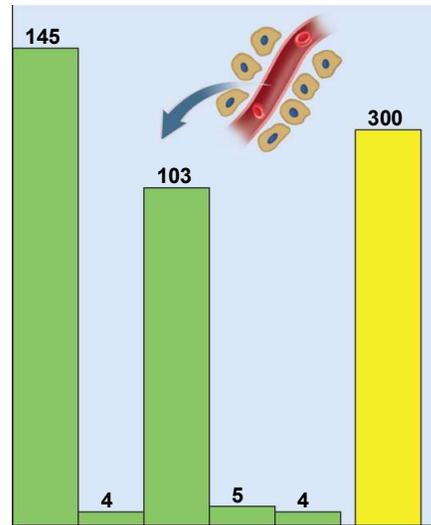


- Physiological **functions of electrolytes**
 - affect body's water distribution within compartments // osmotic pressure
 - Ions help maintain acid base balance
 - chemically reactive and participate in metabolism // cofactors for some enzymes
 - determine electrical potential (charge difference) across cell membranes /// resting membrane potentials

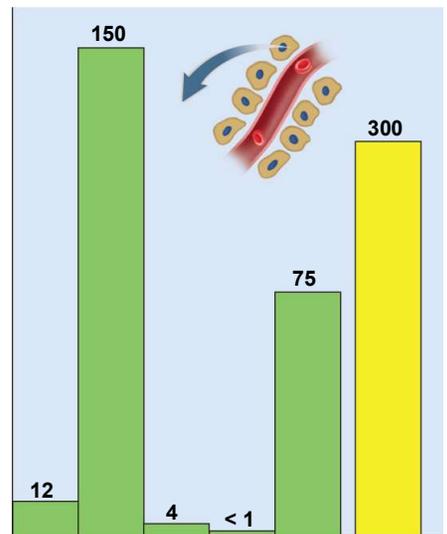
Electrolyte Balance

- major cations /// Na^+ , K^+ , Ca^{2+} , and H^+
- major anions /// Cl^- , HCO_3^- (bicarbonate), and PO_4^{3-}
- great differences in the types of electrolyte concentrations of blood plasma and intracellular fluid (ICF) /// But both spaces have the same osmolarity (300 mOsm/L)
- concentrations in tissue fluid (ECF) differ only slightly from those in the plasma

Electrolyte Concentrations & Osmolarity



(a) Blood plasma



Na⁺ K⁺ Cl⁻ Ca²⁺ P_i Osmolarity
(mEq/L) (mOsm/L)

(b) Intracellular fluid

Sodium - Functions

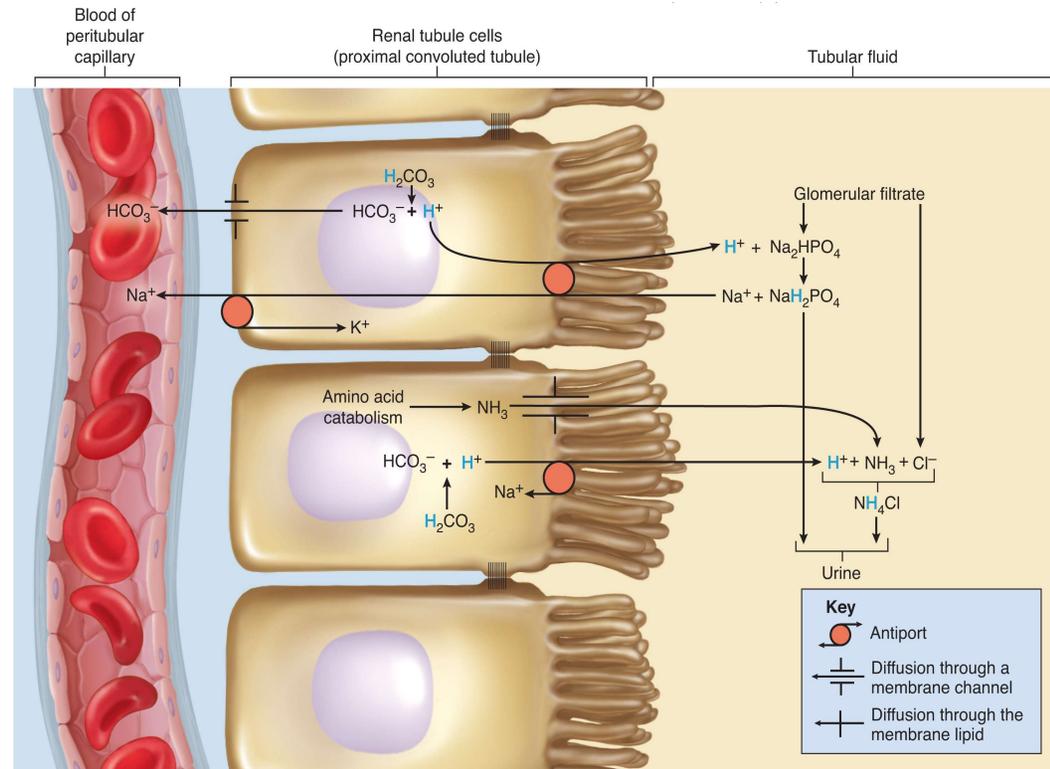
- **Sodium** – major extracellular cation
 - sodium salts accounts for **90% of extracellular fluid's cations**
 - **accounts for 90% to 95% of the osmolarity in the ECF**
 - most significant solute in determining total body water and distribution of water among the fluid compartment
 - principal ions responsible for the **resting membrane potentials**
 - inflow of sodium through membrane gates is an essential event in the depolarization that underlies **nerve and muscle function**
 - **imbalance in sodium may have profound affect on CNS function // cognition & behavior**
 - **provides potential energy for co-transport of many different types of molecules across plasma membranes**

Sodium - Functions

– Na^+ gradient a source of potential energy for **cotransport** of other solutes such as glucose, potassium, and calcium

– Na^+ - K^+ pump /// exchanges intracellular Na^+ for extracellular K^+ --- this pump also generates body heat

– NaHCO_3 has major role in buffering pH in ECF



Aldosterone and Sodium Homeostasis

- adult needs about **0.5 g of sodium per day** /// typical American diet contains 3 – 7 g/day
- primary concern - excretion of excess dietary sodium
- sodium concentration coordinated by **aldosterone** - “salt retaining hormone”
 - primary role in **limiting sodium excretion**
 - **hyponatremia and hyperkalemia directly stimulate the adrenal cortex to secrete aldosterone**
 - hypotension stimulates aldosterone secretion by way of the **renin-angiotensin-aldosterone mechanism**
 - aldosterone receptors in ascending limb of nephron loop, the **distal convoluted tubule**, and cortical part of collecting duct

More About Aldosterone

- aldosterone, a steroid, binds to nuclear receptors
 - activates transcription of a gene for the $\text{Na}^+ - \text{K}^+$ pumps
 - in 10 – 30 minutes enough $\text{Na}^+ - \text{K}^+$ pumps are inserted in the plasma membrane to make a noticeable effect
 - tubules reabsorb more sodium and secrete more hydrogen and potassium
 - water and chloride passively follow sodium
- primary effects of aldosterone
 - less NaCl in urine
 - more potassium urine
 - more protons (more acidic) in urine
- elevated blood pressure inhibits the renin-angiotensin-aldosterone mechanism /// now kidneys reabsorb almost no sodium /// urine may now contain up to 30 g of sodium per day instead of normal 5 g

ADH and Sodium Homeostasis

- **Antidiuretic hormone** **modifies water excretion independently of sodium excretion // uses aquaporins**
 - **high sodium concentration** in the blood stimulate the posterior lobe of the pituitary to release ADH /// kidneys reabsorbs more water /// slows down any further increase in blood sodium concentration
 - **drop in sodium inhibits ADH release** /// more water is excreted, this raises the sodium concentration in the blood

Atrial Natriuretic Peptide and Sodium Homeostasis

- ANP (atrial natriuretic peptide) and BNP (brain natriuretic peptide)
 - inhibit sodium and water reabsorption, and the secretion of renin and ADH
 - kidneys eliminate more sodium and water lowering blood pressure
- Others hormones affecting hydration:
 - estrogen mimics aldosterone and women retain water during pregnancy
 - progesterone reduces sodium reabsorption and has a diuretic effect

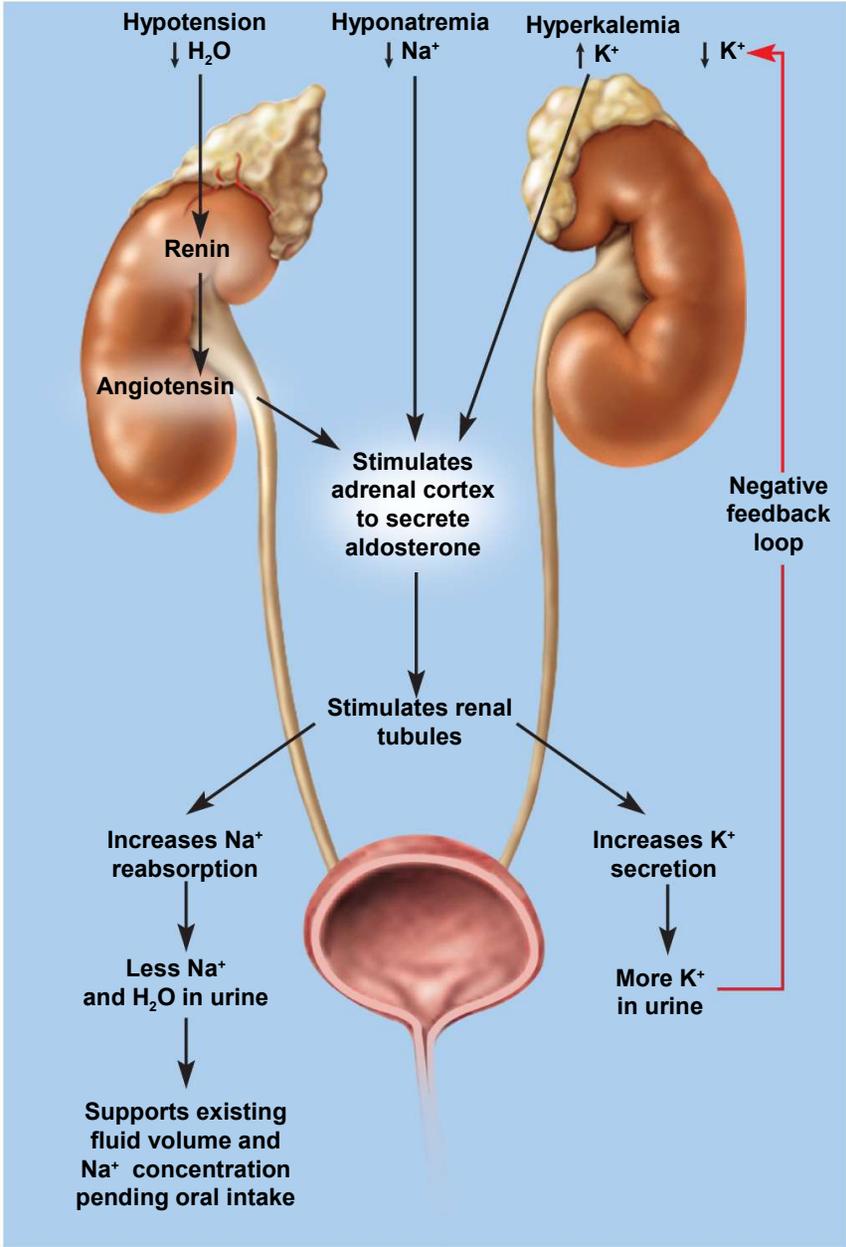
Sodium - Imbalances

- **hypernatremia**
 - plasma sodium concentration greater than 145 mEq/L
 - from administration of IV saline
 - water retention, hypertension and edema
- **hyponatremia**
 - plasma sodium concentration less than 130 mEq/L
 - person loses large volumes of sweat or urine, replacing it with drinking plain water
 - result of excess body water, quickly corrected by excretion of excess water

Potassium - Homeostasis

- potassium homeostasis is closely linked to sodium
- 90% of K^+ in glomerular filtrate is reabsorbed by the PCT // rest excreted in urine
- DCT and cortical portion of collecting duct secrete K^+ in response to blood levels
- Aldosterone stimulates renal secretion of K^+ // Antiport / Sodium reabsorbed and potassium excreted

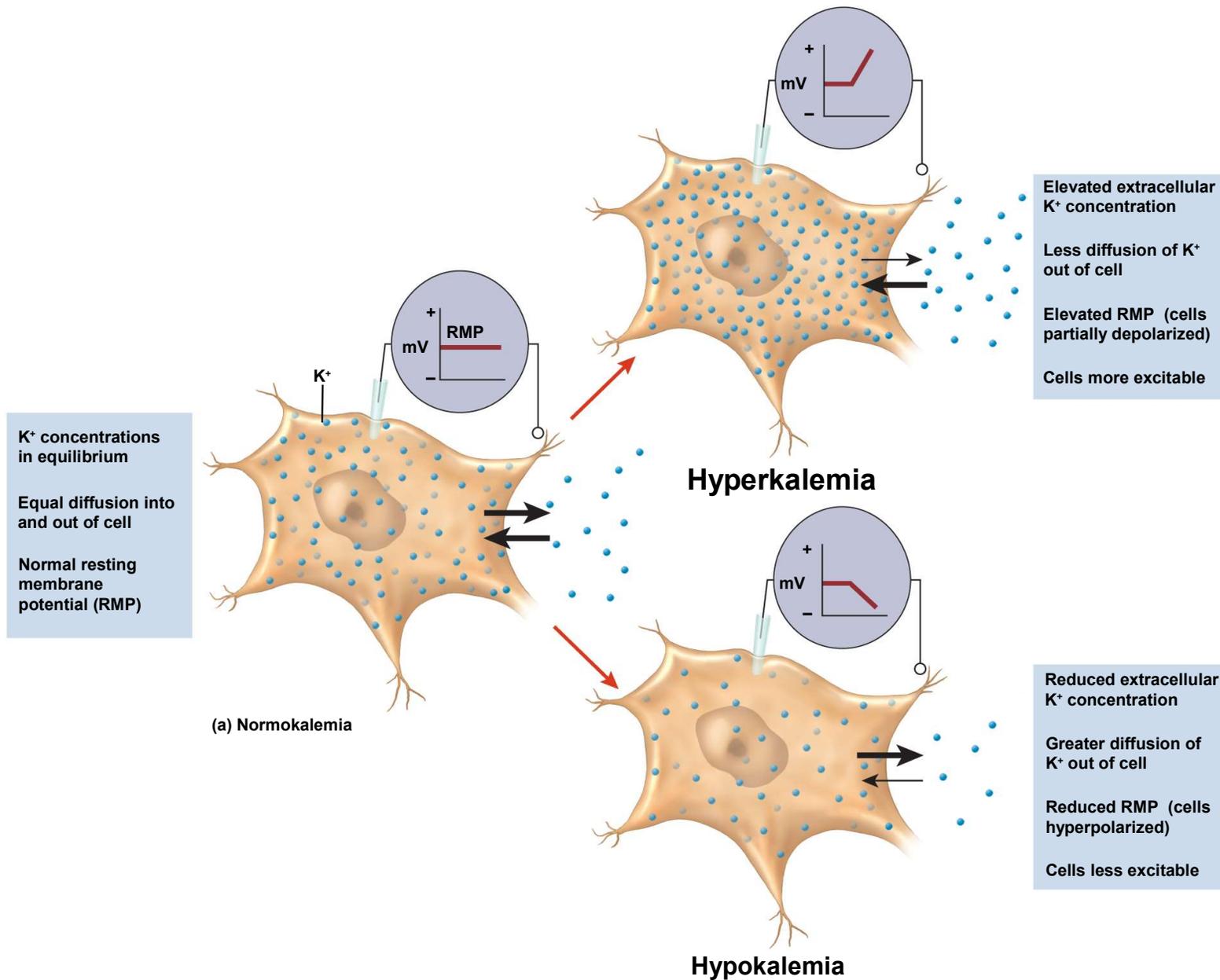
Secretion and Effects of Aldosterone



Potassium - Imbalances

- This is potentially the most dangerous imbalance of any electrolyte.
- **hyperkalemia**
 - greater than 5.5 mEq/L
 - effects depend on whether the potassium concentration rises quickly or slowly
 - **concentration rises quickly, (crush injury)**
 - sudden increase in extracellular K^+
 - nerve and muscle cells abnormally excitable
 - **concentration rises slowly**
 - inactivates voltage-regulated Na^+ channels (can not initiate action potential)
 - nerve and muscle cells become less excitable
 - can produce cardiac arrest
- hypokalemia
 - less than 3.5 mEq/L
 - rarely results from dietary deficiency
 - from sweating, chronic vomiting or diarrhea
 - nerve and muscle cells less excitable
 - muscle weakness, loss of muscle tone, decreased reflexes, and arrhythmias from irregular electrical activity in the heart

Potassium & Membrane Potentials



Chloride - Functions

- most abundant anions in ECF // major contribution to ECF osmolarity
- required for the formation of stomach acid // hydrochloric acid (HCl)
- **chloride shift** that accompanies CO₂ loading and unloading in RBCs
- major role in regulating body pH

Chloride - Homeostasis

- strong attraction to Na^+ , K^+ and Ca^{2+} , which chloride passively follows
- primary homeostasis achieved as an effect of Na^+ homeostasis
 - as sodium is retained /// chloride ions passively follow

Chloride - Imbalances

- **Hyperchloremia** // result of dietary excess or administration of IV saline
- **Hypochloremia**
 - side effect of hyponatremia
 - sometimes from hyperkalemia or acidosis
- primary effects: **disturbances in acid-base balance**

Calcium - Functions

- lends strength to the skeleton
- activates sliding filament mechanism of muscle contraction
- serves as a second messenger for some hormones and neurotransmitters
- activates exocytosis of neurotransmitters and other cellular secretions
- essential factor in blood clotting

Calcium - Homeostasis

- calcium homeostasis is chiefly regulated by
 - parathyroid hormone (PTH)
 - calcitriol (vitamin D)
 - calcitonin (in children)
 - these hormones affect bone deposition and resorption
 - intestinal absorption and urinary excretion
- cells maintain very low intracellular Ca^{2+} levels
 - to prevent calcium phosphate crystal precipitation
 - phosphate levels are high in the ICF
 - cells must pump Ca^{2+} out
 - keeps intracellular concentration low
 - or sequester Ca^{2+} in smooth ER and release it when needed
 - **calsequestrin** – proteins that bind Ca^{2+} and keep it unreactive in Ca^{2+} storage cells

Calcium - Imbalances

- hypercalcemia – greater than 5.8 mEq/L
 - alkalosis, hyperparathyroidism, hypothyroidism
 - reduces membrane Na⁺ permeability /// inhibits depolarization of nerve and muscle cells
 - concentrations greater than 12 mEq/L causes muscular weakness, depressed reflexes, cardiac arrhythmias
- hypocalcemia – less than 4.5 mEq/L
 - vitamin D deficiency, diarrhea, pregnancy, acidosis, lactation, hypoparathyroidism, hyperthyroidism
 - increases membrane Na⁺ permeability /// nervous and muscular systems become abnormally excitable
 - very low levels result in tetanus, laryngospasm, death

Phosphates - Functions

- **relatively concentrated in ICF** due to hydrolysis of ATP and other phosphate compounds
- inorganic phosphates (P_i) of the body fluids are an equilibrium mixture of phosphate (PO_4^{3-}), monohydrogen phosphate (HPO_4^{2-}), and dihydrogen phosphate ($H_2PO_4^-$)
- components of nucleic acids, phospholipids, ATP, GTP, cAMP, and creatine phosphate
- activates many metabolic pathways by phosphorylating enzymes and substrates such as glucose
- **phosphates may act as a buffer to help stabilize the pH of body fluids**

Phosphates - Homeostasis

- renal control
 - normally phosphate is continually **lost by glomerular filtration**
 - if plasma concentration drops, renal tubules reabsorb all filtered phosphate
- parathyroid hormone
 - increases excretion of phosphate which increases concentration of free calcium in the ECF
 - lowering the ECF concentration of phosphate minimizes the formation of calcium phosphate and helps support plasma calcium concentration
- imbalances not as critical /// body can tolerate broad variations in concentration of phosphate

(This will not be included on the unit exam.)

Disorders of Water Balance

Fluid Deficiency VS Fluid Excess

State of fluid imbalance occurs if there is an abnormality of total volume, concentration, or distribution of fluid among the compartments

Fluid Deficiency

- fluid deficiency results from fluid **output exceeds intake** over long period of time
 - volume depletion (hypovolemia)
 - occurs when proportionate amounts of water and sodium are lost without replacement
 - total body water declines
 - osmolarity remains normal
 - hemorrhage, severe burns, chronic vomiting, or diarrhea
 - dehydration (negative water balance)
 - body eliminates significantly more water than sodium
 - total body water declines
 - osmolarity rises
 - lack of drinking water, diabetes, ADH hyposecretion (diabetes insipidus), profuse sweating, overuse of diuretics
 - infants more vulnerable to dehydration than adults due to high metabolic rate that demands high urine excretion, immature kidneys cannot concentrate urine effectively, greater ratio of body surface to mass
 - affects all fluid compartments (ICF, blood, and tissue fluid)
- most serious effects: circulatory shock due to loss of blood volume, neurological dysfunction due to dehydration of brain cells, infant mortality from diarrhea

Fluid Excess

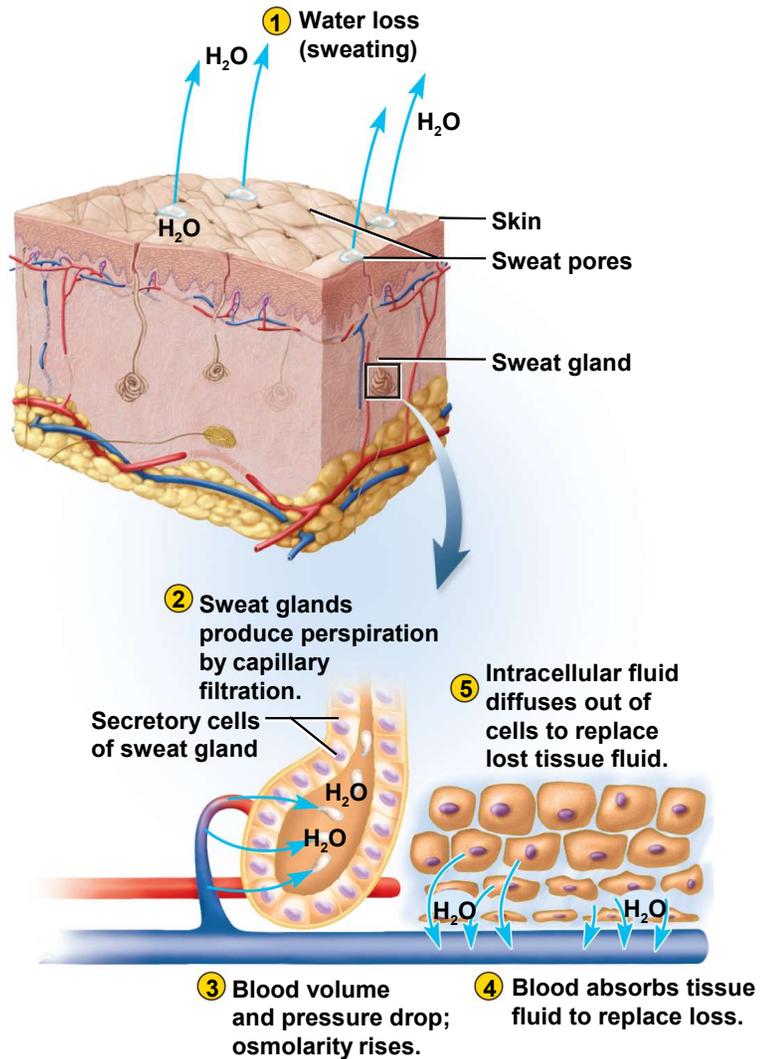
- less common than fluid deficiency
- kidneys are highly effective in **compensating for excessive intake by excreting more urine**
- exception = renal failure which can lead to fluid retention
- **two types of fluid excesses**
 - volume excess (hypervolemia)
 - **both Na⁺ and water retained**
 - ECF remains isotonic
 - caused by aldosterone hypersecretion or renal failure
 - hypotonic hydration
 - water intoxication (positive water balance)
 - **more water than Na⁺ retained** or ingested
 - ECF becomes hypotonic
 - can cause **cellular swelling** // e.g. pulmonary and cerebral edema

Fluid Sequestration

- a condition in which excess fluid **accumulates in a particular location**
 - Example: total body water is normal, but capillares “leak protein” so water moves into interstitial space /// volume of circulating blood drops to cause **circulatory shock**
- most common forms:
 - **edema** - abnormal accumulation of fluid in the interstitial spaces, causing swelling of the tissues
 - **hemorrhage** - another cause of fluid sequestration /// blood that pools in the tissue but is lost to circulation
 - **pleural effusion** – several liters of fluid may accumulate in the pleural cavity /// caused by some lung infections

Dehydration from Excessive Sweating

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- 1) water loss from sweating
- 2) sweat produced by capillary filtration
- 3) blood volume and pressure drop, osmolarity rises
- 4) blood absorbs tissue fluid to replace loss
- 5) tissue fluid pulled from ICF
- 6) all three compartments lose water
- 7) 300 mL from tissue fluid and 700 mL from ICF

Fluid Balance in Cold Weather

- Body conserves heat by constricting blood vessels in the skin
 - Net result = blood shifted to “core” circulation
 - **May cause one or more of the following:**
 - raises blood pressure
 - inhibits secretion of ADH
 - increases secretion of atrial natriuretic peptide
 - Increase urine production (stored in bladder)
 - blood volume reduced
 - exercise dilates vessels in skeletal muscles / more blood in muscle less in systemic circulation
 - insufficient blood for rest of the body can bring on **weakness, fatigue, or fainting (hypovolemic shock)**
 - **Complicating factor**
 - Winter’s cold air is drier
 - With exercise there is an increased respiration
 - water loss via expired gasses also reducing blood volume
- Cold weather plus volume loss from respiratory and urinary systems cause a state of reduced blood volume (hypovolemia)
- **This explains why there is a high incident of heart attacks when people shovel snow in the winter!**

Fluid Replacement Therapy

- one of the most significant problems in the treatment of seriously ill patients is the restoration and maintenance of proper fluid volume, composition, and distribution among fluid compartments
- **fluids may be administered to:**
 - replenish total body water
 - restore blood volume and pressure
 - shift water from one fluid compartment to another
 - restore and maintain electrolyte and acid-base balance
- **drinking water is the simplest method**
 - does not replace electrolytes
 - broths, juices, and sports drinks replace water, carbohydrates, and electrolytes

Fluid Replacement Therapy

Patients who cannot take fluids by mouth

enema – fluid absorbed through the colon

parenteral routes – fluid administration other than digestive tract

intravenous (I.V.) route is the most common

subcutaneous (sub-Q) route

intramuscular (I.M.) route

other parenteral routes

Fluid Replacement Therapy

plasma volume expanders /// hypertonic solutions or colloids that are retained in the bloodstream and drag interstitial water into it by osmosis

used to combat hypotonic hydration by drawing water out of swollen cells
can draw several liters of water out of the intracellular compartment within a few minutes

For patients who cannot eat – isotonic 5% dextrose (glucose) solution has **protein sparing effect** /// fasting patients lose as much as 70 to 85 grams of protein per day - I.V. glucose reduces this by half

patients with renal insufficiency – given slowly through I.V. drip