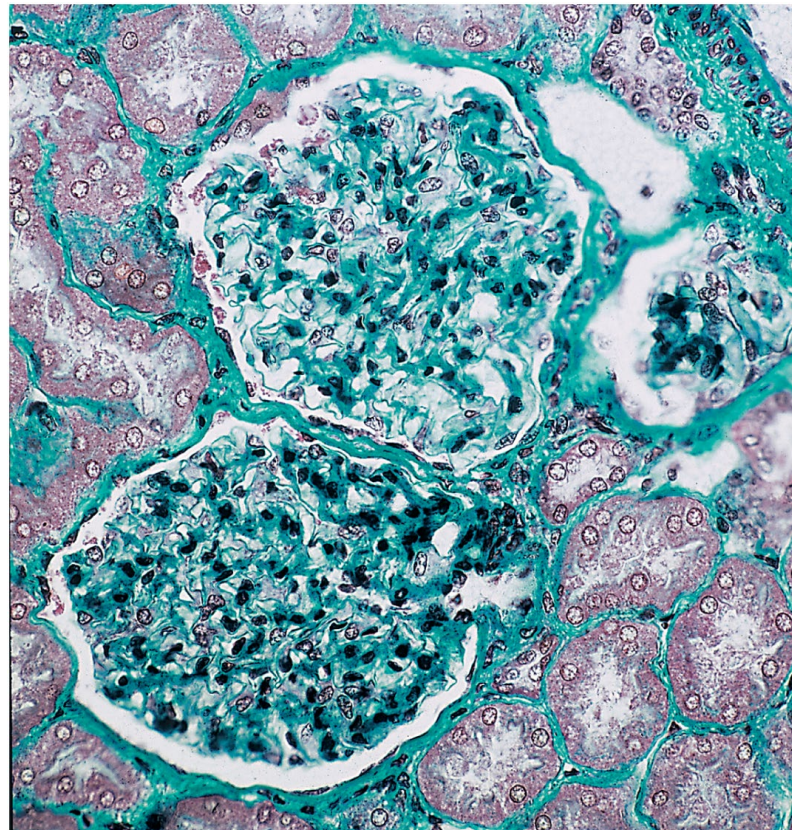


Chapter 24

Water, Electrolytes, and Acid-Base Balance



What must be in “Balance” to maintain homeostasis?

These three “**inseparable components**” of the body fluid must 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 is balanced by 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 (71%)

•8% blood plasma and lymphatic fluid (**vascular**) (21%)

•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 (6%)

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 body wt. average 55% - 60% water

–women average slightly less (higher fat content)

–obese and elderly people body wt. as little as 45% by weight

–as we age, we go from “a grape to a raisin.”

What is the 60/40/20 rule for body water?

The 60/40/20 rule is a physiological guideline used to estimate how water is distributed throughout the human body. It states that about 60% of an adult's total body weight is water, with 40% of body weight residing inside cells and 20% residing outside of cells.

This total body water (TBW) is broken down by the rule as follows:

1. Total Body Water (TBW) – 60%

Water makes up about 60% of a standard adult's total body weight. For example, in a 70 kg (154 lbs) adult, this translates to roughly 42 liters of water. Because fat tissue contains very little water, this percentage is typically higher in leaner individuals and lower in people with higher body fat percentages or the elderly.

2. Intracellular Fluid (ICF) – 40%

Roughly 40% of the body's total weight (or about two-thirds of the total body water) is Intracellular Fluid // . This is the fluid contained directly *inside* the cells. In the 70 kg example, this amounts to about 28 liters of fluid.

3. Extracellular Fluid (ECF) – 20%

The remaining 20% of the body's weight (or about one-third of the total body water) is Extracellular Fluid. This represents all the fluid found *outside* of the cells. In a 70 kg adult, this equals about 14 liters.

Fluid Homeostasis Requires Functional Integration of Many Systems

Cellular function requires a **fluid medium** with a carefully controlled composition

Fluid compartments must be “balanced” and maintained by the **collective action of the following systems:**

- Urinary
- Respiratory
- Digestive
- Integument
- Endocrine
- Nervous
- Cardiovascular
- Lymphatic

How Is Water Moved Between Fluid Compartments?

fluid continually exchanged between compartments

water moves between compartment by osmosis

because water moves easily through plasma membranes, osmotic gradients never last for very long between ICV and ECV

if an imbalance arises, osmosis restores balance within seconds

the osmolarity between the intracellular and extracellular are 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*
- How will water balance change with a liver disease? Why?*

The osmolarity of the human body is between 275 mOsm and 295 mOsm (test benchmark = 300 mOsm)

How water moves between different fluid compartments?

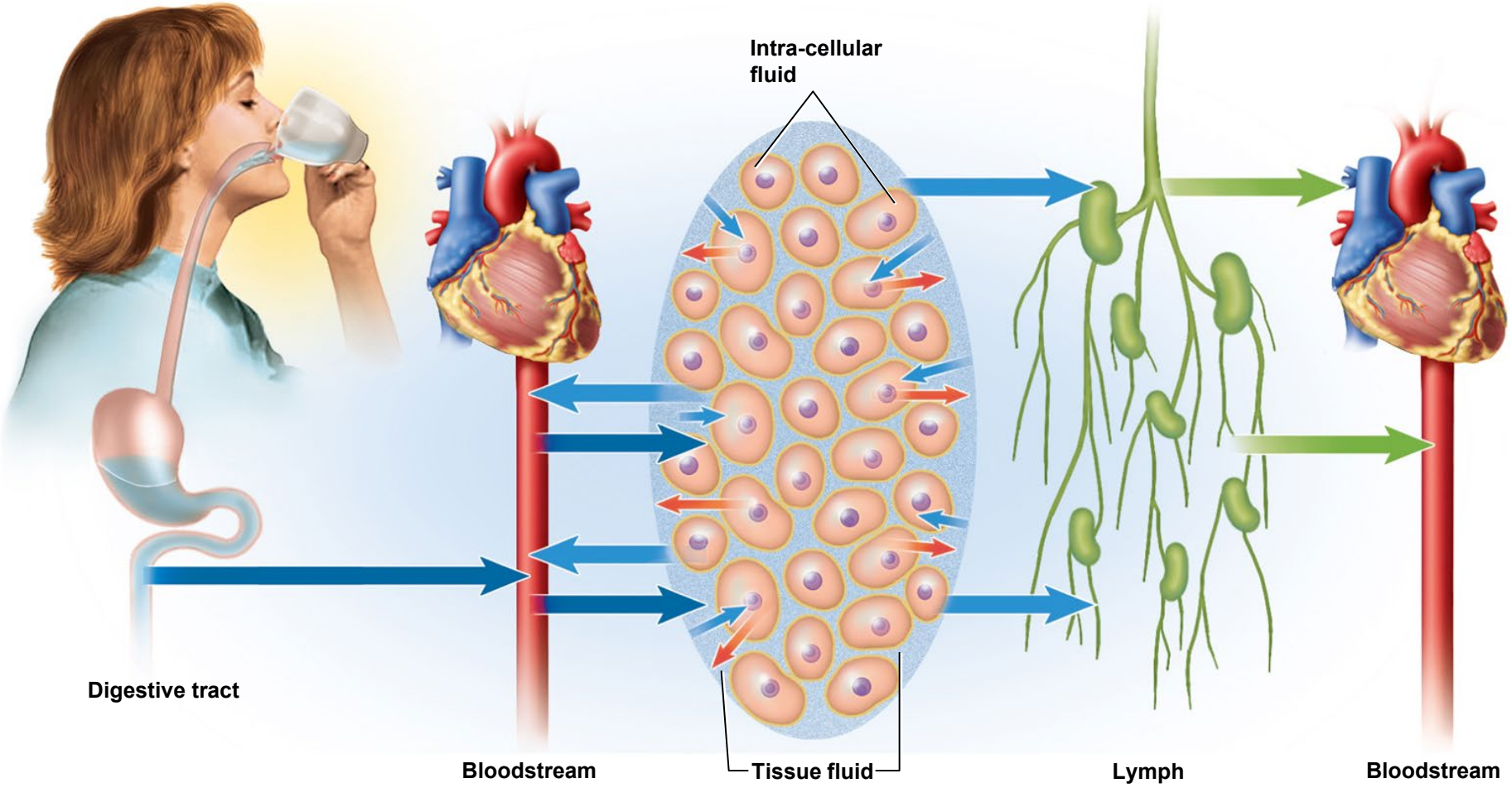
- The movement of water (i.e. osmosis) from one fluid compartment to another is determined by the relative concentrations of solutes
- Electrolytes play the principal role in governing the body's water distribution and total water content
- Electrolytes – they are the most abundant solute particles

Water follows (i.e. obligate) electrolyte movement!

sodium salts major cation in ECF

potassium salts major cation in ICF

Water Movement Between Fluid Compartments



Fluid Balance (Loss = Gain)

Fluid balance is when daily gains and losses are equal /// **about 2,500 mL/day**

Water comes from two sources

preformed water (2,300 mL/day or 2.3 L/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

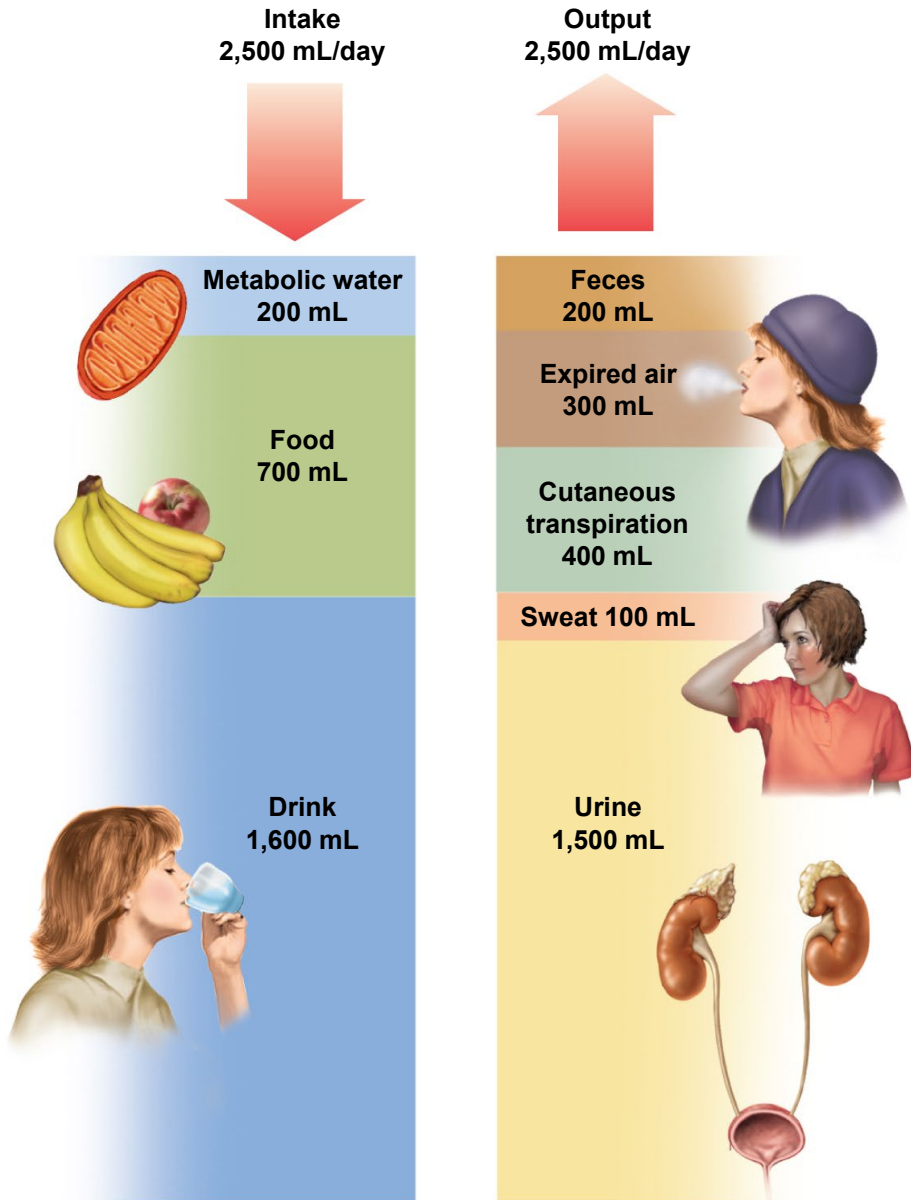
- > 1,500 mL/ day is in urine & feces
- > 100 mL/day is sweat through glands in resting adult

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

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

Fluid Balance



Prolong heavy work may raise respiratory water loss to 650 mL/day and perspiration as much as 5 L/day

How is fluid intake regulated?

Thirst is a conscious sensation that set into motion two different subconscious stimuli. This changes our behavior and we seek fluid intake.

What two stimuli triggers thirst?

- 1) dehydration
- 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 located in hypothalamus communicate with nuclei in the hypothalamus and cerebral cortex (**conscious and unconscious responses**)

hypothalamus produces antidiuretic hormone /// promotes water conservation

cerebral cortex dictates our behavior, so we seek water intake

How is fluid intake regulated?

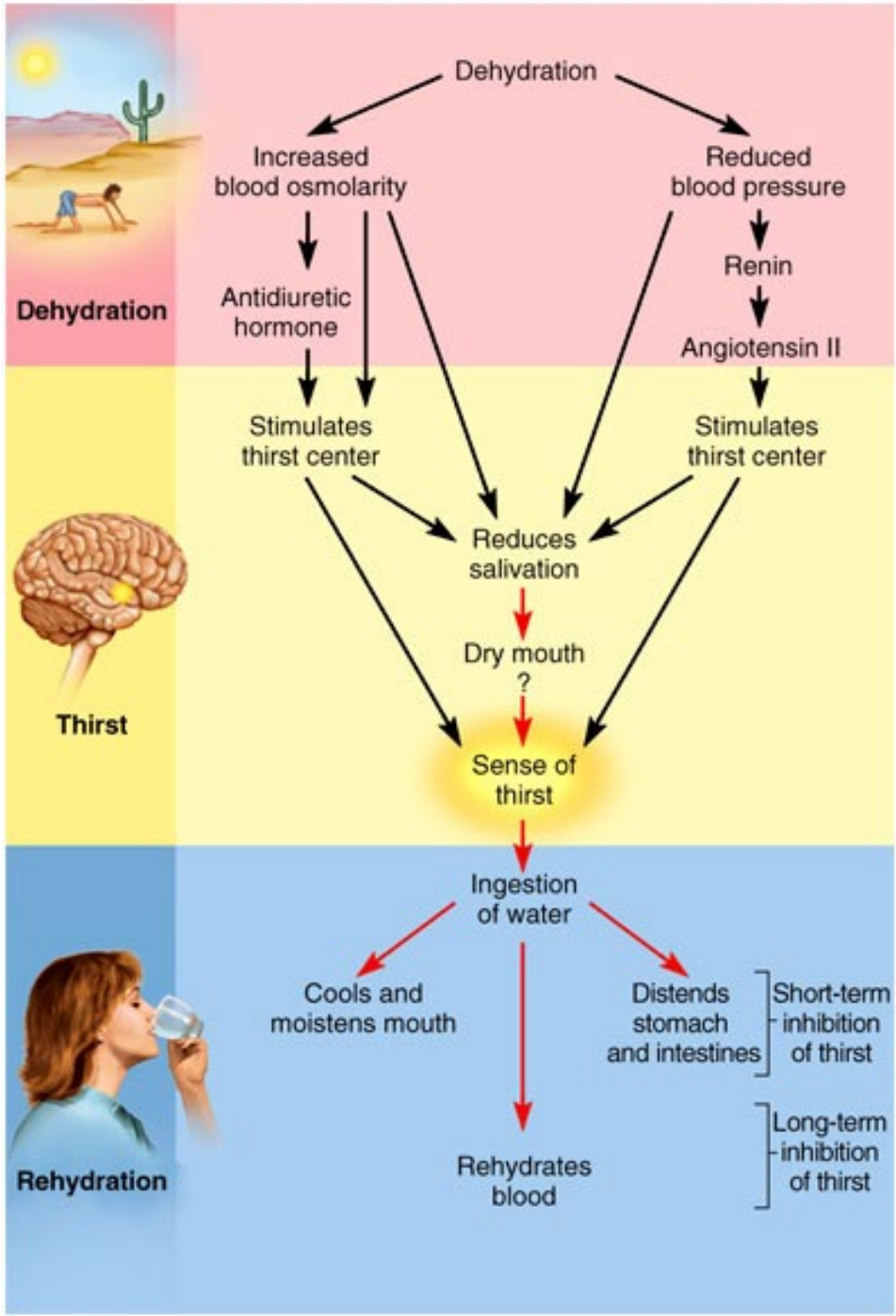
Tissue in kidneys (juxamedullary cells) sense reduced blood pressure

BP drops as blood volume is reduced

activates the renin – angiotensin - aldosterone mechanism

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

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



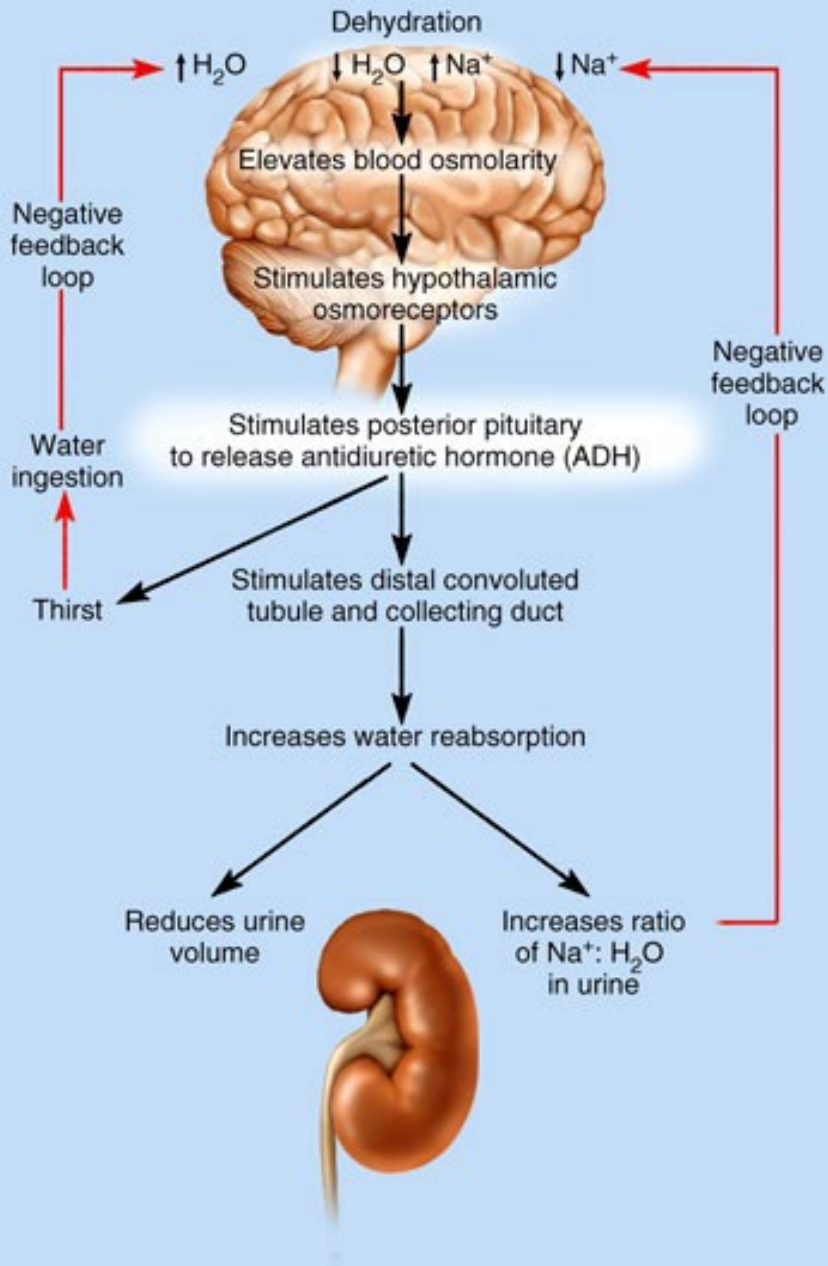
Dehydration, Thirst, and Rehydration

You become intensely thirsty when

> 2% to 3% increase in osmolarity

> 10% to 15% blood volume loss

you will also lose strength and exhibit mental confusion



ADH Secretion

Dehydration or high sodium concentration in plasma will cause release of antidiuretic hormone

What will alcohol do to ADH secretions?

Is it wise to drink alcohol on extremely hot days?

Thirst Satiation Mechanisms

Long term inhibition of thirst

- after drinking water - absorption of water across small intestine
- reduces osmolarity of blood
- stops the osmoreceptor response
- promotes more capillary filtration
- Increase filtration produces more “watery” saliva
- change require **30 minutes** or longer to take effect

Thirst Satiation Mechanisms

Short term inhibition of thirst

cooling and moistening of mouth quenches thirst

also distension of stomach

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 consumption of too much water

rapid over consumption of hypotonic water **potentially life threatening** // why?

Regulation of Water Output

Aldosterone VS Antidiuretic Hormone (1 of 2)

The only way to control the amount of water output is through variation in urine volume

kidneys can't replace water or electrolyte /// only will slow the rate of water and electrolyte loss until you ingest more water and electrolytes

Two mechanisms regulated by hormones:

–1st = Aldosterone hormone (minor role in changing tonicity)

changes in urine volume linked to adjustments in **Na⁺ reabsorption** /// as Na⁺ is reabsorbed water follows

this increases blood pressure // now GFR increases which results in greater filtration volume

Regulation of Water Output

2nd hormone = Antidiuretic hormone

concentrates the urine / becomes darker color

ADH secretion stimulated by hypothalamic osmoreceptors in response to dehydration

aquaporins in cytoplasm inserted into plasma membrane // if need new aquaporins synthesized in response to ADH

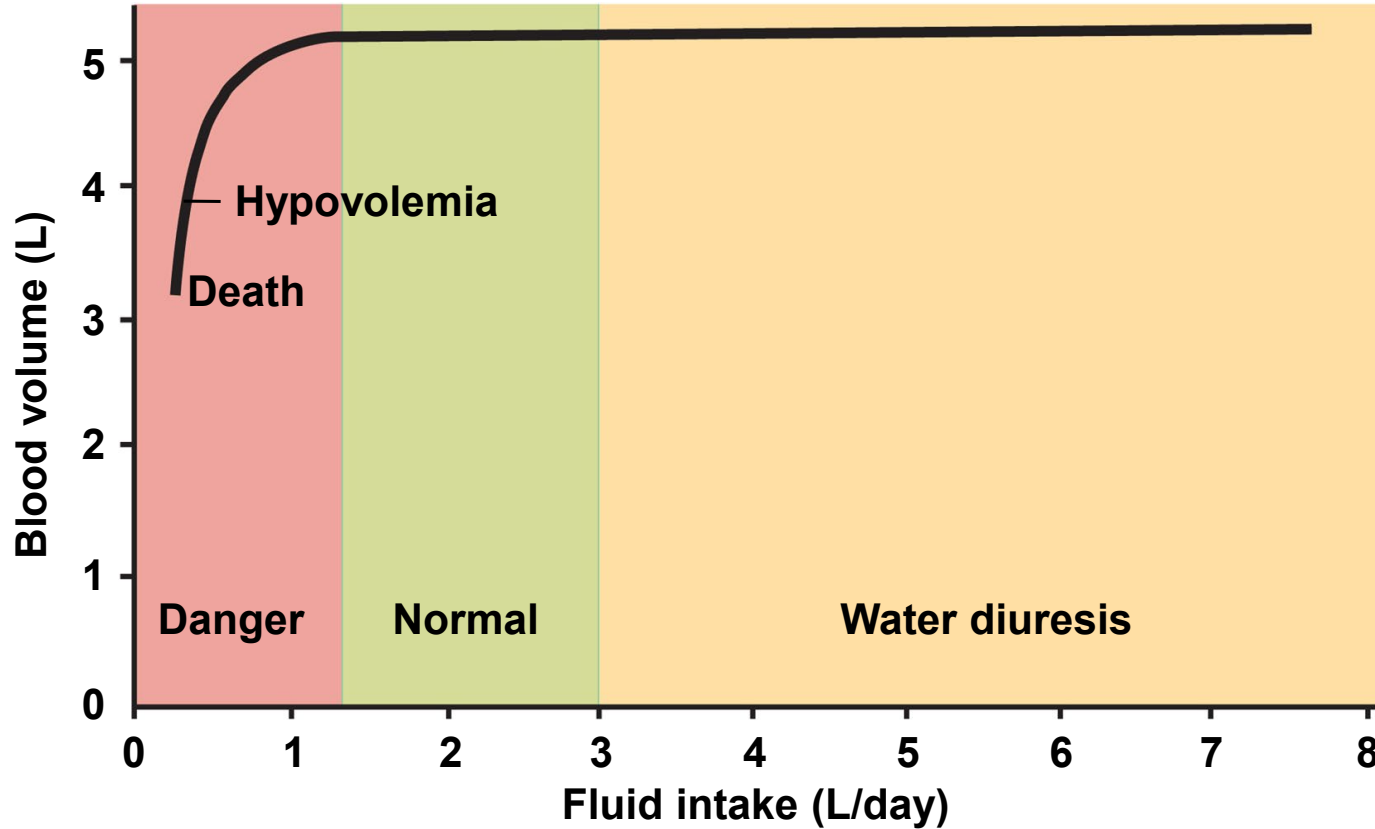
membrane proteins in renal collecting ducts whose job is to channel water back into renal medulla interstitial fluid, but Na⁺ is still excreted

urine decrease 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 able to lower blood tonicity /// aldosterone has little affect to lower blood tonicity (Why?)

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

Acid-Base Balance

Acid-base balance are critical “fluid components” /// must be regulated to maintain homeostasis!

metabolism depends on enzymes which are sensitive to pH

slight deviation from the normal pH can shut down entire metabolic pathways // denature proteins!

alter the structure and function of macromolecules // proteins

failure in pH homeostasis will result in death

changes in pH may also cause imbalance in ions across plasma membranes // affects resting membrane potentials and action potentials.

Acid-Base Balance

7.35 to 7.45 is the normal pH range (test benchmark 7.4 pH)
of blood and tissue fluid

only able to live a couple hours if pH is below 7 or above 7.7,

If pH below 6.8 and above 8 then death is rapid

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 is determined by concentration of **free hydrogen ions (H⁺) // protons**

Molecules that release H⁺ (proton) are acids (proton donors)

strong acids like hydrochloric acid (HCl) ionize freely /// gives up all H⁺
/// rapidly lowers pH of a solution

weak acids like carbonic acid (H₂CO₃) ionize only slightly /// keeps most
H⁺ chemically bound // does not rapidly affect pH

Ammoniochloride (NH₃Cl) is also a weak acid

Acids and Bases

bases – molecules that accept 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

What is the difference between a salt, an acid and a base?

Buffers

Anything that **resists a change in pH**

Buffers are able to convert strong acids or strong bases into weak acids and weak bases

Two different types of buffers

1st = physiological buffer – organ systems that excrete acids (CO_2) or bases “out of the body”

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

2nd = chemical buffer = a substance that binds H^+ and removes it from solution (but not from body) // occurs as proton 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 proteins

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



reversible reaction important in ECF



/// lowers pH by releasing H^+



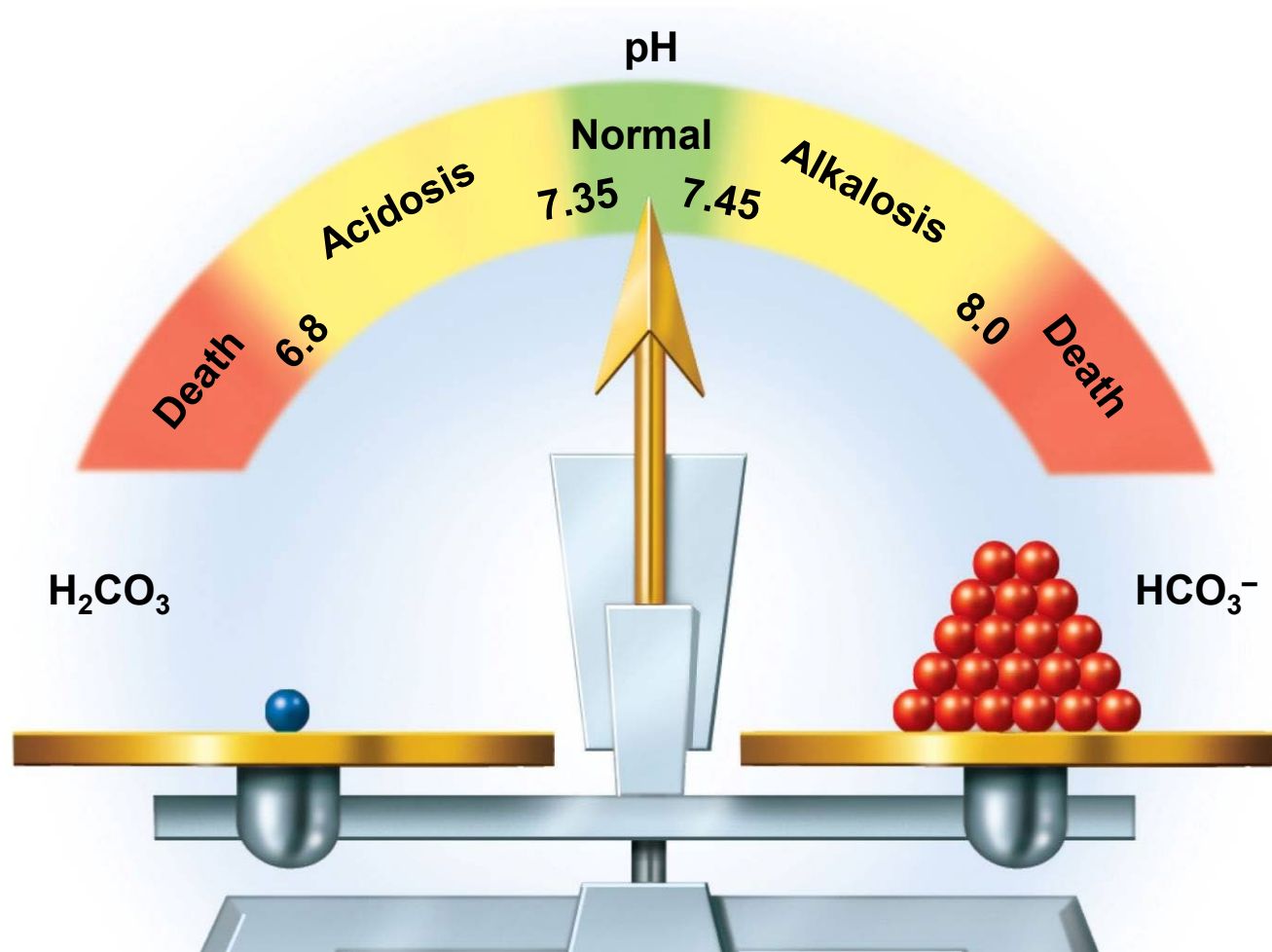
/// raises pH by binding H^+

functions best in the **lungs and kidneys** to constantly remove CO_2

> to lower pH (more acidic), kidneys excrete HCO_3^-

> to raise pH (more alkaline), kidneys excrete H^+ and lungs excrete CO_2

Acid-Base Balance



20:1

As metabolism produces acids, the protons are buffered by bicarbonate, a weak base. This results in the formation of carbon dioxide which then is excreted from the body by the respiratory system. $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$

Phosphate Buffer System

a solution of HPO_4^{2-} and H_2PO_4^-



reactions that proceed to the right release free H^+ and decreasing pH number (more acidic), and movement to the left increase pH number to make pH more alkaline

more important **buffering the ICF and renal tubules** /// here the 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 in part to certain side groups of their amino acid's "R groups"

Amino acids also have at each end of the protein:

carboxyl (-COOH) groups which releases H⁺ when pH begins to rise

amino (-NH₂) groups that bind H⁺ when pH gets too low

Respiratory Control of pH

CO₂ is constantly produced by aerobic metabolism

normally eliminated by the lungs at an equivalent rate



Retain carbon dioxide lowers pH by releasing H⁺



Expire carbon dioxide 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 may neutralize more acid or base than either the respiratory system or chemical buffers

renal tubules secrete H^+ into the tubular fluid

most protons binds to bicarbonate, ammonia, and phosphate buffers

bound and free H^+ are excreted in the urine

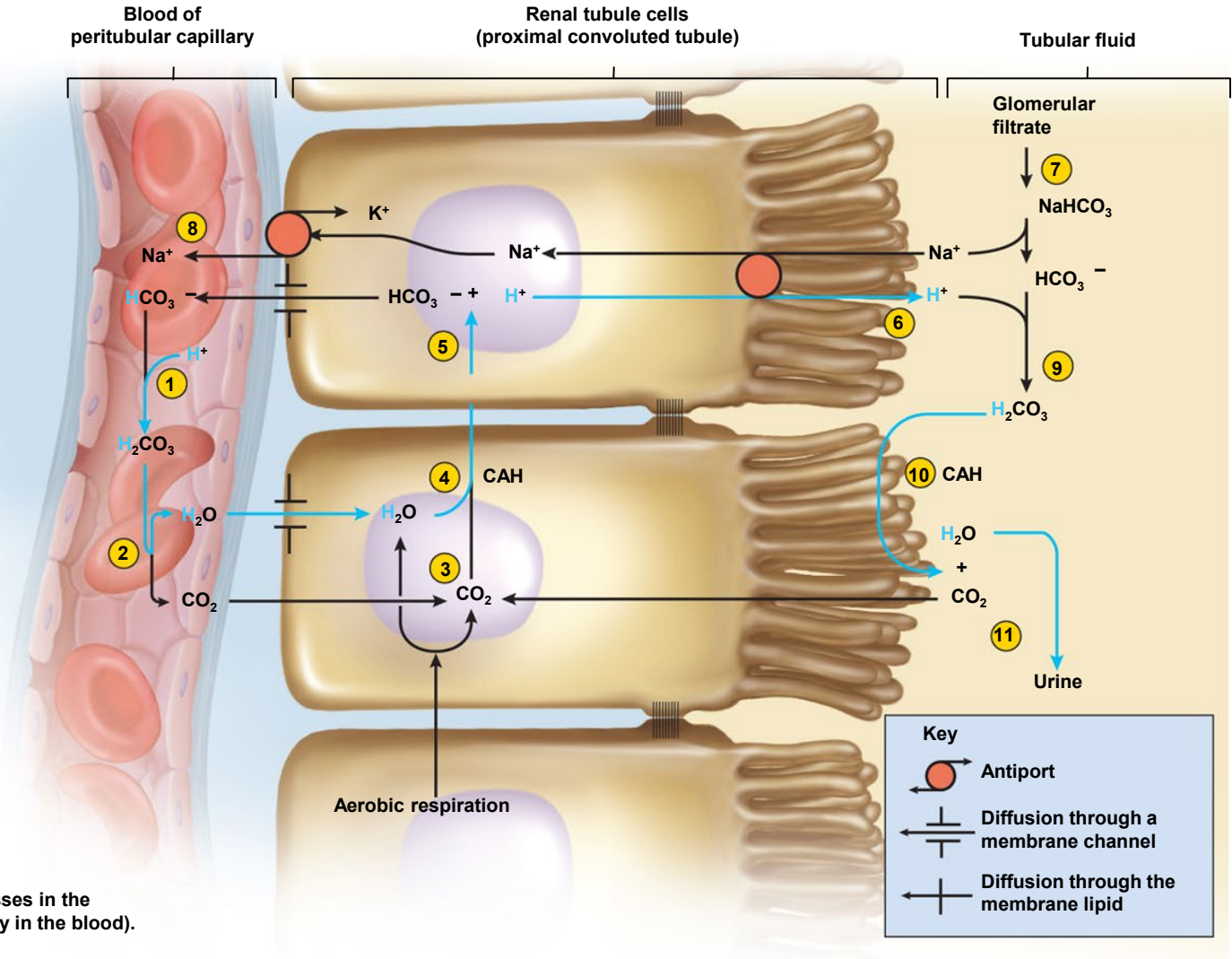
kidney actually expelling H^+ from the body, not just “binding it to another molecule

blood buffer systems only reduce proton concentration by binding protons to other molecules

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 to 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 in previous slide)

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, then secretion of H^+ stops

limiting pH = 4.5

Limiting pH

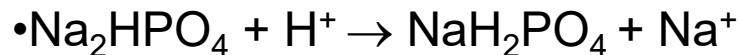
This is prevented by buffers in tubular fluid

bicarbonate system – all bicarbonate ions in tubular fluid are used to neutralize H^+

- so there are no HCO_3^- in the urine
- the more acid the kidneys secrete means less sodium is in the urine

phosphate system - di-basic sodium phosphate is contained in glomerular filtrate

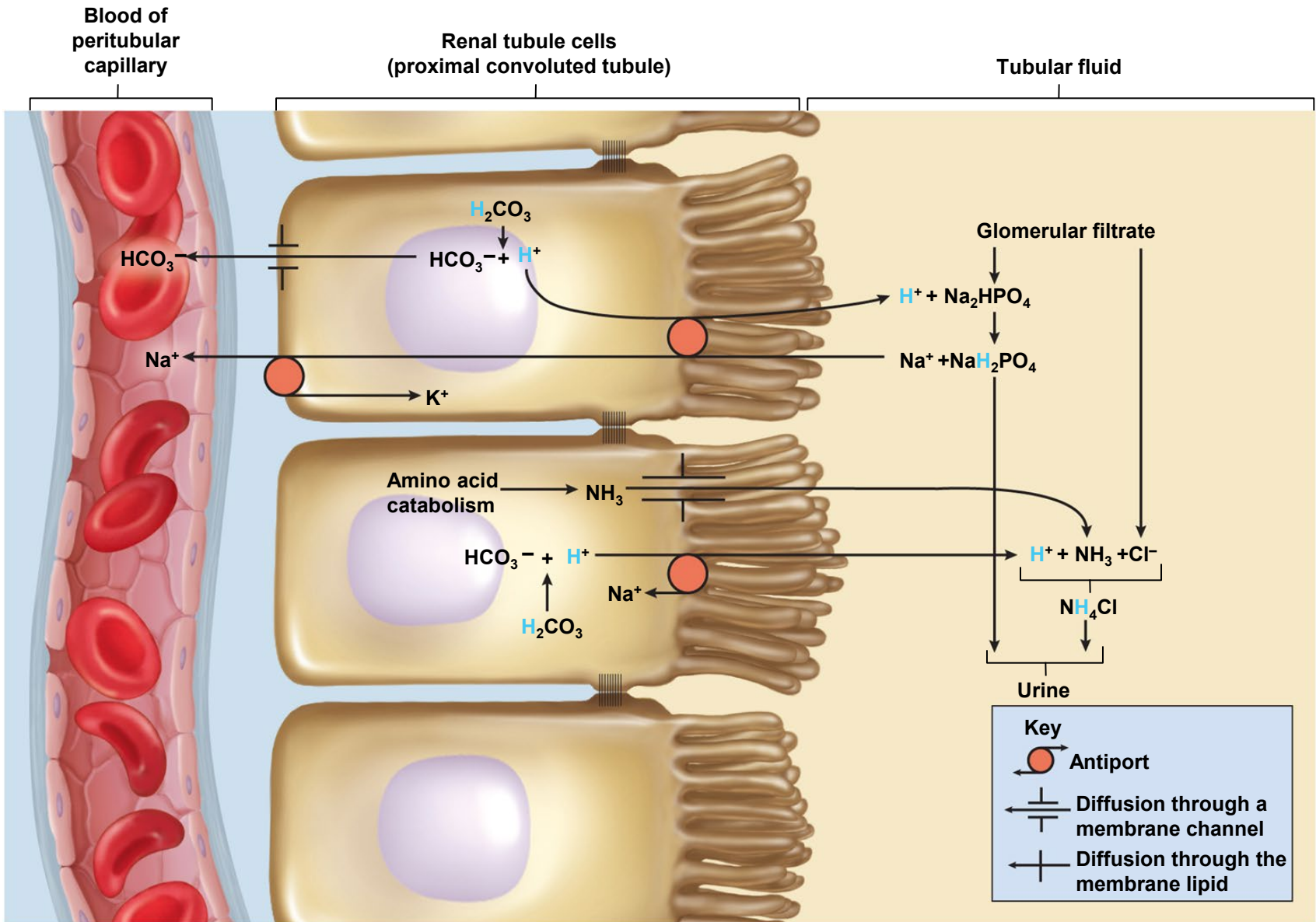
• reacts with some of the H^+ replacing a Na^+ in the buffer which passes into the urine



ammonia (NH_3) - from amino acid catabolism acts as a base to neutralize acid



Ammonium Chloride Buffering Mechanisms in Urine



Acidosis

A Disorder of Acid-Base Balance

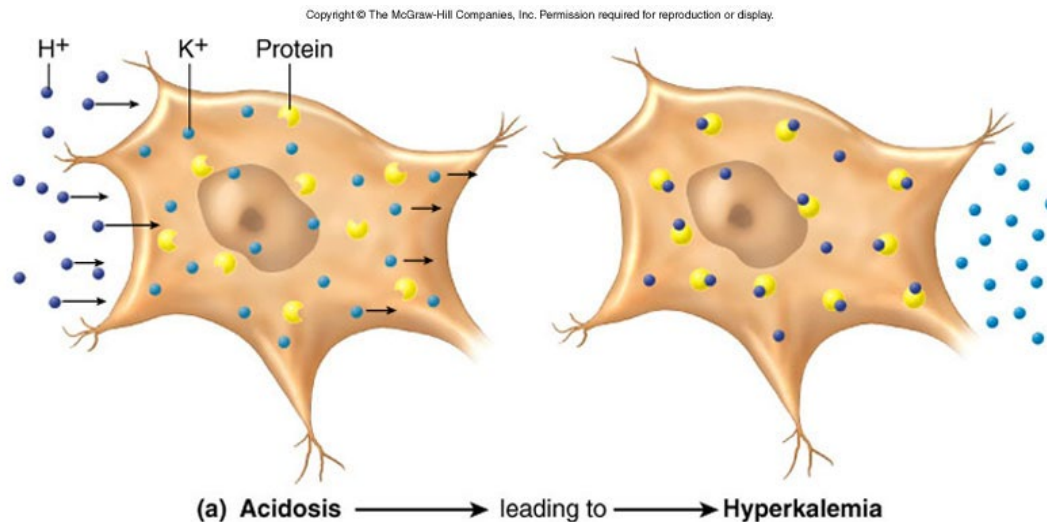
Acidosis = pH below 7.35

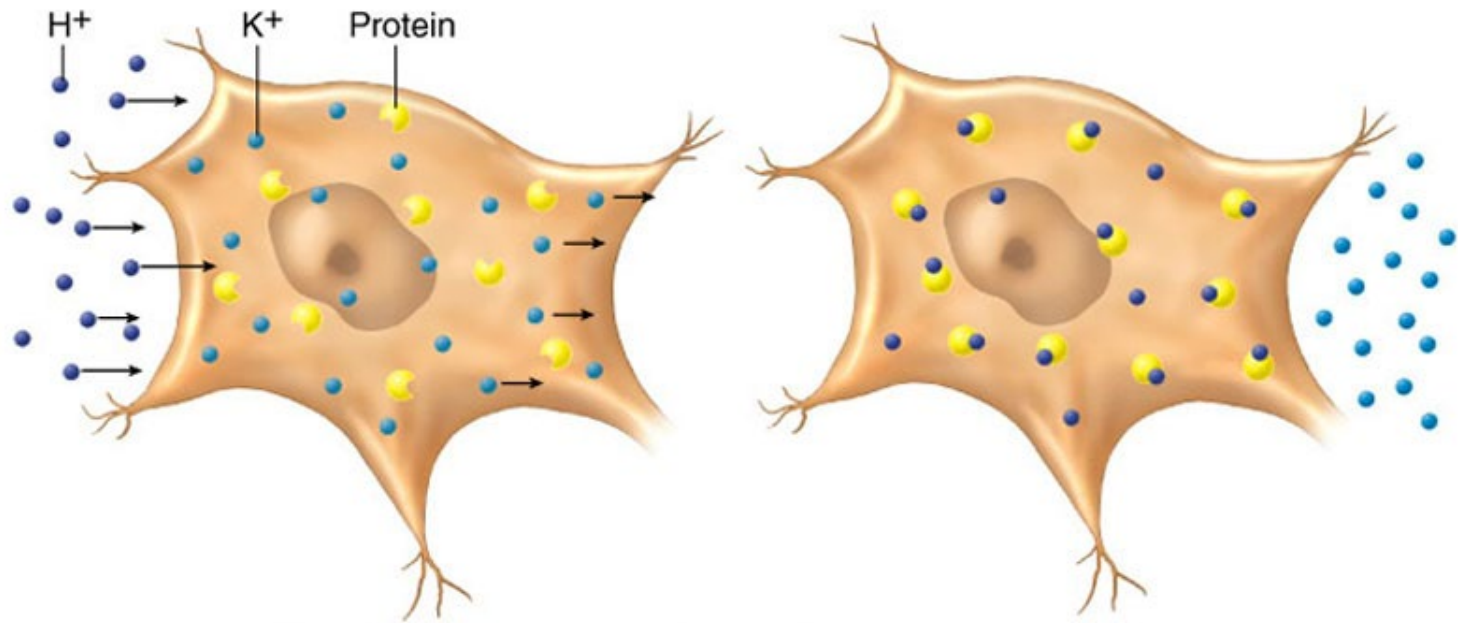
H⁺ diffuses into cells and drives out K⁺ /// H⁺ buffered by protein in ICF // this allow for even more H⁺ to diffuse into cell and more **potassium out** // net loss of cations from cell

Resting membrane potential more negative than normal (hyperpolarized)

Nerves and muscles harder to stimulate // why **acidosis depresses the CNS** and causes symptoms like confusion, disorientation, and coma.

This elevates K⁺ concentration in ECF /// now ECF = **hyperkalemia**





(a) Acidosis \longrightarrow leading to \longrightarrow Hyperkalemia

Alkalosis

A Disorder of Acid-Base Balance

Alkalosis

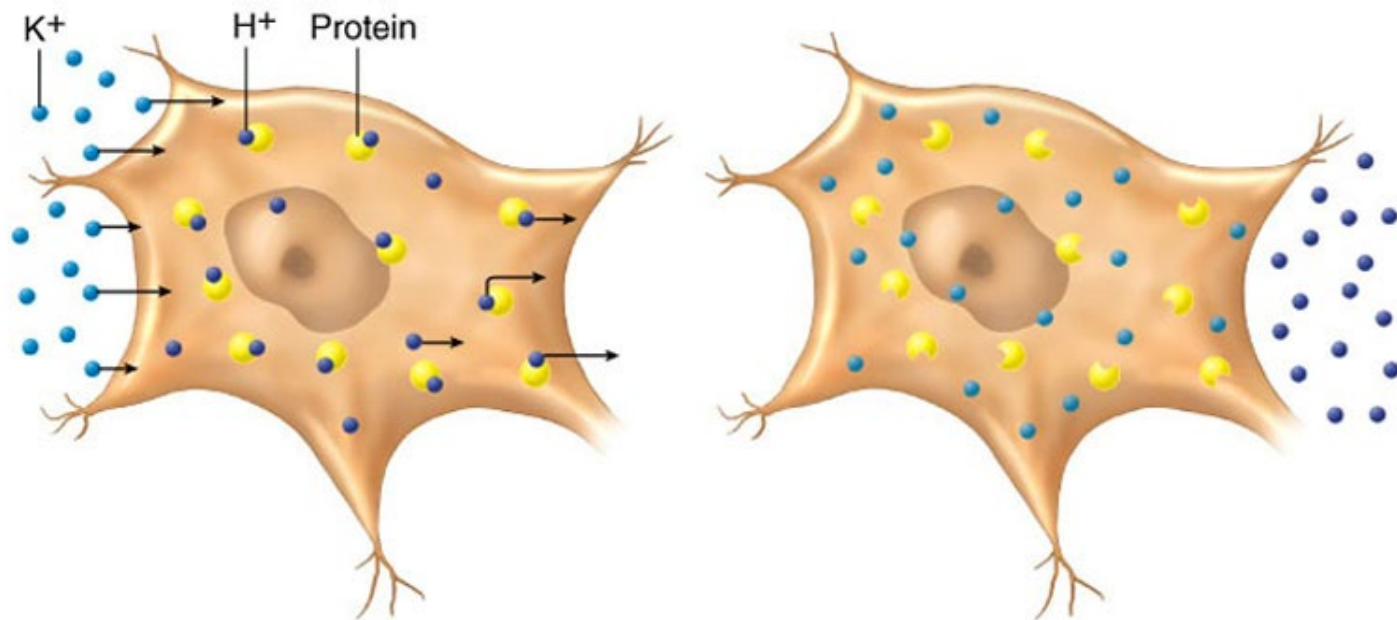
Alkalosis = pH above **7.45**

–H⁺ diffuses out of cells

–K⁺ diffuses in /// causes hypokalemia

–lowers resting membrane potential

This results in making the nervous system More excitable. Neurons fire Spontaneously and overstimulate skeletal muscles, causing muscle spasm, tetanus, convulsions, or respiratory paralysis.



(b) Alkalosis → leading to → Hypokalemia

What Causes Acid-Base Balances?

When you have an acid-base imbalance then it will be caused by either the respiratory system or metabolism:

–**Respiratory acidosis or respiratory alkalosis**

–**Metabolic acidosis or metabolic alkalosis**

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 not enough CO₂ in the blood

What Causes Acid-Base Balances?

Metabolic acidosis

–increased production of organic acids such as lactic acid in anaerobic fermentation, or 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

pH imbalances caused by respiratory system will be compensated by kidneys

pH imbalance caused by metabolism will be compensated by respiratory system

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.)

Metabolic (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 HCO₃⁻

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

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-}

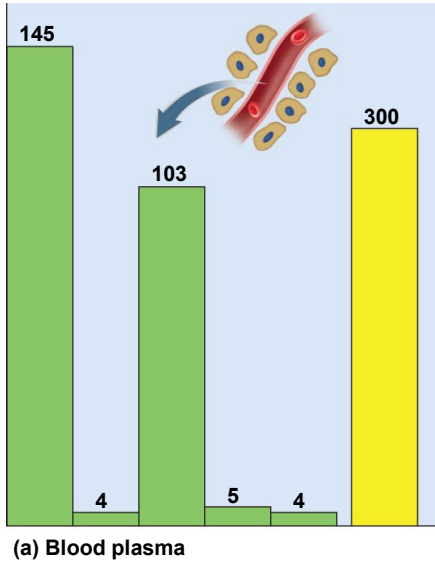
major extracellular cation is sodium

major intracellular cation is potassium

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



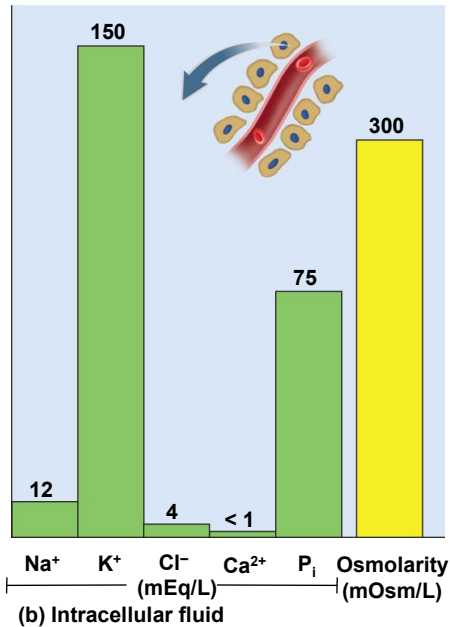
Sodium main extracellular cation

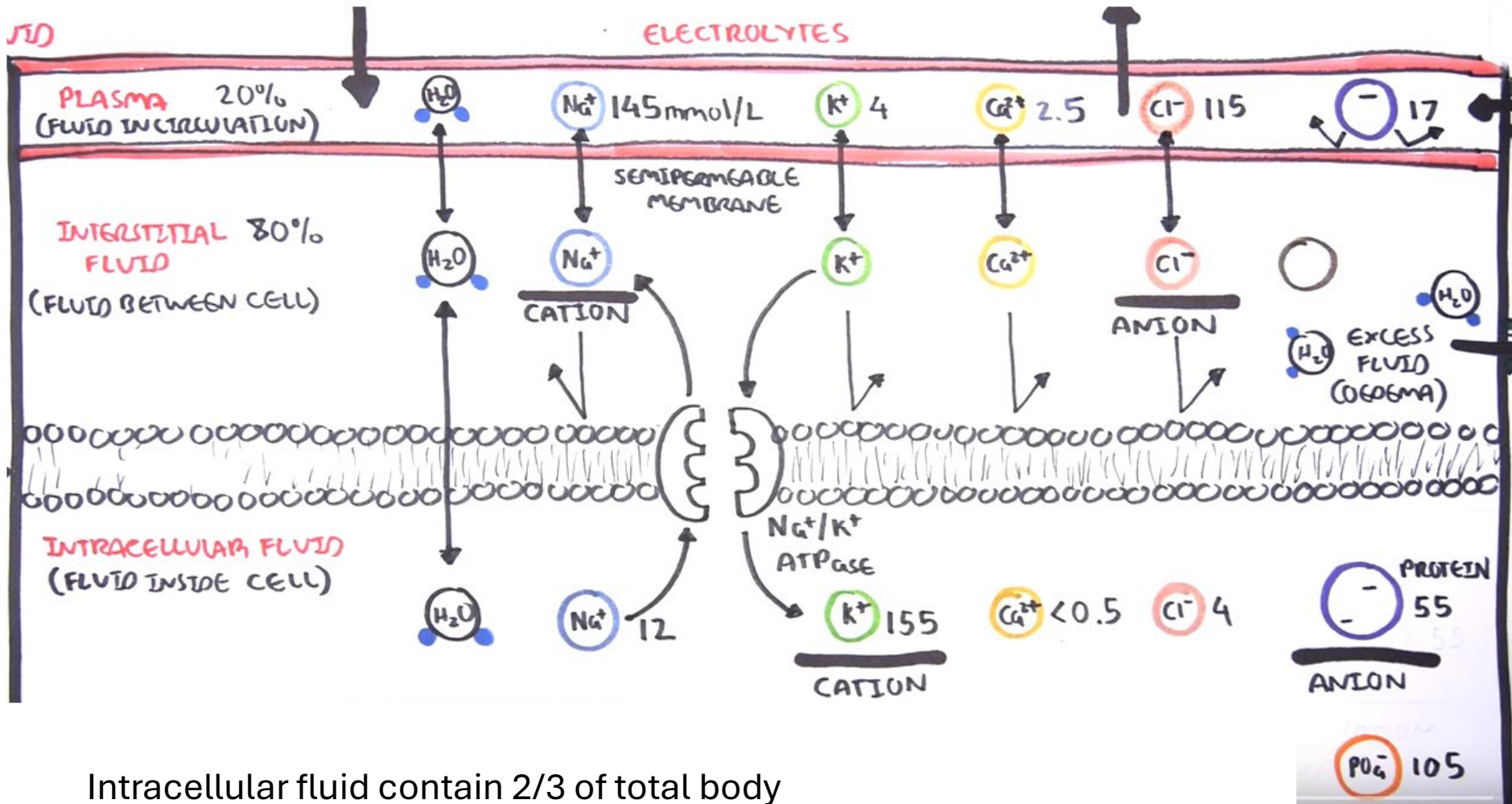
Chloride main extracellular anion

Potassium main intracellular cation

Phosphate main intracellular anion

Bicarbonate important in acid-base balance





Intracellular fluid contain 2/3 of total body water, extracellular fluid contains the rest.

Note: lymphatic system circulates electrolytes between interstitial fluid and plasma

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

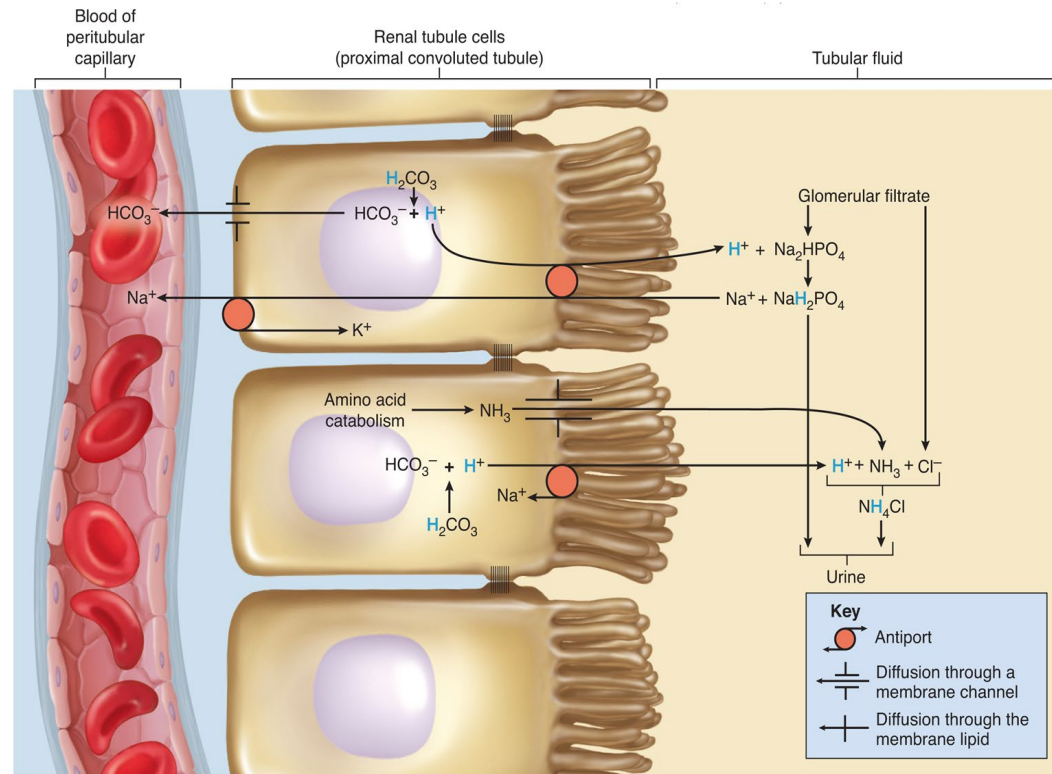
Sodium - Functions

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

Na^+ - K^+ pump /// exchanges intracellular Na^+ for extracellular K^+

this pump also generates body heat and required to maintain resting membrane potential

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 Na⁺-K⁺ pumps**

in **10 – 30 minutes** enough Na⁺-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

with no aldosterone --- **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

Low sodium concentration 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

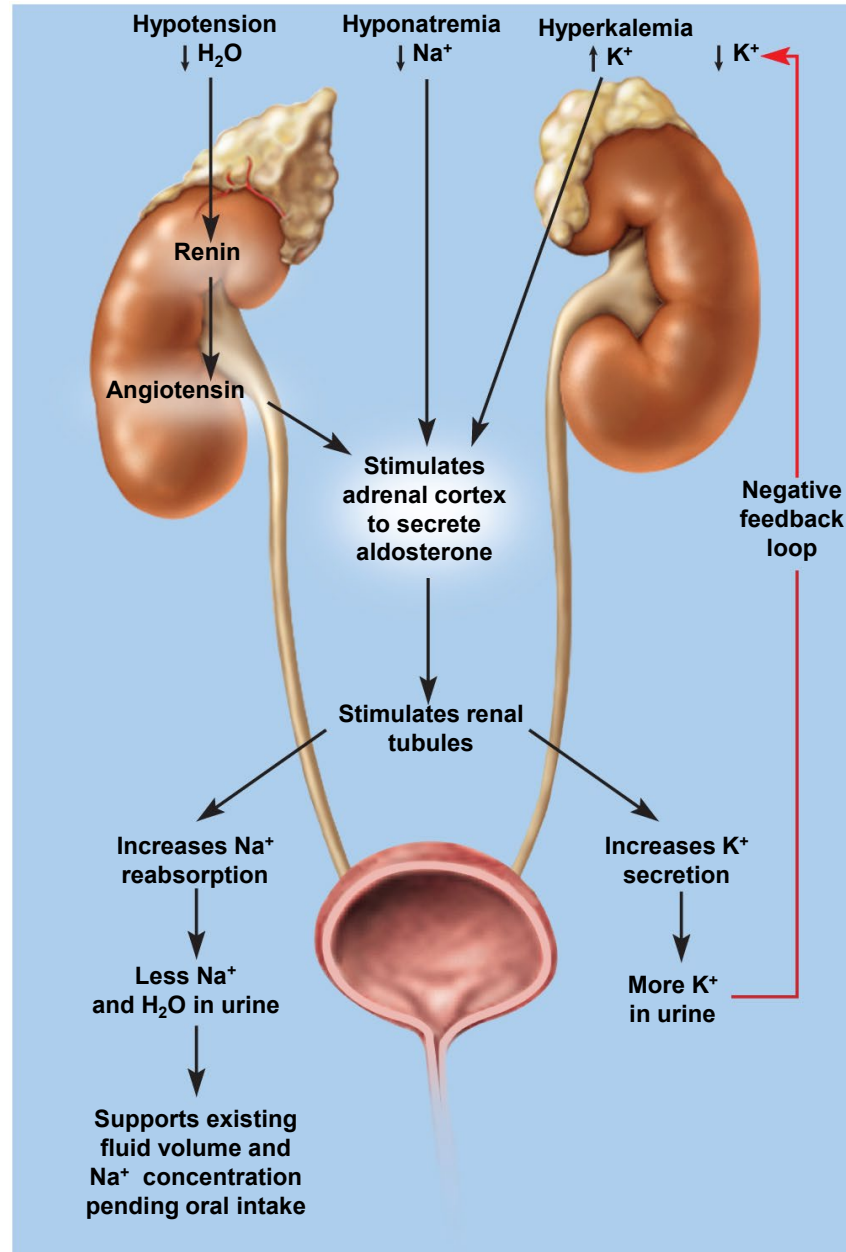
Potassium homeostasis is closely linked to sodium

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 in tubules reabsorbes sodium and potasium 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

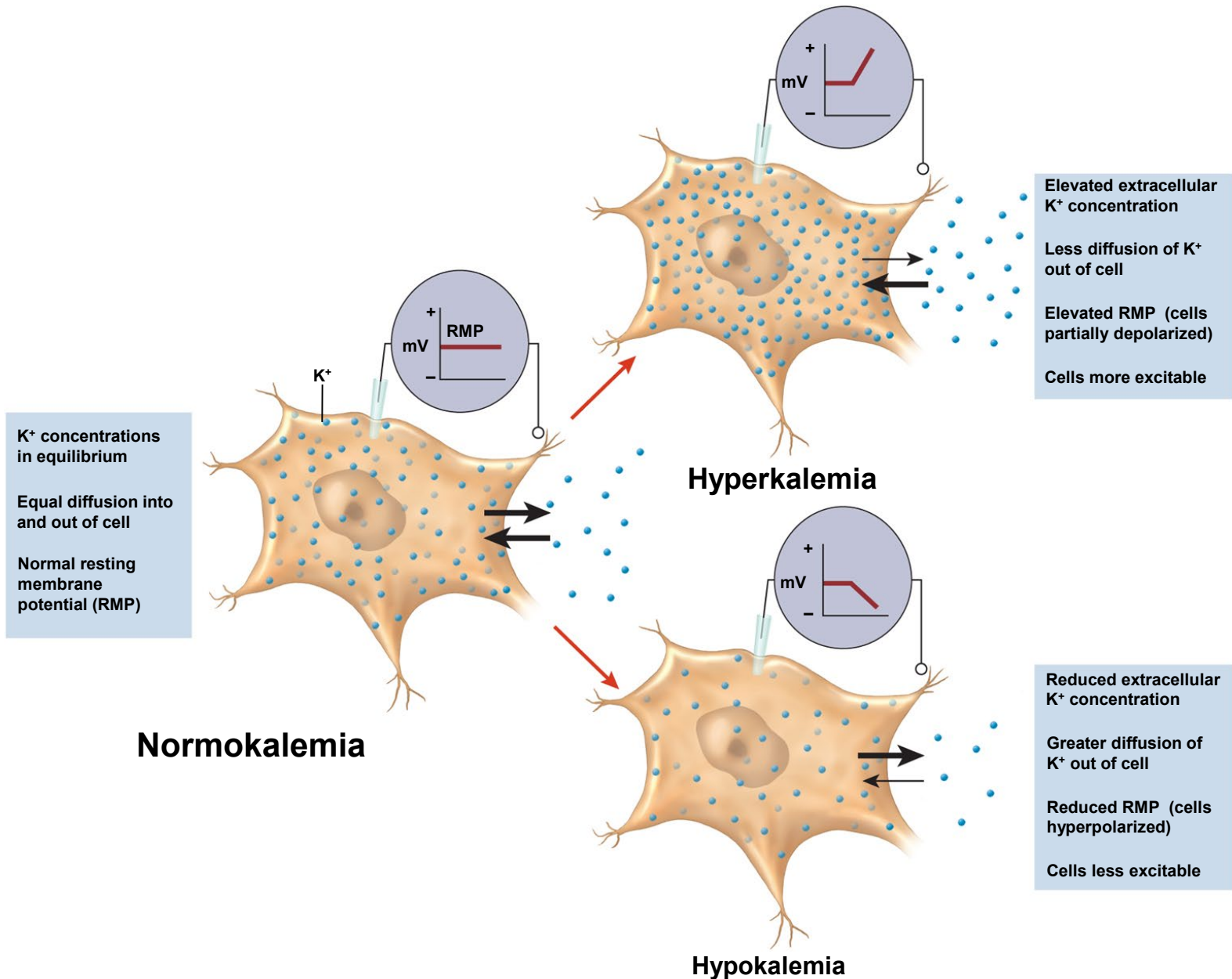
Concentration rises slowly

- inactivates voltage-regulated Na^+ channels (can not initiate action potential)
- nerve and muscle cells become less excitable
- can produce cardiac arrest

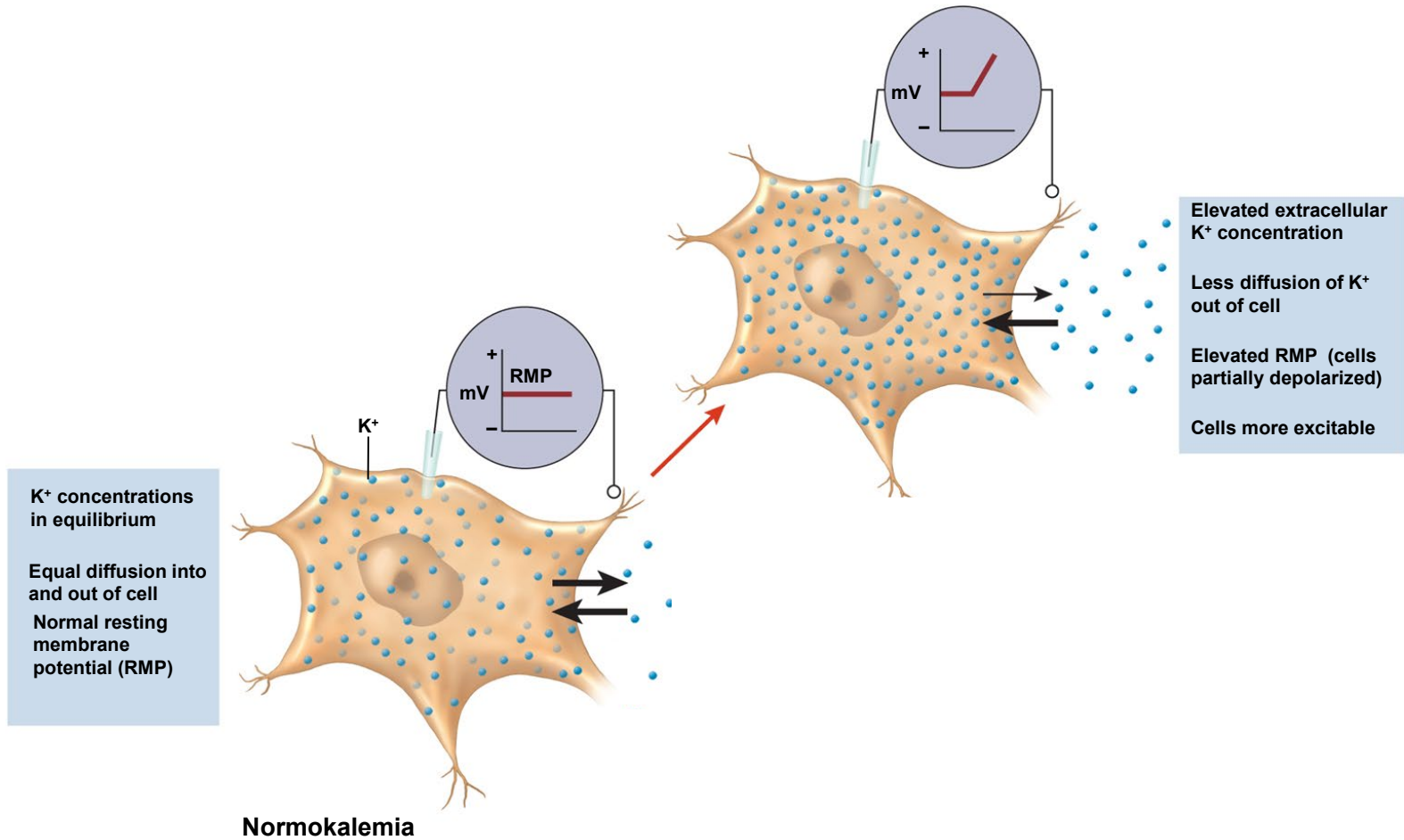
Hypokalemia

- 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

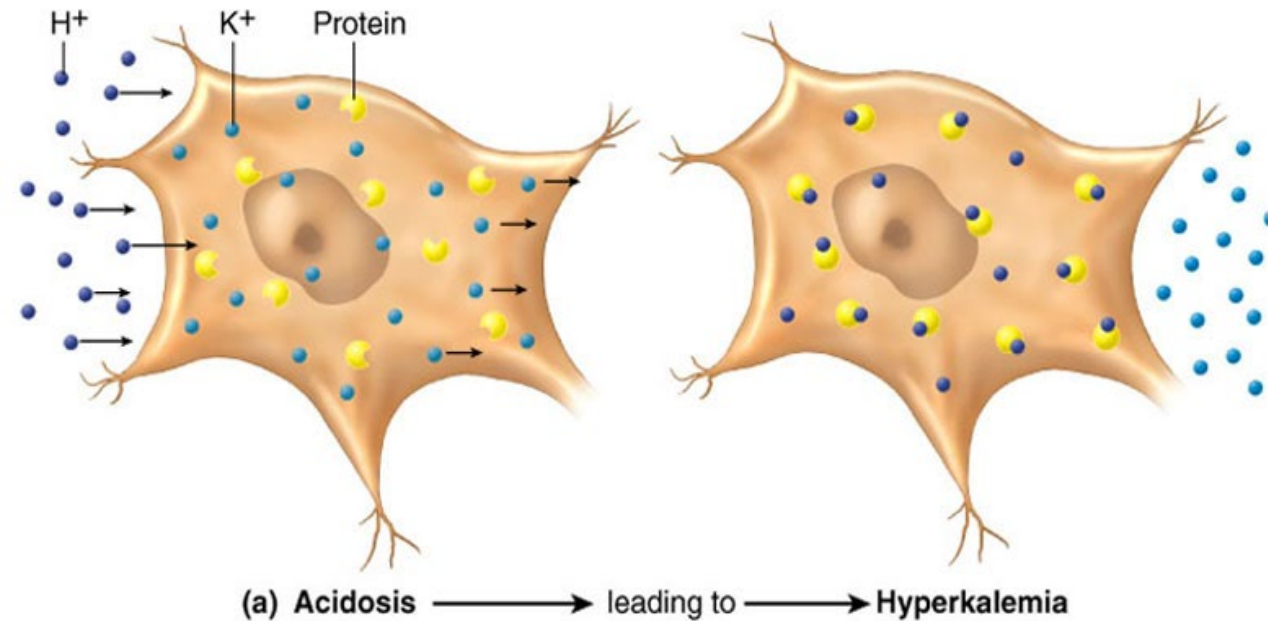


Hyperkalemia Which Increases Excitability



Cells more excitable!
Significance?

Hyperkalemia



Membranes potential moves closer to threshold, nerves partially stimulated, muscles spasms, tetany, convulsions, and respiratory paralysis. // more excitable

Hyperkalemia may also result in a skeletal muscle crush injury or patient given outdated plasma containing many ruptured RBC . Why?

However, if potassium concentration rises slowly over time then voltage regulated sodium channels stop working /// now cell can not initiate an action potential which requires the sodium channels to open /// less excitable /// cause cardiac arrest and respiratory paralysis

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 more acid than chemical buffers

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 non-reactive 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 in 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 capillaries “leak protein” so water moves into interstitial space /// **volume of circulating blood drops to cause circulatory shock**

- most common forms:

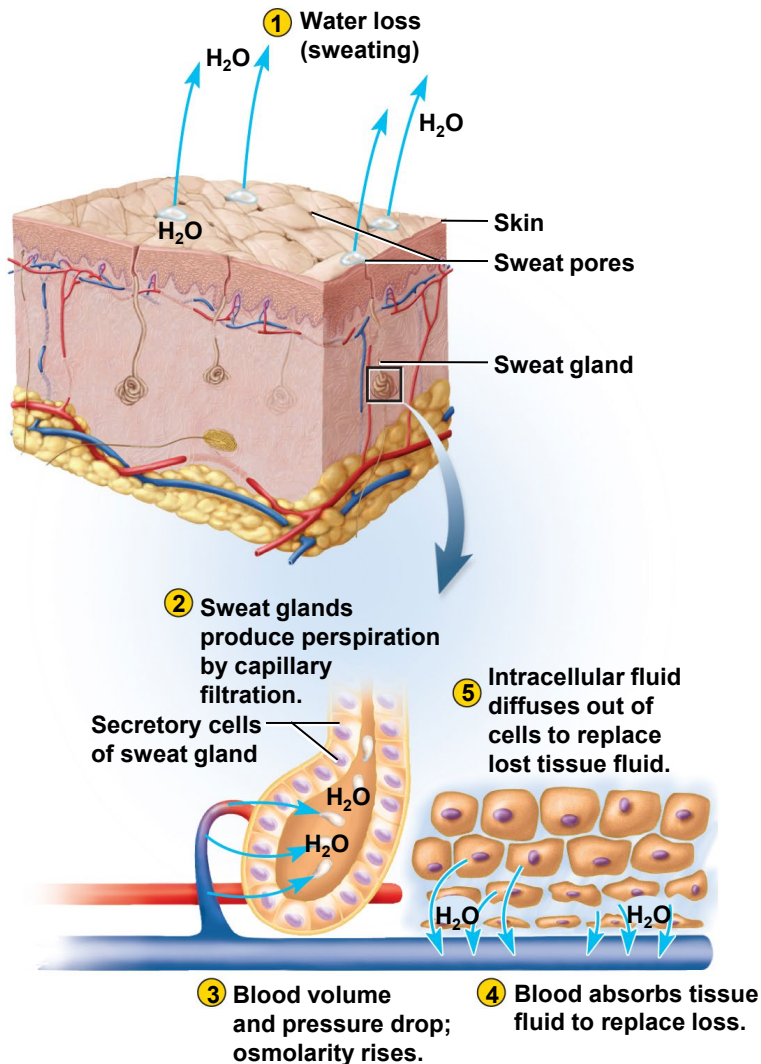
– **edema** - abnormal accumulation of fluid in the interstitial spaces, causing swelling of the tissues

– **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