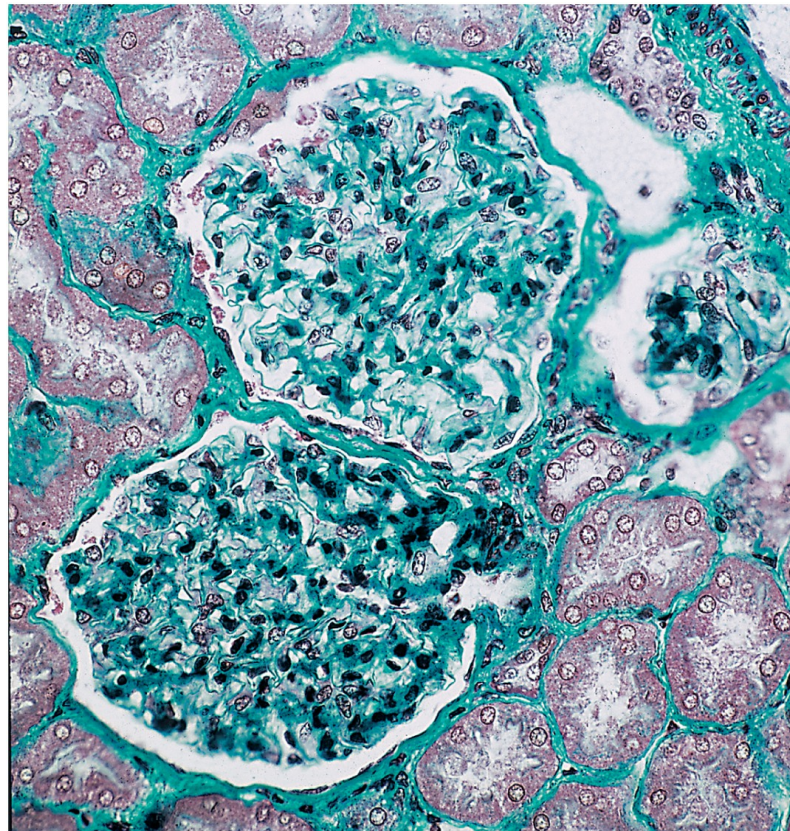


## Chapter 24

# 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

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- 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

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- **Total body water** (TBW) of a 70kg (150 lb) young male is about **40 liters** (We age from a grape to a raisin.)
  - 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

# 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 Is Water Moved Between Fluid Compartments?

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- 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 ICF and ECF
- if an imbalance arises, osmosis restores balance within seconds
- the osmolarity in 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*
  - *the osmolarity of the human body is between 275 mOsm and 295 mOsm*

# Why may there be water movement 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!

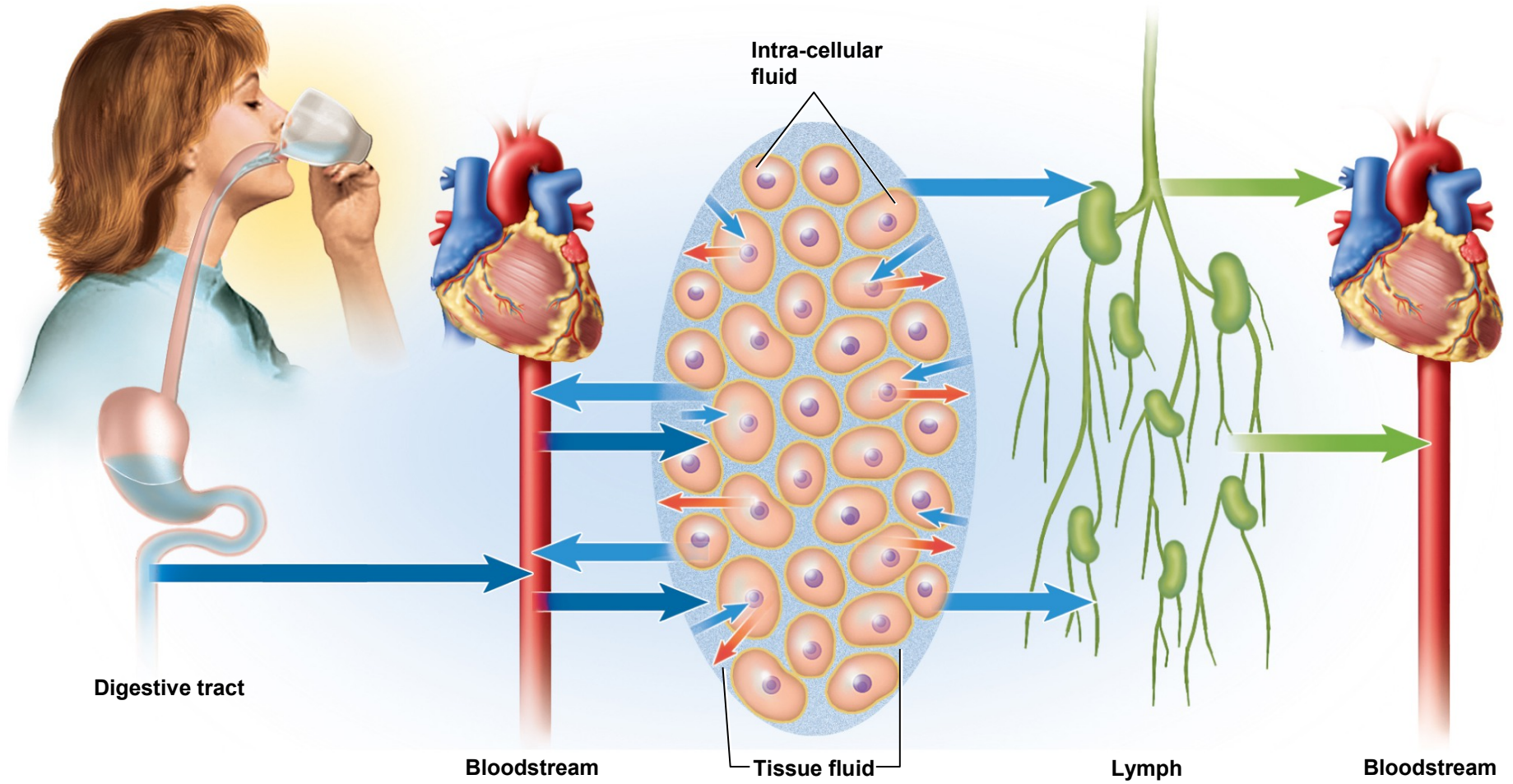
sodium salts major cation in ECF

potassium salts major cation in ICF





# Water Movement Between Fluid Compartments



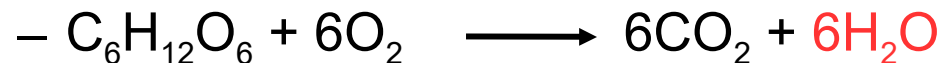




# Fluid Balance (Loss = Gain)

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- 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 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?

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## Two Types of Water Losses

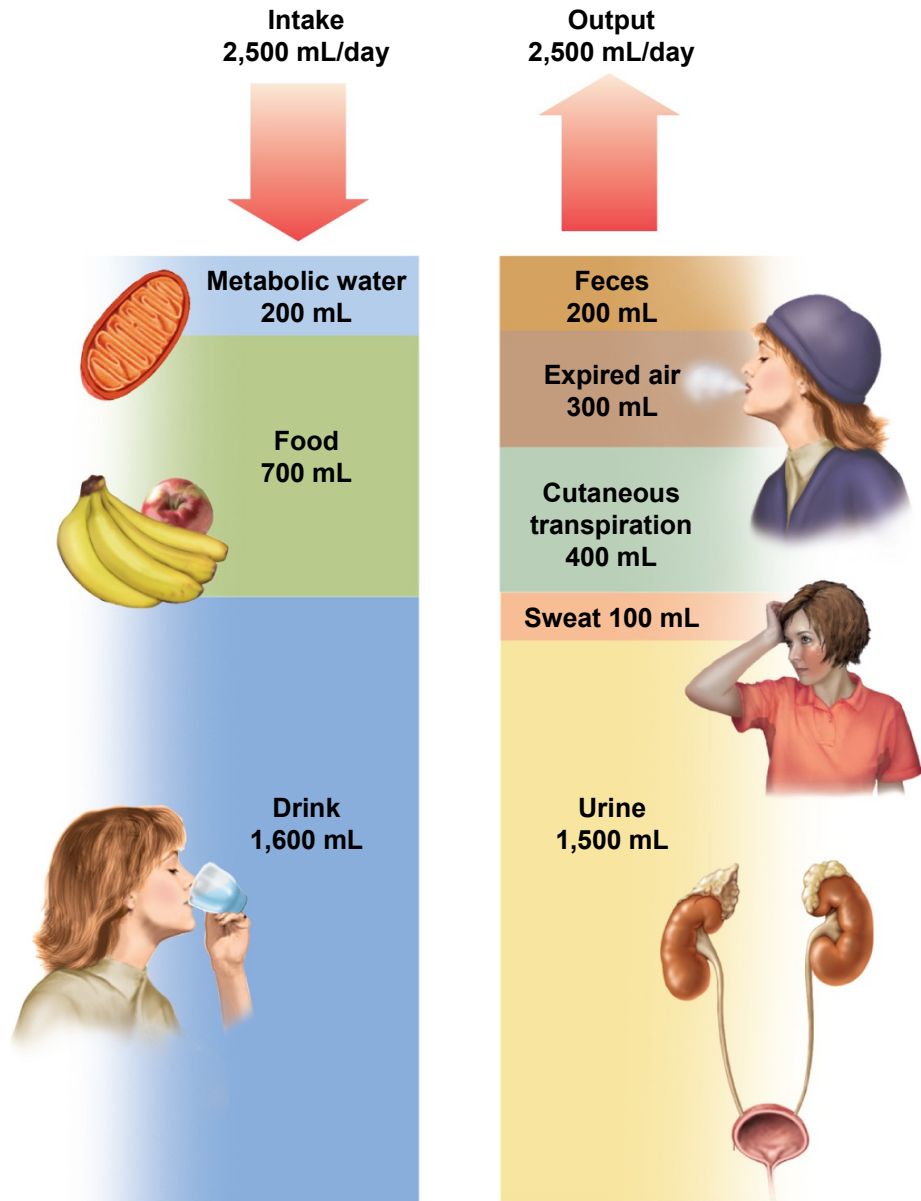
**Sensible water loss** /// this is observable

- > 1,500 mL/ day is in urine
- > 200 mL/day is in feces
- > 100 mL/day is sweat 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
- > 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



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 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

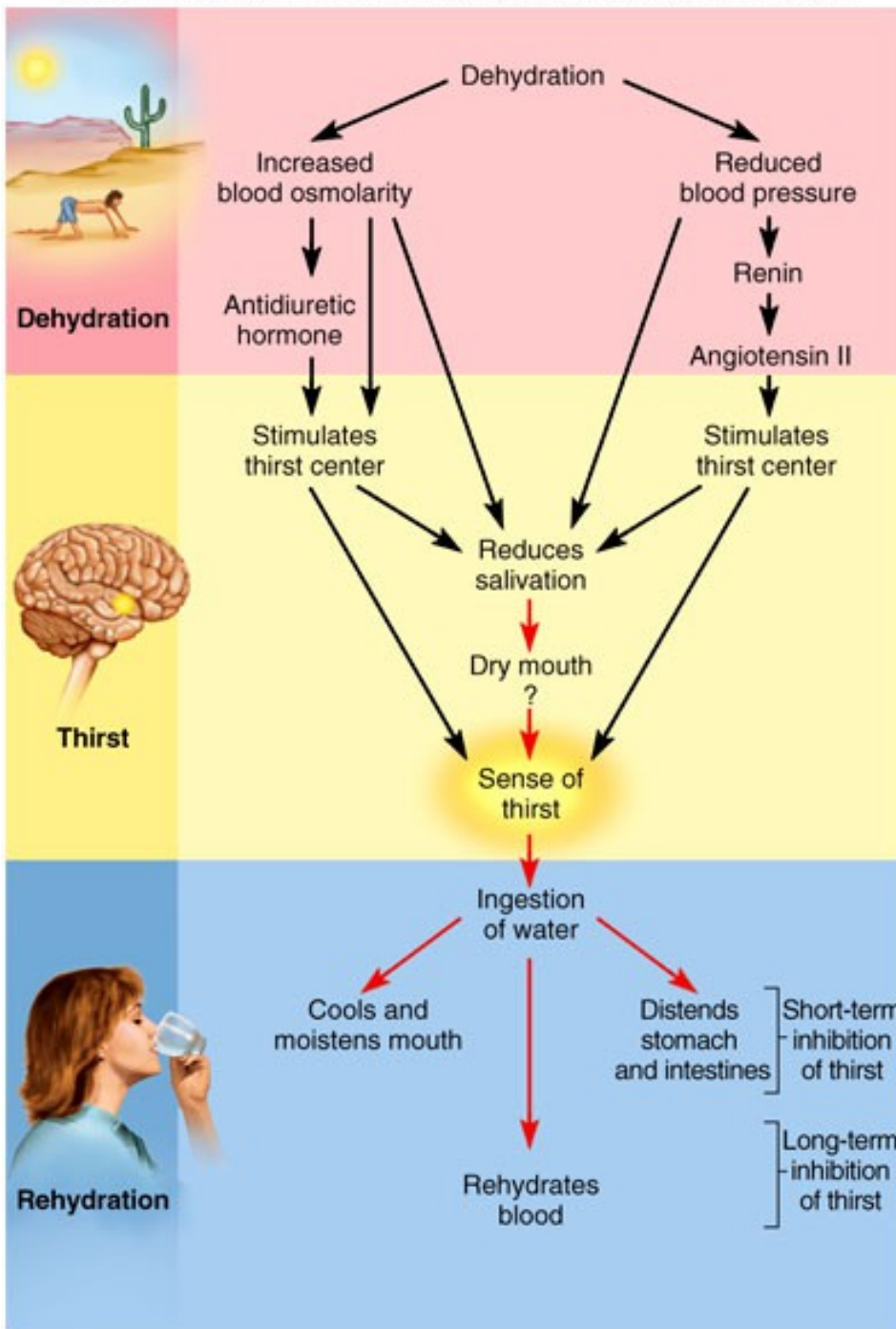
intense sense of thirst occurs with 2-3% increase in plasma osmolarity

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
  - after drinking water - absorption of water across 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

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 electrolytes
  - kidneys can only slow the rate of water and electrolyte loss until you ingest water and electrolytes
- Two mechanisms regulated by hormones:
  - 1<sup>st</sup> = Aldosterone hormone (minor role in changing tonicity)
    - changes in urine volume linked to adjustments in **Na<sup>+</sup> reabsorption**
    - as Na<sup>+</sup> is reabsorbed water follows but increases blood pressure so GFR increases which results in more water loss!

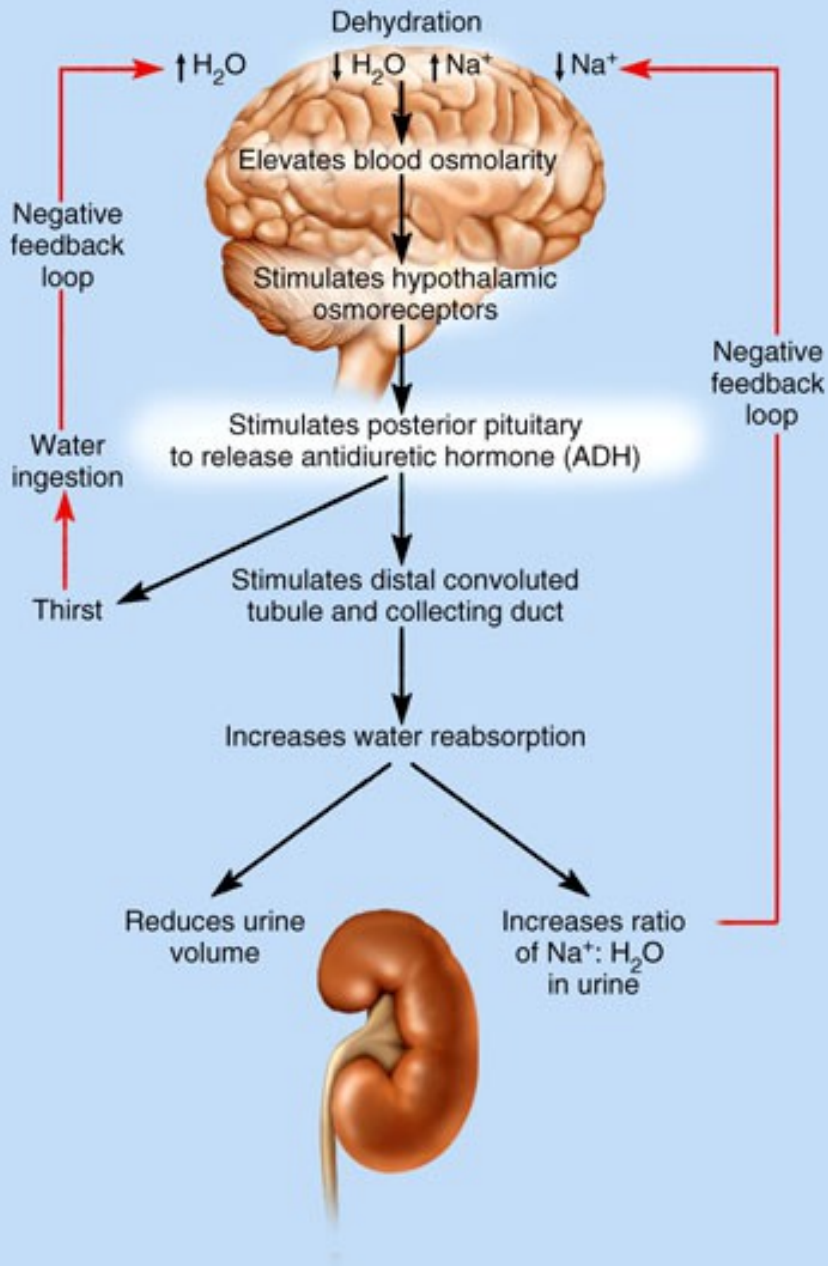
# Regulation of Water Output

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## – 2<sup>nd</sup> = Anitdiuretic hormone

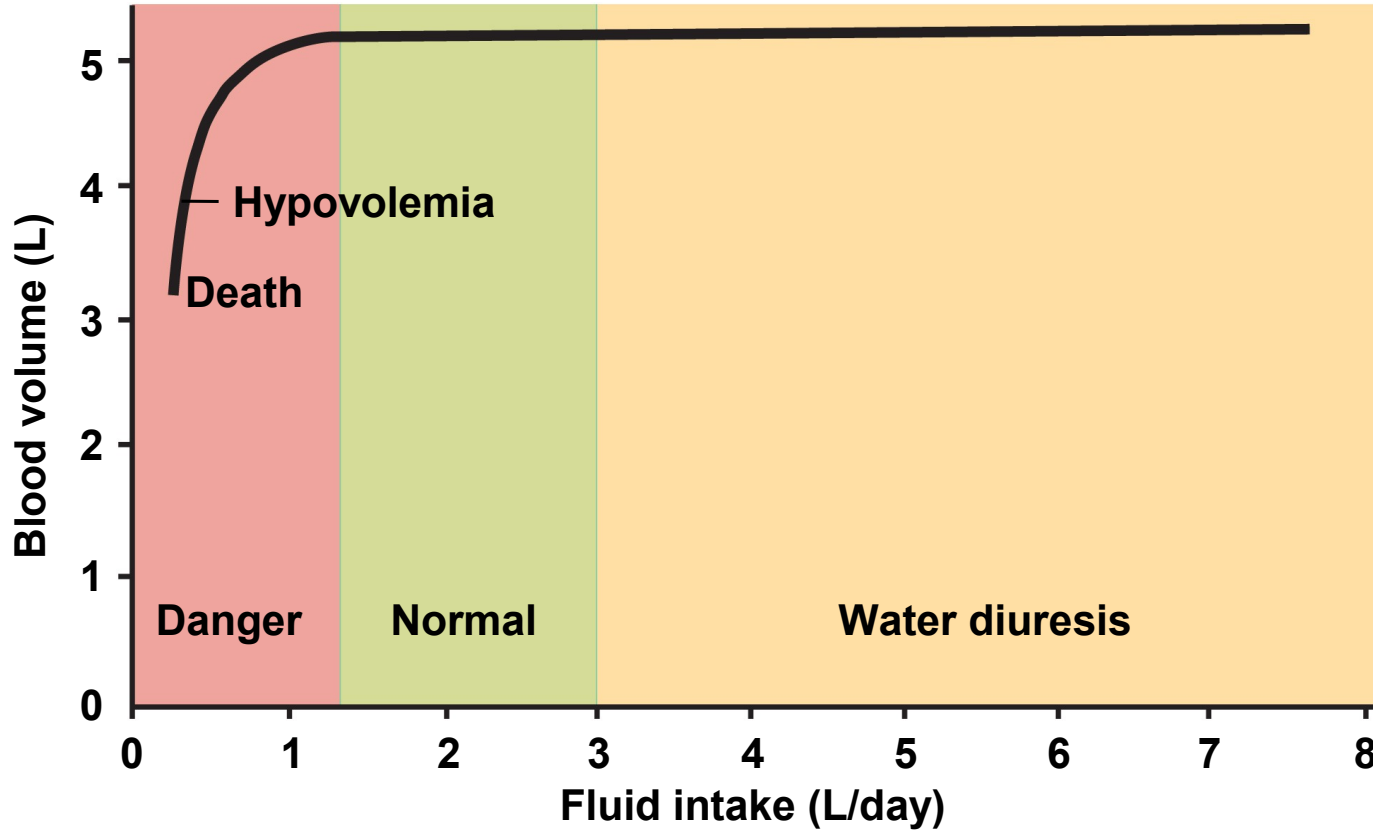
- concentrates the urine / becomes darker color
- ADH secretion stimulated by hypothalamic osmoreceptors in response to dehydration
- **aquaporins** synthesized in response to ADH
  - membrane proteins in renal collecting ducts whose job is to channel water back into renal medulla, Na<sup>+</sup> is still excreted
  - urine // 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 able to lower blood tonicity /// aldosterone does not lower blood tonicity (Why?)



## ADH Secretion

*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

---



- Critical “fluid components” (i.e.  $H^+$  or protons) that 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
  - alter the structure and function of macromolecules
  - 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 ( $H^+$ )**
- any molecule able to release  $H^+$  (proton) is an acid
  - **strong acids** like hydrochloric acid ( $HCl$ ) ionize freely /// gives up all of its  $H^+$  // rapidly lowers pH of a solution
  - **weak acids** like carbonic acid ( $H_2CO_3$ ) ionize only slightly /// keeps most  $H^+$  chemically bound // does not rapidly affect pH
- *Review: What is the difference between a salt and an acid or base?*

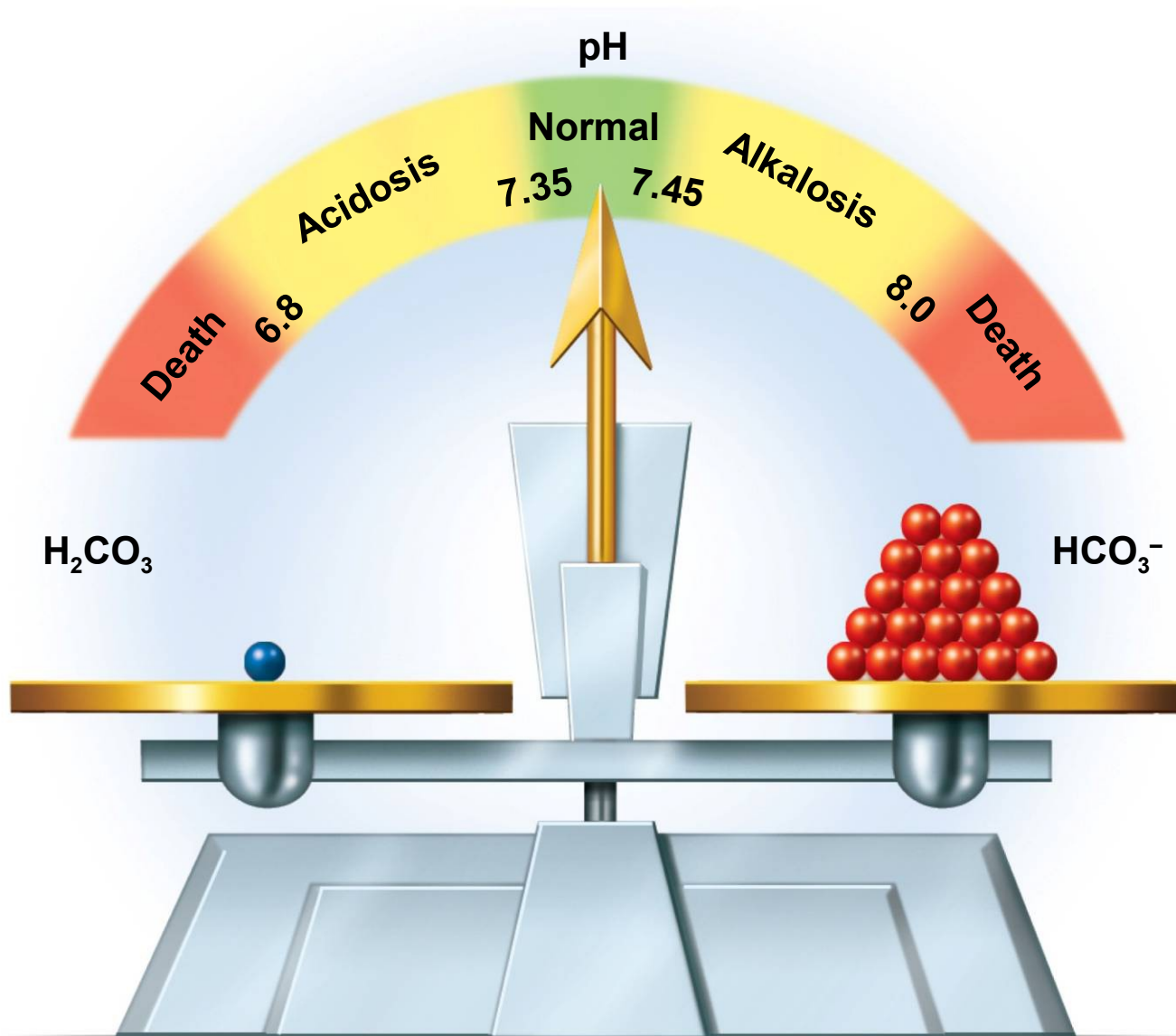


# Acids and Bases

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- **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



20:1

# Buffers

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- any mechanism that **resists change in pH**
- convert strong acids or bases to weak acids and bases
- there are two types of buffers
- **physiological buffer** – organ systems that excrete acids, bases, or CO<sub>2</sub>
  - **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

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**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**
- **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**
    - $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{HCO}_3^- + \text{H}^+$
  - **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  $\text{H}^+$
    - $\text{CO}_2 + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{HCO}_3^- + \text{H}^+$ 
      - raises pH by binding  $\text{H}^+$
- 
- functions best in the **lungs and kidneys** to constantly remove  $\text{CO}_2$ 
    - to lower pH (more acidic), kidneys excrete  $\text{HCO}_3^-$
    - to raise pH (more alkaline), kidneys excrete  $\text{H}^+$  and lungs excrete  $\text{CO}_2$

# Phosphate Buffer System

---

- a solution of  $\text{HPO}_4^{2-}$  and  $\text{H}_2\text{PO}_4^-$
- $\text{H}_2\text{PO}_4^- \leftrightarrow \text{HPO}_4^{2-} + \text{H}^+$ 
  - reactions that proceed to the right release free  $\text{H}^+$  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**
  - 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

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- 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<sup>+</sup> when pH begins to rise
- **others have amino (-NH<sub>2</sub>) side groups** that bind H<sup>+</sup> when pH gets too low

# Respiratory Control of pH

---

- CO<sub>2</sub> 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<sup>+</sup>
  - $\text{CO}_2 \text{ (expired)} + \text{H}_2\text{O} \leftarrow \text{H}_2\text{CO}_3 \leftarrow \text{HCO}_3^- + \text{H}^+$ 
    - raises pH by binding H<sup>+</sup>
- Increased CO<sub>2</sub> and a decrease in the pH number (i.e. more acidic) **stimulate pulmonary ventilation**
- Decreased CO<sub>2</sub> and an increase in the pH number (i.e. more alkaline or basic) **inhibits pulmonary ventilation**

# Renal Control of pH

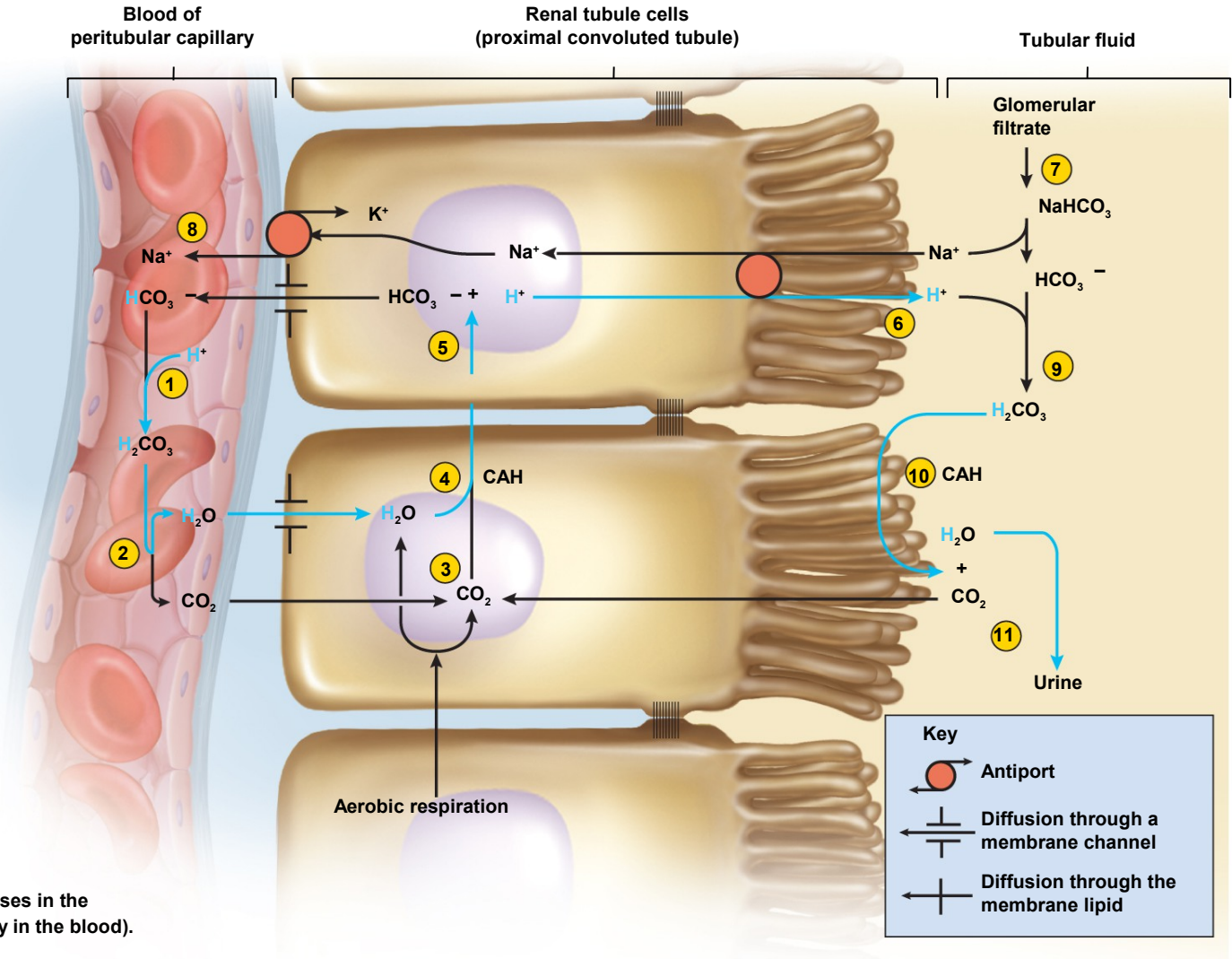
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- the kidneys can neutralize more acid or base than either the respiratory system or chemical buffers
- renal tubules secrete  $H^+$  into the tubular fluid
  - most protons binds to bicarbonate, ammonia, and phosphate buffers
  - bound and free  $H^+$  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<sup>+</sup> Secretion and Excretion in Kidney

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- 1 H<sup>+</sup> in blood reacts with HCO<sub>3</sub><sup>-</sup> to form H<sub>2</sub>CO<sub>3</sub>.
- 2 H<sub>2</sub>CO<sub>3</sub> decomposes into H<sub>2</sub>O and CO<sub>2</sub>, which enter the tubule cell.
- 3 Tubule cells acquire CO<sub>2</sub> from blood, tubular fluid, and their own aerobic respiration.
- 4 Carbonic anhydrase (CAH) combines H<sub>2</sub>O and CO<sub>2</sub> to re-form H<sub>2</sub>CO<sub>3</sub>.
- 5 H<sub>2</sub>CO<sub>3</sub> ionizes to form HCO<sub>3</sub><sup>-</sup> (which returns to the blood) and H<sup>+</sup>.
- 6 Na<sup>+</sup>-H<sup>+</sup> antiport exchanges H<sup>+</sup> for Na<sup>+</sup>.
- 7 NaHCO<sub>3</sub> from glomerular filtrate decomposes into Na<sup>+</sup> and HCO<sub>3</sub><sup>-</sup>. Na<sup>+</sup> is pumped into tubule cell.
- 8 Na<sup>+</sup> is removed by Na<sup>+</sup>-K<sup>+</sup> pump at the base of the cell.
- 9 HCO<sub>3</sub><sup>-</sup> reacts with H<sup>+</sup> from tubule cell to form H<sub>2</sub>CO<sub>3</sub>.
- 10 CAH on brush border decomposes H<sub>2</sub>CO<sub>3</sub> to H<sub>2</sub>O and CO<sub>2</sub> again.
- 11 CO<sub>2</sub> enters the tubular cell and H<sub>2</sub>O passes in the urine (carrying the H<sup>+</sup> 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**

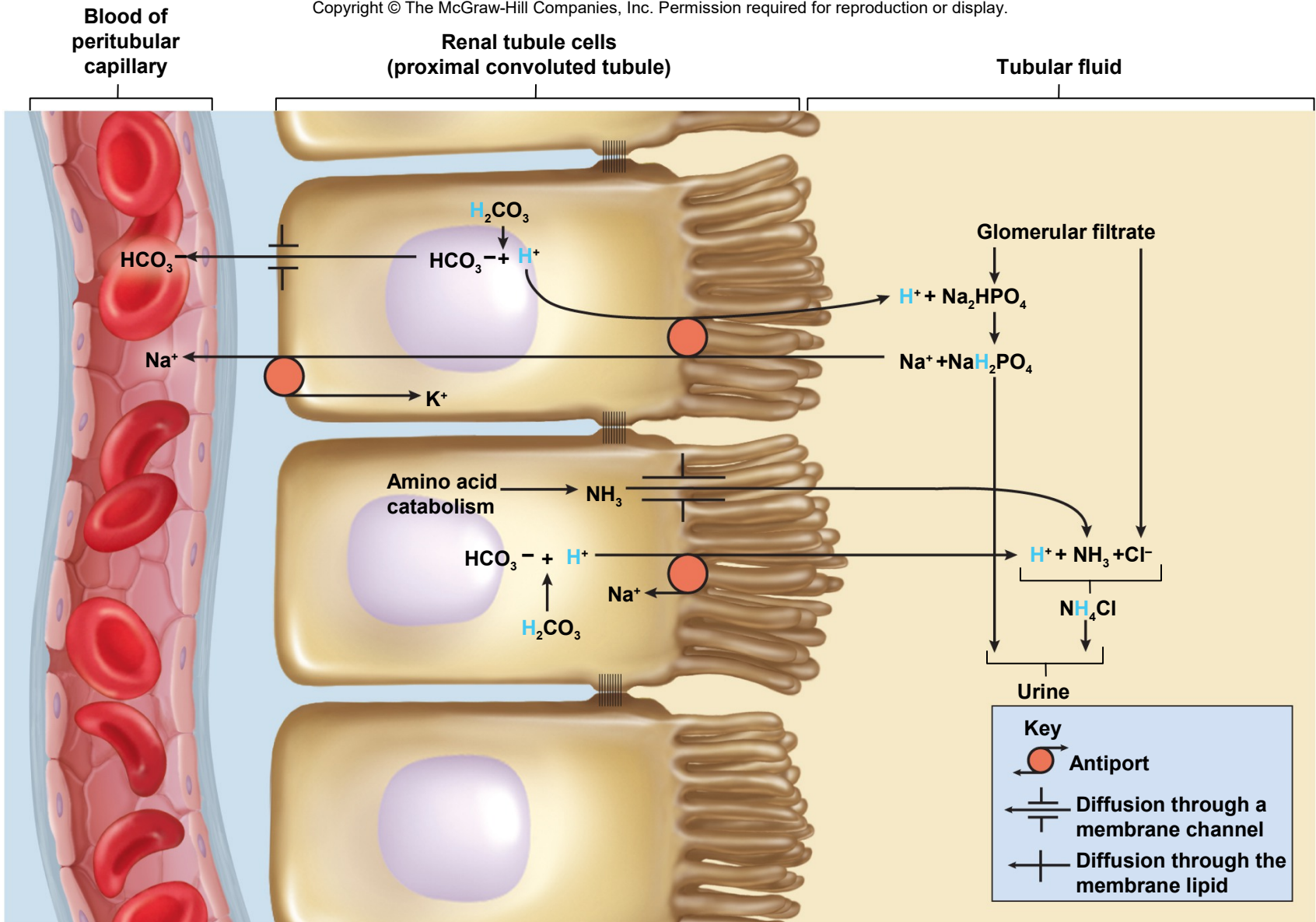
# Limiting pH

---

- this is prevented by buffers in tubular fluid
  - **bicarbonate system** – all bicarbonate ions in tubular fluid are used to neutralize  $H^+$ 
    - so there is 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
    - $Na_2HPO_4 + H^+ \rightarrow NaH_2PO_4 + Na^+$
  - **ammonia** ( $NH_3$ ) - from amino acid catabolism acts as a base to neutralize acid
    - $NH_3 + H^+$  and  $Cl^- \rightarrow NH_4Cl$  (ammonium chloride – a weak acid)

# Ammonium Chloride Buffering Mechanisms in Urine

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# Disorders of Acid-Base Balance / Acidosis



- 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
- this elevates  $K^+$  concentration in ECF /// now ECF = **hyperkalemia**
- because of the hyperkalemia  $>$   $K^+$  diffuses out of the cell at a slower rate (note this is through potassium channels and not the sodium-potassium ATP pump) // result in plasma membrane being less polarized (now less as negative as under normal conditions) /// **closer to threshold**
- *Review action potential: remember it is  $K^+$  leaving cytoplasm that makes resting membrane potential “negative” // if not enough  $K^+$  leave cytoplasm then cell is closer to threshold – closer to an action potential!*





membrane now in state of partial depolarized, (i.e. moved closer to threshold)

nerve and muscle cells are now more easily stimulated

when nerves partially stimulated you may get **muscle spasms, tetany, convulsions, respiratory paralysis, heart arrested**

**This condition will occur if extracellular potassium rising rapidly (i.e. crush injury, infusion of old RBC, veterinary inject dogs with potassium to euthanize.)**

## Disorders of Acid-Base Balance / Acidosis

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- Metabolic acidosis will cause a slower rate of increase in extracellular potassium concentration
- Also likely to cause hyperkalemia. Outcome the same but the mechanism is different.
- Hyperkalemia caused by slow increase in potassium inactivates the voltage regulated sodium pumps.
- This deactivates the sodium-potassium-ATPase-pump
- Now the membrane can not initiate an action potential.
- Result in respiratory paralysis and cardiac arrest.

# Disorders of Acid-Base Balance / Alkalosis

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- **In alkalosis**

- pH above **7.45**
- $H^+$  diffuses out of cells
- $K^+$  diffuses in
- causes hypokalemia
- CNS depression, confusion, disorientation, coma, possibly death

# Disorders of Acid-Base Balances

---



- When you have an acid-base imbalance then it will be caused by one of the following:
  - **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 CO<sub>2</sub> 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
  - CO<sub>2</sub> eliminated faster than it is produced not enough CO<sub>2</sub> in the blood



# Disorders of Acid-Base Balances

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- **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
  - 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

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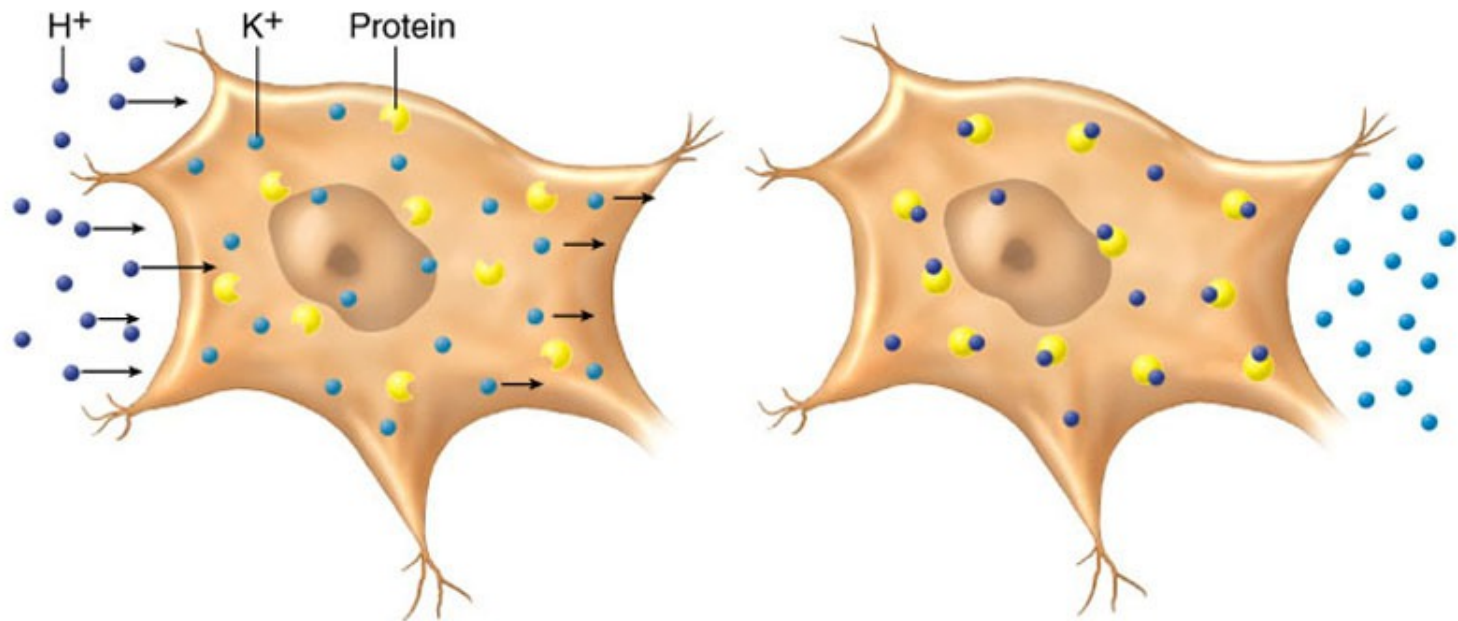
- **Respiratory compensation**
  - **changes in pulmonary ventilation** to correct changes in pH of body fluids by expelling or retaining CO<sub>2</sub>
  - **hypercapnia** (excess CO<sub>2</sub>) - stimulates pulmonary ventilation eliminating CO<sub>2</sub> and allowing pH to rise
  - **hypocapnia** (deficiency of CO<sub>2</sub>) reduces ventilation and allows CO<sub>2</sub> accumulate lowering pH

# Compensation for Acid-Base Imbalances (cont.)

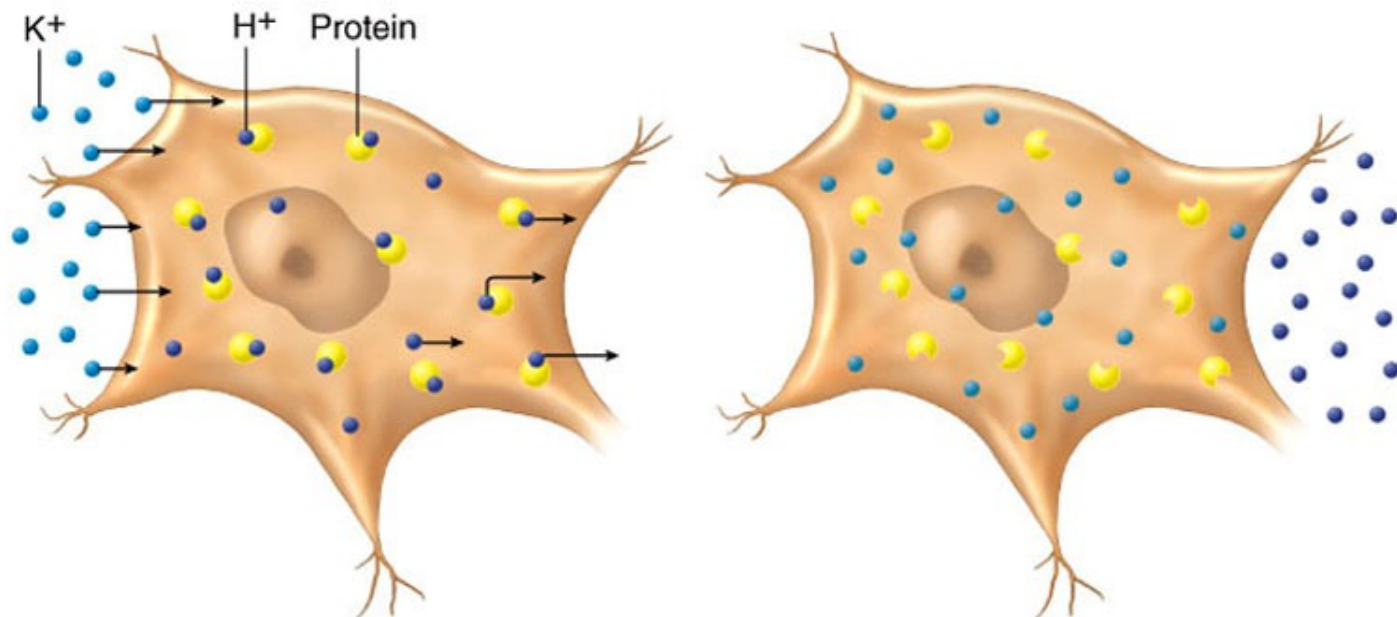
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- **Metabolic (Renal) Compensation**
  - an adjustment of pH by changing the rate of H<sup>+</sup> secretion by the renal tubules
  - slow, but better at restoring a fully normal pH
  - in **acidosis**, urine pH may fall as low as 4.5 due to excess H<sup>+</sup>
    - renal tubules increase rate of H<sup>+</sup> secretion elevating pH
  - in **alkalosis** as high as 8.2 because of excess HCO<sup>3-</sup>
    - renal tubules decrease rate of H<sup>+</sup> 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



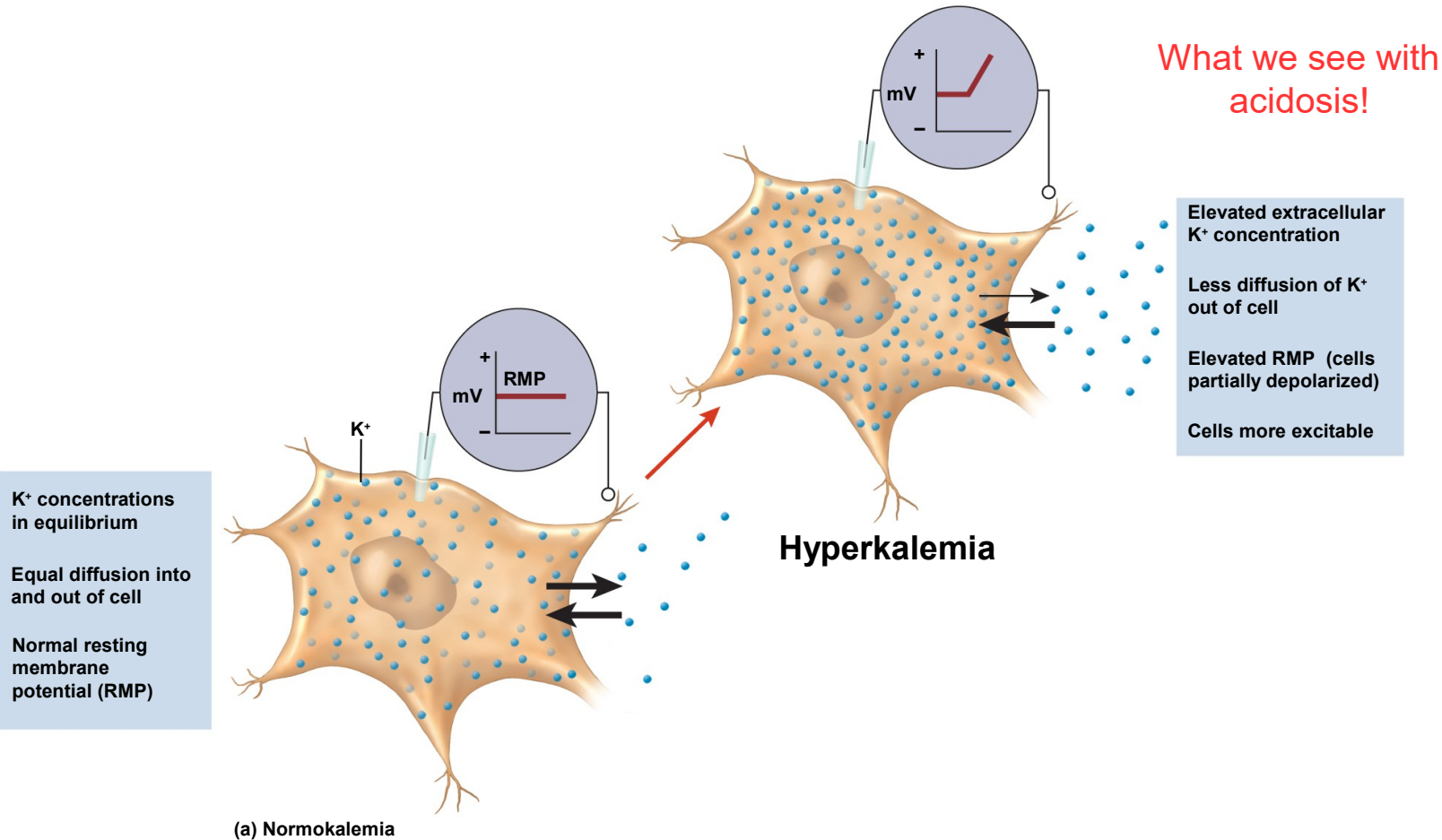


(a) Acidosis leading to Hyperkalemia



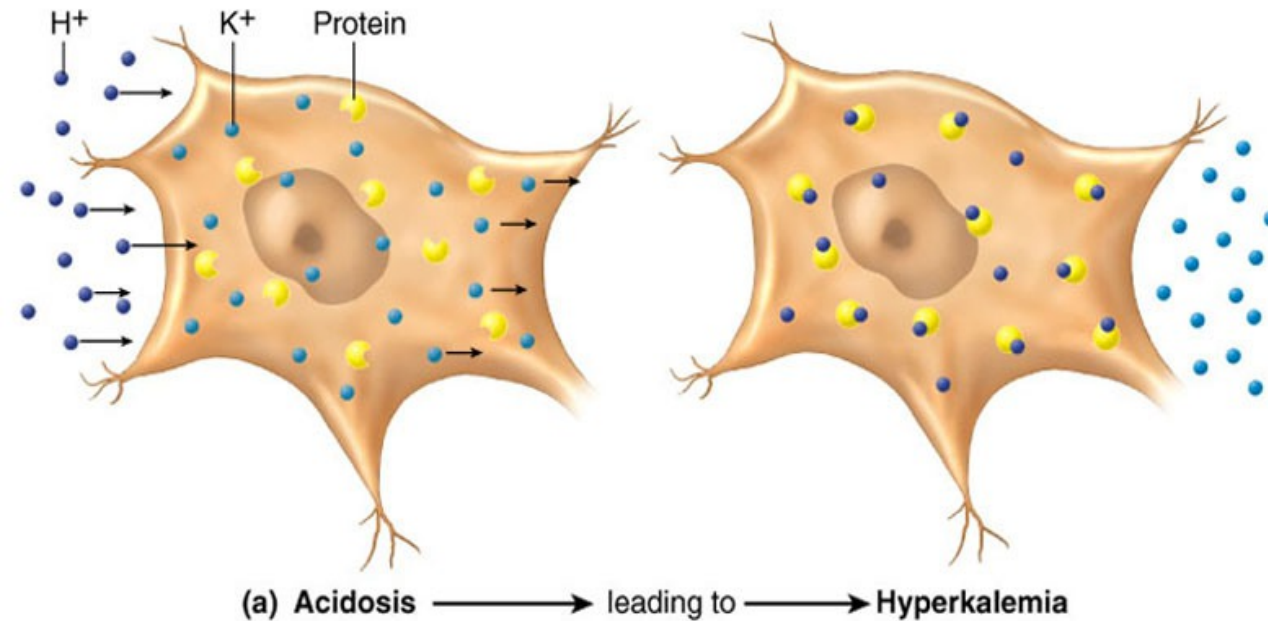
(b) Alkalosis leading to Hypokalemia

# Acidosis Caused Hyperkalemia Which Increases Excitability



Cells more excitable!  
Significance?

# Hyperkalemia



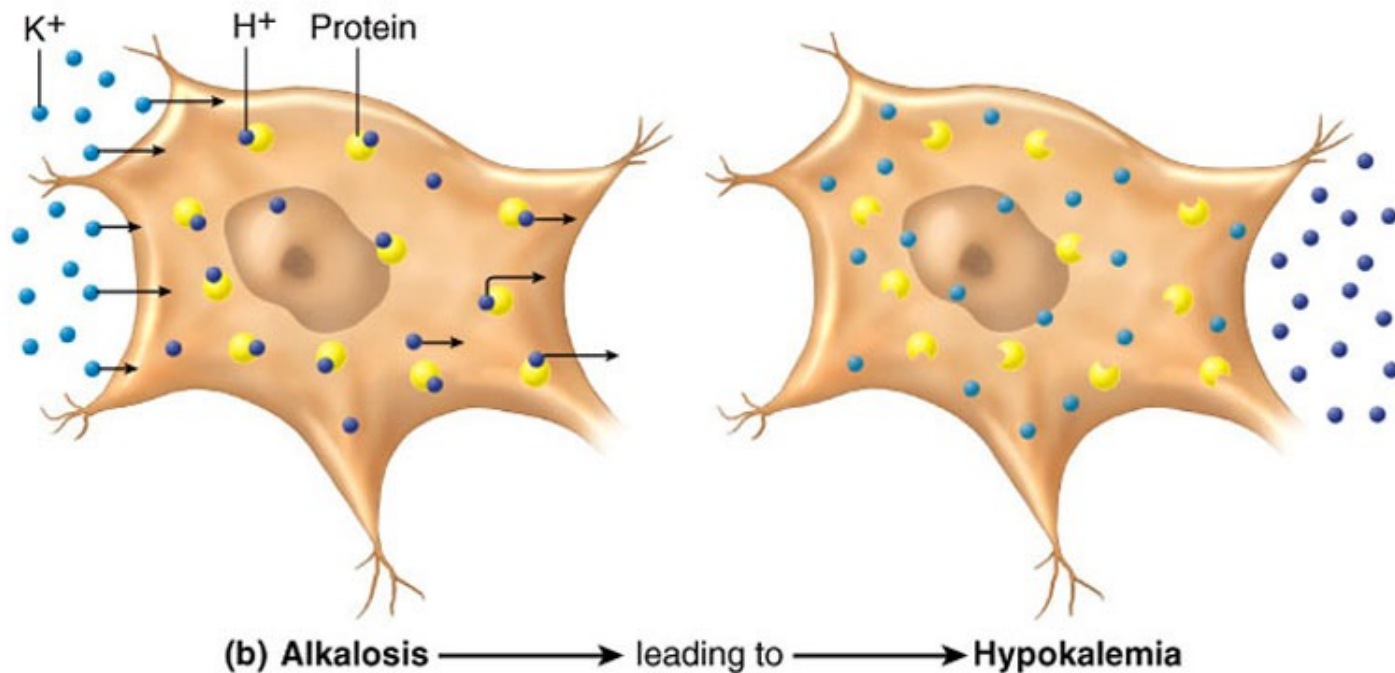
Membranes potential moves closer to threshold, nerves partially stimulated, muscles spasms, tetany, convulsions, and respiratory paralysis. // more excitable

Hyperkalemia may also result in a skeletal muscle crush injury or patient given out dated 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

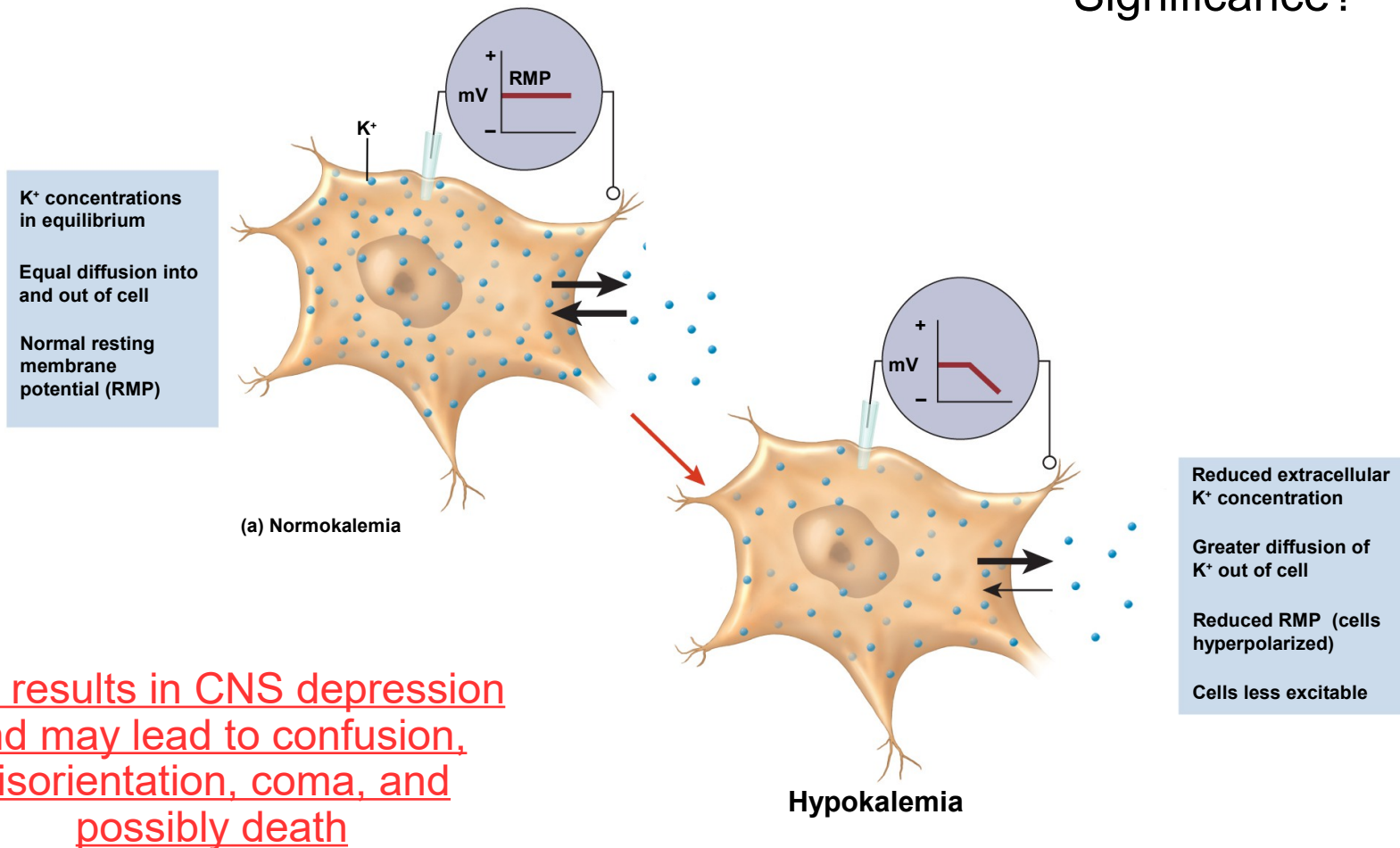
Plasma membrane becomes hyperpolarized!

This results in CNS depression and may lead to confusion, disorientation, coma, and possibly death

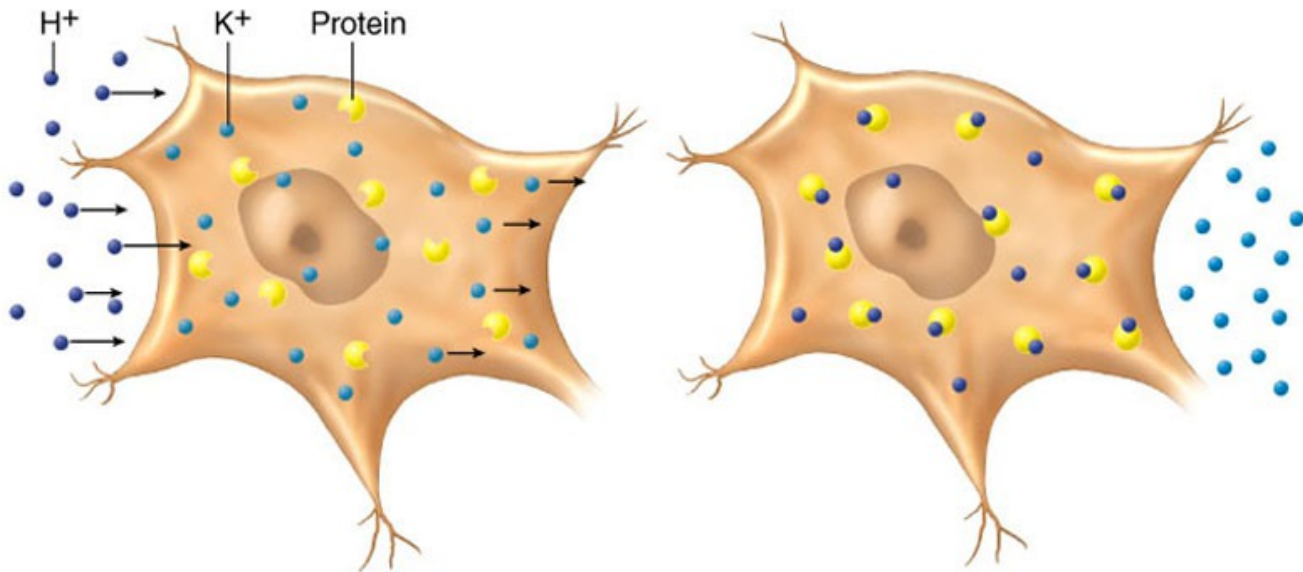


# Alkalosis Causes Hypokalemia Which Decreases Excitability

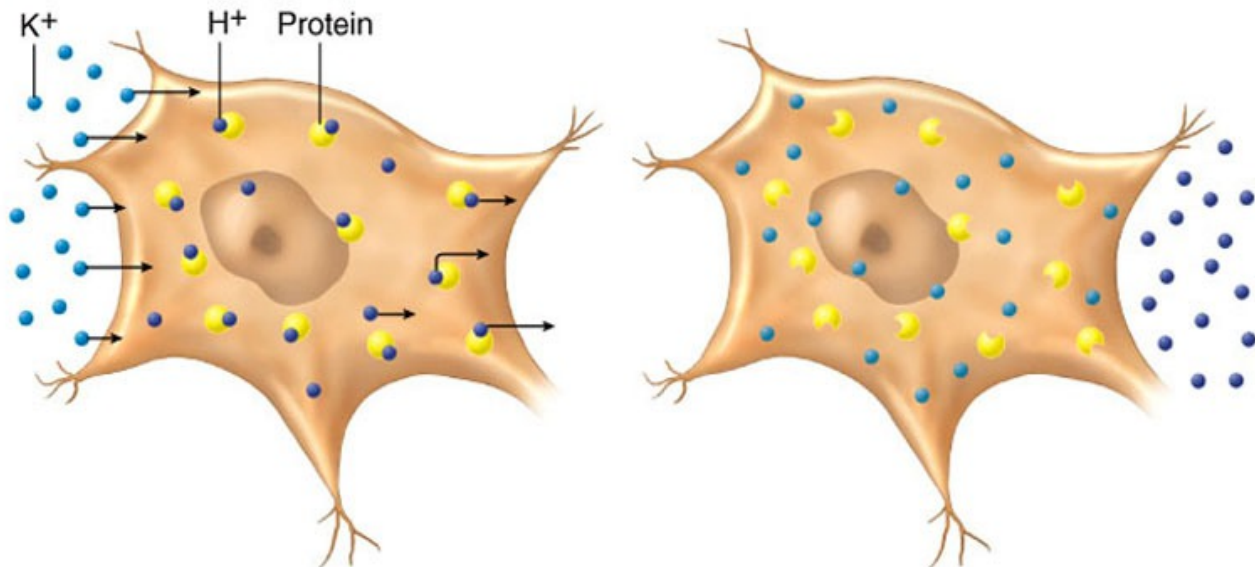
Cells less excitable!  
Significance?







(a) Acidosis → leading to → Hyperkalemia



(b) Alkalosis → leading to → Hypokalemia

# Electrolytes Balance in Body Fluids

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- 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

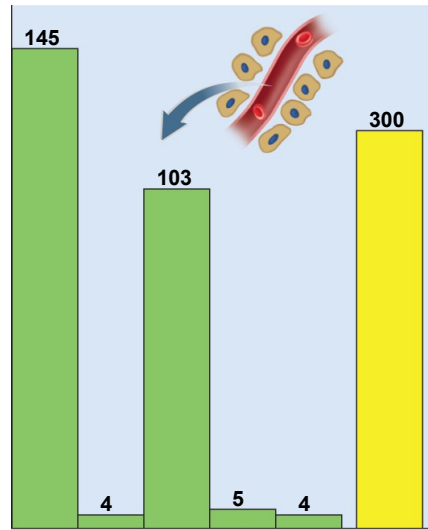
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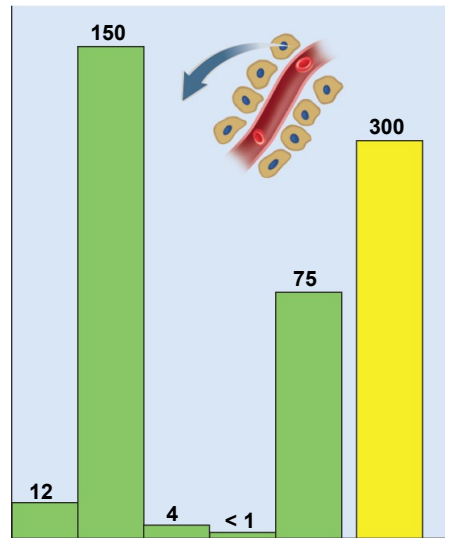
- major cations ///  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ , and  $\text{H}^+$
- major anions ///  $\text{Cl}^-$ ,  $\text{HCO}_3^-$  (bicarbonate), and  $\text{PO}_4^{3-}$
- major extracellular cation is sodium
- major intracellular cation is potassium
- great differences in the types of 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



(a) Blood plasma



(b) Intracellular fluid

# Sodium - Functions

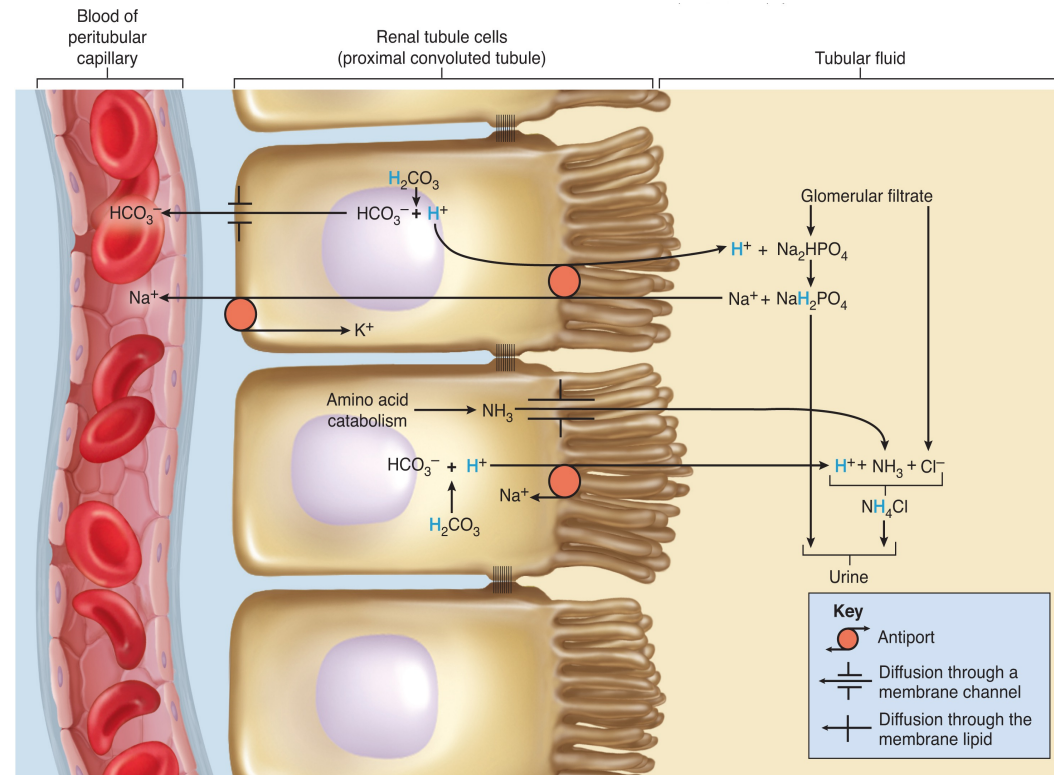
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- **Sodium** – major extracellular cation
  - sodium salts accounts for 90% of extracellular fluid's cations
  - **accounts for 90% to 95% of the osmolarity in the ECF**
  - most significant solute in determining total body water and distribution of 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

- $\text{Na}^+$  gradient a source of potential energy for **co-transport** of other solutes such as glucose, potassium, and calcium
- $\text{Na}^+$ -  $\text{K}^+$  pump /// exchanges intracellular  $\text{Na}^+$  for extracellular  $\text{K}^+$  --- this pump also generates body heat / required to maintain resting membrane potential
- $\text{NaHCO}_3$  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

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- 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
  - 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
  - **drop in sodium inhibits ADH release** /// more water is excreted, this raises the sodium concentration in the blood

# Atrial Natriuretic Peptide and Sodium Homeostasis

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- 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



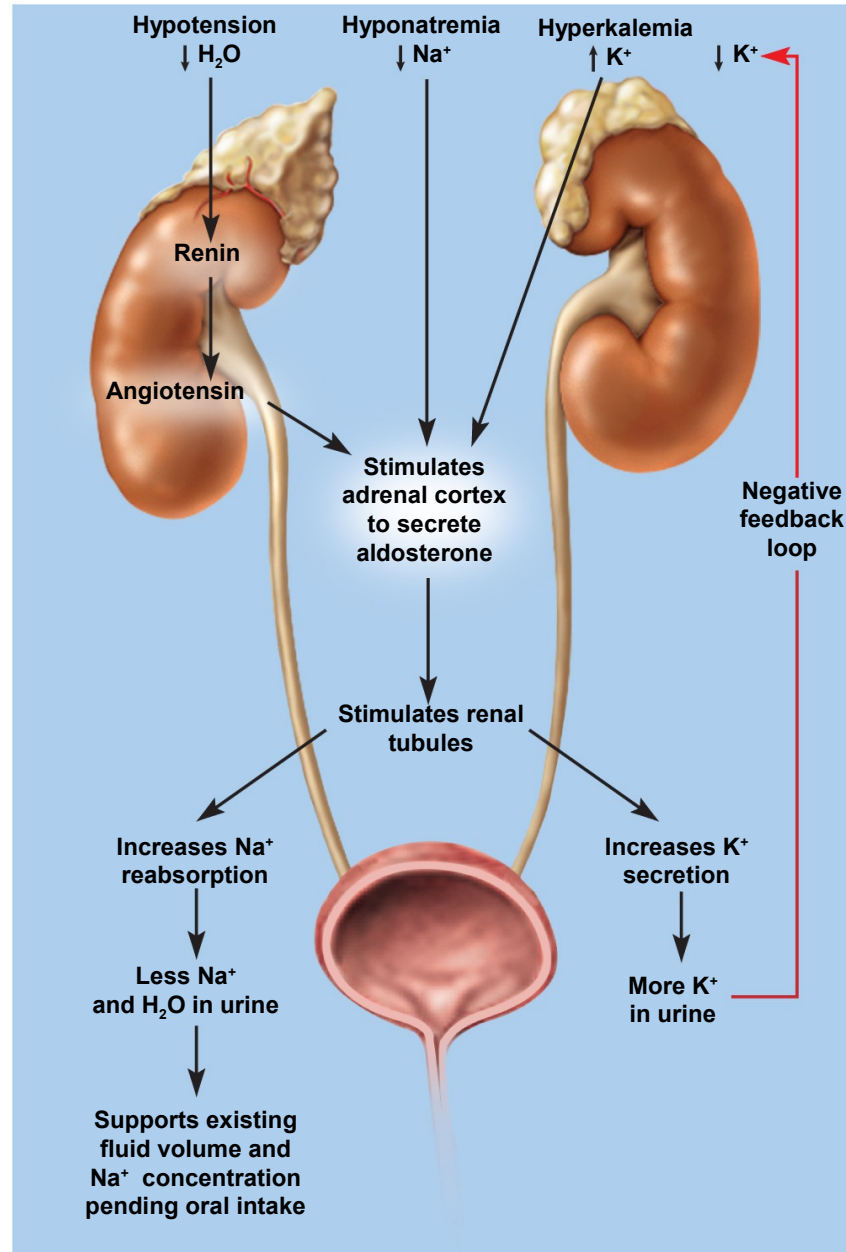


# Potassium - Homeostasis

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- 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



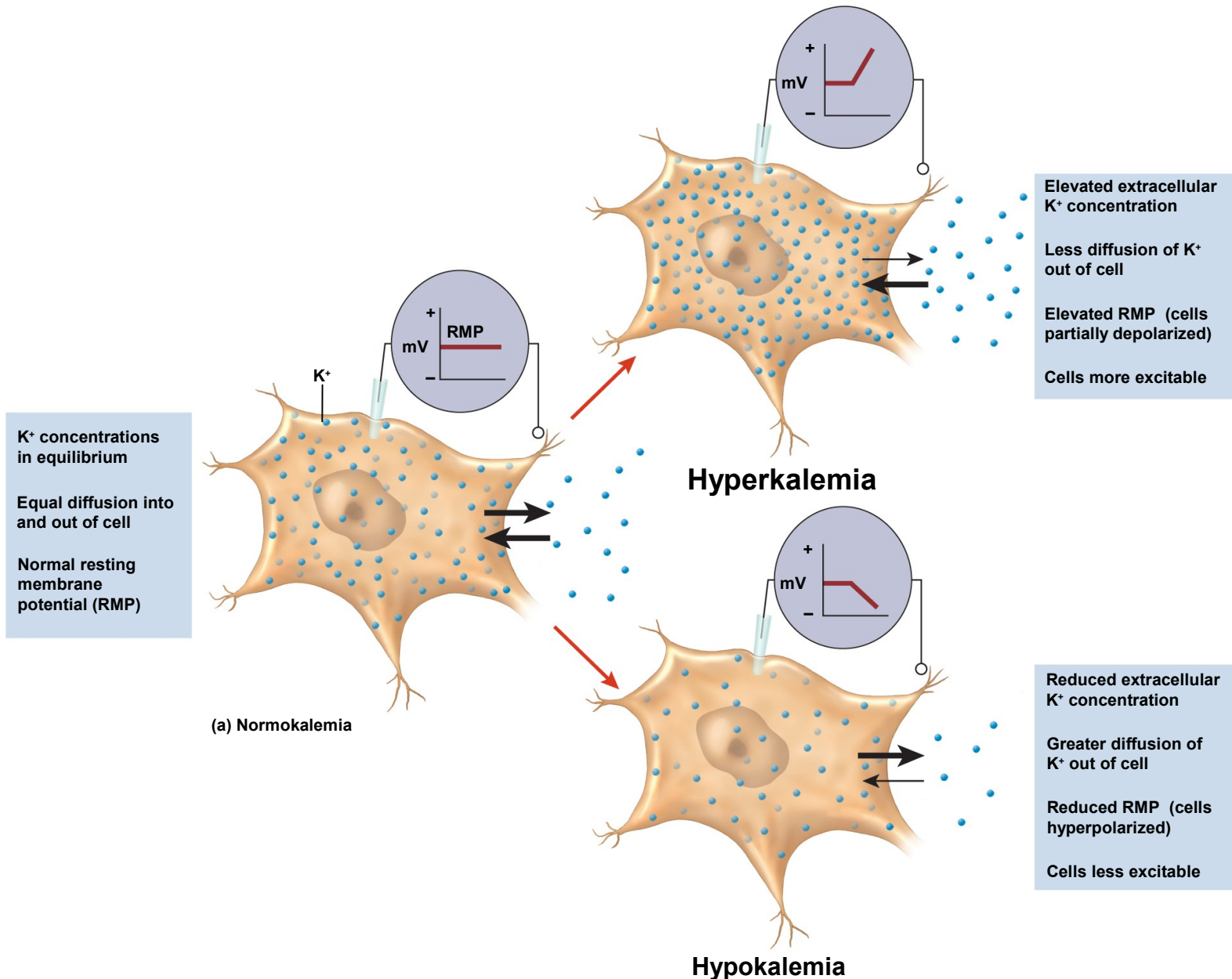
# Potassium - Imbalances

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- 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



# Respiratory Control of pH

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- This is the basis for the strong buffering capacity of the respiratory system.
  - the addition of CO<sub>2</sub> to the body fluids raises the H<sup>+</sup> concentration and lowers pH
  - the removal of CO<sub>2</sub> has the opposite effects
- neutralizes 2 to 3 times more acid than chemical buffers

# Chloride - Functions

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- most abundant anions in ECF // major contribution to ECF osmolarity
- required for the formation of stomach acid // hydrochloric acid (HCl)
- **chloride shift** that accompanies CO<sub>2</sub> loading and unloading in RBCs
- major role in regulating body pH

# Chloride - Homeostasis

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- strong attraction to  $\text{Na}^+$ ,  $\text{K}^+$  and  $\text{Ca}^{2+}$ , which chloride passively follows
- primary homeostasis achieved as an effect of  $\text{Na}^+$  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

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- 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

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- 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  $\text{Ca}^{2+}$  levels
  - to prevent calcium phosphate crystal precipitation // phosphate levels are high in the ICF
  - cells must pump  $\text{Ca}^{2+}$  out
  - keeps intracellular concentration low
  - or sequester  $\text{Ca}^{2+}$  in smooth ER and release it when needed
  - **calsequestrin** – proteins that bind  $\text{Ca}^{2+}$  and keep it non-reactive in  $\text{Ca}^{2+}$  storage cells

# Calcium - Imbalances

---

- hypercalcemia – greater than 5.8 mEq/L
  - alkalosis, hyperparathyroidism, hypothyroidism
  - reduces membrane Na<sup>+</sup> 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<sup>+</sup> permeability /// nervous and muscular systems become abnormally excitable
  - very low levels result in tetanus, laryngospasm, death

# Phosphates - Functions

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- **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

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- 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

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- 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<sup>+</sup> and water retained**
    - ECF remains isotonic
    - caused by aldosterone hypersecretion or renal failure
  - hypotonic hydration
    - water intoxication (positive water balance)
    - **more water than Na<sup>+</sup> retained** or ingested
    - ECF becomes hypotonic
    - can cause **cellular swelling** // e.g. pulmonary and cerebral edema



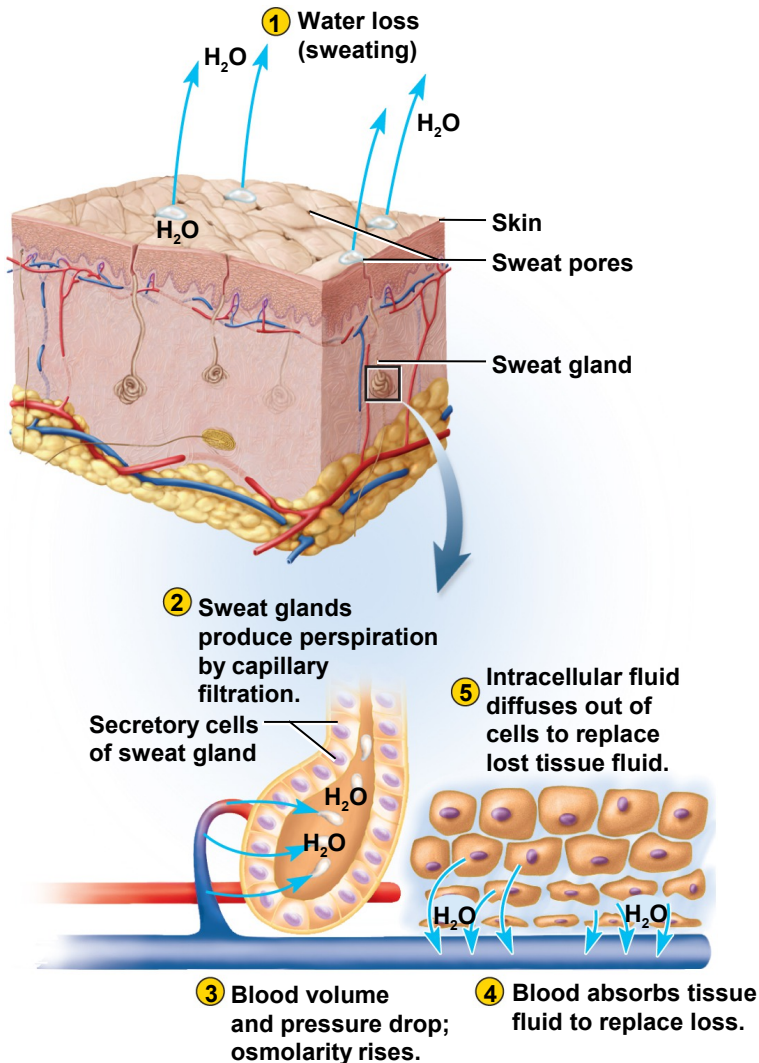
# Fluid Sequestration

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- 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

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- 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

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- 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