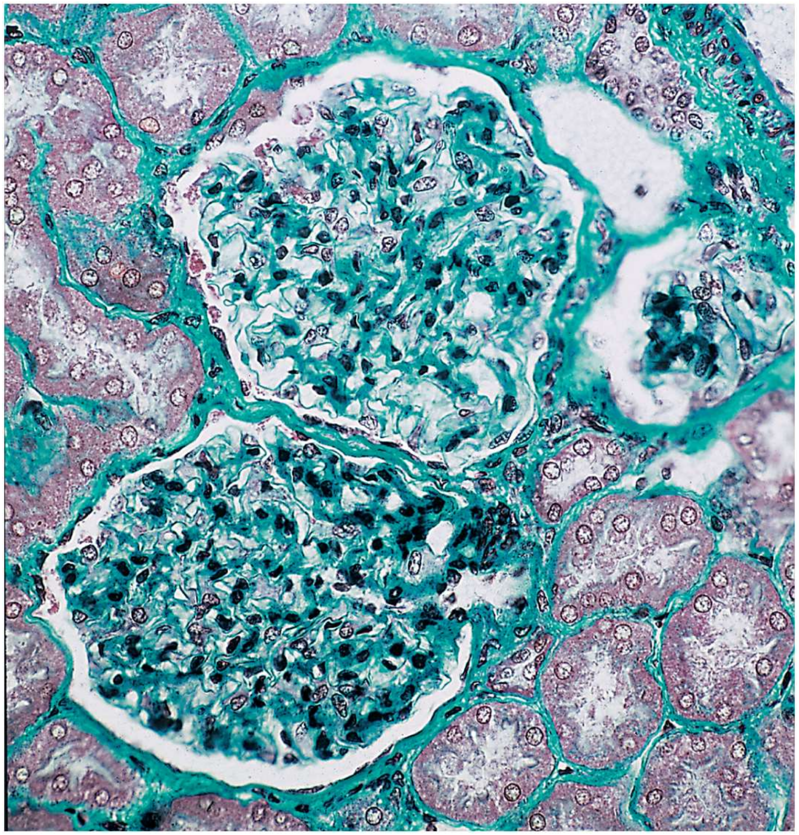
Chapter 27

Homeostatic Balance

Water / Electrolytes / pH



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 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

What Needs to Be “Balanced”

- 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

What Needs to Be “Balanced”

- **three “components” of the fluid needs to be controlled by homeostatic mechanisms**
  - **<u>water balance</u>** *//* average daily water intake and loss are equal
  - **<u>electrolyte balance</u>** *//* the amount of electrolytes absorbed by the small intestine balance with the amount lost from the body, usually in urine
  - **<u>acid-base balance</u>** *//* the body rids itself of acid (hydrogen ion – H^+) at a rate that balances metabolic production

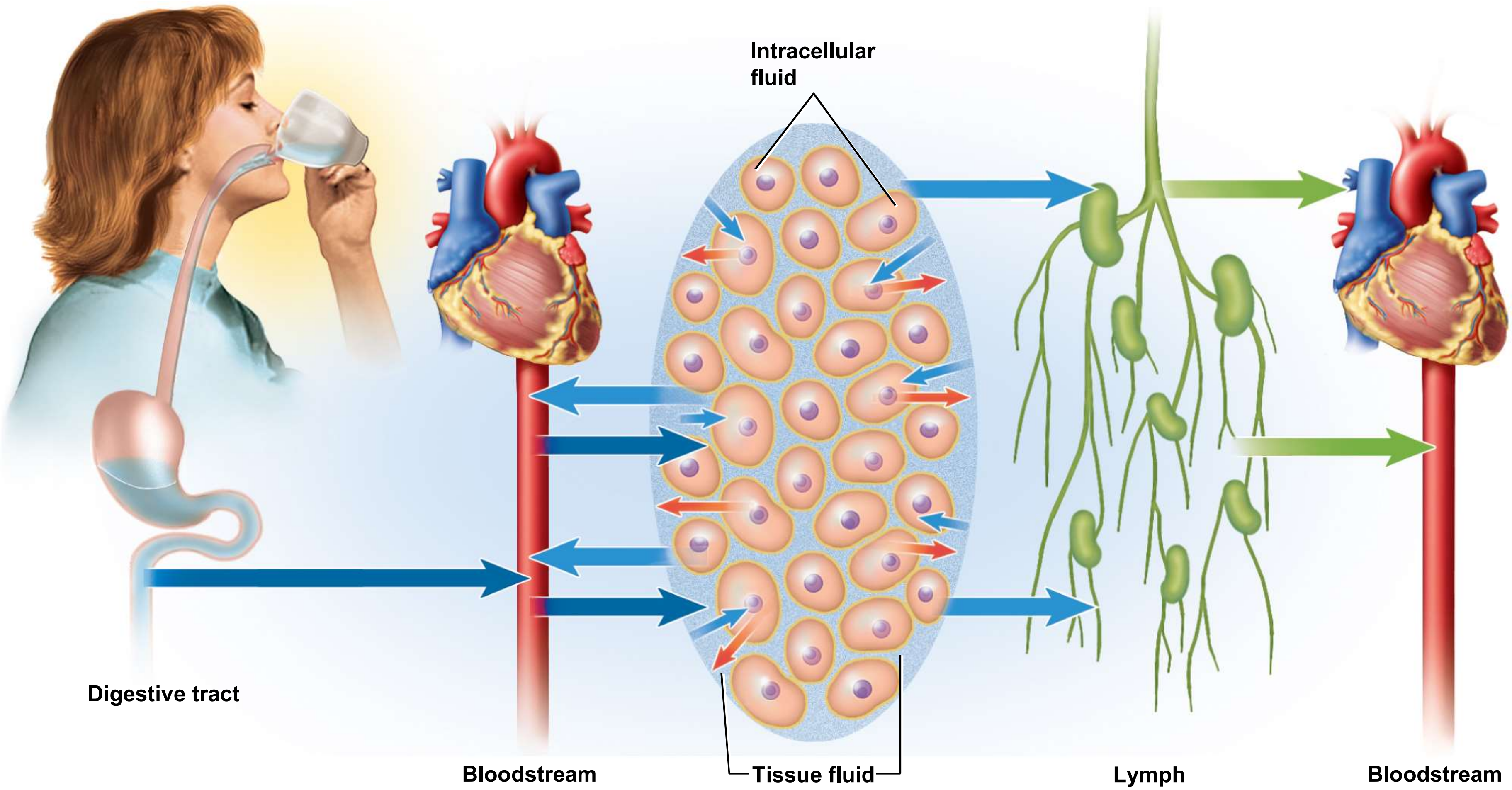
Water Movement Between Fluid Compartments

- fluid continually exchanged between compartments
- water moves across membranes by **osmosis**
- because water moves easily through plasma membranes, **osmotic gradients** never last for very long
- if imbalance arises, osmosis restores balance within seconds so the intracellular and extracellular osmolarity are equal
  - *if osmolarity of the tissue fluid rises, water moves out of the cell*
  - *if it falls, water moves in*

Water Movement Between Fluid Compartments

- osmosis from one fluid compartment to another is determined by the relative concentrations of solutes in each compartment
  - **electrolytes** – they are the most abundant solute particles / water follows electrolyte movement!
  - **sodium salts** in **ECF**
  - **potassium salts** in **ICF**
- **electrolytes** play the principal role in governing the body's water distribution and total water content

Water Movement Between Fluid Compartments



Water Balance & Gain

- **fluid balance** - 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)

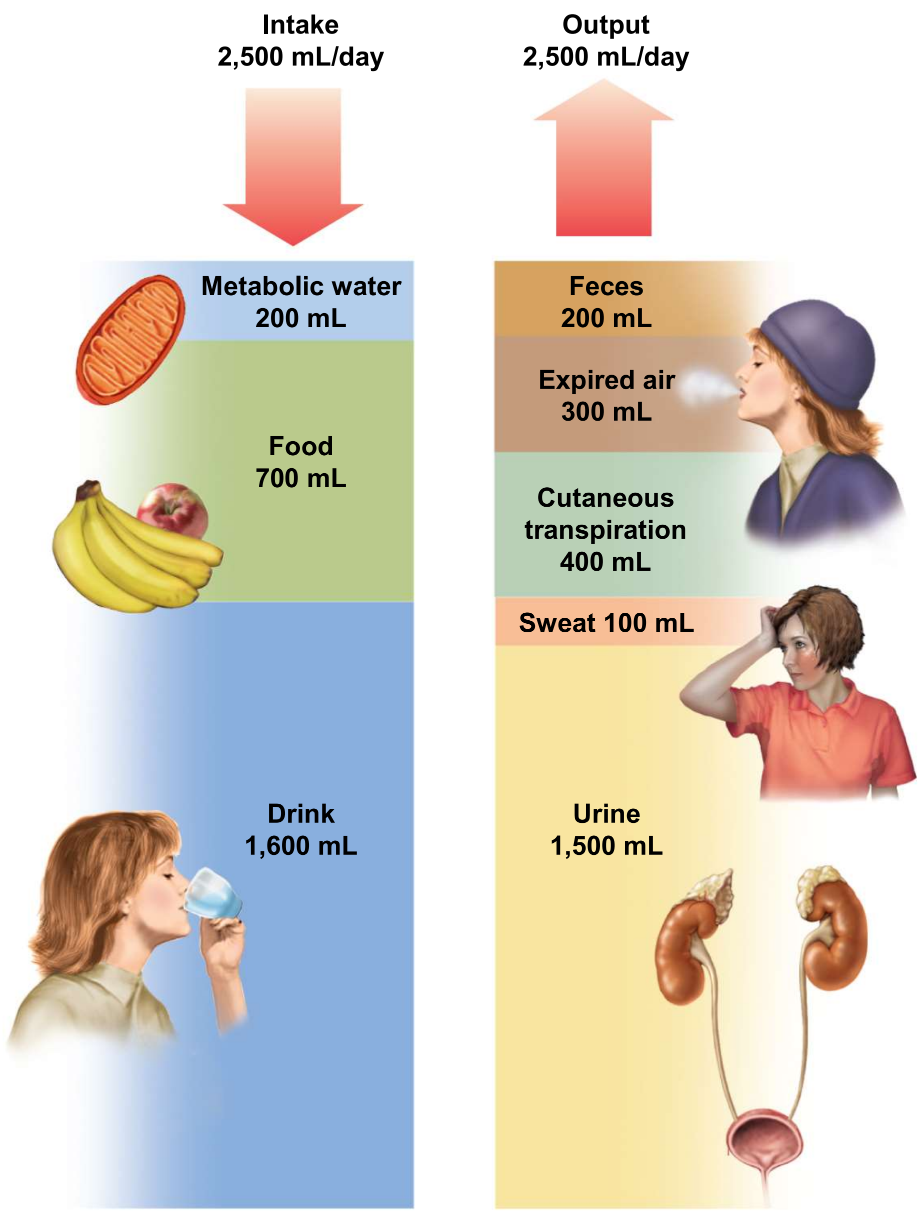
    - by-product of aerobic metabolism and dehydration synthesis

      – $C_6H_{12}O_6 + 6O_2 \longrightarrow 6CO_2 + 6H_2O$

Water Loss

- sensible water loss 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 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



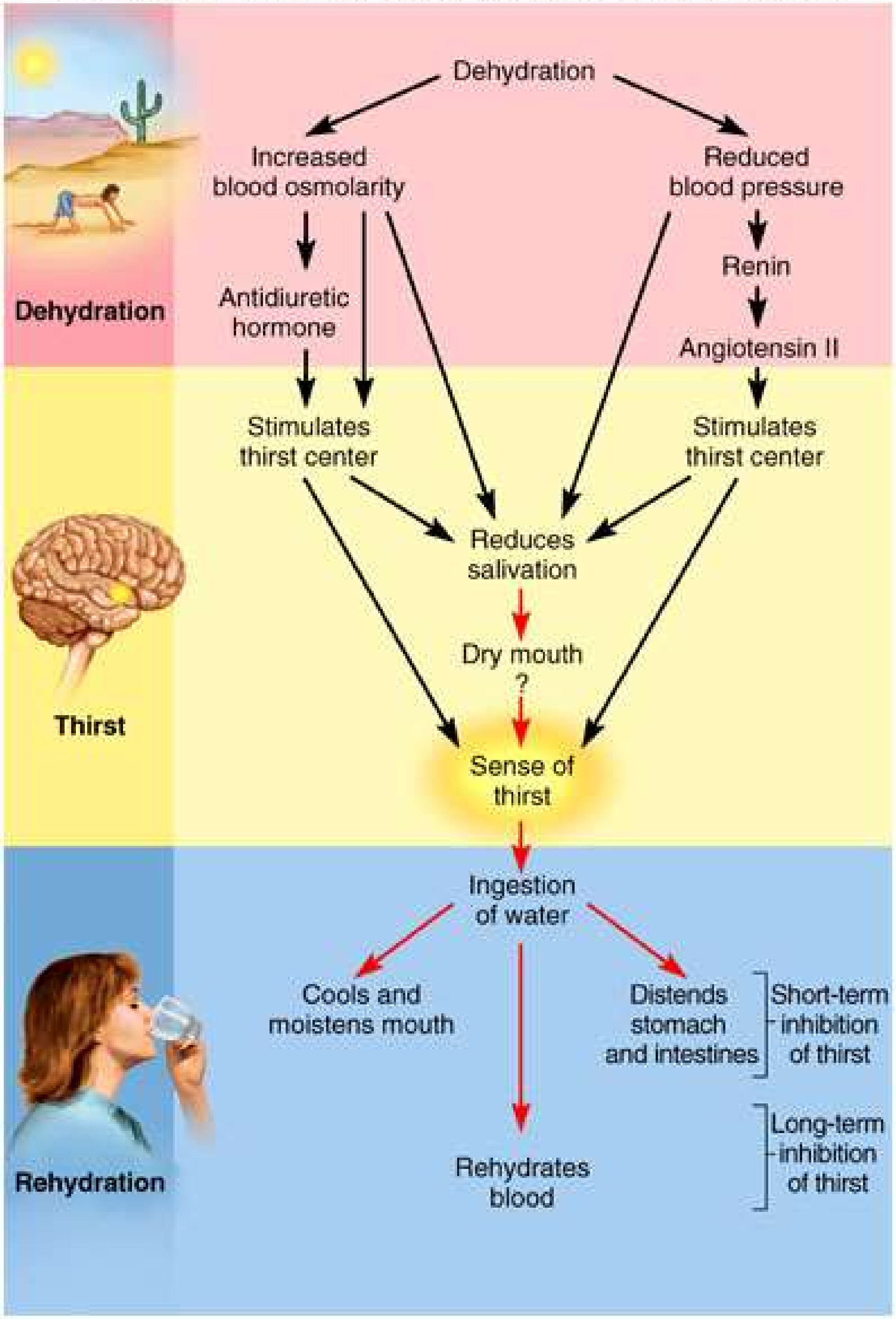
Regulation of Fluid Intake

- Thirst is the “sense” that governs fluid intake
  - dehydration results in
    - <u>increase blood osmolarity</u>
    - low blood volume “linked to” low blood pressure
  - osmoreceptors in hypothalamus sense increase in osmolarity
    - osmoreceptors communicate with the hypothalamus and cerebral cortex
    - hypothalamus produces antidiuretic hormone
    - promotes water conservation

Regulation of Fluid Intake (cont.)

- tissue in kidneys sense reduced blood pressure
  - activates the renin - angiotensin mechanism
  - BP drops (concurrent rise in osmolarity of ECF) with a drop in blood volume
- salivation is inhibited with thirst
  - sympathetic signals from thirst center to salivary glands
- cerebral cortex produces conscious sense of thirst
  - Mediated by Angiotensin and ADH
  - intense sense of thirst with 2-3% increase in plasma osmolarity
  - Or 10-15% blood loss

Dehydration, Thirst, and Rehydration



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

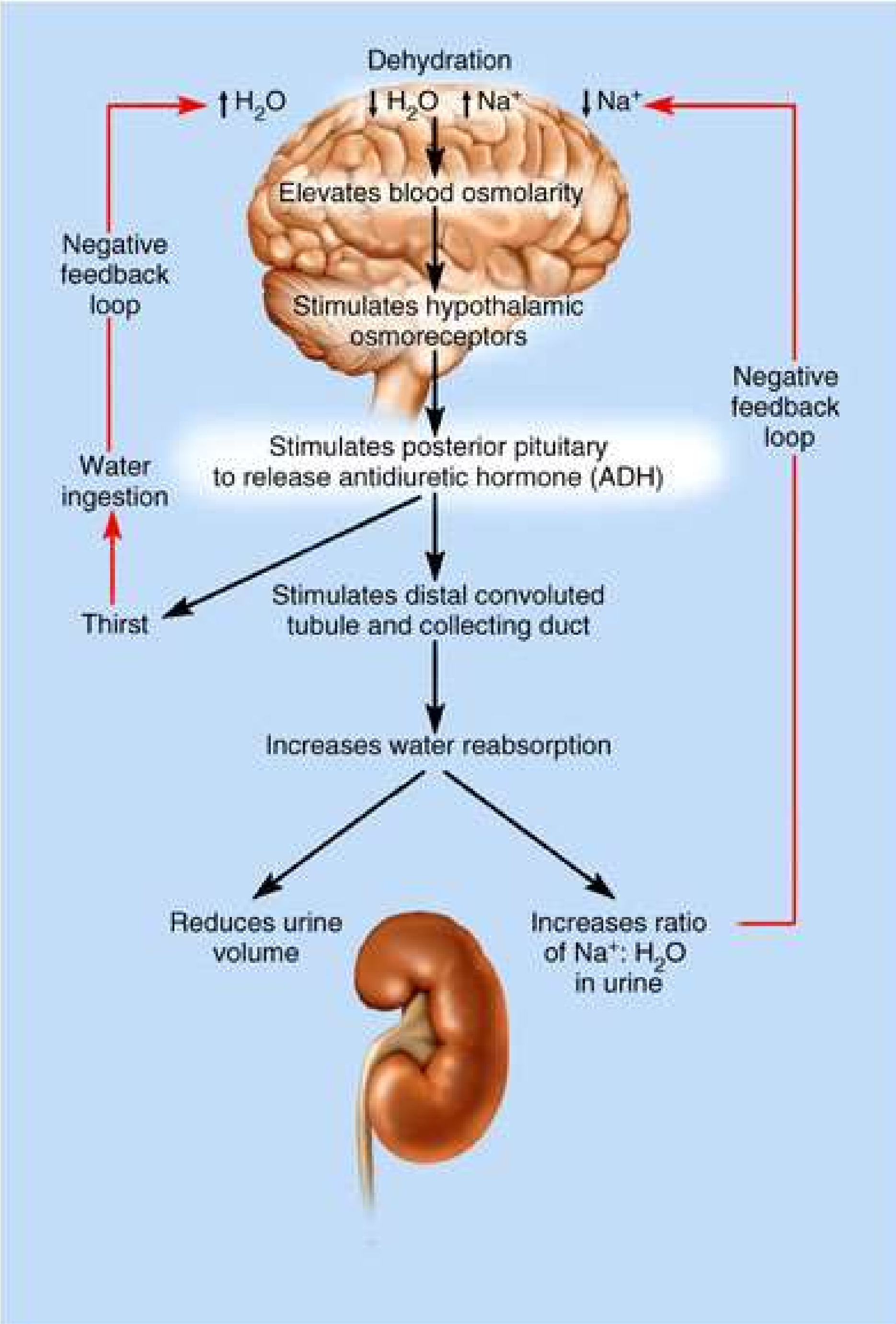
- short term inhibition of thirst
  - cooling and moistening of mouth quenches thirst
  - distension of stomach and small intestine
  - 30 to 45 min of satisfaction // must be followed by water being absorbed into the bloodstream or thirst returns
  - short term response designed to prevent overdrinking

Regulation of Water Output (1 of 2)

- only way to control water output in a significant way is through variation in urine volume
  - kidneys can't replace water or electrolytes
  - only slow rate of water and electrolyte loss until water and electrolytes can be ingested
- Two mechanisms regulated by hormones:
  - Aldosterone hormone
    - changes in urine volume linked to adjustments in **Na^+ reabsorption**
    - as Na^+ is reabsorbed water follows

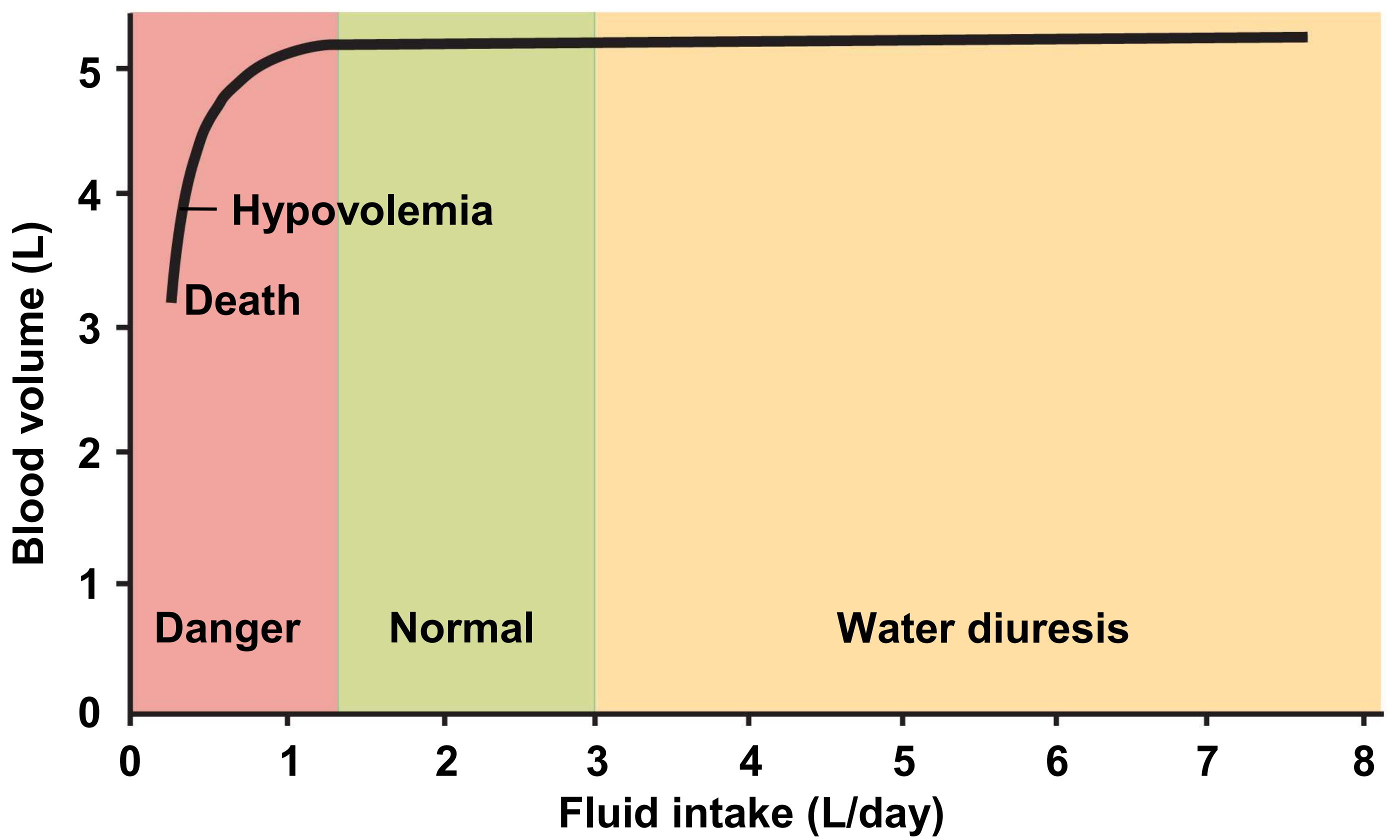
Regulation of Water Output (2 0f 2)

- 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



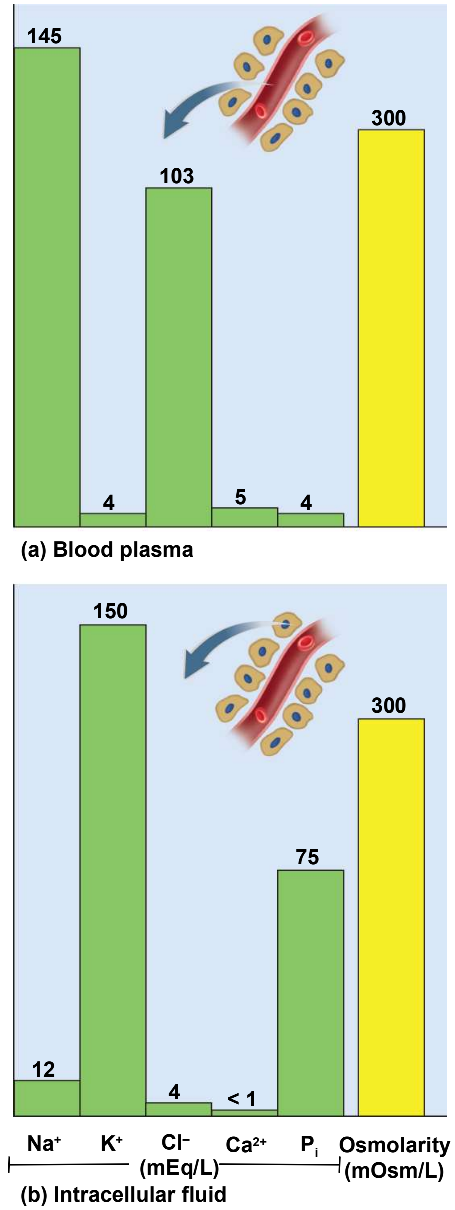
Secretion and Effects of ADH

Blood Volume and Fluid Intake



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

Electrolyte Concentrations & Osmolarity



Acid-Base Balance

- This is one of the most important homeostatic mechanisms
  - metabolism depends on enzymes, and enzymes are sensitive to pH
  - <u>slight deviation from the normal pH can shut down entire metabolic pathways</u>
  - slight deviation from normal pH can alter the structure and function of macromolecules

Acid-Base Balance

- 7.35 to 7.45 is the normal pH range of blood and tissue fluid
- 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

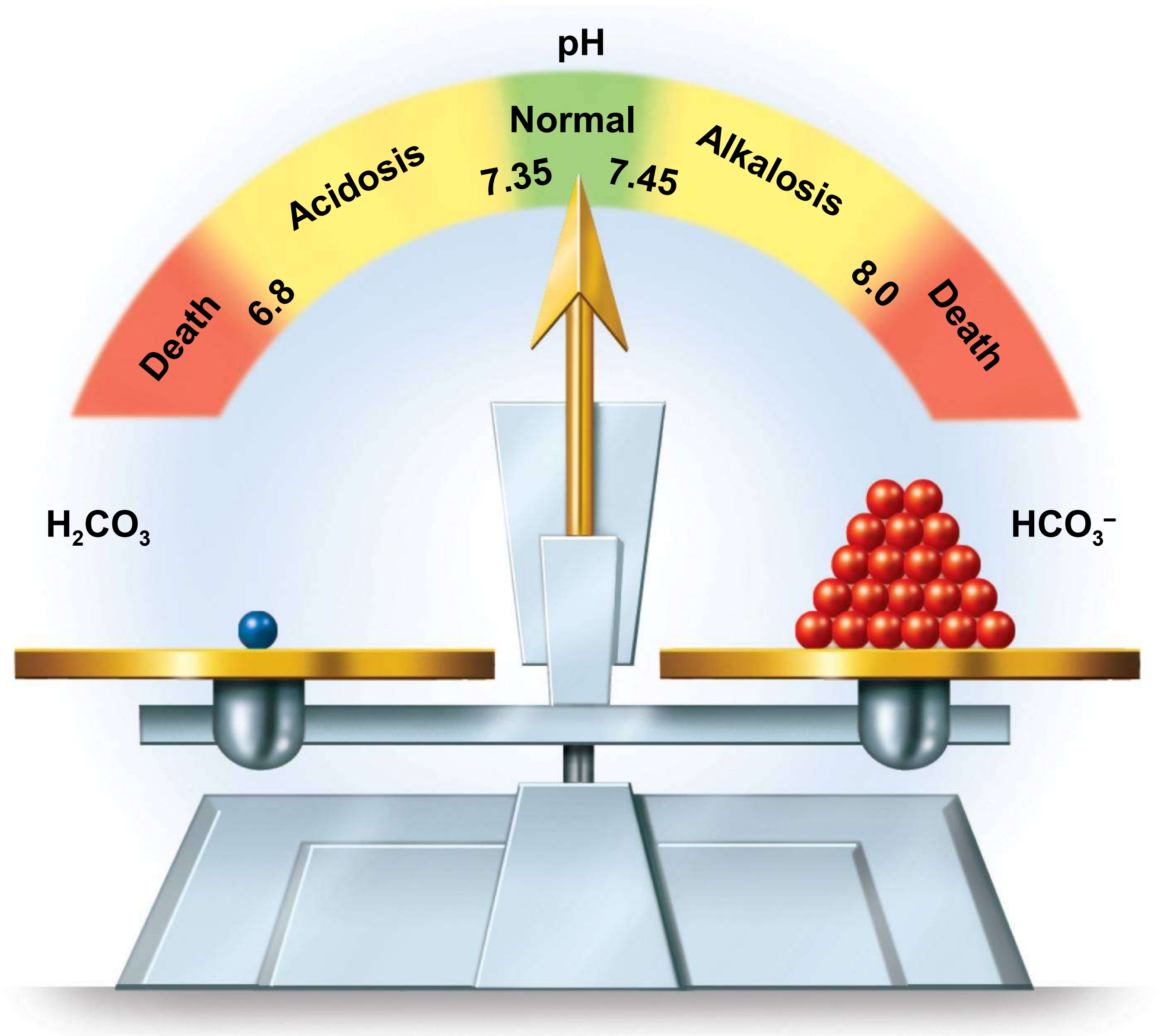
Acids and Bases

- 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

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



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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 CO_2
  - **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**
  - $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$

- **reversible reaction** important in ECF
  - $CO_2 + H_2O \longrightarrow H_2CO_3 \longrightarrow HCO_3^- + H^+$
    - lowers pH by releasing H^+
  - $CO_2 + H_2O \longleftarrow H_2CO_3 \longleftarrow HCO_3^- + H^+$
    - 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 $H_2PO_4^-$
- $H_2PO_4^- \leftrightarrow HPO_4^{2-} + H^+$
  - 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 ($-NH_2$) 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 CO_2 to the body fluids raises the H^+ concentration and lowers pH
  - the removal of CO_2 has the opposite effects
- neutralizes 2 to 3 times as much acid as chemical buffers

Respiratory Control of pH

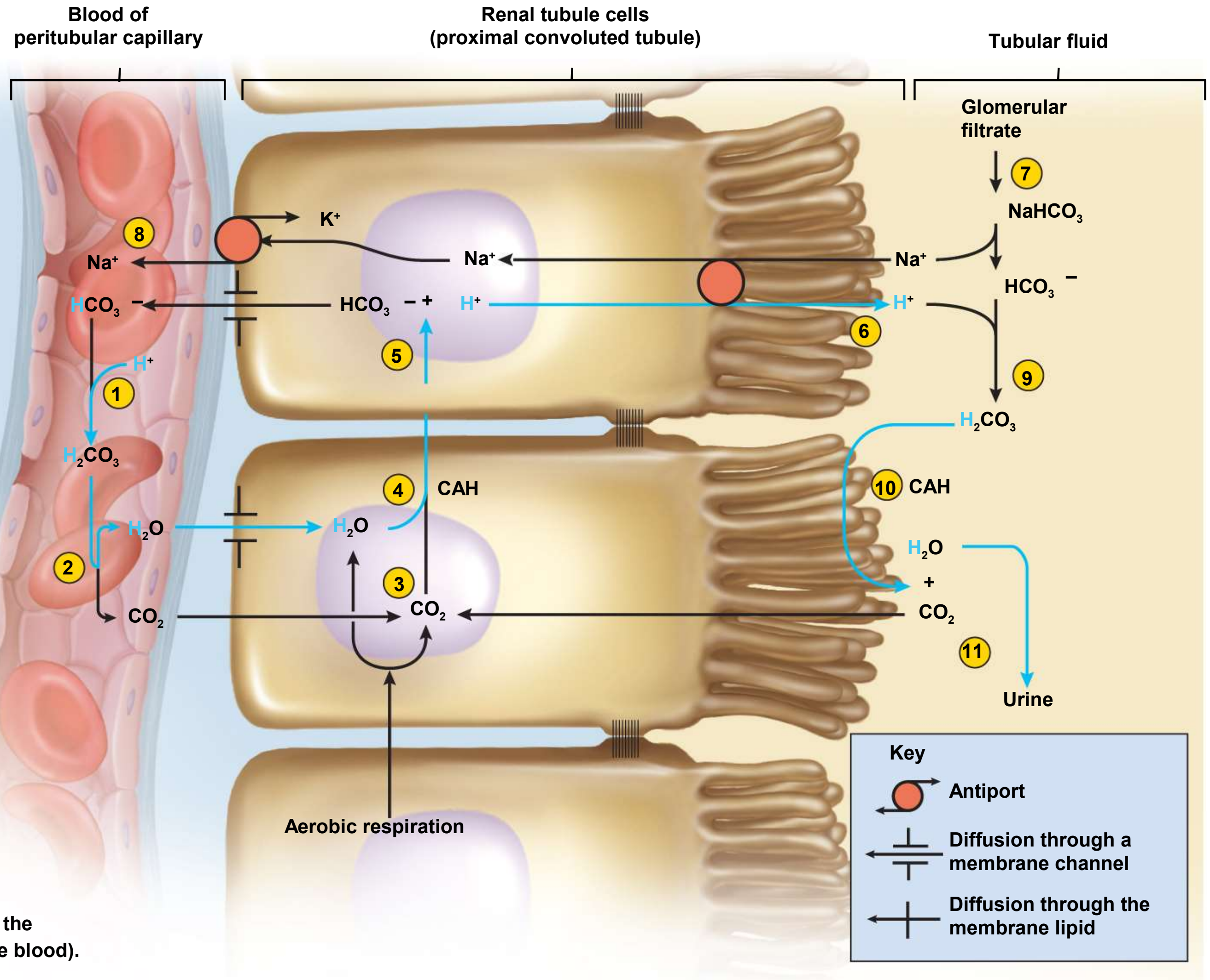
- CO_2 is constantly produced by aerobic metabolism
  - normally eliminated by the lungs at an equivalent rate
  - $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$
    - lowers pH by releasing H^+
  - CO_2 (expired) $+ H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+$
    - raises pH by binding H^+
- increased CO_2 and a decrease in the pH number (i.e. more acidic) stimulate pulmonary ventilation
- Decreased C02 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
  - <u>other buffer systems only reduce its concentration by binding it to other chemicals</u>

H^+ Secretion and Excretion in Kidney

1. H^+ in blood reacts with HCO_3^- to form H_2CO_3.
2. H_2CO_3 decomposes into H_2O and CO_2, which enter the tubule cell.
3. Tubule cells acquire CO_2 from blood, tubular fluid, and their own aerobic respiration.
4. Carbonic anhydrase (CAH) combines H_2O and CO_2 to re-form H_2CO_3.
5. H_2CO_3 ionizes to form HCO_3^- (which returns to the blood) and H^+.
6. Na^+–H^+ antiport exchanges H^+ for Na^+.
7. $NaHCO_3$ from glomerular filtrate decomposes into Na^+ and HCO_3^-. Na^+ is pumped into tubule cell.
8. Na^+ is removed by Na^+–K^+ pump at the base of the cell.
9. HCO_3^- reacts with H^+ from tubule cell to form H_2CO_3.
10. CAH on brush border decomposes H_2CO_3 11111to H_2O and CO_2 again.
11. CO_2 enters the tubular cell and H_2O passes in the urine (carrying the H^+ that was originally in the blood).



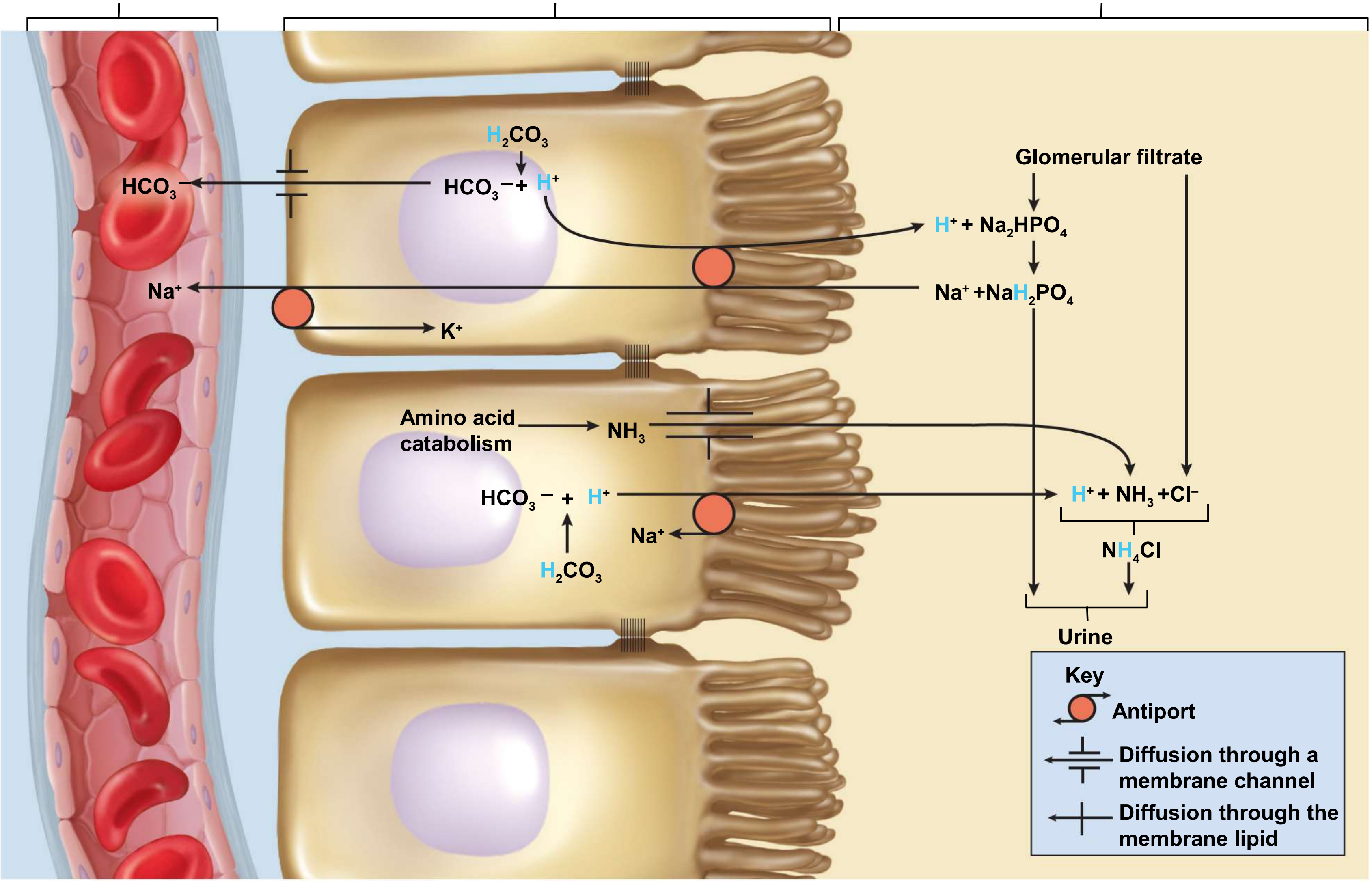
Limiting pH

- 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 *<u>prevented by buffers in tubular fluid</u>*
  - **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
    - $NH_3 + H^+$ and $Cl^- \rightarrow NH_4Cl$ (ammonium chloride – a weak acid)

Buffering Mechanisms in Urine



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
    - H^+ buffered by protein in ICF
    - causes membrane hyperpolarization
    - nerve and muscle cells are hard to stimulate
    - <u>CNS depression may lead to confusion, disorientation, coma, and possibly death</u>

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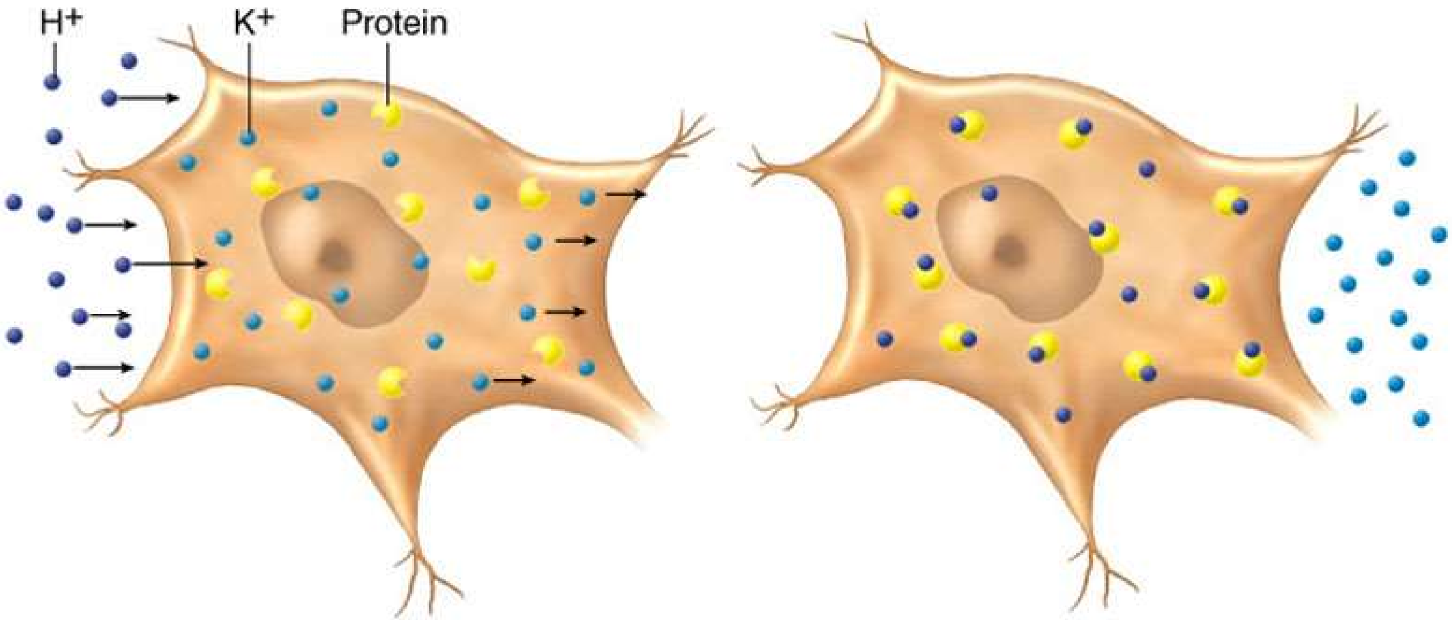

(a) **Acidosis** → leading to → **Hyperkalemia**

Disorders of Acid-Base Balance / Alkalosis

- **In alkalosis**
  - pH above **7.45**
  - H^+ diffuses out of cells
  - K^+ diffuses in
  - membranes depolarized, nerves overstimulated, muscles causing spasms, tetany, convulsions, respiratory paralysis
  - a person cannot live for more than a few hours if the blood pH is below 7.0 or above 7.7

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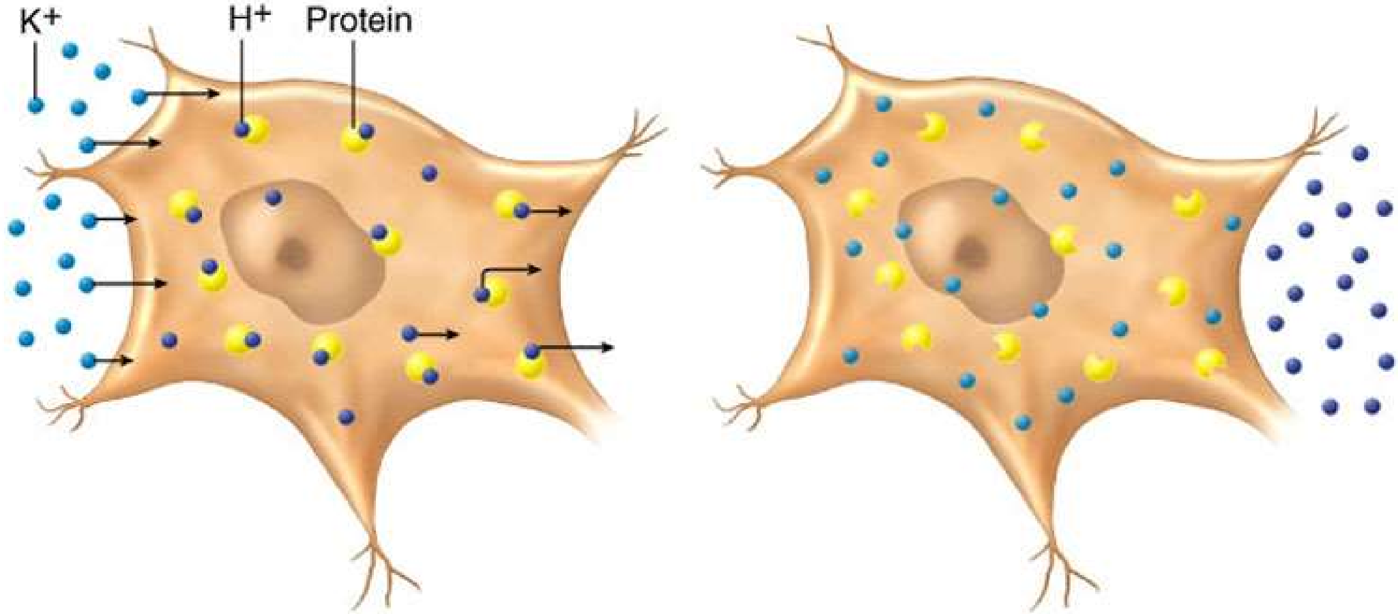

(b) Alkalosis ⟶ leading to ⟶ **Hypokalemia**

Disorders of Acid-Base Balances

- Acid-base imbalances fall into one of two categories:
  - **Respiratory**
  - **Metabolic**
- **Respiratory acidosis**
  - occurs when rate of alveolar ventilation fails to keep pace with the body's rate of CO_2 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_2 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

  1. the **kidneys** compensate for pH imbalances of **respiratory origin**

  1. 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

Compensation for Acid-Base Imbalances

- **Respiratory compensation**
  - changes in pulmonary ventilation to correct changes in pH of body fluids by expelling or retaining CO_2
  - **hypercapnia** (excess CO_2) - stimulates pulmonary ventilation eliminating CO_2 and allowing pH to rise
  - **hypocapnia** (deficiency of CO_2) reduces ventilation and allows CO_2 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

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 draw 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

- **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