Electrolytes

osmolality & acid-base balance

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Electrolyte Balance

maintenance of water homeostasis

Electrolytes

- Ions capable of carrying an electrical charge
  - Anion: (-) → Anode
  - Cation: (+) → Cathode
- Important physiologic electrolytes include: Na^{+}, K^{+}, Ca^{+2}, Mg^{+2}, Cl^{-}, HCO_3^{-}), SO_4^{-2}, phosphates ($H_2PO_4^{-}$, HPO_4^{-2}), sulfate (and some organic anions, such as lactate

Biological Process/Function	Ions Involved
water volume maintenance and osmotic regulation	Na^{+}, K^{+}, Cl^{-}
myocardial rhythm and contractility	K^{+}, Ca^{+2}, Mg^{+2}
cofactors in enzyme activation	Ca^{+2}, Mg^{+2}, Zn^{+2}
regulation of adenosine triphosphatase (ATPase) ion pumps	Mg^{+2}
blood coagulation	Ca^{+2}, Mg^{+2}
neuromuscular excitability	K^{+}, Ca^{+2}, Mg^{+2}
production and use of ATP from glucose	Mg^{+2}, PO_4^{-}
acid–base balance (pH)	K^{+}, Cl^{-}, HCO_3^{-}

Because many of these functions require electrolyte concentrations to be held within **very narrow ranges**, the body has complex systems for monitoring and maintaining electrolyte concentrations

Water

- The average water content of the human body varies from **40% to 75%** of total body weight, and declines with age and especially with obesity (higher fat content)
- Responsible for:
  - transporting nutrients to cells
  - determining cell volume
  - removal of waste products by way of urine
  - acting as the body's coolant by way of sweating

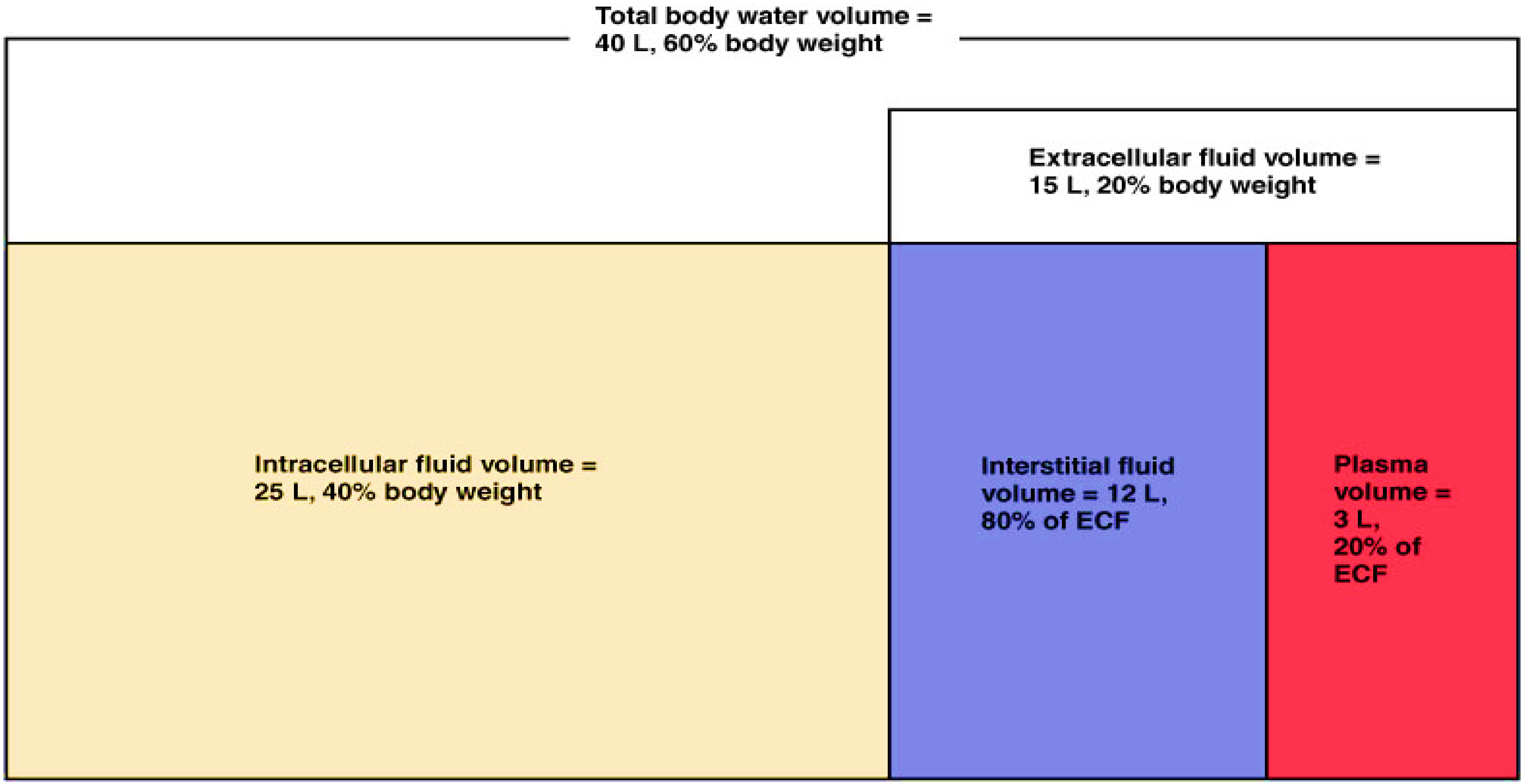
Solvent for all processes in the human body

Water

- **Intracellular fluid (ICF):** is the fluid inside the cells and accounts for about two-thirds of total body water
- **Extracellular fluid (ECF):** accounts for the other one-third of total body water, subdivided into:
  - intravascular ECF (plasma)
  - interstitial cell fluid that surrounds the cells in the tissue

Water

- Normal plasma is about 93% water, with the remaining volume occupied by lipids and proteins
- The concentrations of ions within cells and in plasma are maintained both by energy-consuming active transport processes and by diffusion or passive transport processes

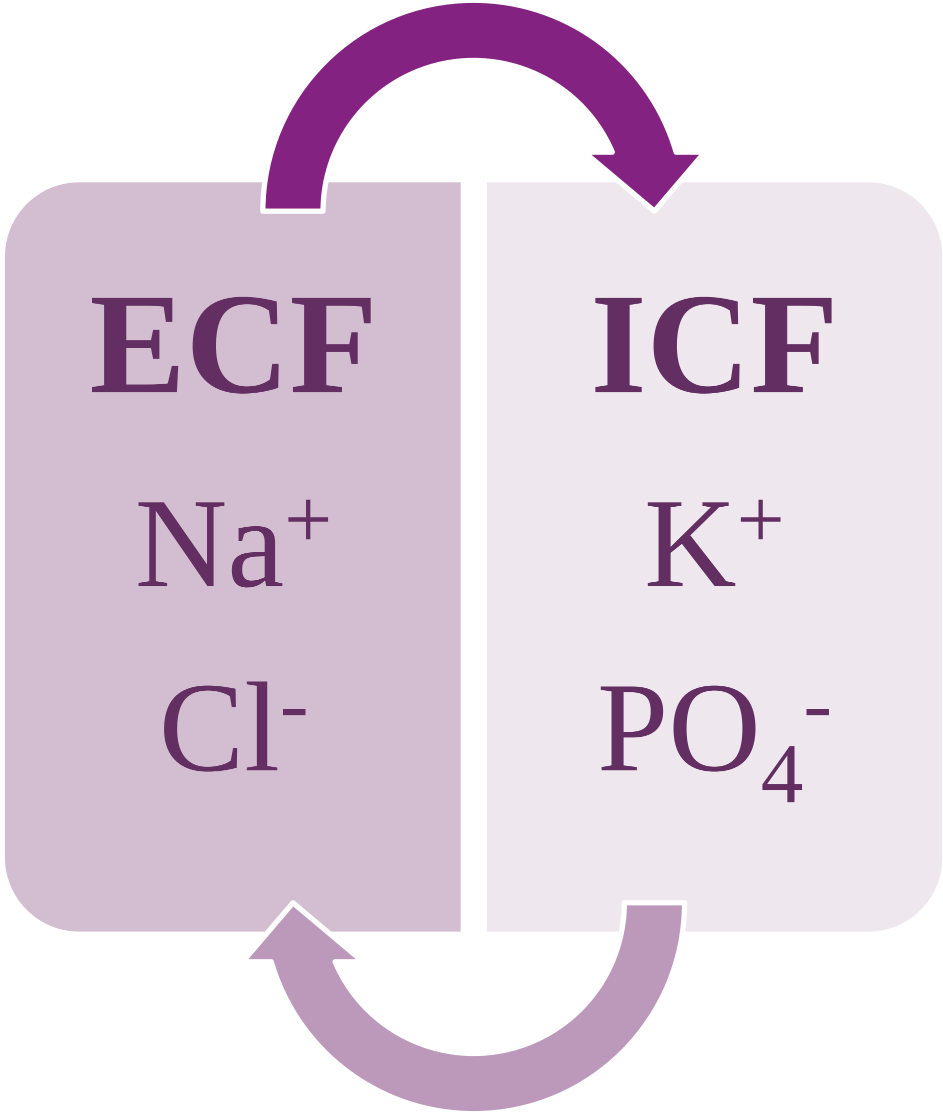

Total body water volume =
40 L, 60% body weight
Extracellular fluid volume =
15 L, 20% body weight
Intracellular fluid volume =
25 L, 40% body weight
Interstitial fluid
volume = 12 L,
80% of ECF
Plasma
volume =
3 L,
20% of
ECF

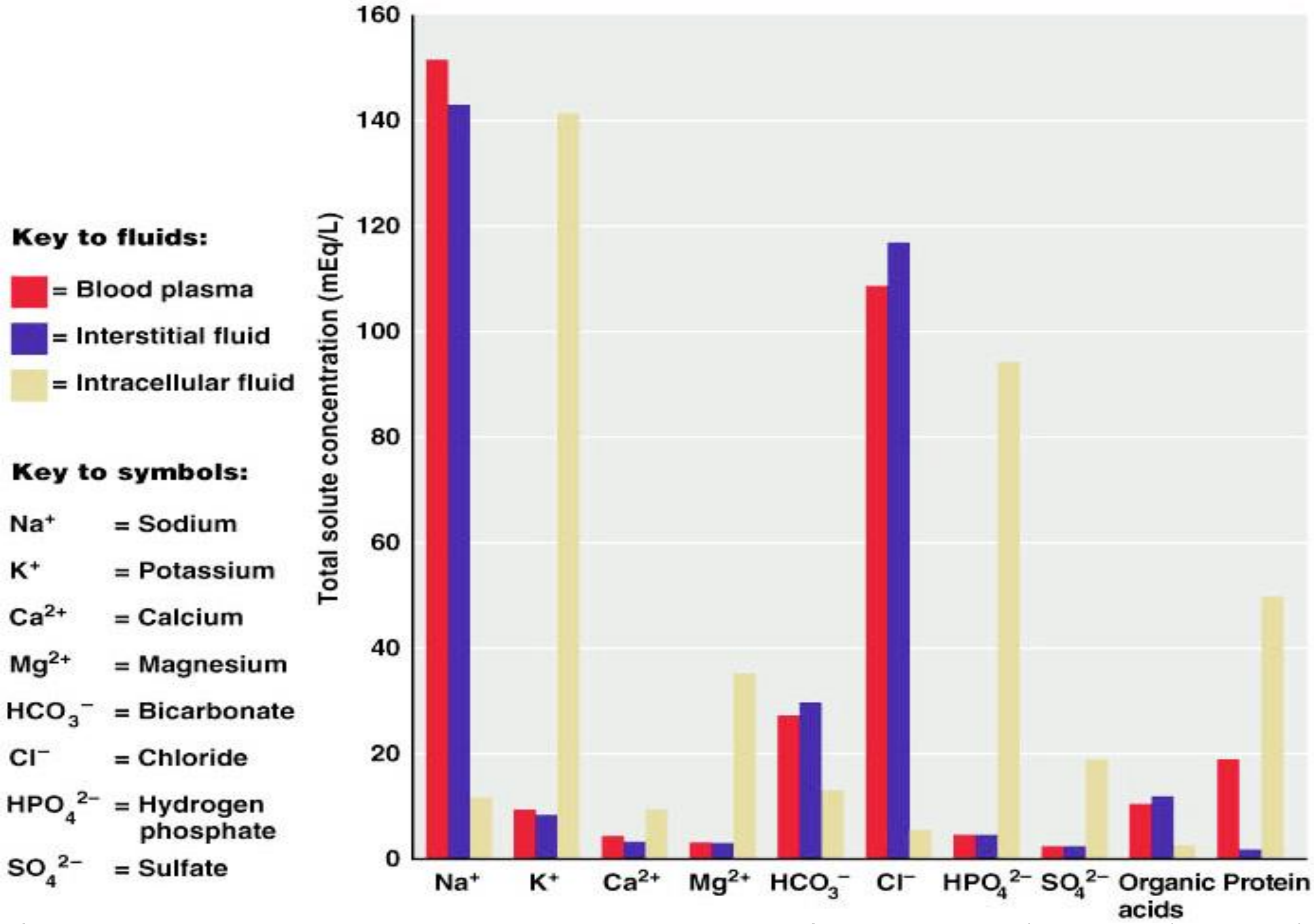
ECF vs. ICF

- Distribution of water in the various body fluid compartments is controlled by maintaining the concentration of electrolytes and proteins in the each compartment
- Because most biologic membranes are **freely permeable to water** but not to ions or proteins, the concentration of ions and proteins on either side of the membrane will influence the flow of water across a membrane

Osmoregulation

ECF vs. ICF




Key to fluids:
= Blood plasma
= Interstitial fluid
= Intracellular fluid
Key to symbols:
Na^+ = Sodium
K^+ = Potassium
Ca^{2+} = Calcium
Mg^{2+} = Magnesium
HCO_3^- = Bicarbonate
Cl^- = Chloride
HPO_4^{2-} = Hydrogen phosphate
SO_4^{2-} = Sulfate
Total solute concentration (mEq/L)
160
140
120
100
80
60
40
20
0
Na^+
K^+
Ca^{2+}
Mg^{2+}
HCO_3^-
Cl^-
HPO_4^{2-}
SO_4^{2-}
Organic acids
Protein

Osmolality

- Osmolality is a physical property of a solution that is based on the concentration of solutes (expressed as millimoles) per kilogram of solvent (w/w)
- The sensation of thirst and arginine vasopressin hormone (AVP), also known as antidiuretic hormone (ADH), secretion are stimulated by the hypothalamus in response to an increased osmolality of blood
- The natural response to thirst is to consume more fluids, increasing the water content of the ECF and decreasing the osmolality of the plasma

Osmolality

- ADH (antidiuretic hormone) and thirst are stimulated by the hypothalamus in **response to increased osmolality**
- ADH is secreted by the posterior pituitary gland, and acts on the cells in the kidneys to increase water reabsorption
- Osmolality is the parameter to which the hypothalamus responds, it affects Na^{+} concentration in plasma, consequently regulating blood volume

Normal plasma osmolality: 275-295 mOsm/kg

Osmolality

- The hypothalamic thirst center is stimulated:
  - By a decline in plasma volume of 10%–15%
  - By increases in plasma osmolality of 1–2%
  - Via baroreceptor input, angiotensin II, and other stimuli

Blood Volume

- Adequate blood volume is essential to maintain blood pressure and ensure good perfusion to all tissues and organs
- Regulation of both Na^+ and water is interrelated in controlling blood volume
- The renin–angiotensin–aldosterone hormone system responds primarily to a **decreased blood volume**

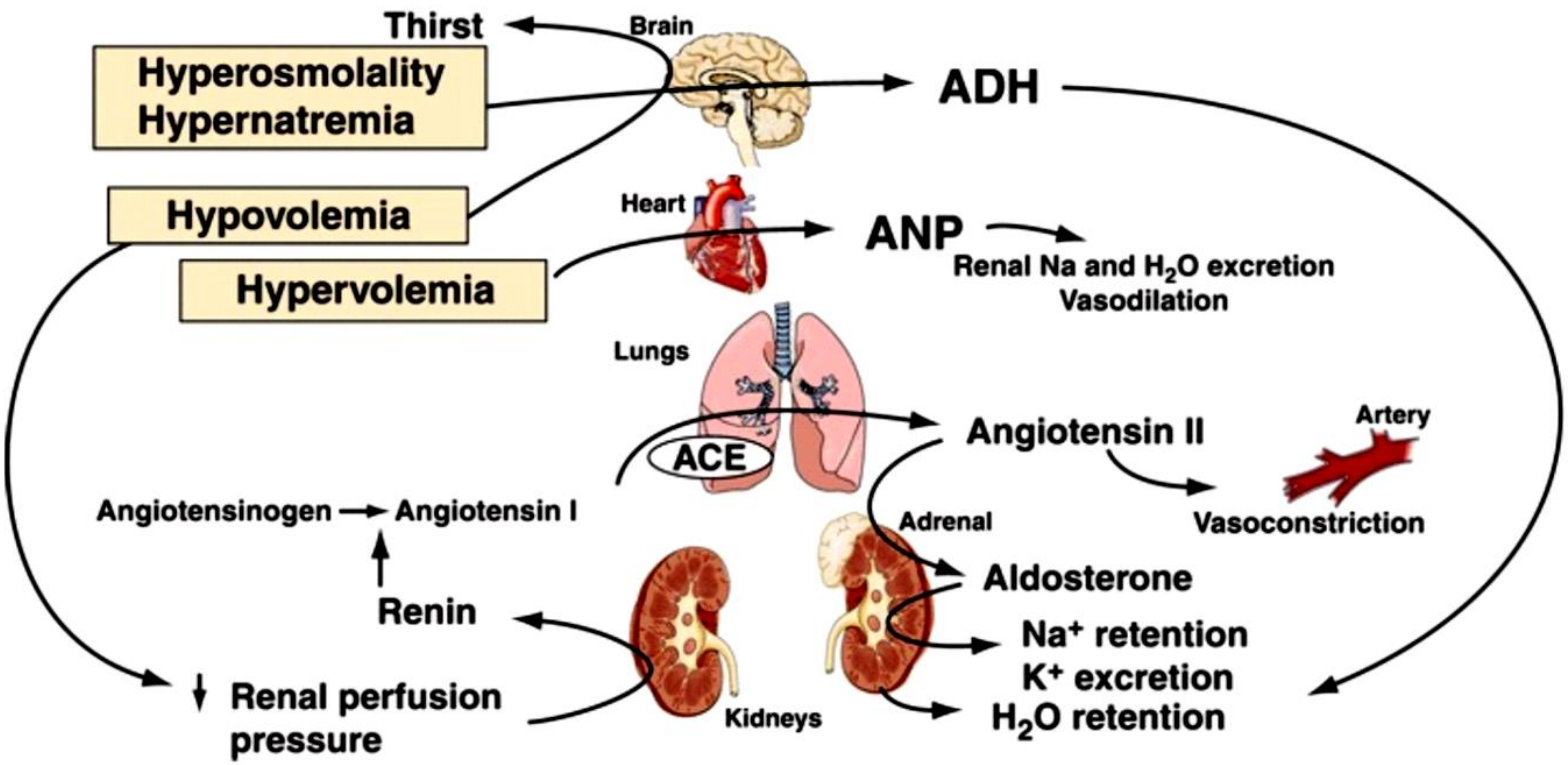


FIGURE 16.1 Responses to changes in blood osmolality and blood volume. ANP, atrial natriuretic peptide; ADH, antidiuretic hormone; ACE, angiotensin-converting enzyme. The primary stimuli are shown in *boxes* (e.g., hypovolemia).

The Electrolytes

ions and their distribution

Sodium (Na^+)

- Na^+ is the most abundant cation in the ECF, representing 90% of all extracellular cations, and largely determines the osmolality of the plasma
- Na^+ concentration in the ECF is much larger than inside the cells
- Because a small amount of Na^+ can diffuse through the cell membrane, the two sides would eventually reach equilibrium

To prevent equilibrium and to ensure a concentration gradient, active transport systems, such as **ATPase ion pumps**, are present in all cells

Sodium (Na^+)

- The plasma Na^+ concentration depends greatly on the intake and excretion of water and, to a somewhat lesser degree, on the renal regulation of Na^+
- Three processes are of primary importance:
  - Intake of water in response to thirst, as stimulated or suppressed by plasma osmolality
  - Excretion of water, largely affected by ADH release in response to changes in either blood volume or osmolality
  - Blood volume status, which affects Na^+ excretion through aldosterone, angiotensin II, and ANP

Sodium (Na^+)

- The kidneys have the ability to conserve or excrete large amounts of Na^+, depending on the Na^+ content of the ECF and the blood volume
- Normally, 60% to 75% of filtered Na^+ is reabsorbed in the proximal tubule. Some Na^+ is also reabsorbed in the loop and distal tubule

Normal plasma Na^+= 136-145 mEq/L (or mmol/L)

Hyponatremia

- Hyponatremia is defined as a serum/plasma level less than 135 mmol/L, and levels below 130 mmol/L are clinically significant
- Decreased levels may be caused by:
  - Increased Na^+ loss
  - Increased water retention
  - Water imbalance

Hyponatremia

- Increased Na^+ loss in the urine can occur with:
  - Decreased aldosterone production
  - Certain diuretics (thiazides)
  - Ketonuria
  - A salt-losing nephropathy (with some renal tubular disorders)
- K^+ deficiency also causes Na^+ loss because of the inverse relationship of the two ions in the renal tubules

Hyponatremia

- Increased water retention causes dilution of plasma Na^+ as with acute or chronic renal failure, nephrotic syndrome, hepatic cirrhosis and congestive heart failure (CHF)
- Urine Na^+ levels can be used to differentiate the cause for increased water retention:
  - Urine Na^+ is $\geq$20 mmol/d, acute or chronic renal failure is the likely cause
  - Urine Na^+ is less than 20 mmol/d, water retention may be a result of nephrotic syndrome, hepatic cirrhosis, or CHF

Hyponatremia

- SIADH (syndrome of inappropriate secretion of antidiuretic hormone) causes an increase in water retention because of increased ADH production
- A defect in ADH regulation has been associated with pulmonary disease, malignancies, central nervous system (CNS) disorders, infections, or trauma

Hyponatremia

With Low Osmolality

Increased sodium loss

Increased water retention

With Normal Osmolality

Increased nonsodium cations

Lithium excess

Increased γ-globulins—cationic (multiple myeloma)

Severe hyperkalemia

Severe hypermagnesemia

Severe hypercalcemia

Pseudohyponatremia

Hyperlipidemia

Hyperproteinemia

Pseudohyperkalemia as a result of in vitro hemolysis

With High Osmolality

Hyperglycemia

Mannitol infusion

Hypernatremia

- Hypernatremia (increased serum Na^+ concentration) results from:
  - Excess loss of water relative to Na^+ loss
  - Decreased water intake
  - Increased Na^+ intake or retention
- Loss of hypotonic fluid may occur either by the kidney or through profuse sweating, diarrhea, or severe burns
- Can result from loss of water in **diabetes insipidus**, either because the kidney cannot respond to ADH or because ADH secretion is impaired

Hypernatremia

Excess Water Loss
Diabetes insipidus
Renal tubular disorder
Prolonged diarrhea
Profuse sweating
Severe burns

Decreased Water Intake
Older persons
Infants
Mental impairment

Increased Intake or Retention
Hyperaldosteronism
Sodium bicarbonate excess
Dialysis fluid excess

Hypernatremia

Urine Osmolality <300 mOsm/kg

Diabetes insipidus (impaired secretion of AVP or kidneys cannot respond to AVP)

Urine Osmolality 300–700 mOsm/kg

Partial defect in AVP release or response to AVP

Osmotic diuresis

Urine Osmolality >700 mOsm/kg

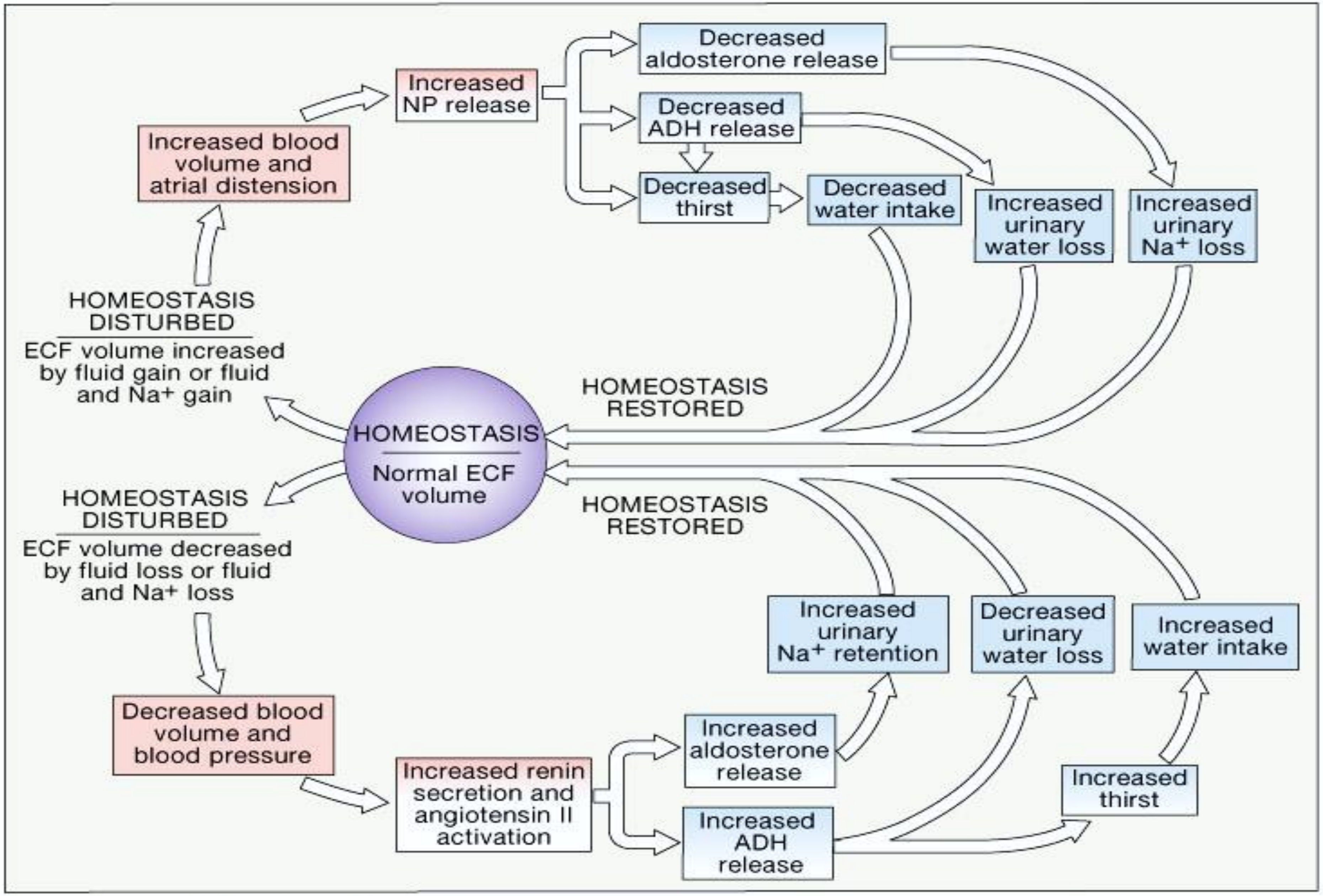
Loss of thirst

Insensible loss of water (breathing, skin)

GI loss of hypotonic fluid

Excess intake of sodium

Commonly, hypernatremia occurs in those persons who may be thirsty but who are unable to ask for or obtain water, such as adults with altered mental status and infants


Increased blood volume and atrial distension
Increased NP release
Decreased aldosterone release
Decreased ADH release
Decreased thirst
Decreased water intake
Increased urinary water loss
Increased urinary Na+ loss
HOMEOSTASIS DISTURBED
ECF volume increased by fluid gain or fluid and Na+ gain
HOMEOSTASIS RESTORED
HOMEOSTASIS
Normal ECF volume
HOMEOSTASIS DISTURBED
ECF volume decreased by fluid loss or fluid and Na+ loss
HOMEOSTASIS RESTORED
Increased urinary Na+ retention
Decreased urinary water loss
Increased water intake
Decreased blood volume and blood pressure
Increased renin secretion and angiotensin II activation
Increased aldosterone release
Increased ADH release
Increased thirst

Potassium (K^+)

- The major intracellular cation in the body, with a concentration 20 times greater inside the cells
- Many cellular functions require that the body maintain a low ECF concentration of K^+ ions. As a result, only 2% of the body's total K^+ circulates in the plasma

Normal serum K^+= 3.5 - 5.1 mEq/L (or mmol/L)

Potassium (K^+)

- Functions of K^+ in the body include regulation of:
  - neuromuscular excitability
  - contraction of the heart
  - ICF volume
  - H^+ concentration

The K^+ concentration has a major effect on the contraction of skeletal and cardiac muscles

Potassium (K^+)

- Renal tubular reabsorption and secretion is important in the regulation of K^+ balance
- Reabsorption of K^+ occurs in the proximal tubules; influenced by aldosterone, K^+ is secreted in the urine exchange for Na^+
- Most individuals consume far more K^+ than needed; the excess is excreted in the urine but may accumulate to toxic levels if renal failure occurs
- Three factors influence the distribution of K^+ between cells and ECF:

Potassium (K^+)

- K^+ loss occurs whenever Na^+/K^+ ATPase pump is inhibited
- Insulin promotes entry of K^+ into skeletal muscle and liver
- Cathecholamines promote cellular entry of K^+

Hypokalemia

Gastrointestinal Loss

Vomiting

Diarrhea

Gastric suction

Intestinal tumor

Malabsorption

Cancer therapy—chemotherapy, radiation therapy

Large doses of laxatives

Renal Loss

Diuretics—thiazides, mineralocorticoids

Nephritis

Renal tubular acidosis

Hyperaldosteronism

Cushing's syndrome

Hypomagnesemia

Acute leukemia

Cellular Shift

Alkalosis

Insulin overdose

Decreased Intake

Hyperkalemia

Decreased Renal Excretion
Acute or chronic renal failure (GFR < 20 mL/min)
Hypoaldosteronism
Addison's disease
Diuretics

Cellular Shift
Acidosis
Muscle/cellular injury
Chemotherapy
Leukemia
Hemolysis

Increased Intake
Oral or intravenous potassium replacement therapy

Artifactual
Sample hemolysis
Thrombocytosis
Prolonged tourniquet use or excessive fist clenching

Chloride (Cl^-)

- The major extracellular anion, and its precise function in the body is not well understood
- It is involved in maintaining osmolality, blood volume, and electric neutrality. In most processes, Cl^- shifts secondarily to a movement of Na^+ or HCO_3^-

Normal serum Cl^-= 98-107 mmol/L

Chloride (Cl^-)

- Cl^- ingested in the diet is almost completely absorbed by the intestinal tract
- Cl^- is then filtered out by the glomerulus and passively reabsorbed, in conjunction with Na^+, by the proximal tubules
- Excess Cl^- is excreted in the urine and sweat
- Cl^- disorders are often a result of the same causes that disturb Na^+ levels because Cl^- passively follows Na^+

Bicarbonate

- The second most abundant anion in the ECF and a major component of the buffering system
- Total CO_2 comprises the bicarbonate ion (HCO_3^-), H_2CO_3, and dissolved CO_2, with HCO_3^- accounting for more than 90% of the total CO_2 at physiologic pH

Normal serum HCO_3^- = 22-26 mEq/L (or mmol/L)

Bicarbonate

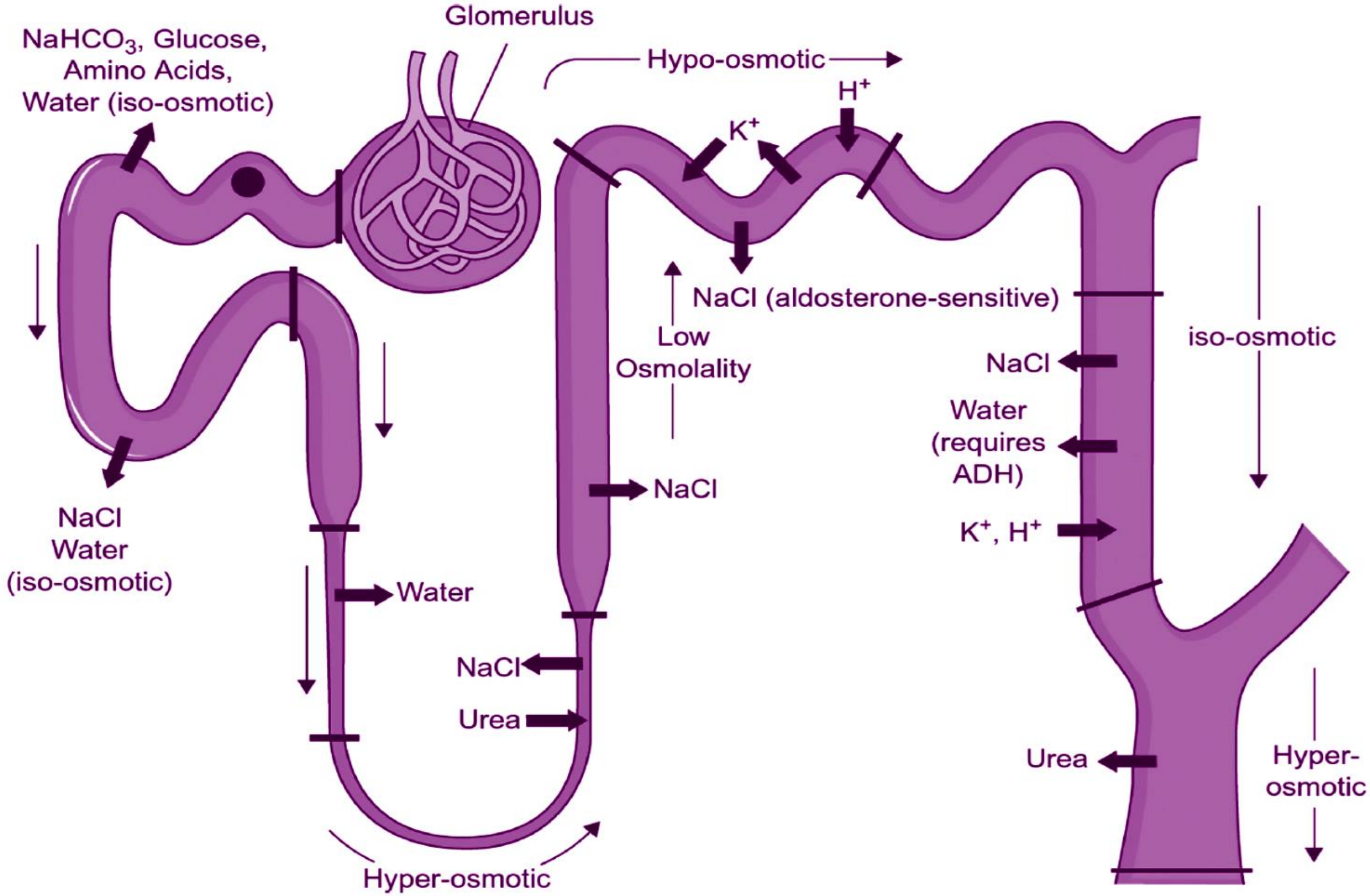
- Carbonic anhydrase in RBCs converts CO_2 and H_2O to H_2CO_3, which dissociates into H^+ and HCO_3^-

$$CO_2 + H_2O \xleftrightarrow{CA} H_2CO_3 \xleftrightarrow{CA} H^+ + HCO_3^-$$

- This process converts potentially toxic CO_2 in the plasma to an effective buffer: HCO_3^-
- HCO_3^- buffers excess H^+ by combining with acid, then eventually dissociating into H_2O and CO_2 in the lungs where the acidic gas CO_2 is eliminated

Bicarbonate

- Most of the HCO_3^- in the kidneys (85%) is reabsorbed by the proximal tubules, with 15% being reabsorbed by the distal tubules
- **In alkalosis**, with a relative increase in HCO_3^- compared with CO_2, the kidneys increase excretion of HCO_3^- into the urine, carrying along a cation such as Na^+
- **In acidosis**, excretion of H^+ into the urine is increased. In addition, HCO_3^- reabsorption is virtually complete



37.3 Principal transport processes in the renal nephron. ADH = antidiuretic hormone.

Anion Gap

- Used to evaluate electrolytes (Na^+, K^+, Cl^-, HCO_3^-)
- Calculated as the difference between measured anions and measured cations.
- Formula: $AG=(Na^+ + K^+)- (Cl^- + HCO_3^-)$

Normal anion gap= 10-20 mmol/L

Anion Gap

- Increased AG can be seen in:
  - Uncontrolled diabetes (due to lactic & keto acids)
  - Severe renal disorders
  - Hypernatremia
  - Lab errors
- A decrease in AG is rare; it occurs more often due to test/instrument errors

Acid-Base Balance

Definitions

- An **acid** is a substance that can donate hydrogen ions (H+) when dissolved in water
- A **base** is a substance that can accept hydrogen ions
- **pH** of a solution is defined as the negative log of the hydrogen ion concentration

A decrease in one pH unit represents a 10-fold increase in H+ concentration

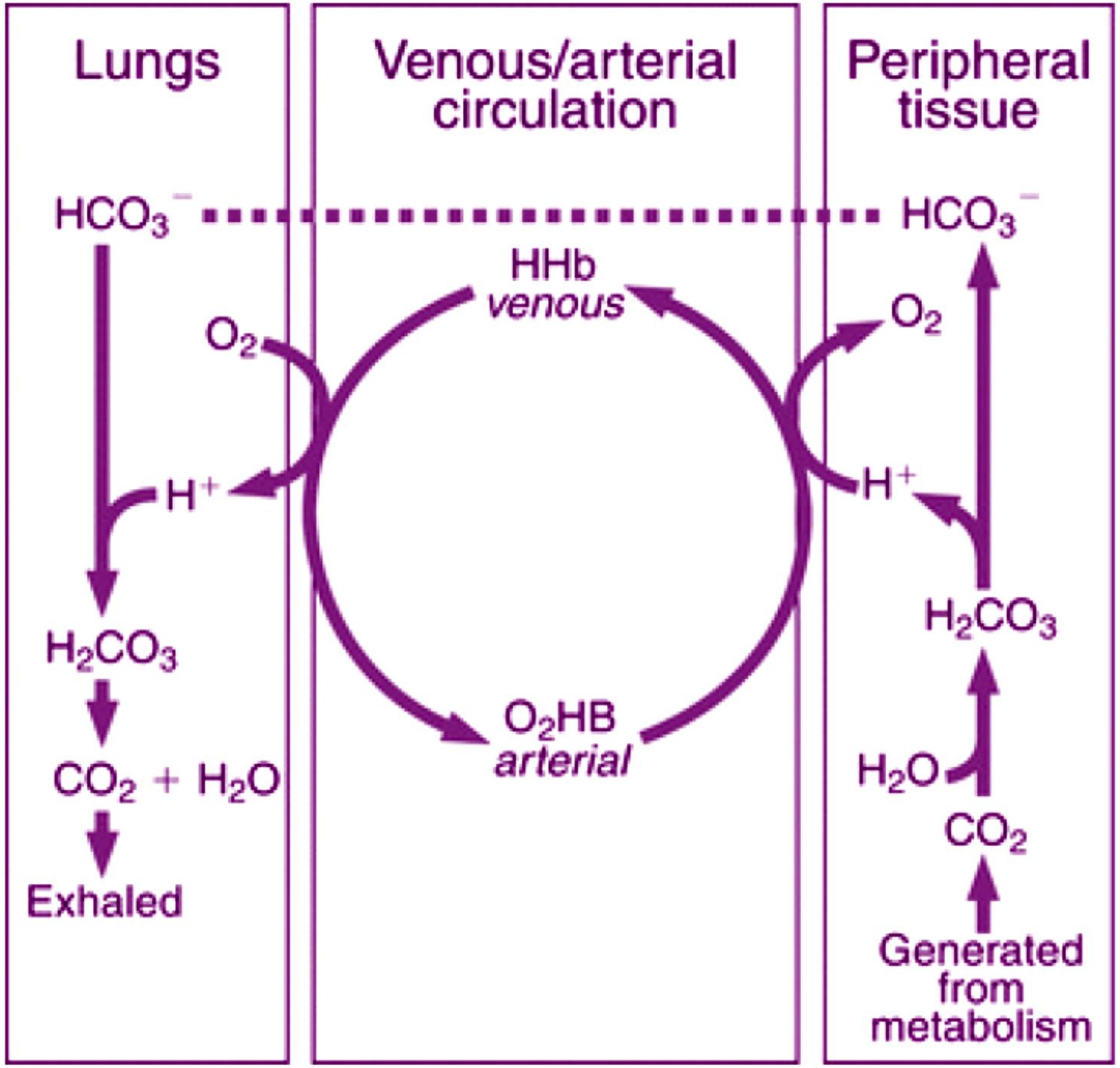
Buffering

- The concentration of H^+ in the ECF is maintained within a narrow range from 36-44 nmol/L (pH 7.35-7.45)
- Through mechanisms that involve the lungs and kidneys, the body controls and excretes H^+ in order to maintain pH homeostasis
- Imbalances between the rate of acid formation and excretion can occur and can lead to alterations in consciousness, neuromuscular irritability, tetany, coma, and death

A **buffer** consists of a weak acid and a salt of its conjugate base, and it resists the change in pH upon adding acid or base.

In plasma, the **bicarbonate–carbonic acid** system, is one of the principal buffers

Buffering


Lungs
Venous/arterial circulation
Peripheral tissue
HCO3−
HCO3−
HHb
venous
O2
O2
H+
H+
H2CO3
H2CO3
CO2 + H2O
O2HB
arterial
H2O
CO2
Exhaled
Generated from metabolism

Buffering

- Proteins and phosphates are also involved in buffering, primarily in the intracellular fluids
- Most circulating proteins have a net negative charge and are capable of binding H^+
- The kidneys regulate the excretion of both acid and base, making them an important player in the regulation of acid–base balance

Disorders

- When blood pH is less than the reference range (7.35-7.45), it is termed **acidemia**. A pH greater than the reference range is termed **alkalemia**
  - Acidemia will result if the hydrogen ion concentration increases through increased PCO_2 concentrations or decreases in the bicarbonate concentration
  - Alkalemia will result with hydrogen ion concentrations that are decreased, either from decreased PCO_2 or increased concentrations of bicarbonate

Disorders

- When blood pH is less than the reference range (7.35-7.45), it is termed **acidemia**. A pH greater than the reference range is termed **alkalemia**
  - Acidemia will result if the hydro … tration

The acid–base status of a patient can be fully characterized by measuring H^+ concentration and PCO_2 in arterial or arterialized capillary blood specimens; HCO_3^- is then obtained by calculation

Disorders

- Acid–base disorders fall into two main categories:
  - Respiratory disorders: A primary defect in ventilation affects the PCO_2
  - Metabolic disorders: The primary defect may be the production of nonvolatile acids, or ingestion of substances that give rise to them, in excess of the kidney’s ability to excrete these substances

Electrolytes are ions capable of carrying an electrical charge

The body has complex systems for monitoring and maintaining electrolyte concentrations

ECF (Na^+, Cl^-) vs. ICF (K^+, PO_4^-)

Through the lungs and kidneys, the body maintains pH homeostasis