Chapter 27: Fluid, electrolyte, and acid-base homeostasis

Fluid (water) balance

Homeostasis of body fluid volume

Water is critical for body functions

- Water is the main component of all body fluids
- The body is about 60% water
- Found both inside and outside the cells
- Functions
  - Helps regulate body temperature, blood pressure
  - Transports nutrients
  - Excretion of waste products

Body Fluid Compartments

- Intracellular fluid (ICF)
  - inside cells
  - About 2/3 of body fluid
- Extracellular fluid (ECF)
  - Interstitial fluid between cells
  - 80% of ECF
  - Plasma in blood
  - 20% of ECF
  - Also includes lymph, cerebrospinal fluid, synovial fluid, aqueous humor

Fluid Balance

- Cell membranes separate body fluids into distinct compartments
  - Cell membranes separate ICF from surrounding interstitial fluid
  - Blood vessel walls separate interstitial fluid from plasma
  - Although fluids are constantly moving from one compartment to another, the volume of fluid in each compartment remains fairly stable – an example of homeostasis

Fluid Balance

- The body is in fluid balance when water and solutes are correctly proportioned among compartments
- Water moves in and out of body compartments by osmosis.
- The concentration of electrolytes (salts) determines water movement.
- Fluid balance means water balance, but also implies electrolyte balance
  - the two are inseparable
Daily Water Gain and Loss

Water gain normally equals water loss, so the body maintains a constant volume.

Water balance and the kidney

- Fluid balance is related to electrolyte balance
- BUT intake of water and electrolytes rarely is proportional
- Kidneys excrete
  - excess water through dilute urine
  - excess electrolytes through concentrated urine

Water balance: Regulation of water intake

- The main way to regulate body water balance is by adjusting the volume of water intake
  - how much you drink
- The stimulus for water intake is dehydration → thirst sensations
  - Decreases blood volume, increases blood osmolarity
  - Stimulates thirst center in hypothalamus

Water gain normally equals water loss, so the body maintains a constant volume.

Water balance: Regulating water and salt loss

- Loss of body water or excess salts depends mainly on regulating how much is lost in the urine
- Under normal conditions, water loss (urine volume) is adjusted by 4 hormones:
  - Antidiuretic hormone (ADH)
  - Atrial natriuretic peptide (ANP)
  - Angiotensin II
  - Aldosterone

Renin-angiotensin-aldosterone system

- Renin increases formation of angiotensin II
- Angiotensin II and aldosterone promote urinary Na+ and Cl- reabsorption (and water by osmosis)
- Dehydration → What happens to urine volume?
Major hormone regulating water loss is ADH

- Also known as vasopressin
- Produced by hypothalamus, released from posterior pituitary
- Promotes insertion of aquaporin-2 into collecting duct cells
- Permeability to water increases
- Produces concentrated urine

Homeostasis of body fluid volume

1. The countercurrent mechanism establishes an osmotic gradient in the renal medulla
   - this enables kidneys to produce concentrated urine when ADH is present
2. ADH
   - Causes water to be reabsorbed in collecting duct → concentrated urine
   - In the absence of ADH, kidneys produce dilute urine

Regulation of water loss in urine

- Angiotensin II
  - Stimulates secretion of aldosterone
- Aldosterone
  - Promotes reabsorption of NaCl and water
  - Reduces loss of water in urine
- Atrial natriuretic peptide (ANP)
  - Promotes natriuresis, increase excretion of Na+ accompanied by water
  - Increases loss of water in urine
- ADH
  - Increases water reabsorption by increasing number of aquaporins in collecting duct
  - Reduces loss of water in urine

Regulation of water loss in urine

- Reduces loss of water
  - Angiotensin II
  - Aldosterone
    - ↑ Na+ (and water) retention
- ADH
  - ↑ water reabsorption

- Increases loss of water
  - ANP
    - ↑ Na+ excretion and water loss

Water balance: movement of water between interstitial fluid and intracellular fluid

- The survival of a cell depends on its ability to balance water uptake and loss

Water Intoxication

Water intoxication – drinking water faster than the kidneys can excrete it
Osmosis
- Movement of WATER into and out of the cell
  - driven by different concentrations of solutes (salts and proteins) inside and outside the cell
  - No energy is needed
  - Osmosis is important in biology because organisms are mostly water

Electrolyte balance

Electrolytes in body fluids
- Serve 4 general functions
  - Control osmosis of water between body fluid compartments
  - Help maintain the acid-base balance
  - Carry electrical current
    - allows production of action potentials
  - Serve as cofactors needed for optimal activity of enzymes

Concentrations of electrolytes in body fluids
- Typically expressed in milliequivalents per liter (mEq/liter)
  - Plasma and interstitial fluid (the ECF compartments) are similar
    - Chief difference is plasma contains many more proteins

ICF differs considerably from ECF
- ECF
  - most abundant ion is Na+
- ICF
  - most abundant ion is K+
  - Na+/K+ pumps play major role in keeping K+ high inside cells and Na+ high outside cell

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Edema
- Excess Na\(^+\) in the body can result in edema
  - When kidney doesn’t excrete enough Na\(^+\), water is osmotically retained
  - Results in ↑ blood volume, ↑ BP and edema, abnormal accumulation of interstitial fluid

Hypovolemia
- Excess loss of Na\(^+\) causes excessive loss of water
- Hypovolemia – an abnormally low blood volume
  - Usually due to inadequate secretion of aldosterone associated with adrenal insufficiency

Test your understanding
- JR just ate a very salty meal. His blood Na\(^+\) level skyrocketed briefly before returning to normal. What caused this return to homeostasis?
  - The excess Na\(^+\) was excreted in the urine. How did this affect urine volume?
  - What factors helped maintain body water (and salt) balance?
    - ANP increases loss of Na\(^+\) (and Cl\(^-\)) in urine, accompanied by water

Acid-base balance

pH – measures the H\(^+\) concentration of a solution
- Base
  - pH above 7
- Neutral
  - pH=7
- Acid
  - pH below 7

Why is pH important?
- Chemical reactions within cells are sensitive to pH
- Small changes in pH can alter enzyme activity
- For example
  - the pH of blood is between 7.35 and 7.45
  - you would only live for a few minutes if it were to fall to 7.0 or rise to 7.8
Acid-base balance

- Major homeostatic challenge is keeping H+ concentration (pH) of body fluids at appropriate level
  - The normal pH of extracellular fluid is 7.35-7.45
- The overall acid-base balance of the body is maintained by
  - Buffer systems
  - Respiratory system: exhalation of CO₂
  - Kidney: excretion of H+

What is a buffer?

- Most buffer systems of the body consist of a weak acid and the salt of that acid (which functions as a weak base)
- Buffers prevent rapid, drastic changes in the pH of body fluids by converting strong acids and bases into weak acids and bases.
- Buffers work within fractions of a second

3 important buffer systems

- **The protein buffer system**
  - the most abundant buffer in body cells and plasma
  - the protein hemoglobin is an especially good buffer in RBCs.
- **The bicarbonate buffer system**
  - an important regulator of blood pH and is based on the bicarbonate ion (HCO₃⁻).
- **The phosphate buffer system**
  - an important regulator of pH, both in RBCs and in the kidney tubular fluids.

Protein buffer system

![Overview of amino acid buffering functions](Copyright 2009, John Wiley & Sons, Inc.)

- Amino acids can accept or donate hydrogen ions, making them excellent buffers.
- Proteins typically have hundreds of amino acids, making them superb buffers.

Bicarbonate buffer system

\[ \text{H}_2\text{O} + \text{CO}_2 \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \]

- Quick overview: carbon dioxide is converted into bicarbonate ions in the blood.
- Bicarbonate ions serve to maintain a pH of 7.4 in the blood
- Bicarbonate ion (HCO₃⁻) acts as weak base and carbonic acid (H₂CO₃) acts as weak acid
- Because CO₂ and H₂O combine to form H₂CO₃, this buffer system cannot protect against pH changes due to respiratory problems in which there is an excess or shortage of CO₂

Phosphate buffer system

- Mechanism is similar to bicarbonate buffer system
- Dihydrogen phosphate (H₂PO₄⁻) acts as a weak acid and is able to buffer strong bases
  \[ \text{OH}^- + \text{H}_2\text{PO}_4^- \rightarrow \text{H}_2\text{O} + \text{HPO}_4^{2-} \]
- Monohydrogen phosphate (HPO₄²⁻) acts as a weak base
  \[ \text{H}^+ + \text{HPO}_4^{2-} \rightarrow \text{H}_2\text{PO}_4^- \]
- Phosphates are important regulators of pH in the cytosol

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Regulation of blood pH by the respiratory system

- The simple act of breathing plays an important role in maintaining pH
- Changes in the rate and depth of breathing can alter pH of body fluids within minutes
  \[ \text{H}_2\text{O} + \text{CO}_2 \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \]
- An increase in the rate of breathing causes more \( \text{CO}_2 \) to be exhaled, and \( \text{H}^+ \) levels fall (blood becomes more basic, increased pH).
- When less \( \text{CO}_2 \) is exhaled, \( \text{CO}_2 \) levels increase → blood becomes more acidic

Test your understanding

- If you hold your breath for 30 sec, what is likely to happen to your blood pH?
  - \( \text{CO}_2 \) levels? Increase
  - Blood pH? Blood becomes more acidic/ pH falls

pH control by the kidneys

- The kidneys excrete \( \text{H}^+ \) and reabsorb \( \text{HCO}_3^- \) to aid in maintaining pH
- Cells in the PCT and collecting ducts secrete hydrogen ions into the tubular fluid
- These two types of cells help maintain body fluid pH by excreting excess \( \text{H}^+ \) when pH is too low or by excreting excess \( \text{HCO}_3^- \) when the pH is too high

Secretion of \( \text{H}^+ \) by intercalated cells in the collecting duct

- Intercalated cells of collecting duct include proton pumps that secrete \( \text{H}^+ \) into tubule fluid
- \( \text{H}^+ \) in the urine is buffered by \( \text{HPO}_4^{2-} \) and \( \text{NH}_3 \)
- Urine can be up to 1000 times more acidic than blood due to the proton pumps in the collecting ducts of the kidney

Acid-base imbalances

- Normal pH range of arterial blood 7.35-7.45
  - Acidosis – blood pH below 7.35
  - Alkalosis – blood pH above 7.45
- Major physiological effect of
  - Acidosis – depression of synaptic transmission in CNS
  - Alkalosis – overexcitability of CNS and peripheral nerves

Physiological responses to normalize arterial blood pH

- Changes in blood pH that lead to acidosis or alkalosis can be compensated to return pH to normal
  - Complete – brought within normal range
  - Partial – still too low or high
- Compensation mechanisms
  - Respiratory – change blood \( \text{CO}_2 \) levels by hyperventilation or hypoventilation
  - Renal – secretion of \( \text{H}^+ \) and reabsorption of bicarbonate
Respiratory acidosis

- Characterized by
  - high partial pressure of CO$_2$ ($P_{CO_2}$) in blood
  - decreased pH

- Causes:
  - Inadequate exhalation of CO$_2$
  - Reduced gas exchange in the lungs
  - emphysema, pulmonary edema, airway obstruction

- Kidneys can help raise blood pH by increasing excretion of H$^+$

- Rx: increase exhalation of CO$_2$
  - providing ventilation therapy

Respiratory alkalosis

- Characterized by
  - Abnormally low $P_{CO_2}$ in blood
  - increased pH

- Cause: hyperventilation
  - due to oxygen deficiency from high altitude or pulmonary disease, stroke or severe anxiety

- Renal compensation can help

- One simple treatment: breathe into paper bag for short time
  - Higher than normal CO$_2$ level in air in bag

Metabolic acidosis/alkalosis

- Results from changes in bicarbonate (HCO$_3^-$) concentration

- Metabolic acidosis
  - abnormally low bicarbonate level
  - decreased pH

- Causes
  - Loss of HCO$_3^-$ from severe diarrhea or renal dysfunction
  - Accumulation of an acid other than carbonic acid – ketosis
  - Failure of kidneys to excrete H$^+$ derived from metabolism of dietary proteins

- Metabolic alkalosis
  - Abnormally high HCO$_3^-$ in blood

- Causes:
  - Nonrespiratory loss of acid - vomiting of acidic stomach contents
  - Excessive intake of alkaline drugs (antacids)

- Treatment
  - Hypoventilation can help
  - Give fluid solutions to correct Cl-, K+ and other electrolyte deficiencies and correct cause of alkalosis

Diagnosis of acid-base imbalances

- Careful evaluation of blood chemistry using a 4-step process:
  1. Note whether the pH is high (alkalosis) or low (acidosis)
  2. Then decide which value – $P_{CO_2}$ or HCO$_3^-$ – is out of the normal range
  3. Is the cause of the problem respiratory or metabolic?
  4. Look at the value that doesn’t correspond with the observed pH change. Is compensation partly correcting the pH imbalance?