Chapter 26
Balance
Part 2. Acid/Base Balance

Acid–Base Balance
- Precisely balances production and loss of hydrogen ions (pH)
- The body generates acids during normal metabolism, tends to reduce pH
- Kidneys:
  - Secrete hydrogen ions into urine
  - Generate buffers that enter bloodstream in distal segments of distal convoluted tubule (DCT) and collecting system
- Lungs: affect pH balance through elimination of carbon dioxide

Acid–Base Balance
- pH of body fluids is altered by the introduction of acids or bases
- Acids and bases may be strong or weak
- Strong acids dissociate completely (only HCl is relevant physiologically)
- Weak acids do not dissociate completely and thus affect the pH less (e.g. carbonic acid)

pH Imbalances
- Acidosis: physiological state resulting from abnormally low plasma pH
- Alkalosis: physiological state resulting from abnormally high plasma pH
- Both are dangerous but acidosis is more common because normal cellular activities generate acids
- Why is pH so important?

Carbonic Acid
- Carbon Dioxide in solution in peripheral tissues interacts with water to form carbonic acid
- Carbonic Anhydrase (CA) catalyzes dissociation of carbonic acid into H+ and HCO3-
- Found in:
  - cytoplasm of red blood cells
  - liver and kidney cells
  - parietal cells of stomach
  - many other cells

CO₂ and pH
- Most CO₂ in solution converts to carbonic acid and most carbonic acid dissociates (but not all because it is a weak acid)
- P CO₂ is the most important factor affecting pH in body tissues
- P CO₂ and pH are inversely related
- Loss of CO₂ at the lungs increases blood pH
Hydrogen Ions (H\(^+\))

- Are gained:
  - at digestive tract
  - through cellular metabolic activities
- Are eliminated:
  - at kidneys and in urine
  - at lungs (as CO\(_2\) + H\(_2\)O)
  - must be neutralized in blood and urine to avoid tissue damage
- Acids produced in normal metabolic activity are temporarily neutralized by buffers in body fluids

Buffers

- Dissolved compounds that stabilize pH by providing or removing H\(^+\)
- Weak acids or weak bases that absorb or release H\(^+\) are buffers

Buffer Systems

- **Buffer System**: consists of a combination of a weak acid and the anion released by its dissociation (its conjugate base)
- The anion functions as a weak base:
  \[ \text{H}_2\text{CO}_3 \text{ (acid)} \leftrightarrow \text{H}^+ + \text{HCO}_3^- \text{ (base)} \]
- In solution, molecules of weak acid exist in equilibrium with its dissociation products (meaning you have all three around in plasma)

Buffer Systems in Body Fluids

Protein Buffer Systems

- Depend on free and terminal amino acids
- Respond to pH changes by accepting or releasing H\(^+\)
- If pH rises:
  - carboxyl group of amino acid dissociates, acting as weak acid, releasing a hydrogen ion
- If pH drops:
  - carboxylate ion and amino group act as weak bases
  - accept H\(^+\)
  - form carboxyl group and amino ion
- Proteins that contribute to buffering capabilities:
  - plasma proteins
  - proteins in interstitial fluid
  - proteins in ICF

3 Major Buffer Systems

1. **Protein buffer systems**:
   - help regulate pH in ECF and ICF
   - interact extensively with other buffer systems
2. **Carbonic acid–bicarbonate buffer system**:
   - most important in ECF
3. **Phosphate buffer system**:
   - buffers pH of ICF and urine
Amino Acids in Protein Buffer Systems

The Hemoglobin Buffer System
- CO₂ diffuses across RBC membrane: no transport mechanism required
- As carbonic acid dissociates: bicarbonate ions diffuse into plasma
- in exchange for chloride ions (chloride shift)
- Hydrogen ions are buffered by hemoglobin molecules
- the only intracellular buffer system with an immediate effect on ECF pH
- Helps prevent major changes in pH when plasma $P_{CO_2}$ is rising or falling

The Carbonic Acid–Bicarbonate Buffer System
- Formed by carbonic acid and its dissociation products
- Prevents changes in pH caused by organic acids and fixed acids in ECF
- H⁺ generated by acid production combines with bicarbonate in the plasma
- This forms carbonic acid, which dissociates into CO₂ which is breathed out

Limitations of the Carbonic Acid Buffer System
1. Cannot protect ECF from changes in pH that result from elevated or depressed levels of CO₂ (because CO₂ is part of it)
2. Functions only when respiratory system and respiratory control centers are working normally
3. Ability to buffer acids is limited by availability of bicarbonate ions

The Phosphate Buffer System
- Consists of anion $H_2PO_4^-$ (a weak acid)
- Works like the carbonic acid–bicarbonate buffer system
- Is important in buffering pH of ICF
### Problems with Buffer Systems
- Provide only temporary solution to acid–base imbalance
- Do not eliminate H⁺ ions
- Supply of buffer molecules is limited

### Maintenance of Acid–Base Balance
- Requires balancing H⁺ gains and losses
- For homeostasis to be preserved, captured H⁺ must either be:
  - permanently tied up in water molecules through CO₂ removal at lungs OR
  - removed from body fluids through secretion at kidney
- Thus, problems with either of these organs cause problems with acid/base balance
- Coordinates actions of buffer systems with:
  - respiratory mechanisms
  - renal mechanisms

### Respiratory Compensation
- Is a change in respiratory rate that helps stabilize pH of ECF
- Occurs whenever body pH moves outside normal limits
- Directly affects carbonic acid–bicarbonate buffer system

### Respiratory Compensation
\[ \text{H}_2\text{CO}_3 \text{ (acid)} \leftrightarrow \text{H}^+ + \text{HCO}_3^- \text{ (base)} \]
- Increasing or decreasing the rate of respiration alters pH by lowering or raising the P\(_{\text{CO}_2}\)
  - When P\(_{\text{CO}_2}\) rises, pH falls as addition of CO₂ drives buffer system to the right (adding H⁺)
  - When P\(_{\text{CO}_2}\) falls, pH rises as removal of CO₂ drives buffer system to the left (removing H⁺)

### Renal Mechanisms
Support buffer systems by:
1. secreting or absorbing H⁺ or HCO₃⁻
2. controlling excretion of acids and bases
3. generating additional buffers

### Renal Compensation
- Is a change in rates of H⁺ and HCO₃⁻ secretion or reabsorption by kidneys in response to changes in plasma pH
- Kidneys assist lungs by eliminating any CO₂ that enters renal tubules during filtration or that diffuses into tubular fluid en route to renal pelvis
- Hydrogen ions are secreted into tubular fluid along:
  - proximal convoluted tubule (PCT)
  - distal convoluted tubule (DCT)
  - collecting system
Buffers in Urine

- The ability to eliminate large numbers of H+ in a normal volume of urine depends on the presence of buffers in urine (without them, we’d need to dilute the H+ with like 1000x more water)
  1. Carbonic acid–bicarbonate buffer system
  2. Phosphate buffer system
    (these two provided by filtration)
  3. Ammonia buffer system:
    - Tubular deamination creates NH₃, which diffuses into the tubule and buffers H+ by grabbing it and becoming NH₄⁺
    - Bicarbonate is reabsorbed along with Na⁺

Kidney Tubules and pH Regulation - Buffers

Kidney Tubules and pH Regulation -

Renal Responses to Acidosis

1. Secretion of H⁺
2. Activity of buffers in tubular fluid
3. Removal of CO₂
4. Reabsorption of NaHCO₃

Renal Responses to Alkalosis

1. Rate of H⁺ secretion at kidneys declines
2. Tubule cells do not reclaim bicarbonates in tubular fluid
3. Collecting system actually transports HCO₃⁻ out into tubular fluid while releasing strong acid (HCl) into peritubular fluid
Kidney Tubules and pH Regulation

Regulation of Plasma pH - Alkalosis

Conditions Affecting Acid–Base Balance

1. Disorders affecting:
   - circulating buffers
   - respiratory performance
   - renal function
2. Cardiovascular conditions:
   - heart failure
   - hypotension
3. Conditions affecting the CNS:
   - neural damage or disease that affects respiratory and cardiovascular reflexes

Disturbances of Acid–Base Balance

• Acute phase:
  - the initial phase in which pH moves rapidly out of normal range
• Compensated phase:
  - when condition persists, physiological adjustments occur

Types of Disorders

• Respiratory Acid–Base Disorders
  - Result from imbalance between CO₂ generation in peripheral tissues and CO₂ excretion at lungs
  - Cause abnormal CO₂ levels in ECF
• Metabolic Acid–Base Disorders
  - Result from one of two things:
    • generation of organic or fixed acids
    • conditions affecting HCO₃⁻ concentration in ECF

Respiratory Acidosis

• Most common acid/base problem
• Develops when the respiratory system cannot eliminate all CO₂ generated by peripheral tissues
• Primary sign:
  - low plasma pH due to hypercapnia
• Primarily caused by hypoventilation
• Acute: cardiac arrest, drowning
• Chronic/compensated: COPD, CHF
  - compensated by: increased respiratory rate, buffering by non-carbonic acid buffers, increased H+ secretion
Respiratory Acid–Base Regulation

**Respiratory Alkalosis**
- Least clinically relevant
- Primary sign:
  - high plasma pH due to hypocapnia
- Primarily caused by hyperventilation
- Caused by: stress/panic, high altitude hyperventilation
- Loss of consciousness often resolves or breathing into a bag to increase PCO₂
- Only acute, rarely compensated

**Respiratory Acid–Base Regulation**

**Metabolic Acidosis**
- Caused by:
  - Production of large numbers of fixed or organic acids, H+ overloads buffer system
  - **Lactic acidosis**:
    - produced by anaerobic cellular respiration
    - Also a complication of hypoxia caused by respiratory acidosis (tissue switched to anaerobic)
  - **Ketoacidosis**:
    - produced by excess ketone bodies (starvation, untreated diabetes)
    - Impaired H+ excretion at kidneys
      - Caused by kidney damage, overuse of diuretics that stop Na+ at the expense of H+ secretion
    - Severe bicarbonate loss (diarrhea – loss of bicarbonate from pancreas, liver that should have been reabsorbed)

**Metabolic Acidosis**
- Second most common acid/base problem
- Respiratory and metabolic acidosis are typically linked:
  - low O₂ generates lactic acid
  - hypoventilation leads to low PO₂
- Compensated by:
  - Respiratory: increased RR (eliminate CO₂)
  - Renal: secrete H+, reabsorb and generate HCO₃⁻
Metabolic Alkalosis

- Caused by elevated HCO₃⁻ concentrations
- Bicarbonate ions interact with H⁺ in solution forming H₂CO₃
- Reduced H⁺ causes alkalosis
- Causes:
  - Alkaline tide: gastric HCl generation after a meal (temporary)
  - Vomiting: greatly increased HCl generation due to loss in vomit
- Compensation:
  - Respiratory: reduced RR
  - Increased HCO₃⁻ loss at kidney, Retention of HCl

Detection of Acidosis and Alkalosis

- Includes blood tests for pH, P_CO₂ and HCO₃⁻ levels:
  - recognition of acidosis or alkalosis
  - classification as respiratory or metabolic

Diseases

- Kidney Damage: can cause increase in glomerular permeability, plasma proteins enter capsular space. Causes:
  - Proteinuria
  - Decrease (BCOP), increase CsCOP (result?)
- Blocked urine flow (kidney stone, etc.)
  - CsHP rises (effect?)
- Nephritis (inflammation)
  - Causes swelling, also increases CsHP
Diuretics

- Caffeine: reduces sodium reabsorption
- Alcohol: blocks ADH release at post. pot.
- Mannitol: adds osmotic particle that must be eliminated with water
- Loop diuretics: inhibit ion transport in Loop of Henle, short circuit conc grad in medulla
- Aldosterone blockers e.g. spironolactone (can cause acidosis)

Dialysis

- In chronic renal failure, kidney function can be replaced by filtering the blood through a machine outside of the body.
- Blood leaves through a catheter, runs through a column with dialysis fluid it, exchange occurs with wastes diffusing out (concentration of urea, creatinine, uric acid, phosphate, sulfate in fluid is zero)

Ion Imbalances

- Hyponatremia: nausea, lethargy, and apathy, cerebral edema
- Hypernatremia: neurological damage due to shrinkage of brain cells, confusion, coma
- Hypokalemia: fibrillation, nervous symptoms such as tingling of the skin, numbness of the hands or feet, weakness
- Hyperkalemia: cardiac arrhythmia, muscle pain, general discomfort or irritability, weakness, and paralysis
- Hypocalcemia: brittle bones, parathesias, tetany
- Hypercalcaemia: heart arrhythmias, kidney stones