Chapter 26
Electrolyte & Acid-Base Balance

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figures from Marieb & Hoehn 9th ed.

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Major fluid compartments of the body

Total body water
Volume = 40 L
60% of body weight

Intracellular fluid (ICF)
Volume = 25 L
40% of body weight

Interstitial fluid (IF)
Volume = 12 L
80% of ECF

Extracellular fluid (ECF)
Volume = 15 L
20% of body weight

Plasma
Volume = 3 L, 20% of ECF
Types of Solutes

• Non-electrolytes
  – Not charged. Glucose, lipids, creatinine, urea

• Electrolytes
  – Dissociate into ions in water; e.g., inorganic salts, all acids and bases, some proteins
    • Ions conduct electrical current
  – 1 M salt (NaCl) = 2 M dissolved particles, hence enhanced osmotic “power” to cause fluid shifts compared to 1M glucose or other non-electrolyte
Electrolyte Concentration

Often expressed in “milli-equivalents per liter”
= “millimoles of charge” per liter = mEq/L
= (mmol/L) x (charges per particle)
Examples:
1 mmol/L Na⁺ = 1 mEq/L
1 mmol/L Ca²⁺ = 2 mEq/L
Extracellular and Intracellular Fluids

- Each fluid compartment has distinctive pattern of electrolytes
- ECF
  - All similar
    - Major cation: $\text{Na}^+$
    - Major anion: $\text{Cl}^-$
  - Except: higher protein, lower $\text{Cl}^-$ content of plasma
Normal saline = 0.9% NaCl = 9 g NaCl in 1 L
MW(NaCl)=58.5
(9 g/L)/(58.5 g/mole) = 0.15 mole/L = 150 mM/L
D5W = 5% dextrose in water = 278 mM/L
Extracellular and Intracellular Fluids

- ICF:
  - Low Na\(^+\) and Cl\(^-\)
  - Major cation: K\(^+\)
  - Major anion HPO\(_4\)\(^{2-}\)
  - More soluble proteins than in plasma
Extracellular and Intracellular Fluids

• Electrolytes most abundant solutes in body fluids; determine most chemical and physical reactions

• Bulk of dissolved solutes are proteins, phospholipids, cholesterol, and triglycerides
  – 90% in plasma
  – 60% in IF
  – 97% in ICF
Electrolyte composition of blood plasma, interstitial fluid, and intracellular fluid.

- Blood plasma
- Interstitial fluid
- Intracellular fluid

- **Na⁺** (Sodium)
- **K⁺** (Potassium)
- **Ca²⁺** (Calcium)
- **Mg²⁺** (Magnesium)
- **HCO₃⁻** (Bicarbonate)
- **Cl⁻** (Chloride)
- **HPO₄^{2-}** (Hydrogen phosphate)
- **SO₄^{2-}** (Sulfate)

**Total solute concentration (mEq/L):**
- 160
- 140
- 120
- 100
- 80
- 60
- 40
- 20
- 0
Fluid Movement Among Compartments

- Osmotic and hydrostatic pressures regulate continuous exchange and mixing of fluids
  - Water moves freely along osmotic gradients
  - All body fluid osmolality almost always equal
  - Change in solute concentration of any compartment leads to net water flow
    - ↑ ECF osmolality → water leaves cell
    - ↓ ECF osmolality → water enters cell
Fluid Movement Among Compartments

• Between plasma and IF across capillary walls
  – Fluid leaks from arteriolar end of capillary, reabsorbed at venule end; lymphatics pick up remaining and return to blood
• Between IF and ICF across cell membrane
  – Two-way osmotic flow of water
  – Ions move selectively; nutrients, wastes, gases unidirectional
Figure 26.3  Exchange of gases, nutrients, water, and wastes between the three fluid compartments of the body.

- **Lungs**
  - Oxygen ($O_2$)
  - Carbon dioxide ($CO_2$)

- **Gastrointestinal tract**
  - Nutrients
  - Water ($H_2O$)
  - Ions

- **Kidneys**
  - Water ($H_2O$)
  - Nitrogenous wastes

- **Blood plasma**
  - Oxygen ($O_2$)
  - Carbon dioxide ($CO_2$)
  - Nutrients
  - Water ($H_2O$)
  - Ions

- **Interstitial fluid**
  - Oxygen ($O_2$)
  - Carbon dioxide ($CO_2$)
  - Nutrients
  - Water ($H_2O$)
  - Ions

- **Intracellular fluid in tissue cells**
  - Nitrogenous wastes
Water Balance and ECF Osmolality

• Water intake must = water output = ~ 2500 ml/day
• Water intake: beverages, food, and metabolic water
• Water output: urine (60%), insensible water loss (lost through skin and lungs), perspiration, and feces
Figure 26.4  Major sources of water intake and output.

- **Metabolism**: 10%
- **Foods**: 30%
- **Beverages**: 60%
- **Feces**: 4%
- **Sweat**: 8%
- **Insensible loss via skin and lungs**: 28%
- **Urine**: 60%

**Average intake per day**: 250 ml
**Average output per day**: 100 ml
Maintenance of Body fluid Osmolality

- Osmolality maintained at ~ 280 – 300 mOsm
- Rise in osmolality →
  - Stimulates thirst
  - ADH release
- Decrease in osmolality →
  - Thirst inhibition
  - ADH inhibition
Regulation of Water Intake

• Thirst mechanism driving force for water intake
• Governed by hypothalamic thirst center
  – Hypothalamic osmoreceptors detect ECF osmolality; activated by
  • ↑ Plasma osmolality of 1 – 2%
  • Dry mouth
  • Decreased blood volume or pressure
  • Angiotensin II or baroreceptor input
Regulation of Water Intake

- Drinking of water inhibits the thirst center
- Inhibitory feedback signals include
  - Relief of dry mouth
  - Activation of stomach and intestinal stretch receptors
Figure 26.5 The thirst mechanism for regulating water intake.

- **↑ ECF osmolality**: Osmoreceptors in hypothalamus
  - ↓ Saliva
  - Dry mouth
  - Hypothalamic thirst center
  - Sensation of thirst; person takes a drink
  - Water moistens mouth, throat; stretches stomach, intestine
  - Water absorbed from GI tract
  - ↓ ECF osmolality
  - ↓ Plasma volume (5–10%)

  - ↓ Blood pressure
  - Granular cells in kidney
  - Renin-angiotensin-aldosterone mechanism
  - ↑ Angiotensin II

- **Physiological response**
  - Initial stimulus
  - Result

- **Result**
  - Increases, stimulates
  - Reduces, inhibits
Regulation of Water Output

• **Obligatory water losses**
  – Insensible water loss from lungs and skin
  – Feces
  – Minimum daily sensible water loss of 500 ml in urine to excrete wastes

• **Solute concentration and volume of urine**
a function of fluid intake, diet, and water loss via other avenues
Regulation of Water Output: Influence of ADH

• Water reabsorption in collecting ducts proportional to ADH release
• ↓ ADH → dilute urine and ↓ volume of body fluids
• ↑ ADH → concentrated urine; reabsorption of water → ↑ volume of body fluids
• Hypothalamic osmoreceptors sense ECF solute concentration and regulate ADH accordingly
Regulation of Water Output: Influence of ADH

• Other factors may trigger ADH release
  – Large changes in blood volume or pressure
    • E.g., ↓ BP → ↑ ADH release due to blood vessel baroreceptors and renin-angiotensin-aldosterone mechanism
    • Factors lowering blood volume: intense sweating, vomiting, or diarrhea; severe blood loss; traumatic burns; and prolonged fever
Figure 26.6 Mechanisms and consequences of ADH release.

- **ECF osmolality**
- **Na⁺ concentration in plasma**

Stimulates:

- Osmoreceptors in hypothalamus

Inhibits:

- Baroreceptors in atria and large vessels

Stimulates:

- Posterior pituitary

Releases Antidiuretic hormone (ADH)

Targets:

- Collecting ducts of kidneys

Effects:

- Water reabsorption

Results in:

- ECF osmolality
- Plasma volume

Scant urine
Disorders of Water Balance

• Principal abnormalities of water balance
  – Dehydration
  – Hypotonic hydration
  – Edema
Disorders of Water Balance: Dehydration

- Negative fluid balance
  - ECF water loss due to: hemorrhage, severe burns, prolonged vomiting or diarrhea, profuse sweating, water deprivation, diuretic abuse, endocrine disturbances
  - Signs and symptoms: "cottony" oral mucosa, thirst, dry flushed skin, oliguria
  - May lead to weight loss, fever, mental confusion, hypovolemic shock, and loss of electrolytes
Consequences of dehydration. If more water than solutes is lost, cells shrink.
Disorders of Water Balance: Hypotonic Hydration

- Cellular overhydration, or water intoxication
- Occurs with renal insufficiency or rapid excess water ingestion
- ECF osmolality ↓ → hyponatremia → net osmosis into tissue cells → swelling of cells → severe metabolic disturbances (nausea, vomiting, muscular cramping, cerebral edema) → possible death
- Treated with hypertonic saline
(b) **Consequences of hypotonic hydration (water gain).**
If more water than solutes is gained, cells swell.
Disorders of Water Balance: Edema

• Atypical accumulation of IF → tissue swelling (not cell swelling)
• Result of ↑ fluid out of blood or ↓ fluid into blood
• ↑ fluid out of blood caused by
  – Increased capillary hydrostatic pressure or permeability
    • Capillary hydrostatic pressure increased by incompetent venous valves, localized blood vessel blockage, congestive heart failure, ↑ blood volume
    • Capillary permeability increased by ongoing inflammatory response
Edema

• ↓ fluid returning to blood result of
  – Imbalance in colloid osmotic pressures, e.g., hypoproteinemia (↓ plasma protein levels → low colloid osmotic pressure)
    • Fluids fail to return at venous ends of capillary beds
    • Results from protein malnutrition, liver disease, or glomerulonephritis
Edema

- Also caused by blocked (or surgically removed) lymphatic vessels
  - Cause leaked proteins to accumulate in IF
  - ↑Colloid osmotic pressure of IF draws fluid from blood
- Increases diffusion distance for nutrients and oxygen
- Results in low blood pressure and severely impaired circulation
Electrolyte Balance

• Electrolytes are salts, acids, bases, some proteins

• **Electrolyte balance** usually refers only to salt balance

• Salts control fluid movements; provide minerals for excitability, secretory activity, membrane permeability

• Salts enter body by ingestion and metabolism; lost via perspiration, feces, urine, vomit
Central Role of Sodium

- Most abundant cation in ECF
  - Sodium salts in ECF contribute 280 mOsm of total 300 mOsm ECF solute concentration
- Only cation exerting significant osmotic pressure
  - Controls ECF volume and water distribution
  - Changes in Na\(^+\) levels affects plasma volume, blood pressure, and ECF and IF volumes
Central Role of Sodium

• Na\(^+\) leaks into cells; pumped out against its electrochemical gradient
• Na\(^+\) moves back and forth between ECF and body secretions (e.g., digestive secretions)
• Renal acid-base control mechanisms are coupled to sodium ion transport
Sodium Concentration Versus Sodium Content

• Concentration of $\text{Na}^+$
  – Determines osmolality of ECF; influences excitability of neurons and muscles
  – Remains stable due to water shifts out of or into ICF

• Content of $\text{Na}^+$
  – Total body content determines ECF volume and therefore blood pressure
Table 26.2 Sodium Concentration and Sodium Content

<table>
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*ADH and thirst are also required to maintain blood volume and for long-term control of blood pressure.
Regulation of Sodium Balance

• No known receptors that monitor Na⁺ levels in body fluids
• Na⁺-water balance is linked to blood pressure and blood volume control mechanisms
• Changes in blood pressure or volume trigger neural and hormonal controls to regulate Na⁺ content
Regulation of Sodium Balance: Aldosterone

- Regardless of aldosterone presence
  - 65% $\text{Na}^+$ reabsorbed in proximal tubules; 25% reclaimed in nephron loops
  - $\text{Na}^+$ never secreted into filtrate
- Water in filtrate follows $\text{Na}^+$ if ADH is present
  - $\uparrow \text{Na}^+$ in urine $\Rightarrow \uparrow$ water loss
Aldosterone

• **Aldosterone** → decreased urinary output; increased blood volume
  – By active reabsorption of remaining Na\(^+\) in distal convoluted tubule and collecting duct
• Also causes increased K\(^+\) secretion
Regulation of Sodium Balance: Aldosterone

- Renin-angiotensin-aldosterone mechanism main trigger for aldosterone release
  - Granular cells of JGC secrete renin in response to
    - Sympathetic nervous system stimulation
    - ↓ filtrate NaCl concentration
    - ↓ stretch (due to ↓ blood pressure) of granular cells
Regulation of Sodium Balance: Aldosterone

• Renin catalyzes production of **angiotensin II**
  – Prompts aldosterone release from adrenal cortex
  – $\uparrow \text{Na}^+$ reabsorption by kidney tubules
• Aldosterone release also triggered by elevated $\text{K}^+$ levels in ECF
• Aldosterone brings about its effects slowly (hours to days)
Figure 26.8  Mechanisms and consequences of aldosterone release.

- ↑K⁺ concentration in the ECF
- ↓Body Na⁺ content triggers renin release, increasing angiotensin II

- Stimulates
  - Adrenal cortex
    - Releases
      - Aldosterone
        - Targets
          - Kidney tubules
            - Effects
              - ↑Na⁺ reabsorption
              - ↑K⁺ secretion
              - Restores
                - Homeostatic plasma levels of Na⁺ and K⁺
Regulation of Sodium Balance: ANP

• Released by atrial cells in response to stretch (↑ blood pressure)

• Effects
  – Decreases blood pressure and blood volume
    • ↓ ADH, renin and aldosterone production
    • ↑ excretion of Na\(^+\) and water
  • Promotes vasodilation directly and also by decreasing production of angiotensin II
Figure 26.9 Mechanisms and consequences of ANP release.

- **Stretch of atria of heart due to ↑ BP**
  - Releases
  - **Atrial natriuretic peptide (ANP)**
    - Targets
      - **JG complex of the kidney**
        - **↓ Renin release**
          - **↓ Angiotensin II**
            - **Vasodilation**
          - **Collecting ducts of kidneys**
            - **↓ Na+ and H2O reabsorption**
              - **Results in ↓ Blood volume**
              - **Results in ↓ Blood pressure**
      - **Hypothalamus and posterior pituitary**
        - **↓ ADH release**
      - **Adrenal cortex**
        - **↓ Aldosterone release**
          - **Inhibits**

Negative feedback
Influence of other Hormones

• Female sex hormones
  – Estrogens: ↑ NaCl reabsorption (like aldosterone)
    • → H₂O retention during menstrual cycles and pregnancy
  – Progesterone: ↓ Na⁺ reabsorption (blocks aldosterone)
    • Promotes Na⁺ and H₂O loss
• Glucocorticoids: ↑ Na⁺ reabsorption and promote edema
Cardiovascular Baroreceptors

- **Systemic arterial pressure** rises →
- Nerve activity on baroreceptor afferent fibers increases →
- Activity on efferent sympathetic nerves, including renal sympathetic nerves, decreases →
- Afferent arterioles dilate →
- GFR increases →
- Na\(^{+}\) and water output increase →
- Blood volume decreases →
- **Systemic arterial pressure** falls
Mechanisms regulating sodium and water balance help maintain blood pressure homeostasis.
Regulation of Potassium Balance

• Importance of potassium
  – Affects RMP in neurons and muscle cells (especially cardiac muscle)
    • $\uparrow$ ECF [K$^+$] $\rightarrow$ ↓RMP $\rightarrow$ depolarization $\rightarrow$ reduced excitability
    • $\downarrow$ ECF [K$^+$] $\rightarrow$ hyperpolarization and nonresponsiveness
Regulation of Potassium Balance

- **Hyperkalemia** - too much $K^+$
- **Hypokalemia** - too little $K^+$
- Both disrupt cardiac electrical conduction in heart and can cause sudden cardiac death
Regulation of Potassium Balance

- $K^+$ part of body's buffer system
- $H^+$ shifts in and out of cells in opposite direction of $K^+$ to maintain cation balance, so
  - ECF $K^+$ levels rise with acidosis
  - ECF $K^+$ levels fall with alkalosis
    - Interferes with activity of excitable cells
Regulation of Potassium Balance

- K\(^+\) balance controlled in collecting ducts by regulating amount *secreted* into filtrate (unlike Na, which is never secreted)
- If [K\(^+\)] is high in ECF, more K\(^+\) is secreted
Influence of Plasma Potassium Concentration

• Most important factor affecting $K^+$ secretion is its concentration in ECF

• High $K^+$ diet $\rightarrow$ ↑ $K^+$ content of ECF $\rightarrow$ $K^+$ entry into principal cells $\rightarrow$ $K^+$ secretion

• Low $K^+$ diet or accelerated $K^+$ loss reduces its secretion
Regulation of Potassium Balance

• Second most important regulator of plasma [K\(^+\)] is aldosterone
  – Aldosterone-secreting cells of adrenal cortex are directly sensitive to plasma [K\(^+\)]: they secrete more aldosterone if plasma [K] is high
  – Aldosterone stimulates K\(^+\) secretion (and Na\(^+\) reabsorption) by principal cells of collecting duct, i.e. aldo causes body to lose K in urine

• Abnormal aldosterone levels severely influence K\(^+\) levels
Regulation of Calcium

• 99% of body's calcium in bones
  – Calcium phosphate salts

• Ca$^{2+}$ in ECF important for
  – Blood clotting
  – Cell membrane permeability
  – Secretory activities
  – Neuromuscular excitability - most important
Regulation of Calcium

- **Hypocalcemia** → ↑ excitability and muscle tetany
- **Hypercalcemia** → inhibits neurons and muscle cells, may cause heart arrhythmias
- Calcium balance controlled by parathyroid hormone (PTH) from parathyroid gland
  - Rarely deviates from normal limits
Influence of PTH

• PTH promotes increase in calcium levels by targeting
  – Bones – osteoclasts break down matrix, releasing calcium and phosphate to blood
  – Kidneys – increases calcium reabsorption; decreases phosphate ion reabsorption
  – Small intestine – increases calcium absorption (indirectly through stimulation of kidney to activate vitamin D precursor)
A 45-year-old man was admitted to the hospital with a 6-month history of anorexia, fatigue, and thirst. Approximately 10 years earlier, he had been treated for urinary calculi. Laboratory evaluation showed a serum calcium level of 14.7 mg per deciliter (3.7 mmol per liter; normal range, 8.0 to 10.4 mg per deciliter [2.0 to 2.6 mmol per liter]) and a serum intact parathyroid hormone level of 3844.0 pg per milliliter (normal range, 10.3 to 65.9). Ultrasonography of the neck revealed a 2.2-cm solid mass posterior to the inferior aspect of the left lobe of the thyroid. Technetium-99m–labeled sestamibi scintigraphy showed abnormal uptake in the left parathyroid gland, corresponding in location to the ultrasonographic finding. Radiographs of the hand showed multiple sites of subperiosteal resorption involving the phalanges (arrowheads) and tuftal resorption (asterisks). The patient underwent surgical resection of the neck mass, and histopathological analysis confirmed the suspected diagnosis of primary hyperparathyroidism caused by parathyroid adenoma. After surgical resection, the parathyroid hormone levels quickly returned to normal. Multifocal subperiosteal bone resorption, which is generally considered to be specific for hyperparathyroidism, is not commonly seen today because of earlier diagnosis. Severe hungry bone syndrome developed postoperatively in this patient, requiring high doses of oral and intravenous calcium with 1,25-dihydroxyvitamin D for approximately 4 months to maintain calcium levels.
Figure 16.13 Effects of parathyroid hormone on bone, the kidneys, and the intestine.

- **Hypocalcemia** (low blood Ca^{2+})
  - ↑PTH release from parathyroid gland
    - ↑Osteoclast activity in bone causes Ca^{2+} and PO_{4}^{3-} release into blood
    - ↑Ca^{2+} reabsorption in kidney tubule
    - ↑Activation of vitamin D by kidney
      - ↑Ca^{2+} absorption from food in small intestine
  - ↑Ca^{2+} in blood

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Regulation of Anions

• Cl$^-$ is major anion in ECF
  – Helps maintain osmotic pressure of blood
  – 99% of Cl$^-$ is reabsorbed under normal pH conditions

• When acidosis occurs, fewer chloride ions are reabsorbed

• Other anions have transport maximums and excesses are excreted in urine
Acid-base Balance

• pH affects all functional proteins and biochemical reactions, so closely regulated

• Normal pH of body fluids
  – Arterial blood: pH 7.4
  – Venous blood and IF fluid: pH 7.35
  – ICF: pH 7.0

• **Alkalosis** or alkalemia: arterial pH >7.45
• **Acidosis** or acidemia: arterial pH <7.35
Acid-base Balance

• Most $H^+$ produced by metabolism
  – Phosphorus-containing protein breakdown releases *phosphoric acid* into ECF
  – *Lactic acid* from anaerobic respiration of glucose
  – *Fatty acids and ketone bodies* from fat metabolism
  – $H^+$ liberated when $CO_2$ converted to $HCO_3^-$ in blood
Acid-base Balance

• Concentration of hydrogen ions regulated sequentially by
  – Chemical buffer systems: rapid; first line of defense
  – Brain stem respiratory centers: act within 1–3 min
  – Renal mechanisms: most potent, but require hours to days to effect pH changes
Acid-base Balance: Chemical Buffer Systems

- Strong acids dissociate completely in water; can dramatically affect pH
- Weak acids dissociate partially in water; are efficient at preventing pH changes
- Strong bases dissociate easily in water; quickly tie up $H^+$
- Weak bases accept $H^+$ more slowly
A strong acid such as HCl dissociates completely into its ions.

A weak acid such as H$_2$CO$_3$ does not dissociate completely.
Chemical Buffer Systems

• Chemical buffer: system of one or more compounds that act to resist pH changes when strong acid or base is added
  – Bind $H^+$ if pH drops; release $H^+$ if pH rises

1. Bicarbonate buffer system
2. Phosphate buffer system
3. Protein buffer system
Bicarbonate Buffer System

• Mixture of H$_2$CO$_3$ (weak acid) and salts of HCO$_3^-$ (e.g., NaHCO$_3$, a weak base)
• Buffers ICF and ECF
• Bicarbonate buffer system is the *only* important ECF buffer
Bicarbonate Buffer System

• If strong acid added:
  – $\text{HCO}_3^-$ binds to $\text{H}^+$ and forms $\text{H}_2\text{CO}_3$
    • $\text{HCl} + \text{NaHCO}_3 \rightarrow \text{H}_2\text{CO}_3 + \text{NaCl}$
  – pH decreases only slightly, unless all available $\text{HCO}_3^-$ (alkaline reserve) used up
  – $\text{HCO}_3^-$ concentration closely regulated by kidneys
Bicarbonate Buffer System

• If strong base is added
  – It causes $\text{H}_2\text{CO}_3$ to dissociate and donate $\text{H}^+$
  – $\text{H}^+$ binds to the base (e.g. $\text{OH}^-$)
    • $\text{NaOH} + \text{H}_2\text{CO}_3 \rightarrow \text{NaHCO}_3 + \text{H}_2\text{O}$
  – pH rises only slightly
  – $\text{H}_2\text{CO}_3$ supply is almost limitless (from CO$_2$ released by respiration) and is subject to respiratory control
Phosphate Buffer System

- Action nearly identical to bicarbonate buffer
- Components are sodium salts of:
  - Dihydrogen phosphate ($\text{H}_2\text{PO}_4^-$), a weak acid
  - Monohydrogen phosphate ($\text{HPO}_4^{2-}$), a weak base
- Unimportant in buffering plasma
- Effective buffer in urine and ICF, where phosphate concentrations are high
Protein Buffer System

- Intracellular proteins are most plentiful and powerful buffers; plasma proteins also important
- Protein molecules are amphoteric (can function as both weak acid and weak base)
  - When pH rises, organic acid or carboxyl (COOH) groups release $H^+$
  - When pH falls, NH$_2$ groups bind $H^+$
- Hemoglobin functions as intracellular buffer
Physiological Buffering Systems

- Respiratory and renal systems
  - Regulate amount of acid or base in body
  - Act more slowly than chemical buffer systems
  - Have more capacity than chemical buffer systems
Acid-Base Balance

• Chemical buffers cannot eliminate excess acids or bases from body
  – Lungs eliminate volatile carbonic acid by eliminating CO₂
  – Kidneys eliminate nonvolatile (fixed) acids produced by cellular metabolism (phosphoric, uric, and lactic acids and ketones) to prevent metabolic acidosis
  – Kidneys also regulate blood levels of alkaline substances; renew chemical buffers
Respiratory Regulation of H⁺

- Respiratory system eliminates CO₂ (an acid)
- A reversible equilibrium exists in blood
  - CO₂ + H₂O ⇌ H₂CO₃ ⇌ H⁺ + HCO₃⁻
- During CO₂ unloading reaction shifts to left (and H⁺ incorporated into H₂O)
- During CO₂ loading reaction shifts to right (and H⁺ buffered by proteins)
Respiratory Regulation of H⁺

• **Hypercapnia** (high plasma \([\text{CO}_2]\)) activates “central” (brain) chemoreceptors
  – → Increased respiratory rate and depth

• Rising plasma \([\text{H}^+]\) activates peripheral chemoreceptors
  – → Increased respiratory rate and depth
  – Which causes more exhalation of \(\text{CO}_2\)
  – Which causes plasma \([\text{H}^+]\) to fall

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-
\]
Respiratory Regulation of H⁺

• Alkalosis depresses respiratory center
  – Respiratory rate and depth decrease
  – H⁺ concentration increases

• Respiratory system impairment causes acid-base imbalances
  – Hypoventilation $\rightarrow$ respiratory acidosis
  – Hyperventilation $\rightarrow$ respiratory alkalosis
Renal Mechanisms of Acid-Base Balance

• Most important renal mechanisms are
  – Conserving (reabsorbing) or generating new HCO$_3^-$
  – Excreting HCO$_3^-$

• Generating or reabsorbing one HCO$_3^-$ is equivalent to losing one H$^+$

• Excreting one HCO$_3^-$ is equivalent to gaining one H$^+$
Renal Mechanisms of Acid-Base Balance

• In a sense, bicarbonate ($\text{HCO}_3^-$) comes from splitting of carbonic acid, so the $\text{H}^+$ that gets made in the process must be dealt with.

• When kidney reabsorb bicarbonate, it secretes $\text{H}^+$

• When kidney excretes excess bicarbonate, it retains $\text{H}^+$
Renal Mechanisms of Acid-base Balance

• Renal regulation of acid-base balance depends on kidney's ability to secrete H⁺
• H⁺ is actively secreted and is exchanged with Na⁺ at apical membrane of PCT cells, see figure.
Figure 26.12 Reabsorption of filtered HCO_3^- is coupled to H^+ secretion.

1. CO_2 combines with water within the tubule cell, forming H_2CO_3.
2. H_2CO_3 is quickly split, forming H^+ and bicarbonate ion (HCO_3^-).
3a. H^+ is secreted into the filtrate.
3b. For each H^+ secreted, a HCO_3^- enters the peritubular capillary blood either via symport with Na^+ or via antiport with Cl^-.
4. Secreted H^+ combines with HCO_3^- in the filtrate, forming carbonic acid (H_2CO_3). HCO_3^- disappears from the filtrate at the same rate that HCO_3^- (formed within the tubule cell) enters the peritubular capillary blood.
5. The H_2CO_3 formed in the filtrate dissociates to release CO_2 and H_2O.
6. CO_2 diffuses into the tubule cell, where it triggers further H^+ secretion.
Renal Mechanisms of Acid-base Balance

• Rate of $H^+$ secretion changes with ECF CO$_2$ levels
  – $\uparrow$ CO$_2$ in peritubular capillary blood $\rightarrow$ $\uparrow$ rate of $H^+$ secretion
  – System responds to both rising and falling $H^+$ concentrations
Go to ch26_acid_base_analysis.ppt
Abnormalities of Acid-Base Balance

• All classed as respiratory or metabolic
  – **Respiratory acidosis and alkalosis**
    • Caused by failure of respiratory system to perform pH-balancing role
    • Single most important indicator is blood $P_{CO_2}$
  – **Metabolic acidosis and alkalosis**
    • All abnormalities other than those caused by $P_{CO_2}$ levels in blood; indicated by abnormal $HCO_3^-$ levels
Respiratory Acidosis and Alkalosis

• Most important indicator of adequacy of respiratory function is $P_{CO_2}$ level (normally 35–45 mm Hg)
  
  $P_{CO_2}$ above 45 mm Hg → respiratory acidosis
  
  • Common cause of acid-base imbalances
  • Due to decrease in ventilation or gas exchange
  • $CO_2$ accumulates in blood
  • Characterized by falling blood pH and rising $P_{CO_2}$
Respiratory Acidosis and Alkalosis

- $P_{CO_2}$ below 35 mm Hg $\rightarrow$ respiratory alkalosis
  - Common result of hyperventilation often due to stress or pain
    - $CO_2$ eliminated faster than produced
Metabolic Acidosis and Alkalosis

- Metabolic acidosis – low blood pH and $\text{HCO}_3^-$
  - Causes
    - Ingestion of too much alcohol ($\rightarrow$ acetic acid)
    - Excessive loss of $\text{HCO}_3^-$ (e.g., persistent diarrhea)
    - Accumulation of lactic acid (exercise or shock), ketosis in diabetic crisis, starvation, and kidney failure
Metabolic Acidosis and Alkalosis

• Metabolic alkalosis much less common than metabolic acidosis
  – Indicated by rising blood pH and HCO$_3^-$
  – Causes include vomiting of acid contents of stomach or by intake of excess base (e.g., antacids)
Effects of Acidosis and Alkalosis

• Blood pH below 6.8 → depression of CNS → coma → death
• Blood pH above 7.8 → excitation of nervous system → muscle tetany, extreme nervousness, convulsions, death often from respiratory arrest
Respiratory and Renal Compensations

- If acid-base imbalance due to malfunction of physiological buffer system, other one tries to compensate
  - Respiratory system attempts to correct metabolic acid-base imbalances
  - Kidneys attempt to correct respiratory acid-base imbalances
Respiratory Compensation

• Changes in respiratory rate and depth
• In metabolic acidosis
  – High H^+ levels stimulate respiratory centers
  – Rate and depth of breathing elevated
  – Blood pH is below 7.35 and HCO_3^- level is low
  – As CO_2 eliminated by respiratory system, P_{CO_2} falls below normal
Respiratory Compensation

- Respiratory compensation for metabolic alkalosis revealed by:
  - Slow, shallow breathing, allowing CO\(_2\) accumulation in blood
  - High pH (over 7.45), elevated HCO\(_3^-\) levels, P\(_{CO_2}\) above 45 mm Hg
Renal Compensation for Respiratory Acid-Base Imbalance

• Hypoventilation causes elevated $P_{CO_2}$
  – Respiratory acidosis
  – Kidneys compensate by excreting more $H^+$ and retaining $HCO_3^-$ (bicarbonate ion). Indicated by above-normal value for plasma $HCO_3^-$. 

• Respiratory alkalosis: low $P_{CO_2}$, high pH
  – Kidneys compensate by retaining more $H^+$ and excreting more $HCO_3^-$. Indicated by below-normal value for plasma $HCO_3^-$. 

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Acid-base Imbalances

- Respiratory system cannot compensate for respiratory acidosis or alkalosis
- Renal system cannot compensate for acid-base imbalances caused by renal problems
Body Water Content: changes with age

- Infants: 73% or more water (low body fat, low bone mass)
- Adult males: ~60% water
- Adult females: ~50% water (higher fat content, less skeletal muscle mass)
  - Adipose tissue least hydrated of all
- Water content declines to ~45% in old age