Acid-Base Balance

Influence of Other Hormones on Sodium Balance

- Estrogens:
  - Enhance NaCl reabsorption by renal tubules
  - May cause water retention during menstrual cycles
  - Are responsible for edema during pregnancy
- Progesterone:
  - Decreases sodium reabsorption
  - Acts as a diuretic, promoting sodium and water loss
- Glucocorticoids – enhance reabsorption of sodium and promote edema

Regulation of Potassium Balance

- Relative ICF-ECF potassium ion concentration affects a cell's resting membrane potential
  - Excessive ECF potassium decreases membrane potential
  - Too little K^+ causes hyperpolarization and nonresponsiveness

Regulation of Potassium Balance

- Hyperkalemia and hypokalemia can:
  - Disrupt electrical conduction in the heart
  - Lead to sudden death
- Hydrogen ions shift in and out of cells
  - Leads to corresponding shifts in potassium in the opposite direction
  - Interferes with activity of excitable cells

Regulatory Site: Cortical Collecting Ducts

- Less than 15% of filtered K^+ is lost to urine regardless of need
- K^+ balance is controlled in the cortical collecting ducts by changing the amount of potassium secreted into filtrate
- Excessive K^+ is excreted over basal levels by cortical collecting ducts
- When K^+ levels are low, the amount of secretion and excretion is kept to a minimum
- Type A intercalated cells can reabsorb some K^+ left in the filtrate

Influence of Plasma Potassium Concentration

- High K^+ content of ECF favors principal cells to secrete K^+
- Low K^+ or accelerated K^+ loss depresses its secretion by the collecting ducts

Influence of Aldosterone

- Aldosterone stimulates potassium ion secretion by principal cells
- In cortical collecting ducts, for each Na^+ reabsorbed, a K^+ is secreted
- Increased K^+ in the ECF around the adrenal cortex causes:
  - Release of aldosterone
  - Potassium secretion
- Potassium controls its own ECF concentration via feedback regulation of aldosterone release

Regulation of Calcium

- Ionic calcium in ECF is important for:
  - Blood clotting
  - Cell membrane permeability
  - Secretory behavior
- Hypocalcemia:
  - Increases excitability
  - Causes muscle tetany

Regulation of Calcium

- Hypercalcemia:
  - Inhibits neurons and muscle cells
  - May cause heart arrhythmias
- Calcium balance is controlled by parathyroid hormone (PTH) and calcitonin

Regulation of Calcium and Phosphate

- PTH promotes increase in calcium levels by targeting:
  - Bones – PTH activates osteoclasts to break down bone matrix
  - Small intestine – PTH enhances intestinal absorption of calcium
  - Kidneys – PTH enhances calcium reabsorption and decreases phosphate reabsorption
- Calcium reabsorption and phosphate excretion go hand in hand

Regulation of Calcium and Phosphate

- Filtered phosphate is actively reabsorbed in the proximal tubules
- In the absence of PTH, phosphate reabsorption is regulated by its transport maximum and excesses are excreted in urine
- High or normal ECF calcium levels inhibit PTH secretion
  - Release of calcium from bone is inhibited
  - Larger amounts of calcium are lost in feces and urine
  - More phosphate is retained

Influence of Calcitonin

- Released in response to rising blood calcium levels
- Calcitonin is a PTH antagonist, but its contribution to calcium and phosphate homeostasis is minor to negligible

Regulation of Magnesium Balance

- Magnesium is the second most abundant intracellular cation
- Activates coenzymes needed for carbohydrate and protein metabolism
- Plays an essential role in neurotransmission, cardiac function, and neuromuscular activity
- There is a renal transport maximum for magnesium
- Control mechanisms are poorly understood

Regulation of Anions

- Chloride is the major anion accompanying sodium in the ECF
- 99% of chloride 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

- Normal pH of body fluids
  - Arterial blood is 7.4
  - Venous blood and interstitial fluid is 7.35
  - Intracellular fluid is 7.0
- Alkalosis or alkalemia – arterial blood pH rises above 7.45
- Acidosis or acidemia – arterial pH drops below 7.35 (physiological acidosis)

Sources of Hydrogen Ions

- Most hydrogen ions originate from cellular metabolism
  - Breakdown of phosphorus-containing proteins releases phosphoric acid into the ECF
  - Anaerobic respiration of glucose produces lactic acid
  - Fat metabolism yields organic acids and ketone bodies
  - Transporting carbon dioxide as bicarbonate releases hydrogen ions

Hydrogen Ion Regulation

- Concentration of hydrogen ions is regulated sequentially by:
  - Chemical buffer systems – act within seconds
  - The respiratory center in the brain stem – acts within 1–3 minutes
  - Renal mechanisms – require hours to days to effect pH changes

Chemical Buffer Systems

- Strong acids – all their H^+ is dissociated completely in water
- Weak acids – dissociate partially in water and are efficient at preventing pH changes
- Strong bases – dissociate easily in water and quickly tie up H^+
- Weak bases – accept H^+ more slowly (e.g., HCO_3^- and NH_3)

Chemical Buffer Systems

- One or two molecules that act to resist pH changes when strong acid or base is added
- Three major chemical buffer systems
  - Bicarbonate buffer system
  - Phosphate buffer system
  - Protein buffer system
- Any drifts in pH are resisted by the entire chemical buffering system

Bicarbonate Buffer System

- A mixture of carbonic acid (H_2CO_3) and its salt, sodium bicarbonate ($NaHCO_3$) (potassium or magnesium bicarbonates work as well)
- If strong acid is added:
  - Hydrogen ions released combine with the bicarbonate ions and form carbonic acid (a weak acid)
  - The pH of the solution decreases only slightly

Bicarbonate Buffer System

- If strong base is added:
  - It reacts with the carbonic acid to form sodium bicarbonate (a weak base)
  - The pH of the solution rises only slightly
- This system is the only important ECF buffer

Phosphate Buffer System

- Nearly identical to the bicarbonate system
- Its components are:
  - Sodium salts of dihydrogen phosphate ($H_2PO_4^-$), a weak acid
  - Monohydrogen phosphate (HPO_4^{2-}), a weak base
- This system is an effective buffer in urine and intracellular fluid

Protein Buffer System

- Plasma and intracellular proteins are the body's most plentiful and powerful buffers
- Some amino acids of proteins have:
  - Free organic acid groups (weak acids)
  - Groups that act as weak bases (e.g., amino groups)
- Amphoteric molecules are protein molecules that can function as both a weak acid and a weak base

Physiological Buffer Systems

- The respiratory system regulation of acid-base balance is a physiological buffering system
- There is a reversible equilibrium between:
  - Dissolved carbon dioxide and water
  - Carbonic acid and the hydrogen and bicarbonate ions

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

Physiological Buffer Systems

- During carbon dioxide unloading, hydrogen ions are incorporated into water
- When hypercapnia or rising plasma H^+ occurs:
  - Deeper and more rapid breathing expels more carbon dioxide
  - Hydrogen ion concentration is reduced
- Alkalosis causes slower, more shallow breathing, causing H^+ to increase
- Respiratory system impairment causes acid-base imbalance (respiratory acidosis or respiratory alkalosis)

Renal Mechanisms of Acid-Base Balance

- Chemical buffers can tie up excess acids or bases, but they cannot eliminate them from the body
- The lungs can eliminate carbonic acid by eliminating carbon dioxide
- Only the kidneys can rid the body of metabolic acids (phosphoric, uric, and lactic acids and ketones) and prevent metabolic acidosis
- The ultimate acid-base regulatory organs are the kidneys

Renal Mechanisms of Acid-Base Balance

- The most important renal mechanisms for regulating acid-base balance are:
  - Conserving (reabsorbing) or generating new bicarbonate ions
  - Excreting bicarbonate ions
- Losing a bicarbonate ion is the same as gaining a hydrogen ion; reabsorbing a bicarbonate ion is the same as losing a hydrogen ion

Renal Mechanisms of Acid-Base Balance

- Hydrogen ion secretion occurs in the PCT and in type A intercalated cells
- Hydrogen ions come from the dissociation of carbonic acid

Reabsorption of Bicarbonate

- Carbon dioxide combines with water in tubule cells, forming carbonic acid
- Carbonic acid splits into hydrogen ions and bicarbonate ions
- For each hydrogen ion secreted, a sodium ion and a bicarbonate ion are reabsorbed by the PCT cells
- Secreted hydrogen ions form carbonic acid; thus, bicarbonate disappears from filtrate at the same rate that it enters the peritubular capillary blood

Reabsorption of Bicarbonate

- Carbonic acid formed in filtrate dissociates to release carbon dioxide and water
- Carbon dioxide then diffuses into tubule cells, where it acts to trigger further hydrogen ion secretion

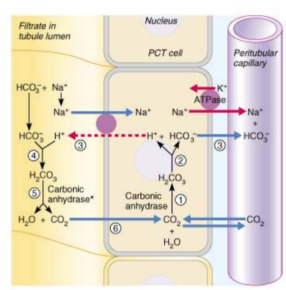

Figure 25.12

Generating New Bicarbonate Ions

- Two mechanisms carried out by type A intercalated cells generate new bicarbonate ions
- Both involve renal excretion of acid via secretion and excretion of hydrogen ions or ammonium ions (NH_4^+)

Generating New Bicarbonate Ions Using Hydrogen Ion Excretion

- Dietary hydrogen ions must be counteracted by generating new bicarbonate
- The excreted hydrogen ions must bind to buffers in the urine (phosphate buffer system)
- Intercalated cells actively secrete hydrogen ions into urine, which is buffered and excreted
- Bicarbonate generated is:
  - Moved into the interstitial space via a cotransport system
  - Passively moved into the peritubular capillary blood

Generating New Bicarbonate Ions Using Hydrogen Ion Excretion

- In response to acidosis:
  - Kidneys generate bicarbonate ions and add them to the blood
  - An equal amount of hydrogen ions are added to the urine

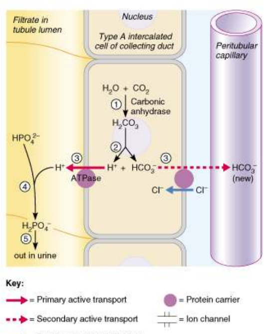

Figure 25.13

Generating New Bicarbonate Ions Using Ammonium Ion Excretion

- This method uses ammonium ions produced by the metabolism of glutamine in PCT cells
- Each glutamine metabolized produces two ammonium ions and two bicarbonate ions
- Bicarbonate moves to the blood and ammonium ions are excreted in urine

Generating New Bicarbonate Ions Using Ammonium Ion Excretion

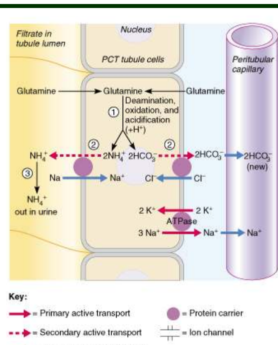

Figure 25.14

Bicarbonate Ion Secretion

- When the body is in alkalosis, type B intercalated cells:
  - Exhibit bicarbonate ion secretion
  - Reclaim hydrogen ions and acidify the blood
- The mechanism is the opposite of type A intercalated cells and the bicarbonate ion reabsorption process
- Even during alkalosis, the nephrons and collecting ducts excrete fewer bicarbonate ions than they conserve

Respiratory Acidosis and Alkalosis

- Result from failure of the respiratory system to balance pH
- P_{CO2} is the single most important indicator of respiratory inadequacy
- Normal P_{CO2}
  - Fluctuates between 35 and 45 mm Hg
  - Values above 45 mm Hg signal respiratory acidosis
  - Values below 35 mm Hg indicate respiratory alkalosis

Respiratory Aciodosis and Alkalosis

- Respiratory acidosis is the most common cause of acid-base imbalance
  - Occurs when a person breathes shallowly, or gas exchange is hampered by diseases such as pneumonia, cystic fibrosis, or emphysema
- Respiratory alkalosis is a common result of hyperventilation

Metabolic Acidosis

- All pH imbalances except those caused by abnormal blood carbon dioxide levels
- Metabolic acid-base imbalance – bicarbonate ion levels above or below normal (22–26 mEq/L)
- Metabolic acidosis is the second most common cause of acid-base imbalance
  - Typical causes are ingestion of too much alcohol and excessive loss of bicarbonate ions
  - Other causes include accumulation of lactic acid, shock, ketosis in diabetic crisis, starvation, and kidney failure

Metabolic Alkalosis

- Rising blood pH and bicarbonate levels indicate metabolic alkalosis
- Typical causes are:
  - Vomiting of the acid contents of the stomach
  - Intake of excess base (e.g., from antacids)
  - Constipation, in which excessive bicarbonate is reabsorbed

Respiratory and Renal Compensations

- Acid-base imbalance due to the inadequacy of a physiological buffer system is compensated for by the other system
  - The respiratory system will attempt to correct metabolic acid-base imbalances
  - The kidneys will work to correct imbalances caused by respiratory disease

Respiratory Compensation

- In metabolic acidosis:
  - The rate and depth of breathing are elevated
  - Blood pH is below 7.35 and bicarbonate level is low
  - As carbon dioxide is eliminated by the respiratory system, P_{CO2} falls below normal
- In respiratory acidosis, the respiratory rate is often depressed and is the immediate cause of the acidosis

Respiratory Compensation

- In metabolic alkalosis:
  - Compensation exhibits slow, shallow breathing, allowing carbon dioxide to accumulate in the blood
- Correction is revealed by:
  - High pH (over 7.45) and elevated bicarbonate ion levels
  - Rising P_{CO2}

Renal Compensation

- To correct respiratory acid-base imbalance, renal mechanisms are stepped up
- In acidosis
  - High P_{CO2} and high bicarbonate levels
    - The high P_{CO2} is the cause of acidosis
    - The high bicarbonate levels indicate the kidneys are retaining bicarbonate to offset the acidosis
- In alkalosis
  - Low P_{CO2} and high pH
    - The kidneys eliminate bicarbonate from the body by failing to reclaim it or by actively secreting it

Assessing Acid-Base Balance Using Blood Values

- Note the pH: this indicates if the person is in acidosis (pH<7.35) or alkalosis (pH>7.45), but it does not tell the cause
- Check the P_{CO2}: excessively high or low P_{CO2} indicate
  - Whether the condition is caused by the respiratory system
  - Whether the respiratory system is compensating
- Check the bicarbonate level: if the respiratory system is not the cause, it is a metabolic condition