Types of IV Solutions

Crystalloid Solutions

Isotonic Solutions	Action/Use	Nursing Considerations
Isotonic saline solution • 0.9% sodium chloride solution (Normal saline, NS, NaCl).	• Contains sodium chloride as the solute, dissolved in sterile water. • Increases vascular and extracellular fluid volumes. • Replaces sodium. • Causes no fluid shift.	• May cause hyperglycemia and/or osmotic diuresis. • May cause fluid overload and generalized edema. • Dilutes hemoglobin and lowers hematocrit levels. • May cause other electrolyte imbalances. • Inflammatory in high doses.
Balanced electrolyte solutions • Ringer's solution. • Lactated Ringer's solution (LR).	• Ringer's solution contains sodium chloride, potassium chloride, and calcium chloride dissolved in sterile water. • Lactated Ringer's solution contains sodium chloride, sodium lactate, potassium chloride, and calcium chloride dissolved in sterile water. • Lactate is metabolized by the liver to form bicarbonate. • Useful in treating metabolic acidosis.	• May cause fluid overload and generalized edema. • Dilutes hemoglobin and lowers hematocrit levels. • May cause other electrolyte imbalances. • Use with caution in clients with renal insufficiency, congestive heart failure, and in conditions in which potassium retention is present. • May be contraindicated in clients with hyperkalemia and hypernatremia. • Excessive administration of LR may result in metabolic alkalosis.

Continued

Types of IV Solutions—cont'd

Crystalloid Solutions		
Hypotonic Solutions	**Action/Use**	**Nursing Considerations**
Dextrose solutions • Dextrose 5% in water (D_5W). • Dextrose 5% in 0.225% saline solution (D_5 ¼ NS). • Dextrose 5% in 0.45% saline solution (D_5 ½ NS).	• Carbohydrate solution, using glucose as the solute. • Provides calories and free water. • Provides glucose for metabolism sparing muscle mass; hydrates cells. • Treats hyperkalemia via dilutional effect. • Promotes sodium diuresis. • Shifts fluid from intravascular space into intracellular and interstitial spaces.	• May cause fluid overload and/or water intoxication. • Isotonic when infused. • Quickly becomes hypotonic as dextrose is rapidly metabolized. • D_5W is often used as a mixing solution (diluent) for IV medications. • Check compatibility before adding medications to a dextrose solution. • May irritate veins. • May worsen hypotension. • May increase edema. • May cause hyponatremia.
Hypotonic saline solution • 0.225% saline solution (¼ NS). • 0.45% saline solution (½ NS).	• Hydrates cells. • Replaces fluids when sodium intake must be restricted. • Shifts fluid out of the intravascular space into the intracellular and interstitial spaces, causing cells to swell.	• May cause fluid overload. • May worsen hypotension because water moves out of the vascular space. • May increase edema because water moves into the cells and interstitial spaces. • May cause dilutional hyponatremia (see Chapter 3) because the sodium content is less than that of plasma.

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Continued

Types of IV Solutions—cont'd

Crystalloid Solutions

Hypertonic Solutions	Action/Use	Nursing Considerations
Dextrose solutions • Dextrose 5% in 0.9% sodium chloride solution (D_5NS). • Dextrose 5% in lactated Ringer's solution (D_5LR).	• Supplies fluid and calories to the body. • Decreases edema. • Replaces electrolytes. • Shifts fluid from intracellular compartment into intravascular space, expanding vascular volume.	• May cause fluid overload. • D_5NS may cause hypernatremia related to sodium content. • Hypertonic solutions may be irritating to veins. • Check compatibility before adding medications to a dextrose solution.
Hypertonic saline solutions • 3% sodium chloride solution (3% NaCl). • 5% sodium chloride solution (5% NaCl).	• Supplies sodium to the body; treats hyponatremia. • Decreases inflammation and increases capillary permeability. • Shifts fluid from intracellular compartment into intravascular space.	• May cause fluid overload. • May cause cells to shrink (cellular dehydration) as fluid is drawn out of the cell. • Hypertonic solutions may be irritating to veins. • May cause hypernatremia. • Use with extreme caution.

Continued

Types of IV Solutions—cont'd

Crystalloid Solutions		
Hypertonic Solutions	**Action/Use**	**Nursing Considerations**
Total parenteral nutrition (TPN) or partial parenteral nutrition (PPN) • Concentrated dextrose in water (20%, 40%, 50%, 60%, or 70%): added to amino acid solutions.	• Provides nutrition when client is unable to tolerate or absorb nutrients via the gastrointestinal system. • Customized based on the clients nutrient and electrolyte needs. • TPN provides all of the client's daily nutritional requirements but not the caloric requirements. • Best for short-term use.	• May cause fluid volume overload and electrolyte imbalances. • TPN is administered via central venous catheter; PPN is administered via peripheral IV catheter. • **Medication should never be added to a TPN/PPN solution.** • Catheter-related bacterial infection is the most common complication of TPN. • TPN/PPN should be administered using an infusion pump. • Usually administered to critically ill clients.

Continued

Types of IV Solutions—cont'd

Colloid Solutions

Types	Action/Use	Nursing Considerations
Albumin (human plasma protein) • 5% and 25% concentrations.	• Natural plasma protein prepared from donor plasma. • Maintains vascular volume by keeping fluid in intravascular space. • Replaces protein and treats shock and burns. • 25% concentration is used to treat hypoproteinemia. • Encourages movement of fluid from the interstitial space to the intravascular space. • Decreases "third-spacing."	• May cause fluid overload. • May cause pulmonary edema. • 5% albumin is equivalent to plasma protein; isotonic. • 25% albumin solution is equivalent to 500 mL of plasma or 2 units of whole blood. • 25% albumin solution must not be used in dehydrated clients without supplemental fluids. • **May cause anaphylaxis (observe for hives, fever, chills, and headache).**
Dextran (polysaccharide) • Low-molecular-weight dextran (Dextran 40). • High-molecular-weight dextran (Dextran 70).	• Synthetic colloid made of glucose polysaccharides. • Expands volume. • Mobilizes interstitial edema. • Prolongs hemodynamic response when given with hetastarch. • Shifts fluid from cells and interstitial spaces into intravascular space.	• May cause hypersensitivity and fluid overload. • Increases risk of bleeding. • Contraindicated in bleeding disorders, congestive heart failure (CHF), and renal failure.

Continued

Types of IV Solutions—cont'd

Colloid Solutions

Types	Action/Use	Nursing Considerations
Hetastarch • 6% and 10% concentrations.	• Synthetic colloid made from corn diluted in normal saline solution. • Expands volume. • Shifts fluid from cells and interstitial spaces into intravascular space.	• May cause hypersensitivity. • May cause fluid overload. • Increases risk of bleeding. • Contraindicated in bleeding disorders, CHF, and renal failure.
Plasma protein fraction • 5% concentration.	• Human plasma protein in normal saline solution. • Expands volume. • Similar to albumin. • Increases osmotic pressure. • Shifts fluid from cells and interstitial spaces into intravascular space.	• May cause fluid overload. • May cause hypertension. • Used interchangeably with albumin. • Lacks clotting factors and should not be considered a plasma substitute.

Blood and Blood Products

Types	Action/Use	Nursing Considerations
Whole blood	• Rarely used. • May be given emergently to an exsanguinating client. • Contains all blood components.	• **No medications or intravenous fluids should be added to or mixed with blood products except normal saline solution.**

Continued

Types of IV Solutions—cont'd

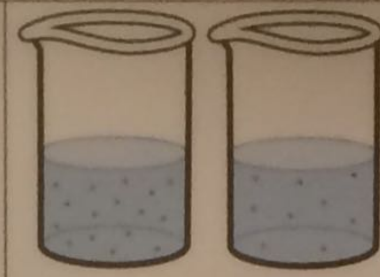
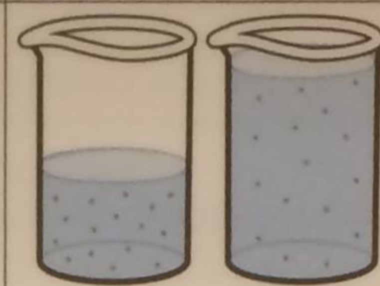
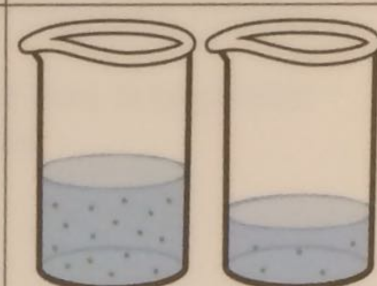
Blood and Blood Products

Types	Action/Use	Nursing Considerations

Packed red blood cells (PRBCs)	• Used to treat acute anemia, chronic anemia, and blood loss.
	• Contains red blood cells in approximately 20% plasma.
	• Contains no clotting factors or platelets.
		• All blood and blood products should be administered using an in-line filter primed with normal saline solution.
		• When administering any blood product, observe for:
		  • **Acute hemolytic reaction:** Fever, chills, flushing, low back pain, tachycardia, hypotension, vascular collapse, cardiac arrest.
		  • **Allergic reaction:** Hives, urticaria, flushing, and fever.
		  • **Anaphylaxis:** Urticaria, restlessness, wheezing, shock, cardiac arrest.
		  • **Bacteremia:** Fever, chills, vomiting, diarrhea, hypotension, septic shock.
		• **Circulatory overload:** Pulmonary congestion, restlessness, cough, shortness of breath, hypertension, distended neck veins.
		• **Febrile, nonhemolytic reaction:** Fever, chills, flushing, headache, muscle aches, respiratory distress, cardiac dysrhythmias.

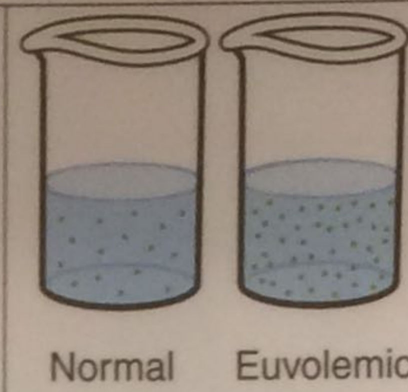
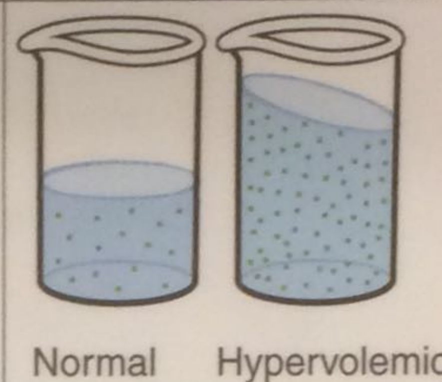
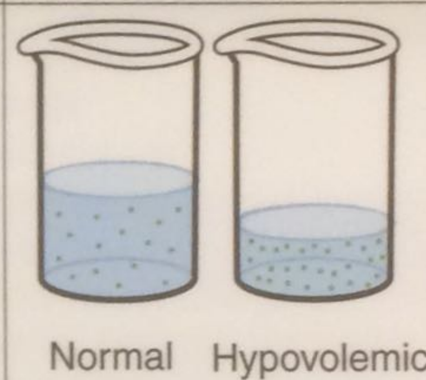
Platelets	• Used to increase low platelet counts or to treat coagulopathies. • Usually given in pools of 6–10 units. • One unit will generally increase platelet count by 6,000 units.	
Fresh frozen plasma (FFP)	• Used to replace clotting factors. • Contains plasma and clotting factors. • Not usually administered until more than 6 units of PRBCs have been infused. • Reverses the effects of warfarin (Coumadin®).	
Cryoprecipitate	• Used to treat hemophilia, fibrinogen deficiency, and disseminated intravascular coagulation. • Contains clotting factors.	

Types of Sodium Imbalance

Type	Description	
	Hyponatremia	
Euvolemic	**Sodium content decreases while total body water remains near normal.** • Usually caused by decreased sodium intake or an actual loss of sodium from the body.	 Normal Euvolemic
Hypervolemic	**Sodium content and total body water increase.** • Client becomes hyponatremic because total body water increases more than the sodium content increases. • ECF volume is increased. • Edema may be noted.	 Normal Hypervolemic
Hypovolemic	**Sodium content and total body water decrease.** • Client becomes hyponatremic because sodium content decreases more than the total body water decreases. • ECF volume is decreased.	 Normal Hypovolemic

Continued

Types of Sodium Imbalance—cont'd

Type	Description	
	Hypernatremia	
Euvolemic	**Sodium content increases while total body water remains near normal.** • Usually caused by excess sodium intake or administration.	
Hypervolemic	**Sodium content increases while total body water remains the same or increases.** • Client becomes hypernatremic because sodium content increases more than the total body water content.	
Hypovolemic	**Sodium content and total body water decrease.** • Client becomes hypernatremic because total body water decreases more than the sodium content decreases.	

Hyponatremia (serum sodium less than 135 mEq/L) is the most common electrolyte imbalance.

Causes of Sodium Imbalance

Hyponatremia	Hypernatremia
Actual Decrease in Sodium	**Actual Increase in Sodium**
• **Sodium loss.** • Vomiting. • Nasogastric suctioning. • Diarrhea. • Excessive diaphoresis. • Burns. • Wound drainage. • Consumption of large quantities of beer (diuretic effect). • Kidney disease. • Medications (act directly on the kidney to produce hyponatremia). • **Inadequate sodium intake.**	• **Sodium gain.** • Excessive oral sodium intake. • Inability to ingest water. • Administration of hypertonic tube feedings without adequate water. • Administration of hypertonic intravenous solutions (hypertonic saline solution, sodium bicarbonate, total parenteral nutrition). • **Sodium retention.** • Hyperaldosteronism. • Cushing's syndrome. • Corticosteroids. • Acute renal failure.
Relative Decrease in Sodium (dilutional)	**Relative Increase in Sodium (dilutional)**
• **Water gain.** • Decreased aldosterone secretion. • Excessive intake of hypotonic fluids; wound irrigation with hypotonic fluids. • Acute renal failure (nephrotic syndrome). • Heart failure/congestive heart failure. • **Third-spacing** (interstitial accumulation). • **Syndrome of inappropriate antidiuretic hormone secretion (SIADH).**	• **Water loss.** • Vomiting. • Diarrhea. • Decreased fluid intake. • Burns. • Diabetes insipidus. • Mineralocorticoid excess. • Increased insensible loss (hyperventilation, excessive diaphoresis).

Potassium and Magnesium Imbalances

- Most potassium and magnesium within the body is stored inside the cells.
- Potassium and magnesium are obtained through dietary intake; almost all foods contain at least some magnesium.

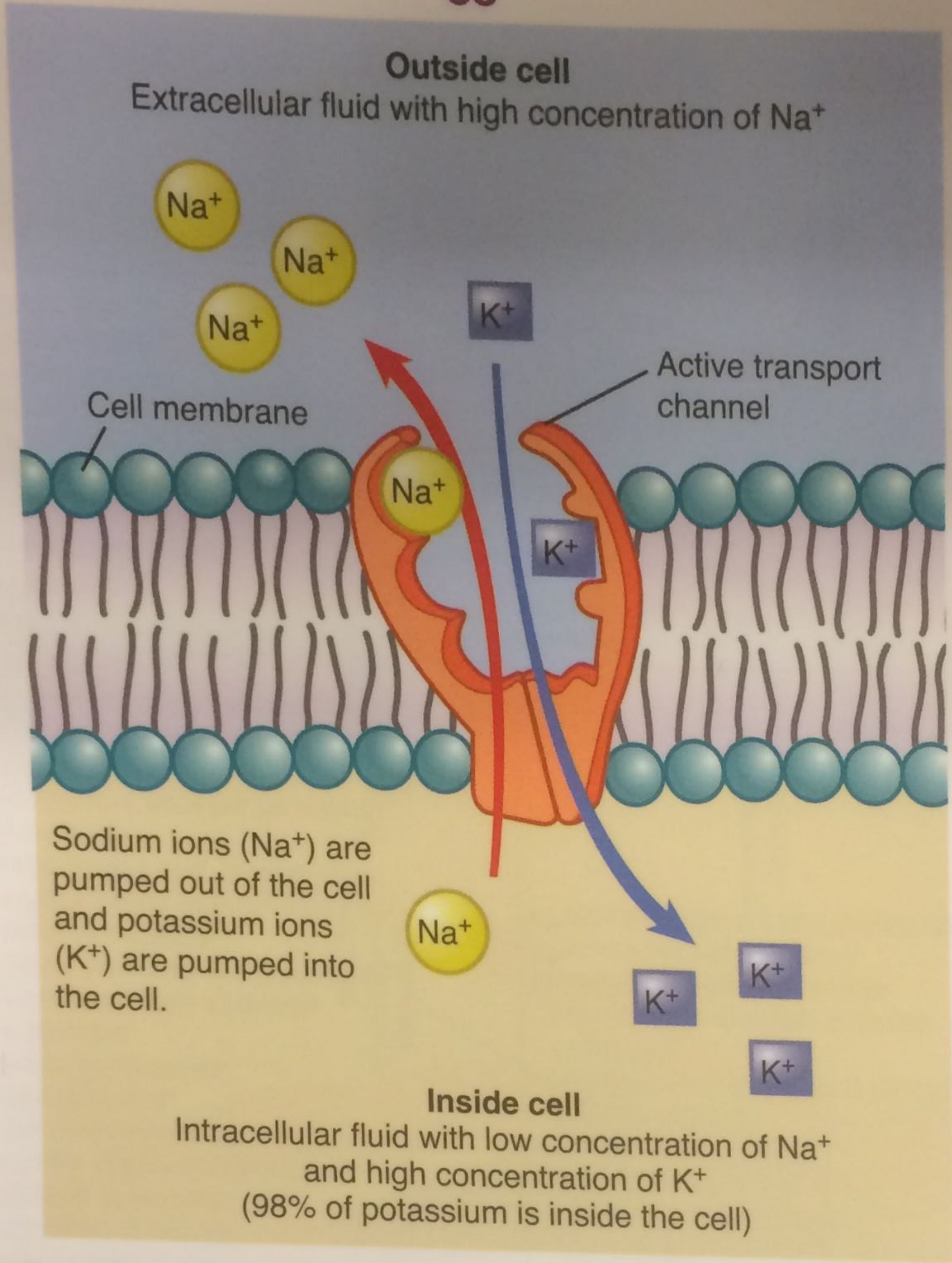
Potassium Imbalance

POTASSIUM (K^+):

- **It is the most common cation in the intracellular fluid compartment (ICF).**
- **Even small changes in potassium concentration can cause major alterations in how the body functions, producing life-threatening cardiac dysrhythmias.**
- It plays a significant role in cardiac muscle, skeletal muscle, and smooth muscle activity.
- Assists with maintaining acid-base balance.
- Moves by active transport across cell membranes.
- The sodium-potassium pump within the cell membrane maintains the concentrations of potassium in the ICF and extracellular fluid (ECF) compartment.
- There is only a small amount of potassium found in the ECF.
- Potassium is excreted and conserved by the kidneys.
- Aldosterone enhances kidney excretion of potassium.
- The primary source of potassium is dietary intake, usually in a sufficient amount to meet the body's needs.
- Recommended daily intake of potassium is 4700 mg for adults.

Normal serum potassium levels are maintained within a narrow range from 3.5 mEq/L to 5.0 mEq/L.

Critical serum potassium levels are less than 2.5 meq/l or greater than 6.5 meq/l.



Sodium-potassium pump.

Causes of Potassium Imbalance

Hypokalemia	Hyperkalemia
Actual Decrease in Potassium	**Actual Increase in Potassium**

Potassium Loss
• Vomiting.
• Prolonged gastric suctioning.
• Chronic diarrhea.
• Eating disorders.
• Major surgical procedures.
• Hemorrhage.
• Medications.
  • corticosteroids.
  • insulins.
  • loop/thiazide diuretics.
• Stimulation of the sympathetic nervous system.
  • Particularly with β_2-agonists.
Inadequate Potassium Intake/ Absorption
• Prolonged nothing by mouth (NPO) status.
• Ingestion of clay (bentonite).
• IV therapy with potassium-deficient solutions.
	Potassium Retention
	• Acute renal failure.
	• Chronic kidney disease.
	• Glomerulonephritis.
	• Obstructive uropathy.
	• Addison's disease.
	• Medications.
	  • ACE inhibitors.
	  • angiotensin II receptor blockers.
	  • NSAIDS.
	  • potassium-sparing diuretics
	Excessive Potassium Intake
	• Potassium replacement.
	• Potassium-based salt substitutes.

Relative Decrease in Potassium (dilutional)	**Relative Increase in Potassium (dilutional)**

Extracellular Shifts
• Familial periodic paralysis.
  • A rare genetic disorder characterized by transient episodes of profound hypokalemia.
• Third-spacing.
• Water gain.
	Extracellular Shifts
	• Metabolic acidosis.
	• Massive tissue trauma.
	  • Burns.
	  • Rhabdomyolysis.
	  • Surgical procedures.
	  • Tumor invasion.
	• Water loss.

Calcium and Phosphate Imbalances

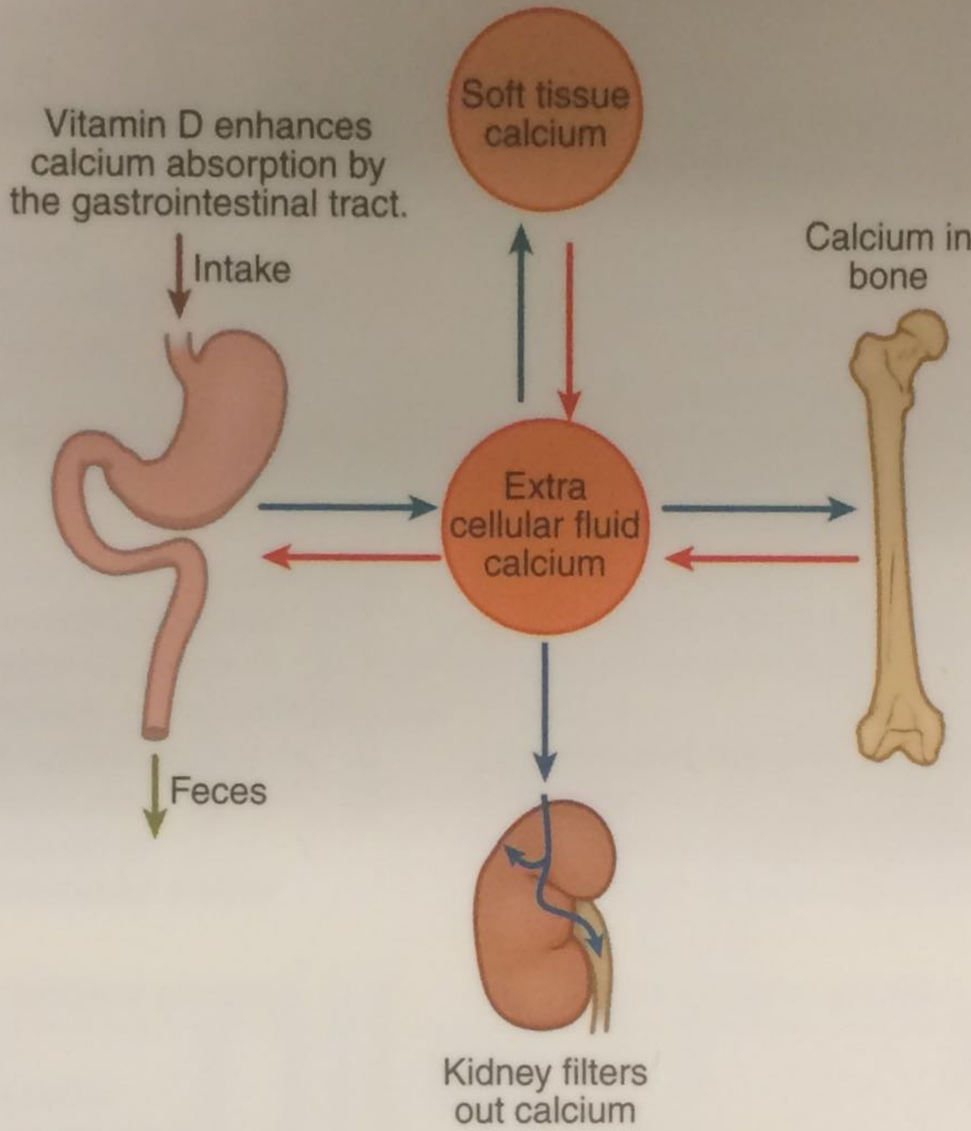
- Calcium (Ca^{2+}) is a mineral with functions related closely to phosphorous and magnesium.
- Phosphorous (P) is never found as a free element on Earth.
- Phosphorous binds with oxygen molecules to form organic phosphate (PO_4), which is distributed throughout the body.
- Calcium (Ca^{2+}) and phosphorous (P) have an inverse relationship; an increase in serum calcium level will result in a proportional decrease in serum phosphate level (equal and opposite change).

Calcium Imbalance

CALCIUM ($Ca2^{+}$):

- **It is the most abundant mineral in the human body.**
- Approximately 99% of body calcium is located in bones and teeth; the remaining 1% circulates in the extracellular fluid (ECF) and intravascular space.
- It is essential for:
  - Bone health (strength and density).
  - Skeletal and cardiac muscle function.
  - Blood clotting.
  - Nerve impulse transmission.
  - Activation of certain enzymes.
- Calcium is an ion that has two positive charges and exists in the bloodstream in a *bound* form and an *ionized* (unbound, active or free) form.
  - ***Ionized*** calcium is the **active** form and must be maintained in a narrow range.
  - Ionized calcium circulates freely in the blood or other extracellular fluids.
  - Bound calcium is attached to serum proteins, especially albumin.
- Absorption of calcium takes place in the intestines and requires the active form of vitamin D.
- When serum calcium levels become too low, calcium is borrowed from the bones, in response to the secretion of parathyroid hormone (PTH) by the parathyroid gland and calcitrol, a form of vitamin D.
- When excess calcium is present in plasma, PTH secretion is inhibited and the secretion of calcitonin (also know as *thyrocalcitonin* [TCT]) is increased.
- TCT, secreted by the thyroid gland, causes plasma calcium levels to decrease by inhibiting bone reabsorption, inhibiting vitamin D–associated intestinal uptake, and increasing renal excretion of calcium.
- Serum calcium levels are also affected by acid-base balance and plasma protein levels, particularly albumin.

- **The body loses calcium every day; it must be included in dietary intake to meet requirements.**
- Recommended daily intake of calcium is approximately 1000 mg for adults (varies by age and sex).



Normal calcium metabolism.

- *Total* serum calcium levels represent both *bound* and *unbound* calcium.
- Normal *ionized* serum calcium level is 4.6–5.3 mg/dL (adults).

Normal *total* serum calcium level is 8.2–10.2 mg/dL in adults; 7.6–10.8 mg/dL in children.

Teach Client How to Prevent Falls at Home

- Avoid the use of throw rugs; use slip-proof carpet pads if throw rugs are used.
- Maintain a clutter-free environment.
- Avoid wet or slippery floors, and repair floors as necessary.
- Ensure adequate lighting in the home.
- Install handrails on stairs and grab bars in bathrooms.
- Use nonslip bath mats.
- Utilize raised toilet seats.
- Evaluate visual acuity, and treat as necessary.
- Evaluate hearing, and treat as necessary.
- Evaluate mobility, and recommend assistive devices as necessary.

HYPERCALCEMIA:

Teach the Client How to Prevent Calcium Excess

- Avoid foods high in calcium during the acute phase (see High Calcium Foods table on page 103). Avoid or limit dark green leafy vegetables, edible bones of fish, calcium-fortified foods, and dairy products.
- Drink more fluids, especially water, because dehydration may exacerbate hypercalcemia and kidney stone formation.
- Teach the client to read labels on food packages to determine calcium content.

Evaluate and Document

Document All Assessment Findings and Interventions

- Evaluate and document the client's response to interventions and education.
- Ensure that the client or caregiver understands specifics, rationale, potential side effects, and desired effects of treatment regime.
- Include medication administration, nutrition, hydration, dietary restrictions, and foods high in calcium in client teaching.

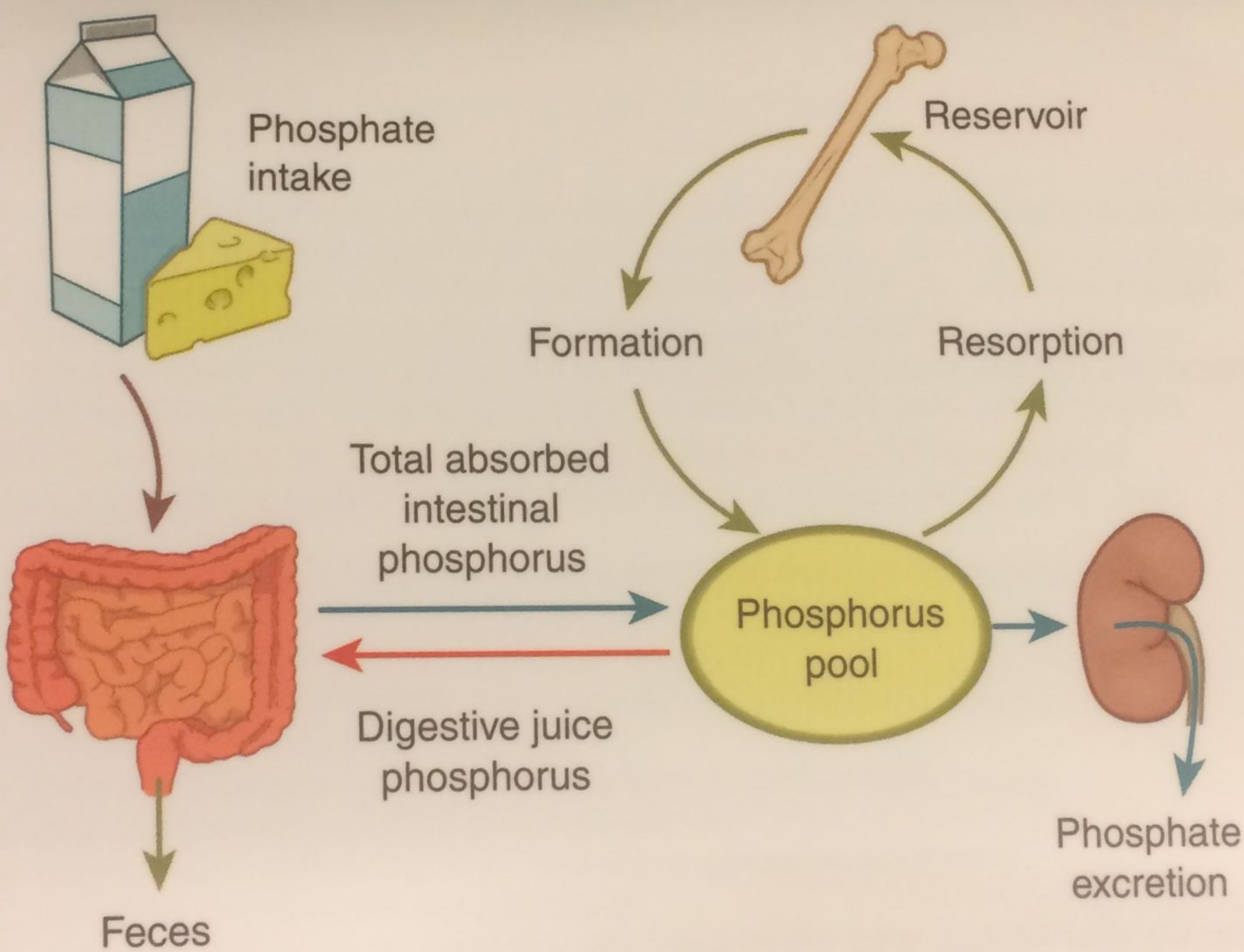
Phosphate Imbalance

PHOSPHATE (Po_4^-):

- **It is the major anion found in intracellular fluid.**
- Although the terms *phosphorus* and *phosphate* are often used interchangeably, phosphorus (P) is actually an essential mineral never found as a free element in nature because of its high reactivity.
  - Phosphorus is found in the body in combination with oxygen as phosphate (Po_4^-).
- It assists in muscle contraction, maintaining heart rhythm, kidney function, nerve conduction, and the functioning of red blood cells.
- Is needed for cell membrane integrity.

- Is a major component of ATP, DNA, and RNA.
- Is involved in protein, fat, and carbohydrate metabolism.
- Approximately 85% of the body's phosphate is bound with calcium in teeth and bones, where it is regulated by parathyroid hormone (PTH); the remainder is located primarily inside the cells.
- Phosphate is excreted in urine and stool.
- **Phosphorus and calcium levels are inversely proportionate.**
- Vitamin D also plays a part in the regulation of phosphate by influencing phosphorus and calcium absorption.
- The primary source of phosphorus is dietary intake; it is plentiful in meats, fish, poultry, milk products, and legumes. The average American diet is high in phosphorus (1–2 g/day).
- Children have higher serum phosphorus levels than adults; newborn levels are nearly twice those of adults.
- **The most dangerous problems associated with phosphate imbalances are due to related calcium imbalances, which can lead to severe cardiovascular and neuromuscular problems.**

Normal serum phosphorus level in adults is 2.5–4.5 mg/dL (3.0–4.5 mEq/L).



Phosphate balance.

Causes of Phosphate Imbalance

Hypophosphatemia	Hyperphosphatemia
Actual Decrease in Phosphate	**Actual Increase in Phosphate**

Phosphate Loss
• Hyperparathyroidism.
• Vomiting.
• Prolonged gastric suctioning.
• Diarrhea.
• Steatorrhea.
• Massive burns.
• Excessive calcium supplementation.
• Medications (act on kidney to increase phosphate excretion).
  • corticosteroids.
  • loop diuretics.
  • thiazide diuretics.
• Chronic kidney disease.
• Pancreatitis.
• Metabolic acidosis.
Inadequate Intake/Impaired Absorption
• Vitamin D deficiency (decreases renal reabsorption of phosphate).
• Prolonged nothing by mouth status.
• Malnutrition.
• Excessive intake of phosphate-binding antacids.
• Malabsorption syndromes.
• Treatment of diabetic ketoacidosis.
• Hyperparathyroidism.
• Hyperglycemia.
• Alcohol abuse.
	Phosphate Gain
	• IV phosphorus infusion.
	• Excessive dietary ingestion of phosphorus.
	• Vitamin D intoxication.
	• Excessive use of phosphate-containing laxatives or enemas.
	Phosphate Retention/Decreased Excretion
	• Vitamin D excess.
	• Chronic kidney disease.
	• Acute renal failure.
	• Hypoparathyroidism.
	• Acromegaly.
	• Vitamin D intoxication.
	• Bisphosphonate therapy.
	• Pseudohyperphosphatemia.
	• Multiple myeloma.
	• Calcium or magnesium deficiency.
	• Inability to be removed by dialysis.

Relative Decrease in Phosphate	**Relative Increase in Phosphate**
Shift From Extracellular Compartment • Glucose and insulin administration. • Hyperglycemia. • Total parenteral nutrition.	**Shift From Intracellular Compartment** • Hemolysis. • Chemotherapy for malignant tumors.

Continued

Types and Causes of Phosphate Imbalance—cont'd

Hypophosphatemia	Hyperphosphatemia
Relative Decrease in Phosphate	**Relative Increase in Phosphate**

Shift From Extracellular Compartment
• Acid-base imbalances (respiratory alkalosis, metabolic acidosis).
• Alcohol withdrawal.
• Refeeding syndrome.
• Hungry bone syndrome.
• Medications (hormonal effects cause phosphate to shift into cells):
  • Catecholamines.
  • Hormones.
  • Insulins.
	Shift From Intracellular Compartment
	• Tumor lysis syndrome.
	• Rhabdomyolysis.
	• Hypoparathyroidism.
	• Acid-base disorders (lactic acidosis, diabetic ketoacidosis, respiratory acidosis).
	• Sepsis/severe infection.
	• Crush injuries/tissue trauma.

Nursing Assessment for Phosphate Imbalance

	Hypophosphatemia	Hyperphosphatemia
Assess Vital Signs		
Blood pressure	• Possibly decreased.	• Possibly decreased.
Heart rate	• Decreased.	• Possibly decreased.
Respiratory rate	• Decreased.	• Possibly decreased, depends on degree of accompanying hypocalcemia.
Temperature	• WNL.	• Within normal limits.

Continued

Acid-Base Imbalance

Review of Acid-Base Balance

Acid-Base Balance

- Is influenced by the production and elimination of hydrogen (H^+) ions.
- pH is a measure of the free hydrogen ion level in body fluids.
- The pH of a solution can range from 1 (highest concentration of hydrogen ions) to 14 (lowest concentration of hydrogen ions).
- A pH of 7 is considered neutral.
- The body's pH is normally maintained in a narrow range, which is slightly alkaline.

The normal pH range of blood is 7.35–7.45.

- Requires balancing acids and bases in the body.
- Balance is regulated primarily by the lungs and kidneys.
  - Both regulatory systems attempt to correct acid-base imbalances so the pH can be returned to normal; this process is called *compensation.*
  - The lungs work much quicker than the kidneys in compensating for imbalances.
- Acid-base imbalances impair the functioning of many organs by:
  - altering the response of excitable membranes.
  - making the heart, nerves, muscles, and gastrointestinal tract either more or less active.
  - reducing the function of hormones and enzymes.
  - affecting the distribution of electrolytes.
  - decreasing the effectiveness of many drugs.
- Even small changes in the pH of body fluids can cause major problems in functioning.

Blood (serum) pH

	6.8		7.35		7.45		7.8	
Death		Acidosis		Normal		Alkalosis		Death

A BLOOD pH LESS THAN 6.8 OR GREATER THAN 7.8 IS USUALLY FATAL

Acids

Substances that release hydrogen ions (H^+) when dissolved in water, increasing the concentration of H^+ and lowering pH (acidosis).

- **Carbonic acid** forms when carbon dioxide (CO_2) combines with water in the body; levels are normally controlled by the lungs through the retention or excretion of carbon dioxide. It may lead to respiratory acidosis or alkalosis.
- **Sulfuric acid** is produced by the body as a byproduct of protein metabolism through the breakdown of sulfur-containing amino acids.
- **Fatty acids** and **ketones** form as a byproduct of fat breakdown.
- **Lactic acid** forms when cells metabolize under anaerobic conditions and glucose breakdown is incomplete.

Bases

Substances that bind free hydrogen ions in water, reducing the concentration of hydrogen ions, and increasing pH (alkalosis).

- **Bicarbonate (HCO_3^-)** is the principle alkaline substance (base) in the body.
- HCO_3^- binds with free hydrogen ions in the extracellular fluid (ECF) and intracellular fluid (ICF) to decrease hydrogen ion concentration.
- HCO_3^- and hydrogen ion levels are controlled by the kidneys; problems of regulation lead to metabolic *acidosis* or *alkalosis*.
- Venous HCO_3^- levels are higher than arterial levels because CO_2 in the blood is converted into carbonic acid, which can quickly turn into bicarbonate.

Regulation of Acid-Base Balance

Buffers

- The first line of defense against pH changes.
- Bring body fluids back to normal pH range of 7.35–7.45 by either releasing hydrogen ions or binding with hydrogen ions.
- **Bicarbonate (HCO_3^-):** The principle alkaline substance in the body; *slowly* responds to changes in pH.
  - Considered the major buffer in the body; binds free hydrogen ions.
  - Active in the ECF and ICF.
  - The lungs work much quicker than the kidneys in compensating for imbalances.

- **Phosphate:** Is active in the ICF; binds to hydrogen ions, which are then excreted in the urine.
- **Protein buffers:** The most common buffers.
  - Active in the ECF and ICF.
  - Can either bind or release free hydrogen ions as needed.
  - Extracellular protein buffers are albumin and globulins.
  - **Hemoglobin** is a major cell protein buffer; buffers hydrogen ions directly and buffers acids formed during the production of carbon dioxide.

Respiratory System

- The second line of defense against pH changes.
- Responds to pH changes in seconds to minutes after a change is detected, much faster than the kidneys.
- Breathing rids the body of excess CO_2 created through metabolism.
- If the pH is too low (acidic), an increase in the rate and depth of breathing **(hyperventilation)** increases the rate at which CO_2 is exhaled ("blown off") from the lungs, attempting to normalize the pH of arterial blood.
- If the pH is too high (alkaloid), a decrease in the rate and depth of breathing (**hypoventilation**) decreases the rate at which CO_2 is exhaled, decreasing the pH of arterial blood.
- **Carbon dioxide (CO_2):** One of the principle substances that affect pH.
  - CO_2 level is controlled by the lungs and is exhaled during breathing.
  - CO_2 is a natural waste product of carbohydrate metabolism.
  - CO_2 combines with water in the body to form **carbonic acid**, meaning CO_2 is considered an acid.
  - Blood pH is influenced by how much CO_2 is produced by the cells during metabolism versus how rapidly that CO_2 is removed by breathing.

Renal System

- The third line of defense against pH changes.
- Slow response to pH changes (24–48 hr) with the longest duration of the three regulatory mechanisms. When pH changes persist, the kidneys increase excretion and reabsorption of acids or bases (depending on the direction of the pH change).
- When blood hydrogen levels are high (low pH), bicarbonate made in other parts of the body is reabsorbed by the kidneys and put back into circulation to bind with hydrogen ions, increasing the blood pH.
- The kidney tubules can make additional bicarbonate, which can also be reabsorbed.
- The phosphate-buffering system inside the kidney tubules helps to bind free hydrogen ions for excretion in the urine, increasing pH.
- Ammonia, which is formed during protein breakdown, is converted by the kidney into ammonium, which traps hydrogen ions for excretion in the urine, increasing pH.

Compensation

- The body's attempt to bring the pH of the blood back to normal range.
- Both kidneys and lungs can compensate for pH changes.
- The respiratory system is more sensitive to acid-base changes and begins compensation efforts immediately, but efforts are limited and short-lived.
- The renal system is much more powerful but less sensitive; compensatory mechanisms are not fully triggered unless acid-base imbalance persists for several hours to several days.

Full Compensation

- Occurs when the kidney and lungs successfully correct pH imbalance.
- pH is within normal reference range, even though CO_2 and HCO_3^- levels may be abnormal.

Partial Compensation

- Occurs when the kidneys and lungs attempt to correct pH imbalance.
- Prevents acid-base imbalances from becoming life-threatening.
- pH is slightly out of normal reference range.
- CO_2 and HCO_3^- levels may remain abnormal.

Renal Compensation

- Occurs when healthy kidneys attempt to correct acid-base imbalances caused by respiratory problems.
- Activates when the respiratory system is overwhelmed or is not healthy.
- Responds slowly to pH changes (24–48 hr) with longer duration than respiratory compensation.
  - When hydrogen ion levels are low (high pH/alkalosis), the kidneys excrete additional bicarbonate to lower the amount of circulating base and decrease serum pH.
  - When hydrogen ion levels are high (low pH/acidosis), bicarbonate made in other parts of the body is reabsorbed by the kidneys and put back into vascular circulation to bind with the hydrogen ions, which increases the blood pH.
  - The kidney tubules can make additional bicarbonate, which also can be reabsorbed.
  - The phosphate-buffering system inside the kidney tubules helps to bind free hydrogen ions for excretion in the urine, which increases pH.
- When the kidneys can *fully compensate*, the blood pH returns to normal, even though the levels of oxygen and bicarbonate may be abnormal; full compensation is rare.
- When respiratory problems are severe, the kidneys can only *partially compensate*, leaving the blood pH abnormal but preventing the acid-base balance from becoming severe or life-threatening.

Respiratory Compensation

- Occurs when the lungs attempt to correct acid-base imbalances caused by metabolic problems.

- Responds to pH changes in seconds to minutes after a change is detected.
  - Breathing rids the body of excess CO_2 when the serum pH is too low (acidosis).
  - The lungs conserve CO_2 through shallow respirations when the serum pH is too high. (Carbonic acid levels are normally controlled by the lungs through the retention or the excretion of carbon dioxide, and problems of regulation lead to respiratory acidosis or alkalosis.)
  - Breathing increases in rate and depth, decreasing CO_2 levels, and increasing blood pH.
- When the lungs can *fully compensate*, the pH returns to normal.

The body's pH has the narrowest normal range and the tightest control mechanism.

ACID-BASE IMBALANCES MAY BE LIFE-THREATENING!

Acid-Base Values: Normal Range for Adults

Value	Arterial	Venous
pH	7.35–7.45	7.32–7.43
PO_2	80–100 mm Hg	20–49 mm Hg
PCO_2	35–45 mm Hg	41–51 mm Hg
HCO_3^- (bicarbonate)	22–26 mEq/L	24–28 mEq/L
Lactate	3–7 mg/dL	5–20 mg/dL
Anion gap	8–16 mEq/L	8–16 mmol/L

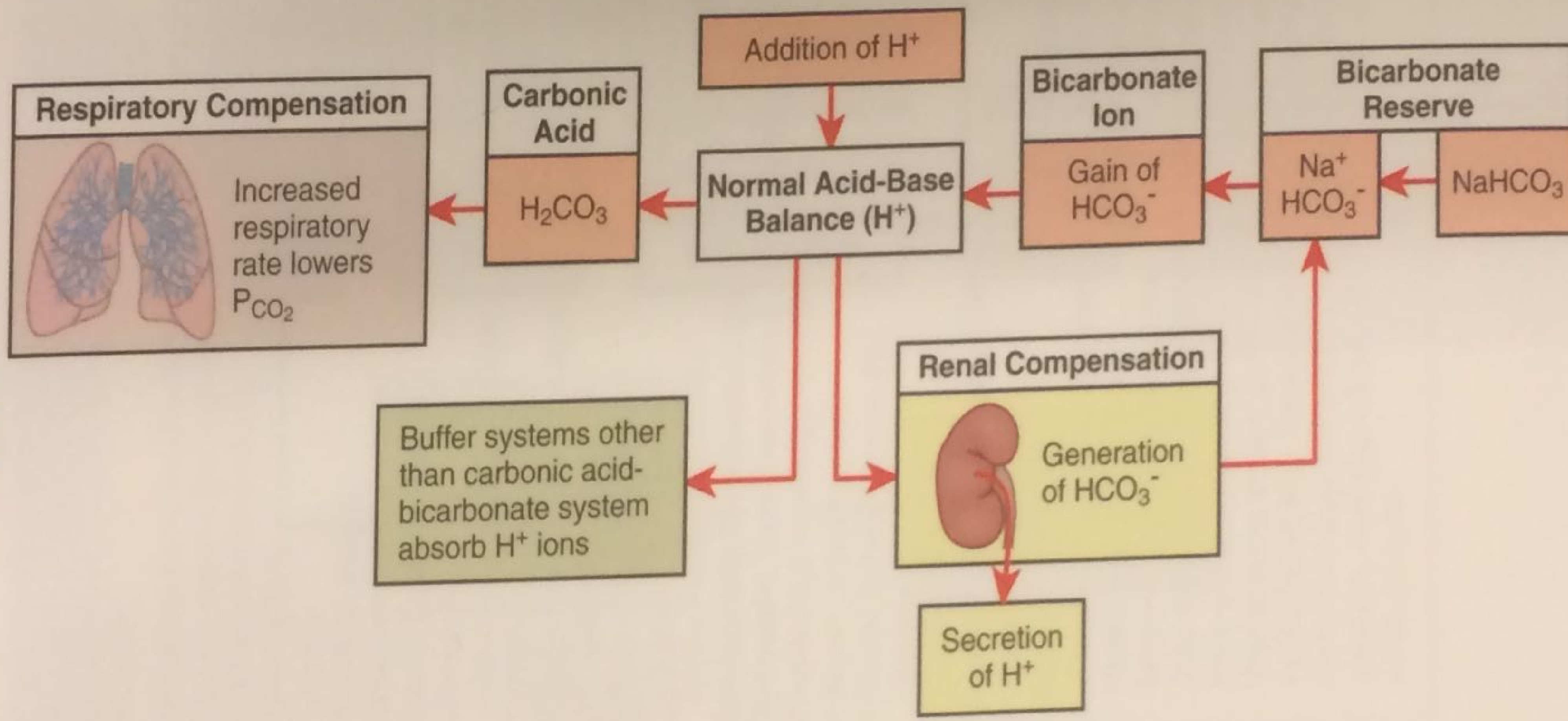
Acid-Base Imbalances

Occur when the body's pH varies from the normal range, resulting in acidosis or alkalosis.

- A pH value **below 7.35** indicates a state of **acidosis**—an increase in the concentration of free hydrogen ions in the blood (higher acid concentration).
- A pH **above 7.45** indicates a state of **alkalosis**—a decrease in the concentration of free hydrogen ions in the blood (lower acid concentration).
- Acidosis and alkalosis are not disease processes. They are:
  - Conditions caused by a disorder or a pathological process.
  - Caused by metabolic problems, respiratory problems, or both!

Types of Acid-Base Imbalances

	Acidosis	Alkalosis
Metabolic	A decrease in blood pH caused by: • Excessive acid production. • Excessive acid intake. • Inadequate elimination of H^+. • Decreased production of HCO_3^-. • Excessive elimination of HCO_3^-.	An increase in blood pH caused by: • Base excess. • Acid deficit.
Respiratory	A decrease in blood pH caused by retention of CO_2 (acid).	An increase in blood pH caused by excessive loss of CO_2 (acid).



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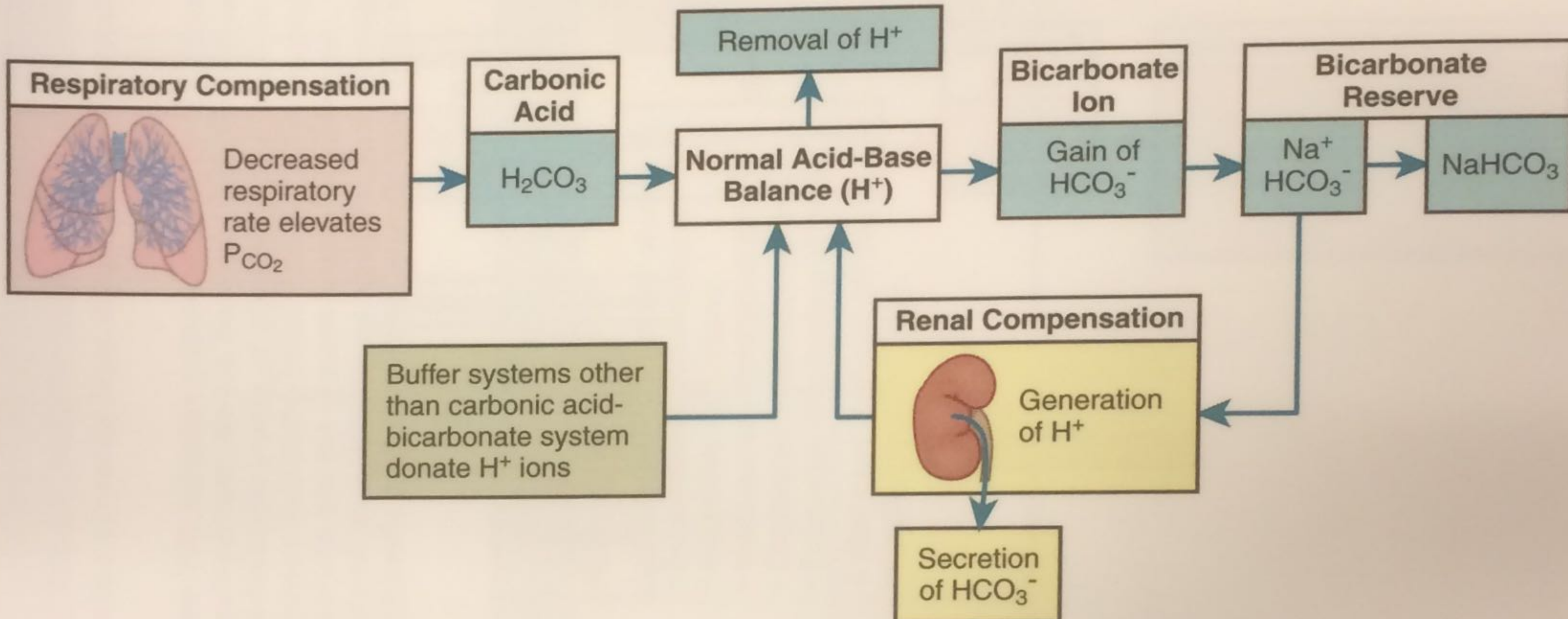
The body's response to acidosis.



The body's response to alkalosis.

Causes of Acid-Base Imbalances

	Acidosis	Alkalosis

Metabolic	**Excessive Acid Production**
	• Poorly controlled diabetes.
	• Diabetic ketoacidosis.
	• Starvation.
	• Sepsis.
	• Cardiac arrest.
	• Shock.
	Excessive Acid Intake
	• Alcohol.
	  • Also causes concurrent respiratory acidosis.
	• Salicylate (aspirin) overdose or toxicity.
	• Excessive infusion of chloride-containing intravenous (IV) fluids.
	Inadequate Elimination of Hydrogen Ions/Decreased Production of HCO_3^-
	• Renal insufficiency.
	• Renal failure (acute or chronic).
	• Pancreatitis.
	Excessive Elimination of HCO_3^-
	• Vomiting, diarrhea.
	Potassium Shift
	• When extracellular potassium levels are high (hyperkalemia), potassium shifts *into* the cells and hydrogen ions shift *out* of the cell, decreasing blood pH (metabolic acidosis). There is a need to keep ICF electrically neutral, and therefore this shift occurs.
		Base Excess
		• Decreased HCO_3^- excretion.
		  • Cushing syndrome.
		• Excessive HCO_3^- administration.
		  • HCO_3^- containing antacids.
		  • Parenteral sodium bicarbonate.
		• Hypochloremia.
		Acid Deficit
		• Prolonged vomiting.
		• Gastric suctioning.
		Potassium Shift
		• When extracellular potassium levels are low (hypokalemia), potassium shifts *out* of the cells and hydrogen ions shift *into* the cells, increasing blood pH (metabolic alkalosis).

Continued

Causes of Acid-Base Imbalances—cont'd

	Acidosis	Alkalosis

Respiratory	**Retained Acid**
	• Hypoventilation/carbon dioxide retention.
	• Central nervous system depression due to anesthesia or overdose of opioids/sedatives.
	• Central nervous system dysfunction/brain injury that affects the respiratory center.
	• Brain tumors.
	• Chest trauma.
	• Neuromuscular disease such as Guillain-Barré syndrome.
	Conditions that Impair Gas Exchange at the Alveolar-Capillary Membrane
	• Chronic obstructive pulmonary disease (COPD)
	• Chronic lung disease.
	• Acute pulmonary edema.
	• Pneumonia.
	• Near-drowning.
	• Airway obstruction/aspiration of foreign body.
	• Injury to respiratory center in the brain.
		Decreased Acid/Excessive Acid Loss
		• Hyperventilation secondary to:
		  • Anxiety.
		  • Stress.
		  • Fear.
		  • Pain.
		  • Head injury.
		  • Stroke.
		  • Asthma.
		  • Pneumonia.
		  • Pulmonary edema.
		  • Pulmonary embolism.
		  • Sepsis.
		  • Thyrotoxicosis.
		  • Salicylate overdose.
		  • Nicotine.
		  • Excessive mechanical ventilation.
		  • Progesterone during pregnancy.
		  • Sepsis and fever (i.e., hypermetabolic states).

Nursing Assessment for Acid-Base Imbalances

Assess Arterial Blood Gases

	Respiratory Acidosis	Metabolic Acidosis	Respiratory Alkalosis	Metabolic Alkalosis
pH	Less than 7.35	Less than 7.35	Greater than 7.45	Greater than 7.45
PaCO2	Greater than 45 mm Hg	Normal or less than 35 mm Hg (CO_2 decreases to compensate)	Less than 35 mm Hg	Greater than 45 mm Hg (CO_2 increases to compensate)
HCO_3^-	**Acute:** Normal or slightly elevated **Chronic:** Greater than 26 mEq/L (HCO_3^- increases to compensate)	Less than 22 mEq/L	Normal or less than 22 mEq/L (HCO_3^- excreted by kidneys to compensate)	Greater than 26 mEq/L

Observe for Signs and Symptoms

	Acidosis	Alkalosis
Cardiovascular	• Tachycardia (mild). • Bradycardia (severe). • Weak peripheral pulses. • Hypotension (result of peripheral dilation). • Arrhythmias due to hyperkalemia.	• Increased heart rate. • Thready pulse. • Normal or low blood pressure. • Increased digoxin toxicity.
Cerebral	• Lethargy. • Confusion. • Headache. • Stupor or coma (severe).	• Confusion. • Lightheadedness. • Headache. • Dizziness. • Anxiety. • Irritability. • Tetany. • Seizures.

Continued

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DNA vectors contain at least one sequence, if not many, recognized by restriction enzymes. A vector also requires an origin of replication and at least one gene for antibiotic resistance to allow for selection of colonies with recombinant plasmids, as described above. The formation of a recombinant plasmid is shown in Figure 6.20.

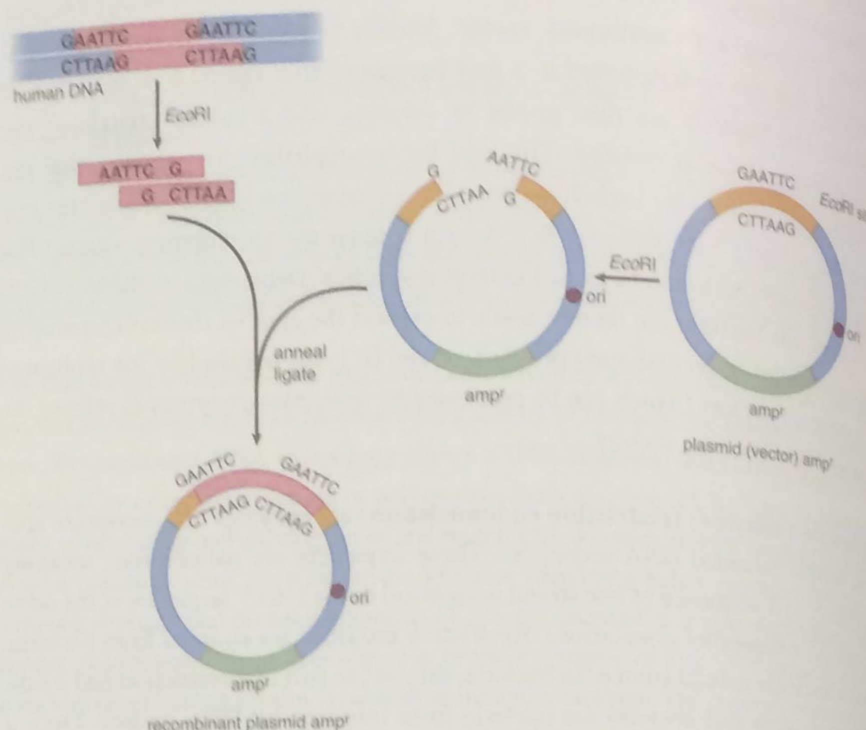

Figure 6.20. Formation of a Recombinant Plasmid Vector
ori: origin of replication; amp^r: gene for resistance to ampicillin (an antibiotic).

DNA LIBRARIES AND cDNA

DNA cloning can be used to produce DNA libraries. **DNA libraries** are large collections of known DNA sequences; in sum, these sequences could equate to the genome of an organism. To make a DNA library, DNA fragments, often digested randomly, are cloned into vectors and can be utilized for further study. Libraries can consist of either genomic DNA or cDNA. **Genomic libraries** contain large fragments of DNA, and include both coding (exon) and noncoding (intron) regions of the genome. **cDNA (complementary DNA)** libraries are constructed by reverse-transcribing processed mRNA, as shown in Figure 6.21. As such, cDNA lacks noncoding regions, such as introns, and only includes the genes that are expressed in the tissue from which the mRNA was isolated. For that reason, these libraries are sometimes called **expression libraries**. While genomic libraries contain the entire genome of an organism, genes may by chance be split into multiple vectors. Therefore, only cDNA libraries can be used to reliably sequence specific genes and identify disease-causing mutations, produce recombinant proteins (such as insulin, clotting factors, or

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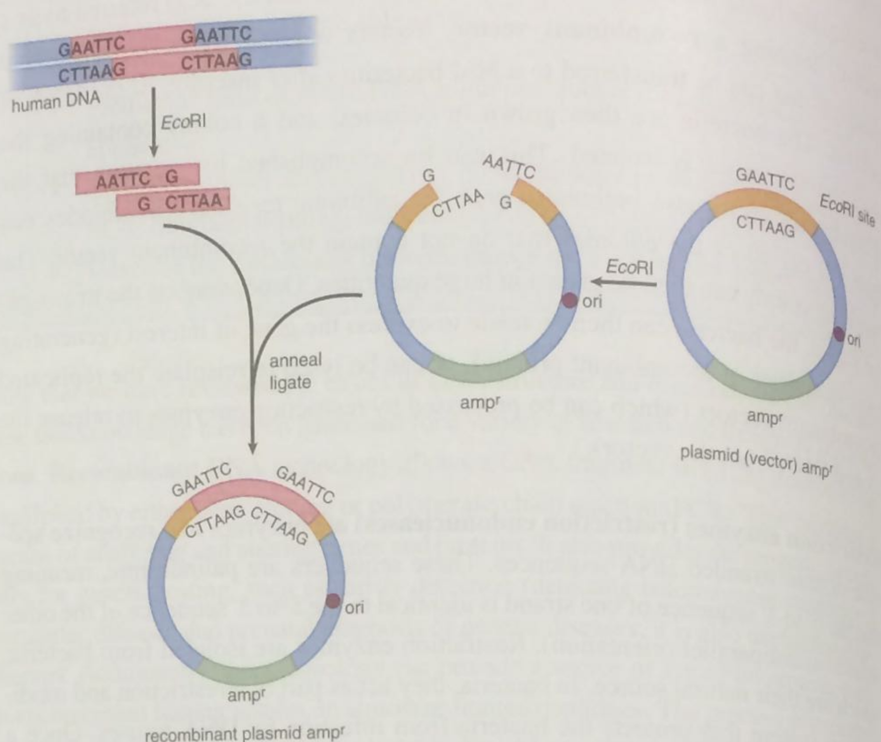

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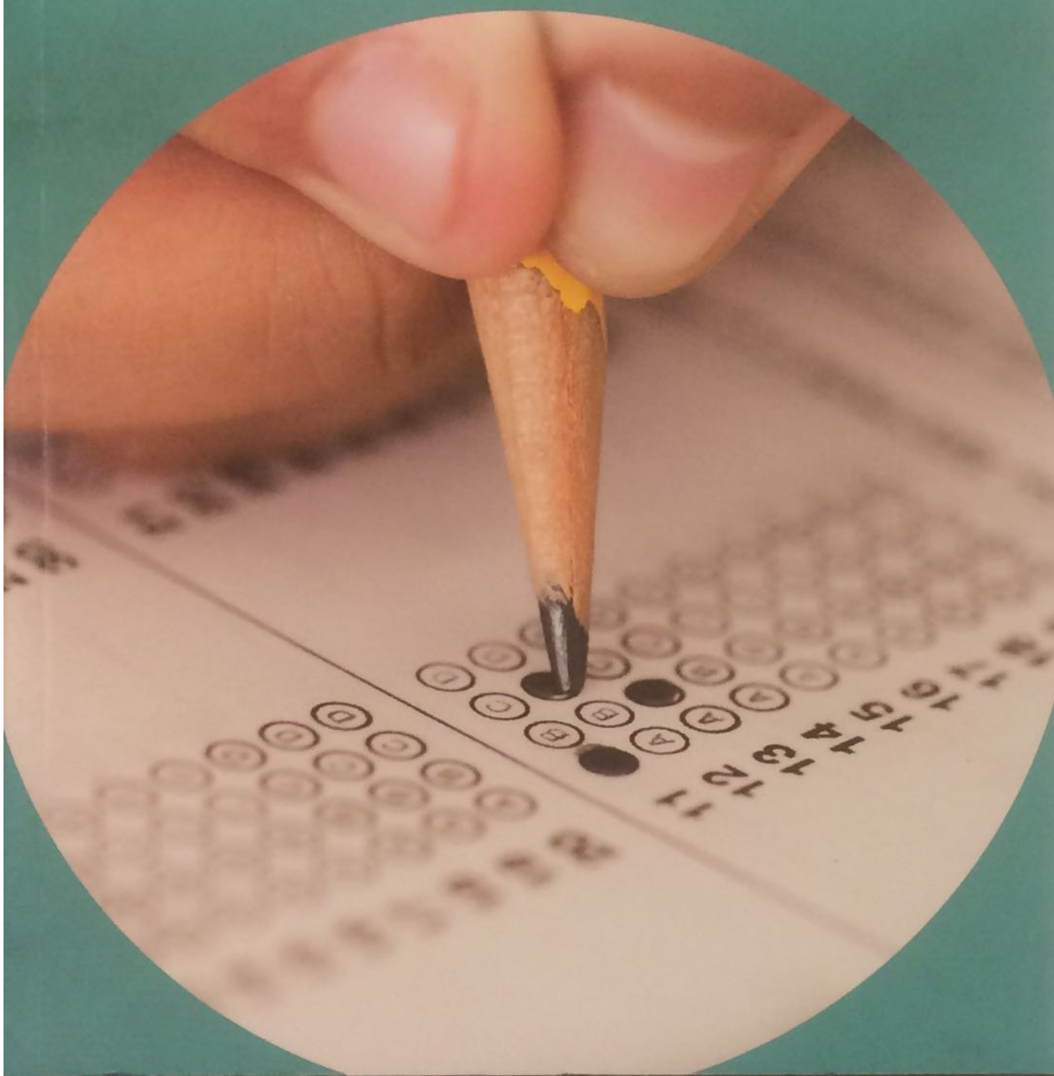

What's Inside:

- Two real Chemistry Subject Tests
- Detailed answer explanations
- Exclusive test-taking tips

Skills Specifications	Approximate Percentage of Test
Recall of Knowledge Remembering fundamental concepts and specific information; demonstrating familiarity with terminology	20%
Application of Knowledge Applying a single principle to unfamiliar and/or practical situations to obtain a qualitative result or solve a quantitative problem	45%
Synthesis of Knowledge Inferring and deducing from qualitative data and/or quantitative data; integrating two or more relationships to draw conclusions or solve problems	35%

How to Prepare

- Take a one-year introductory chemistry course at the college preparatory level.
- Laboratory experience is a significant factor in developing reasoning and problem-solving skills and should help in test preparation even though laboratory skills can be tested only in a limited way in a multiple-choice test.
- Mathematics preparation that enables handling simple algebraic relationships and applying these to solving word problems will help.
- Familiarize yourself with the concepts of ratio and direct and inverse proportions, exponents, and scientific notation.
- Familiarize yourself with directions in advance. The directions in this book are identical to those that appear on the test.

You should have the ability to

- recall and understand the major concepts of chemistry and to apply the principles to solve specific problems in chemistry.
- organize and interpret results obtained by observation and experimentation and to draw conclusions or make inferences from experimental data, including data presented in graphic and/or tabular form.

Notes: (1) A periodic table indicating the atomic numbers and masses of elements is provided for all test administrations.

(2) Calculators aren't allowed to be used during the test.

(3) Problem solving requires simple numerical calculations.

(4) The metric system of units is used.

Score

The total score is reported on the 200 to 800 scale.

Topics Covered

Topics	Approximate Percentage of Test
I. Structure of Matter	25%
Atomic Structure, including experimental evidence of atomic structure, quantum numbers and energy levels (orbitals), electron configurations, periodic trends	
Molecular Structure, including Lewis structures, three-dimensional molecular shapes, polarity	
Bonding, including ionic, covalent, and metallic bonds; relationships of bonding to properties and structures; intermolecular forces such as hydrogen bonding, dipole-dipole forces, dispersion (London) forces	
II. States of Matter	16%
Gases, including the kinetic molecular theory, gas law relationships, molar volumes, density, stoichiometry	
Liquids and Solids, including intermolecular forces in liquids and solids, types of solids, phase changes, and phase diagrams	
Solutions, including molarity and percent by mass concentrations; solution preparation and stoichiometry; factors affecting solubility of solids, liquids, and gases; qualitative aspects of colligative properties	
III. Reaction Types	14%
Acids and Bases, including Brønsted-Lowry theory, strong and weak acids and bases, pH, titrations, indicators	
Oxidation-Reduction, including recognition of oxidation-reduction reactions, combustion, oxidation numbers, use of activity series	
Precipitation, including basic solubility rules	
IV. Stoichiometry	14%
Mole Concept, including molar mass, Avogadro's number, empirical and molecular formulas	
Chemical Equations, including the balancing of equations, stoichiometric calculations, percent yield, limiting reactants	
V. Equilibrium and Reaction Rates	5%
Equilibrium Systems, including factors affecting position of equilibrium (LeChâtelier's principle) in gaseous and aqueous systems, equilibrium constants, equilibrium expressions	
Rates of Reactions, including factors affecting reaction rates, potential energy diagrams, activation energies	
VI. Thermochemistry	6%
Including conservation of energy, calorimetry and specific heats, enthalpy (heat) changes associated with phase changes and chemical reactions, heating and cooling curves, randomness (entropy)	
VII. Descriptive Chemistry	12%
Including common elements, nonmenclature of ions and compounds, periodic trends in chemical and physical properties of the elements, reactivity of elements and prediction of products of chemical reactions, examples of simple organic compounds and compounds of environmental concern	
VIII. Laboratory	8%
Including knowledge of laboratory equipment, measurements, procedures, observations, safety, calculations, data analysis, interpretation of graphical data, drawing conclusions from observations and data	

template DNA, primers, an appropriate DNA polymerase, and all four deoxyribonucleotide triphosphates. In addition, a modified base called a ***dideoxyribonucleotide*** is added in lower concentrations. Dideoxyribonucleotides (ddATP, ddCTP, ddGTP, and ddTTP) contain a hydrogen at C-3', rather than a hydroxyl group; thus, once one of these modified bases has been incorporated, the polymerase can no longer add to the chain. Eventually the sample will contain many fragments (as many as the number of nucleotides in the desired sequence), each one of which terminates with one of the modified bases. These fragments are then separated by size using gel electrophoresis. The last base for each fragment can be read, and because gel electrophoresis separates the strands by size, the bases can easily be read in order.

Real World

The Human Genome Project, initiated in 1991, involved the identification of all 3 billion base pairs of the human DNA sequence. The first draft of this project was completed in 2000. This project demonstrated that although humans appear to be quite different from each other, the sequence of our DNA is, in reality, highly conserved. On average, two unrelated individuals still share over 99.9% of their DNA sequences.

APPLICATIONS OF DNA TECHNOLOGY

In addition to its utility as a research tool, DNA biotechnology has led to a number of therapeutic breakthroughs, ranging from gene therapy—described in this section—to development of personalized chemotherapeutic regimens in cancer by genotyping the tumor cells. DNA technology is also used in industry, including the development of genetically modified foods that are enriched with specific nutrients and testing of the environment for risk assessment and cleanup procedures. As mentioned previously, DNA technology also plays a key role in forensic pathology and crime scene investigation. This is likely only the beginning, as biotechnology continues to be an active area of research.

Gene Therapy

Gene therapy now offers potential cures for individuals with inherited diseases. Gene therapy is intended for diseases in which a given gene is mutated or inactive, giving rise to pathology. By transferring a normal copy of the gene into the affected tissues, the pathology should be fixed, essentially curing the individual. For instance, about half of children with *severe combined immunodeficiency* (SCID) have a mutation in the gene encoding the γ chain common to several of the interleukin receptors. By placing a working copy of the gene for the γ chain into a virus, one can transmit the functional gene into human cells. The first successful case of gene therapy was for SCID (caused by a different mutation) in 1990.

For gene replacement therapy to be a realistic possibility, efficient gene delivery vectors must be used to transfer the cloned gene into the target cells' DNA. Because viruses naturally infect cells to insert their own genetic material, most gene delivery vectors in use are modified viruses. A portion of the viral genome is replaced with the cloned gene such that the virus can infect but not complete its replication cycle, as shown in Figure 6.22. Randomly integrated DNA poses a risk of integrating near and activating a host oncogene. Among the children treated for SCID, a small number have developed leukemias (cancers of white blood cells).

Polymerase Chain Reaction

Polymerase chain reaction (PCR) is an automated process that can produce millions of copies of a DNA sequence without amplifying the DNA in bacteria. PCR is used to identify criminal suspects, familial relationships, and disease-causing bacteria and viruses. Knowing the sequences that flank the desired region of DNA allows for the amplification of the sequence in between. A PCR reaction requires **primers** that are complementary to the DNA that flanks the region of interest, nucleotides (dATP, dTTP, dCTP, and dGTP), and DNA polymerase. The primer has high GC content (40–60% is optimal), as the additional hydrogen bonds between G and C confer stability. The reaction also needs heat to cause the DNA double helix to melt apart (denature). Unfortunately, the DNA polymerase found in the human body does not work at high temperatures. Thus, the DNA polymerase from *Thermus aquaticus*, a bacteria that thrives in the hot springs of Yellowstone National Park at 70°C, is used instead. During PCR, the DNA of interest is denatured, replicated, and then cooled to allow reannealing of the daughter strands with the parent strands. This process is repeated several times, doubling the amount of DNA with each cycle, until enough copies of the DNA sequence are available for further testing.

Bridge

PCR provides a great example of the temperature dependence of enzymes. While human DNA polymerase denatures at the high temperatures required in PCR, the DNA polymerase from *T. aquaticus* functions optimally at these temperatures. Refer to Chapter 2 of *MCAT Biochemistry Review* for more on the link between temperature and enzyme activity.

Gel Electrophoresis and Southern Blotting

Gel electrophoresis is a technique used to separate macromolecules, such as DNA and proteins, by size and charge. Electrophoresis of proteins was discussed in detail in Chapter 3 of *MCAT Biochemistry Review*, but DNA can be separated in a similar way. All molecules of DNA are negatively charged because of the phosphate groups in the backbone of the molecule, so all DNA strands will migrate toward the anode of an electrochemical cell. The preferred gel for DNA electrophoresis is **agarose gel**, and—just like proteins in polyacrylamide gel—the longer the DNA strand, the slower it will migrate in the gel.

Gel electrophoresis is often used while performing a Southern blot. A **Southern blot** is used to detect the presence and quantity of various DNA strands in a sample. DNA is cut by restriction enzymes and then separated by gel electrophoresis. The DNA fragments are then carefully transferred to a membrane, retaining their separation. The membrane is then probed with many copies of a single-stranded DNA sequence. The **probe** will bind to its complementary sequence and form double-stranded DNA. Probes are labeled with radioisotopes or indicator proteins, both of which can be used to indicate the presence of a desired sequence.

DNA SEQUENCING

DNA sequencing has revolutionized the world that we live in. The applications of this technique are far-reaching, from the medical field to criminal courts. A basic sequencing reaction contains the main players from replication, including